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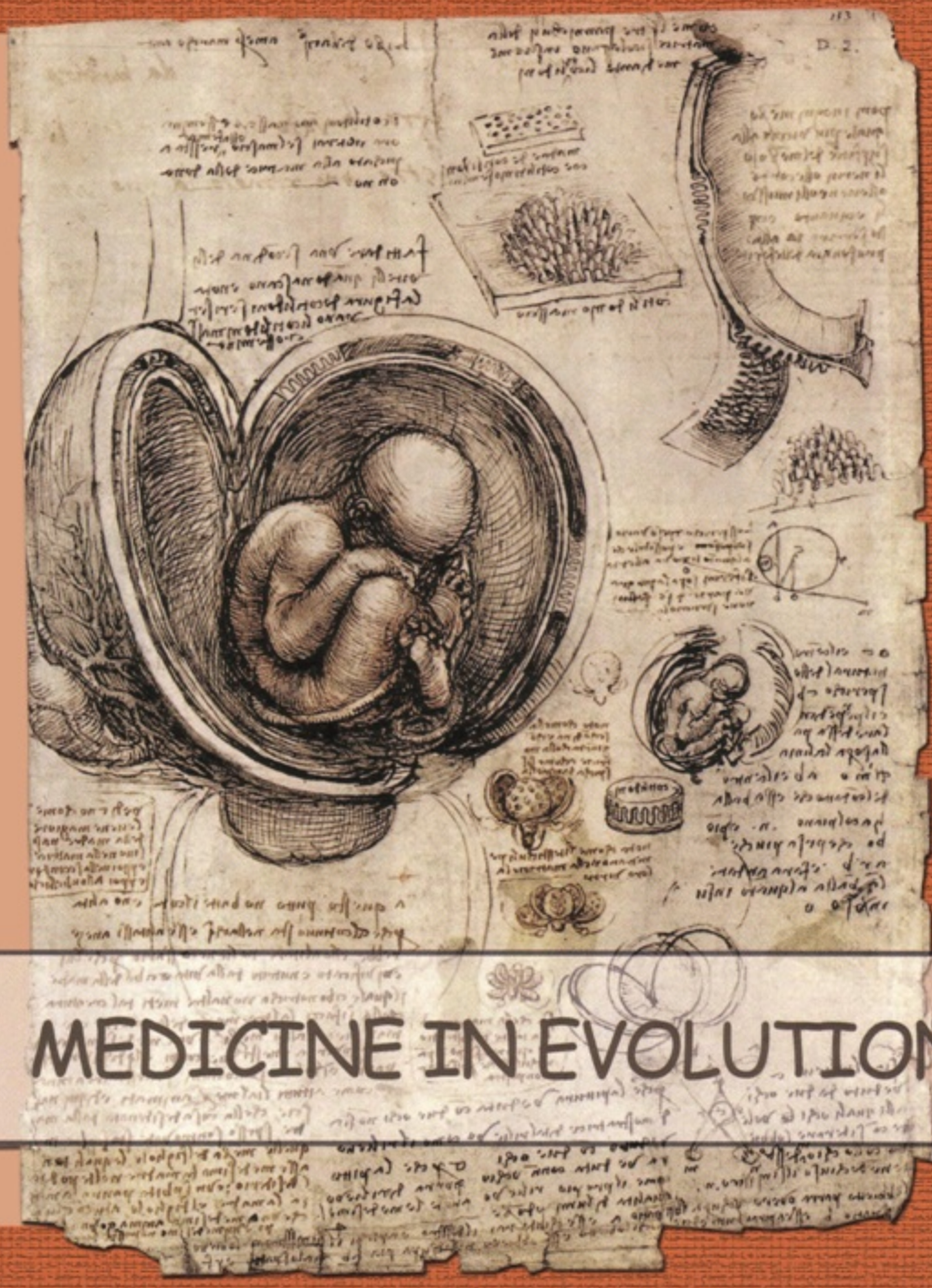

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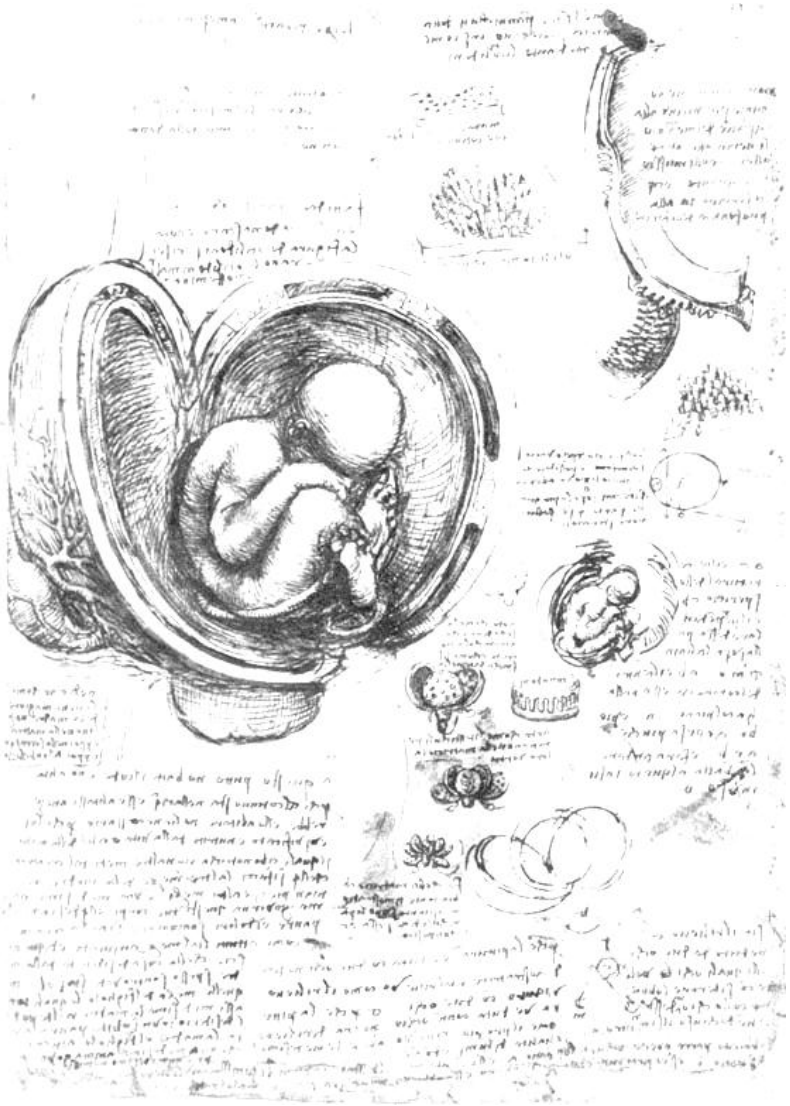

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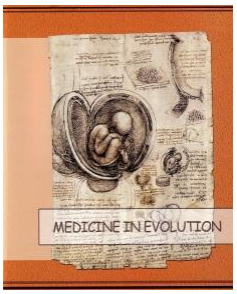
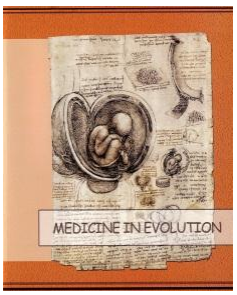


ARTICLES

Multicentre comparative analysis of liver fibrosis in chronic hepatitis C infection. The role of noninvasive markers



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Abstract

Aim and objectives: Comparative analysis of epidemiological indicators and non-invasive markers of liver fibrosis in chronic hepatitis C.

Material and methods: The group included 170 cases of chronic hepatitis C. Inclusion criteria: chronic hepatitis C, gender, age, living place, liver transaminases, total bilirubin and fibrosis score (METAVIR).

Results: Gender comparative analysis was statistically insignificant, with p between 0.3429 and 0.4566; age was statistically insignificant with p between 0.3429 and 0.4566, living place statistically significant with p between 0.0000 and 0.0468. Liver transaminases were statistically relevant, with p between 0.0000 and 0.0479, total bilirubin was incomplete statistically significant, with p between 0.0272 and 0.4474, incipient fibrosis had p between 0.0232 and 0.0415 and advanced fibrosis between 0.0001 and 0.0422, both statistically representative.

Conclusions: Regionally variability of epidemiological indicators and the advanced liver fibrosis revealed the necessity of making a new non-invasive marker, epidemiological dependent, quantifiable, reproducible, for correlation of epidemiological indicators with serum markers.

Keywords: HCV, epidemiology, fibrosis, noninvasive markers

INTRODUCTION

By analyzing different epidemiological trends of hepatitis C (HCV) genotypes and subtypes, it showed that the mode of transmission (or certain medical practices or social behavior) has even greater significance than genetic variability of the virus [1].

The natural history of HCV infection, factors related to host receptivity and enabling environment increases the likelihood of developing chronic hepatitis and hepatic cirrhosis. These include older age at infection, male gender, co-infection with hepatitis B, alcohol consumption in large quantities or low immunity, similar to that in HIV co-infection.

For many years, liver biopsy (LB) was considered ,,the gold standard", due to the possibility of direct histological evaluation of the severity of liver disease.

In the last decade, with the emergence of the possibility of assessment of liver fibrosis by noninvasive markers, between clinicians occurred conflicting views on liver biopsy versus noninvasive markers, due to absolute and relative contraindications (bleeding, pain, coagulopathies and comorbidities) or other considerations [2].

Aim and objectives

Assess the liver fibrosis stage in chronic hepatitis C infection (CHCI) by noninvasive methods in different regions/geographical areas. Observing trends and establishing preconditions for future scientific studies of the epidemiology and assessment of noninvasive markers for CHCI in Romania.

MATERIAL AND METHODS

Multicentre, comparative, retrospective study, developed in different public hospitals from the west of the country, during 2010 -2015.

The study group consisted of a total of 170 cases with CHCI and partitioned as follows: the subgroup 1 -17 cases, diagnosed in the Department of Infectious Diseases from Clinical Emergency Military Hospital ,,Dr. Victor Popescu" Timişoara, subgroup 2 - 63 cases, diagnosed in the Division of Infectious Diseases from Emergency Hospital Petroşani, subgroup 3 - 90 cases, diagnosed in the Division of Gastroenterology from Clinical Emergency County Hospital Oradea.

Selection of cases was done using the following inclusion criteria: main diagnosis of CHCI, framing each case the following parameters: gender, age group, social environment, liver transaminases values, total bilirubin value, fibrosis stage, interpreted by METAVIR score. Determination of the fibrosis stage was achieved both on a liver biopsy (LB), and other noninvasive methods (Fibrotest, Fibroscan).

Statistical processing of results and comparative analysis of subgroups was performed using Microsoft Excel software, version 2007 and SPSS, version 22.0. Subgroups analysis was performed by statistical indicators: weight, median, standard deviation. Testing the consistency of the samples was performed using the independent student t-test, bilateral comparison, testing all three subgroups, taken two by two. Statistical differences were representative when the p value of the test was < 0.05 at a confidence interval (confidence) of 95%.

RESULTS

A comparative analysis of subgroups was performed, by gender, age group, social environment, liver transaminases value, total bilirubin value, fibrosis stage, determined by invasive methods, noninvasive, respectively, both.

Structure of subgroups, according to gender (**Table I**), revealed to subgroup 1 a ratio of male about 58.82% compared to subgroup 2, where it was 49.21% and p value in comparing the 2 subgroups was 0.2101, without statistical significance.

The comparative analysis of the subgroup 2 with the subgroup 3, the ratio of males for subgroup 3 was 37.78% and p value of 0.3429, not significant statistically.

For the comparative analysis of the subgroup 3 with the subgroup 1, p value was 0.1099, not significant statistically.

Table I. Comparative analysis of the study group by gender

Subgroup	Cases number	Gender		P value
	Ratio (%)	Male	Female	
Subgroup 1	17	10	7	0.5389
	100	58.82	41.18	
Subgroup 2	63	31	32	0.2101
	100	49.21	50.79	
Subgroup 3	90	34	56	0.1099
	100	37.78	62.22	

Structure of subgroups, depending on the age group (**Table II**), revealed for the subgroup 1 an average age of 55 years ± 13.09, for subgroup 2 53 years ± 10.75, and for the subgroup 3, 54 years ± 10.80. Comparative analysis of subgroups was not statistically significant, with p values of 0.4566 (subgroup 1 by subgroup 2), 0.3429 (subgroup 2 by subgroup 3) and 0.4489 (subgroup 3 by subgroup 1).

Table II. Comparative analysis of the study group by age group

Subgroup	Cases number	Age group						Median ± standard deviation (SD)	P value
		5-24 years	25-34 years	35-44 years	45-54 years	55-64 years	>65 years		
Subgroup 1	17	-	1	4	3	7	2	55±13.09	0.4566
Subgroup 2	63	-	3	10	22	18	10	53±10.75	0.3429
Subgroup 3	90	1	5	12	35	28	9	54±10.80	0.4489

The structure of subgroups by the social environment (urban or rural) (**Table III**) showed a ratio of 88.24% in urban areas for subgroup 1, a ratio of 88.89% urban in subgroup 2 and 51, 11% urban in subgroup 3. Comparative analysis of subgroups revealed p values of 0.0224 (subgroup 1 by subgroup 2), 0.0000 (subgroup 2 by subgroup 3) and 0.0468 (subgroup 3 by subgroup 1), all with statistical significance.

Table III. Comparative analysis of the study group by social environment

Subgroup	Cases number	Social environment		P value
	Ratio (%)	Urban	Rural	
Subgroup 1	17	15	2	0.0224
	100	88.24	11.76	
Subgroup 2	63	56	7	0.0000
	100	88.89	11.11	
Subgroup 3	90	46	44	0.0468
	100	51.11	48.89	

To monitor the evolution of the disease, to determine liver function and indirect serological markers (noninvasive), laboratory tests were conducted, too. Among the most relevant for our study were hepatic transaminases (glutamic oxaloacetic transaminase and glutamic pyruvic transaminase) and total serum bilirubin.

Table IV. Comparative analysis of the liver transaminases levels in study group

Subgroup	Total cases number	Liver transaminases			P value
		Median ± standard deviation (SD)	Glutamic oxaloacetic transaminase (GOT, IU/L)		
			Normal levels cases number	High levels cases number	
Subgroup 1	17	46 ± 22.65	6	11	0.0000
Subgroup 2	63	94 ± 46.20	10	53	0.0000
Subgroup 3	90	43 ± 28.20	21	69	0.0251
Subgroup	Total cases number	Median ± standard deviation (SD)	Glutamic pyruvic transaminase (GPT, IU/L)		P value
			Normal levels cases number	High levels cases number	
Subgroup 1	17	38 ± 28.68	6	11	0.0000
Subgroup 2	63	125 ± 70.91	12	51	0.0000
Subgroup 3	90	43 ± 30.29	23	67	0.0479

The lot structuring, we had into account both cases: CHCI with normal levels transaminases and CHCI with high levels transaminases. Thus, GOT had a median (**Table IV**) 46 IU / L ± 22.65 for subgroup 1, GPT was 38 IU / L ± 28.68 and p value of 0.0000 (subgroup 1 versus subgroup 2) for both GOT and GPT , as well as statistically significant.

For subgroup 2, median GOT was 94 IU / L ± 46.20, the high levels cases were more numerous than those with normal levels, and median GPT was 125 IU / L ± 70.91, p value being 0.0000 (subgroup 2 compared to subgroup 3) for both liver transaminases levels, with statistical significance.

For subgroup 3, median GOT was 43 IU / L ± 28.20, the high levels cases were more numerous than those with normal levels and median GPT was 43 IU / L ± 30.29, p value being 0.0251 (subgroup 3 compared to subgroup 1) for GOT and, respectively, for GPT 0.0479, both the statistical significance.

Table V. Comparative analysis of the total bilirubin levels in study group

Subgroup	Total cases number	Total bilirubin			P value
		Median ± SD (mg/dL)	Normal levels cases number	High levels cases number	
Subgroup 1	17	0.63 ± 0.21	12	5	0.0463
Subgroup 2	63	0.83 ± 0.30	34	29	0.4474
Subgroup 3	90	0.71 ± 0.41	67	23	0.0272

Structuring of the group, based on the total bilirubin revealed a median of 0.63 mg / dL ± 0.21 (**Table V**) for the subgroup 1, 0.83 mg / dL ± 0.30 for subgroup 2 and 0, 71 mg / dL ± 0.41 for the subgroup 3, with the predominance of the normal levels for all three subgroups. P value in the comparative analysis was 0.0463 (subgroup1 by subgroup 2), 0.4474 (subgroup 2 by subgroup 3) and 0.0272 (subgroup 3 by subgroup 1), with statistical significance only partially (0.0463, respectively 0.0272).

Table VI. Comparative analysis of the fibrosis stage in the study group

Subgroup	Early fibrosis			Total cases number	P value
	Fibrosis stage (METAVIR)				
	F 0 (without fibrosis)	F 1 (mild fibrosis)	F 2 (significant fibrosis)		
Subgroup 1	1	4	1	6	0.0321
Subgroup 2	2	8	16	26	0.0415
Subgroup 3	7	14	15	36	0.0232
Subgroup	Advanced fibrosis			Total cases number	P value
	Fibrosis stage (METAVIR)				
	F 3 (sever fibrosis)	F 4 (hepatic cirrhosis)			
Subgroup 1	4	7		11	0.0322
Subgroup 2	26	11		37	0.0001
Subgroup 3	17	37		54	0.0422

The structure of the subgroups, depending on the method used to determine the fibrosis stage (invasive versus noninvasive) was as follows:

- **LB** - *subgroup 1*: 1 case F0, 4 cases F1, 1 case F2, 2 cases F3, 2 cases F4, representing a ratio of 43.75%, *subgroup 2*: 6 cases F1, F2 14 cases, 21 cases F3, 4 cases F4, representing a ratio of 71.43%, *subgroup 3*: 6 cases F0, 12 cases F1, 14 cases F2, 11 cases F3, 35 cases F4, representing a ratio of 86.67%.
- **Fibrotest** - *subgroup 1*: 1 case F4, representing a ratio of 6.25%, *subgroup 2*: 1 case F0, 1 case F1, 2 cases F2, 2 cases F3, 6 cases F4, representing a ratio of 28.57%, *subgroup 3*: 2 cases F1, 1 case F2, 4 cases F3, 1 case F4, representing a ratio of 8.89%.
- **Fibroscan** - *subgroup 1*: 2 cases F3, 4 cases F4, representing a ratio of 37.5%, *subgroup 2*: 1 case F0, 1 case F1, 3 cases F3, 1 case F4, accounting for a ratio of 7.94%, *subgroup 3:* 1 case F0, 2 cases F3, 1 case F4, representing a ratio of 4.44%.
  There were situations where the fibrosis stage was determined by various methods, both invasive and noninvasive for the same patient. The situation in the subgroups was as follows:
- **LB + Fibrotest** - *subgroup 2*: 1 case Fibrotest F4 (0.77) versus F3 (LB), representing a ratio of 1.59%, *subgroup 3*: 1 case Fibrotest F3 (0.64) versus F2 (LB), 1 case Fibrotest F4 (0.83) versus F3 (LB), representing a ratio of 2.22%.
- **LB + Fibroscan** - *subgroup 2*: 1 case Fibroscan F0-F1 (4.9kPa) versus F2 (LB), 1 case of Fibroscan F3 (12,3kPa) versus F3 (LB), 1 case of Fibroscan F4 (19,1kPa) versus F3 (LB), representing a ratio of 4.76%, *subgroup 3*: 1 case Fibroscan F4 (15,2kPa) versus F3 (PBH), representing a subgroup of 1.11%.
- **Fibroscan + Fibrotest** - *subgroup 3*: 1 case Fibroscan F3 (10.1 kPa) versus F2 (Fibrotest), representing a ratio of 1.11%.

For the comparative statistical analysis (**Table VI**), we structured the subgroups in 2 categories: early fibrosis (no fibrosis - significant fibrosis) and advanced fibrosis (hepatic fibrosis – hepatic cirrhosis). In the first category, the p value was 0.0322 (subgroup 1 compared to subgroup 2), 0.0415 (subgroup 3 compared to subgroup 2) and 0.0232 (subgroup 3 compared to subgroup 1), all the three values were statistically representative.

The second category, had the p value 0.0322 (subgroup 1 compared to subgroup 2), 0.0001 (subgroup 2 compared to subgroup 3) and 0.0422 (subgroup 3 compared to subgroup 1), all three values were statistically representative.

DISCUSSIONS

Analyzed group includes various counties from west of the country and form a multicenter, comparative study of representative population segments both geographical area and for liver pathology.

Thus, subgroup 1 consists of a segment of Timişoara city population and Timiş county, subgroup 2 of a segment of the Oradea population and Bihor county, respectively subgroup 3 of Petroşani municipality and southern Hunedoara county, while being representative for Jiu Valley, region with an apart socio-economic specific.

Structure of subgroups by gender revealed for subgroup 1 a ratio of male gender with 17.64% higher compared to female gender ratio, for subgroup 2 female gender had a ratio with 1.58% higher compared to male gender ratio, for subgroup 3 the ratio of female gender was with 24.44% higher than the ratio for male gender, overall ratio among the global group was with 11.76% higher for female gender compared to male gender. However, the p value for statistical comparative analysis of subgroups was between 0.1099 and 0.5389, without statistically representativeness.

The data obtained are consistent with findings of other scientific studies on the prevalence of CHCI both in Romania and other countries from the EU (France, Germany) [3, 4].

The age and, respectively, age group in the structure of the study group, highlighted values between 53 and 55 years, the higher number of cases being framed in the age group 45-54 years (60 cases), with a ratio of 35.29% in the overall group. The next age group in the ,,top" of CHCI was the age group 55-64 years (53 cases), with a ratio of 31.18% from the global group. The p value, among statistical comparative analysis of subgroups was between 0.3429 and 0.4566, without statistical significance. The data obtained are inconsistent with the results of the latest studies on the prevalence of CHCI in Romania, but are consistent with other global scientific studies in different countries (Australia, Turkey, Canada, Brazil and Egypt) [3, 4].

Another hypothesis, tested and scientific validated, was the heterogeneity of CHCI by gender and age group, being very difficult to create a ,,pattern", mainly due to virus genotype variability and diversity of transmission pathways [3].

The studies that have examined the epidemiological trends for different genotypes and subtypes of HCV, suggested that the mode of transmission (or certain medical practices or social behaviors) have greater importance than even the genetic variability of the virus.

Thus, as long as the transmission routes are kept functional, *any viral subtypes* can explode and trigger a *future epidemic* anywhere in the world [1].

Another phenomenon that occurs in patients with HCV is social discrimination, virtually double discrimination, first due to the social and second due to the disease, for different types of activities such as health care system, predominantly, but also in the workplace or other social activities. In the same time with discrimination are limited the access to information (including medical information), prevention, support and testing services, treatment and medical care.

A third component is the appearance of social stigma. All these aspects lead to installing barriers for certain categories of people who want access to treatment, especially for the poor. These categories have limited knowledge about HCV, route of transmission is often associated with, lack of information on treatment options and rejection in accessing priority social services [5].

Noninvasive markers, specially the indirect ones, were the second major concern of the research team. From these, laboratory tests such as liver transaminases (GOT, GPT) had statistical significance with medians between 43 ± 28.20 and 94 ± 46.20 and the p value was between 0.0000 and 0.0251 for GOT, respectively, medians between 38 ± 28.68 and 125 ± 70.91, the p value was between 0.0000 and 0.0479, for GPT.

The ratio for the cases with normal levels of transaminases in the global group was 21.76% (37 cases) for GOT, respectively, 24.12% (41 cases) for GPT. The number of cases with high levels of transaminases was 78.24% (133 cases) for GOT, respectively, 75.88% (129 cases) for GPT.

The total bilirubin, an important laboratory analysis from the hepatobiliary sphere disorders, had medians between 0.63 ± 0.21 and 0.83 ± 0.30, and the p value for the comparative analysis of subgroups was between 0.0272 and 0.4474, with statistical significance only in part. The ratio for the cases with normal bilirubin levels was 66.47% (113 cases) compared to 33.53% (57 cases) with high bilirubin levels.

In determining the hepatic fibrosis stage, they were used as invasive methods (LB), noninvasive (Fibroscan, Fibrotest) or, in parallel, LB and Fibroscan, LB and Fibrotest, Fibroscan and Fibrotest. Thus, LB was used to diagnose a number of 133 cases (78.24%) from the overall group, Fibroscan 16 cases (9.41%), Fibrotest 21 cases (12.35%), LB and Fibroscan 4 cases (2.35%), LB and Fibrotest 3 cases (1.76%), Fibroscan and Fibrotest 1 case (1.04%).

The structuring and ratio of fibrosis stage (METAVIR) in overall group was: F0 10 cases (5.88%), F1 26 cases (15.29%), F2 32 cases (18.82%), F3 47 cases (27.65%) and F4 55 cases (32.35%).

Depending on the type of fibrosis, global group was divided into two categories: early fibrosis or advanced fibrosis. Comparative analysis of the subgroups, depending on the type of fibrosis showed p values between 0.0232 and 0.0415 for early fibrosis, respectively, advanced fibrosis from 0.0001 to 0.0422, all statistically representative.

A retrospective comparison between the APRI score (aspartate aminotransferase to platelet ratio index) and Fibrotest, with a prevalence of 41% for stage F2, F3, F4 fibrosis [6]. The results are inconsistent with those obtained by our research team, which can be explained by the heterogeneity of global group, each subgroup having distinct epidemiological characteristics.

In the last decade, with the emergence of the possibility of assessment of liver fibrosis by noninvasive markers, between clinicians occurred conflicting views on liver biopsy versus noninvasive markers, due to absolute and relative contraindications (bleeding, pain, coagulopathies and comorbidities) or other considerations

Thus, numerous studies have been conducted among practicing clinicians liver biopsy. In a study conducted in France, the country that introduced noninvasive markers determining for the first time, since 2007, were established ways of settlement of investigations conducted between clinicians and participants, only 4% have recommended biopsy.

In a study conducted in the United States, the cost of a puncture biopsy was 1032 $, with the ability to grow to 2745 $, where complications occur following procedure. In Canada, the average cost of a liver biopsy complications and hospitalization was $ 4,579 [2].

In Romania the estimated cost of a puncture biopsy without complications is 439.12 lei (111.89 $), including food costs (the days of hospitalization), proper handling, medical equipment, medicines, laboratory analyzes, etc.

In conclusion, at this time, after the emergence of new noninvasive techniques, we cannot speak of a ,,gold standard" in diagnosing and assessing of liver fibrosis, all methods currently use, being imperfect reference methods.

CONCLUSIONS

1. Analyzing global group by gender resulted in a higher ratio for females (11.76% higher) but with high variability in the subgroups, from one region to another.
2. The analysis by age group resulted in the highest ratio for the age group 45-54 years (35.29%), with a peak within 53-55 years and with less interregional variability.
3. Structuring the global group by the social environment (urban, rural) led to the conclusion that CHCI is predominant in urban areas (68.82%).
4. Analysis of noninvasive markers, and particularly the indirect ones, concluded that advanced liver transaminases are increased for most cases (78.24% GOT and, respectively, 75.88% GPT), while total bilirubin was normal for the largest majority of cases (66.47%).
5. Analyzing the liver fibrosis stage in the global group structure revealed that the advanced fibrosis had the highest ratio (60%).
6. On one hand, considering limited access to certain investigations (most specialized centers are in cities, the cost is still quite high), on the other hand standardization quite low of laboratory investigations, develop new noninvasive markers, to overcome the limitations of those already ordained.
7. Interregional variability of epidemiological indicators measured, on one hand and advanced stage of liver fibrosis for most cases, on the other hand, have iterated the need to develop a new noninvasive marker, epidemiological-dependent, quantifiable, reproducible, linking epidemiological indicators with biological parameters of disease.

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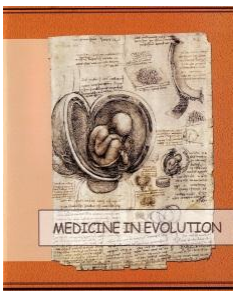
Polydactyly in children – histological diagnosis: a case report



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Abstract

Polidactily is a more frequent condition that emerges in children, developing along with other abnormalities, during fetal evolution and first year of life, often misdiagnosed as another dermatopathological conditions. Associated with genetic autosomal dominant abnormalities like the Ellis-van Crefeld syndrom, it mith become an indicator in parental counseling for future pregnancies and baby outcome. Treatment is not necessary unless mechanical or esthetical benefits are required. We present the case of a 6 month old child, initially misdiagnosed with a finger condyloma, later confirmed as incomplete type 2B polydactyly.

Keywords: incomplete polidactily, children, pathology, falanges

INTRODUCTION

Polidactily (PD) is a frequent condition associated with different genetic anomalies, especially in children. Generally accepted, there are two types of PD as digital duplications: radial or preaxial and ulnar or postaxial PD. Duplications of the second to the fourth fingers are known as central PD. Radial PD is the most common form encountered in white Caucasians, while ulnar PD is more frequent in African-Americans. In Caucasian-type people the incidence varies in between 1:1500 to 1:3300. It seems that PD is associated with autosomal dominant traits, or other limb malformations, like Ellis-van Crefeld, McKusik-Kaufman and Bardet-Biedl, short rib-polydactyly syndrome I, orofacial syndrome III, Bardot-bipedal, Meckel-Gruber, Greg polycephalopolysyndactyly and Palister-Hall syndromes (1). Some authors classified PD taking in account the functional aspect of the duplicated finger. Therefore, it is cited the „A type" PD for complete, functional, finger and „B type" for incomplete, non-functional PD. Other authors preffer to examine histological constituents of PD: „type 1" for soft parts formation only, „type 2" for further bone formation while „type 3" needs the presence of metacarpal complete duplication. Regarding these, type B ulnar polydactyly is far frequent that type A radial PD, respectively type 1 ulnar and type 3 radial ones (2).

CASE REPORT

A six months old boy has been reffered for an apparent condyloma on the ulnar side of the 5th finger at the left hand.

I. Anamnesis

The boy's family states that the child is in good health, active, joyful. The main concern was the upgrowing formation on the left hand, that seemed accelerated being present at the site from his birth.

II. Clinical examination data

At the ulnar side of the fifth finger on the left hand, an indurated-elastic mass was observed, bulging medially, well demarcated, covered with acral skin having no other suspicious modification. The presumtive diagnosis was that of an acral wart or of a congenital condyloma. Dental and oral examination proved no anomalies, as normal primary teeth were about to emerge, with presence of a slight anxiety and whitened gums. At a careful clinical examination the child proved a slight shorter stature (56 cm) with normal weight (7300 grams). No detectable morphogenetic anomalies were observed.

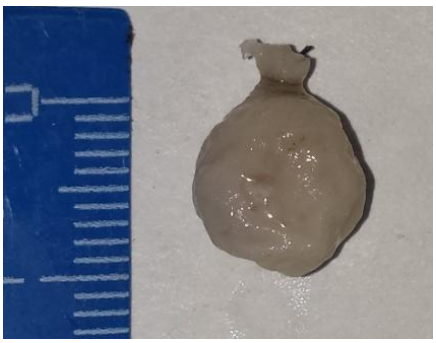

Figure 1. Gross aspect of the nodular mass extracted from the ulnar side of the left hand from a 6 months old boy (personal collection)

III. Laboratory data proved no abnormal deviation of any kind

IV. Additional paraclinical investigations

Although no incidental radiograph was initially neccesary, resection has been performed, and a bioptic tissue has been sent to the anatomical pathology laboratory, in our hospital. It was described as a singular, well demarcated ovoidal white to tan mass, 1 cm in diameter; regarding the sectional aspect, the nodule was slight heteregenous with soft and hardened, calcified areas (Fig. 1). After standard preparation in succesive ethilic and isopropyl alcohool grades (70, 80 and 96^{o}), paraffing embedding with subsequent haematoxilin and eosin staining procedure, having no decalcification, we detected a bulbous skin structure, with acral skin and rete ridges with some elongation (Fig. 2). Various eccrine structure were visible, having alined glomeruli in the mid-dermis. Centrally, we observed varied fibrous structures along with a cartilage-like area, showing enchondral ossification, and a Paccini corpuscule intermingled by neural structures (Fig. 3 and Fig. 4). The final diagnosis was that of an incomplete PD type 2B, for an extranumerary 6th finger on the ulnar side at the left hand.

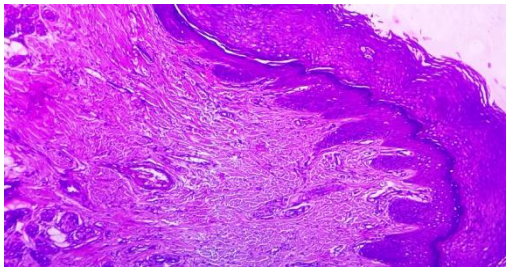

Figure 2. The Vater-Pacinni corpuscule found in side the hypodermis, proving tactile features of the formation (10x20, HE)

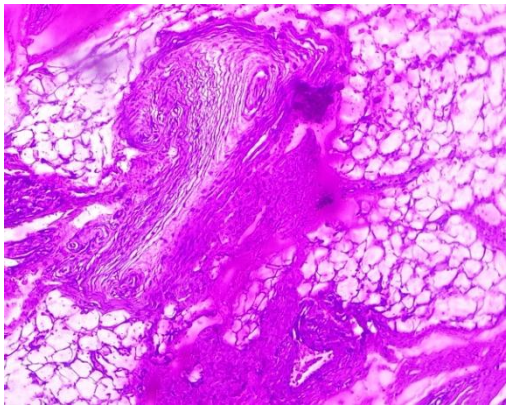

Figure 3. Elongated rete ridges, acral skin with thick keratinization. Various eccrine structures and ductuli are visibile within a dense, collagenous dermis (4x10, HE)

V. Treatment and evolution

The treatment was represented by surgical excision and ligation, hemostasis and minimal esthetic dermal reconstruction of the remaining tisular void. Medical and surgical follow up was decided for the case in matter for as long as one year postoperatory.

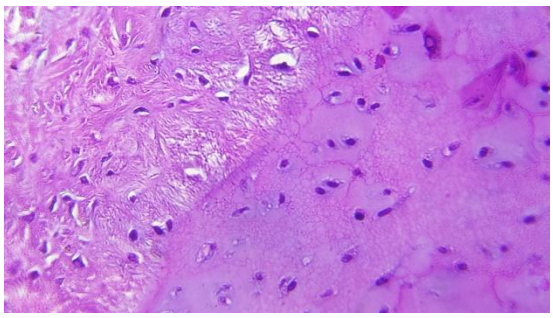

Figure 4. Enchondral ossification inside the hypodermis (10x40, HE)

DISCUSSIONS

The histopathologist should find structures and appendages detectable in a normal finger. Rquired characteristics of the acral skin are, usually, conspicous: a thick lamellar keratin, with elongations of the rete ridges and numerous acrosyringeal structures and eccrine apparati. The presence of nerve structures is obvious and obligatory for histopathological diagnosis criteria. Nail formation with abrupt keratinization, osteoid and a central cartilagenous core are usually found in PD type 2 and 3. In type 1, i.e. a rudimentary digit, histology is less characteristic and may mimic a traumatised neuroma, especially with the abscence of the osteo-cartilagenous structures. In this case, the diagnostic clue remains the rete ridges elongation and presence of the Meissner or Vater-Pacinni corpusculi at the tip of the epidermal cristae toegether with the localisation (3). Diagnosis should be completed with a minutious radiologic examination as well as molecular and genetical testing, if any abnormal genetic syndrome context is suspicioned. Abnormal enchondral ossification may complicate further the diagnosis as differential diagnosis with osteochondrodysplasia, parosteal osteosarcoma and chrondrosarcoma should be verified, due to molecular and immunohistochemical analysis. For example, Ellis-van Crefeld syndrom associated with PD needs molecular testing for definitive diagnosis, represented by complete sequencing and identification of the EVC and EVC2 genes, components of the Hedgehog family genes (Hh) that regulates normal endochondral growth, located on 4p16, within a 17-cM region (4). These mutations together with a detailed necropsy and radiologic study may sustain a certitude diagnosis. In some cases, PD type A may be associated with dental abnormalities, like symmetrical absence of primary teeth with abnormal pitting. A decreased motility on the affected hand might become visible, usually, during the first year of life, although most solitary cases have a normal health and development, sometimes with some degree of muscular weakness not classifiable as a distrophy of any kind (5).

Acknowledgement

We wish to thank to the surgical team of our hospital for complete cooperation with clincal data and anamensis onto this case report to be completed.

Conflict of interests

The authors declare no conflict of interest of any kind.

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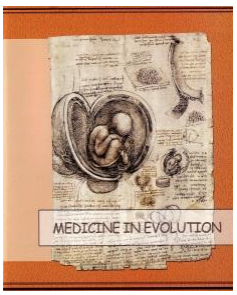
The amount of lipids used during a maximal effort will be influenced through aerobic exercyse capacity



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Abstract

Aim: Increased aerobic capacity may modify the energy system efficiency during specific rowing maximal effort.

Material and method: A cross-sectional study was conducted in February 2016, Bucharest, Romania, on a group of 26 elite male rowers, by applying an indoor VO_{2max} test over a standard distance of 2,000 m. Data collection was conducted through Cosmed Quark CPET equipment/ Concept 2 ergometer.

Results: VT1, in G1 (167.6±1.69 b/min), was statistically significant compared to G2 (161.1±1.93 b/min), through p=0.0178. Activity period of ATP+CP system in G2 was 71.75±5.06 s, while in the G1 group was 51.61±3.52 s. As a result, energy consumption was 152.1±3.04 kcal in G1, while G2 reported an energy consumption of 148.8±3.15 kcal.

Conclusions: The efficiency of energy metabolism is directly proportional to the aerobic capacity, being reported a significant increase in carbohydrate consumption during maximal effort, and a decrease in lipids consumption in association with low VO_2 value.

Keywords: carbohydrates, oxygen, anaerobic, fat

INTRODUCTION

The contribution of energy metabolism and energy resources represented through carbohydrates, respectively lipids, will be directly influenced by the intensity and volume of the performed effort (1). The intensity is defined as a percentage of the determined VO_2 value (2). Thus, it is imposed a hypothesis according to which, during effort, the total volume will determine the amount of energy that will be used, while exercise intensity will determine the energy substrate use during sustained exercise (3). In practical terms, rowing is characterized by dynamic and intense activity on the main muscle groups involving the need for significant force production during each strike performed at high intensity, characterizing the anaerobic competitive effort, and the aerobic general training form (4).

An immediate energy source during a maximal effort is represented by ATP (5). All exercise are dependent of ATP use and degradation, as a fast energy source (6). Thus, the energy value is associated with the activity and efficiency of muscle contraction (6). The total amount of ATP stored in the body is low, being reported different stages of ATP re-synthesis through energy sources such as glycogen and Fat (7). Despite the energy importance, it should be mentioned that ATP is not an energy deposit, but through the contribution of secondary elements activity, ATP will represent the optimal form of energy with influence in cellular activity (8). At the same time, decreased ATP levels will be associated with muscle inefficiencies, fatigue, and an impaired ability to generate force, representing one of the most important elements of muscle contraction (9). From a practical standpoint, fatigue is associated with decreased ability to maintain homeostasis, involving avoidance of decrease ATP level at values that inhibit muscle contraction (10).

Both creatine kinase, and adenylate cyclase reaction promotes ATP re-synthesis during physical effort. Increased process efficiency is associated with different values of creatine kinase (11). From this point, it may be recalled that certain sporting activities such as team sports, weightlifting, and various athletics probes, will additionally benefit from this energy source through the body's ability to re-synthesized ATP, as long as the energy demands will be satisfied (12).

HYPOTHESIS

Respiratory and cardiovascular adaptation during effort is associated with metabolic balance, being likely possible to enhance energy system contribution and efficiency, through increasing aerobic capacity. Thus, increased exercise capacity, through elevated VO_2 value, during general training period, will increase athlete's capacity and energy efficiency during maximal effort.

MATERIAL AND METHODS

A cross-sectional study was conducted in February 2016 on a group of 26 elite male rowers. The activity was initiated after receiving the acceptance of the informed subjects to participate in the study, and the ethical committee approval. The study included a sample of 26 athletes, divided into two groups based on age and activity level (G1/G2). G1, with a number of 14 athletes, was included in the study after a period of 112 days engaged in a general effort which reached 45-87% of VO_2, and 55-85% of the maximum heart rate value. Group G2, with a number of 12 athletes, was included in the study after a total of 112 days engaged in a general effort of 45-93% VO_2, and 55-95% of the maximum heart rate value.

Data collection was performed by conducting an effort test, VO2max, indoor, using Cosmed Quark CPET equipment (Rome, Italy) for cardio-metabolic/ cardio-respiratory measurements, and Concept 2 ergometer in order to sustain the effort. The VO_{2max} test was

performed after a complementary activity conducted to adapt the body to exercise, over a total time of 20 minutes, involving both basic elements in preparing the athletes for the test, as well as ergometer specific activity at a predetermined intensity (55-85% heart rate) in order to simulate the effort. The test was carried out over a distance of 2,000 m without imposing a completion limit time, or an effort developed in different intensity stages. Cardio-respiratory/ cardio-metabolic parameters were determined through Cosmed Quark CPET equipment, while the heart rate value through Cosmed heart rate strip with Bluetooth transmission to the main device. The following parameters were monitored during the effort: heart rate (HR -bpm), respiratory frequency (Rf -b/min), minute ventilation (VE -l/min), maximum rate of oxygen consumption (VO_2 -ml/min), carbon dioxide elimination rate (VCO_2 -ml/min), ventilatory equivalent for oxygen (VE/VO_2),ventilatory equivalent for carbon dioxide (VE/VCO_2), metabolic equivalent (METS), tidal ventilation (VT -l), the amount of oxygen expired (O_2exp -ml), amount of carbon dioxide expired (CO_2exp -ml), respiratory exchange ratio (RER), end tidal CO_2 fraction (FeO_2 -%), end tidal O_2 fraction ($FeCO_2$ -%), end-tidal oxygen tension oxygen ($PetO_2$ -mmHg), end-tidal carbon dioxide tension ($PetCO_2$ -mmHg), partial pressure of carbon dioxide in the arterial blood ($PaCO_2$ -mmHg), partial pressure of oxygen in the arterial blood (PaO_2 -mmHg), the ratio of physiologic dead space over tidal volume (VD/VT), Energy expenditure (Kcal/min), Fat (Lipids -gr/%), CHO (carbohydrates -gr/%), being possible the determination of ventilatory thresholds (VT1, VT2) through the extracted data.

Statistical analysis was performed using GraphPad Prism 7.0 software. The main statistical indicators were: average value (mean), standard error (SE), standard deviation (SD), standard error of the mean (SEM), and coefficient of variation (CV). For data normalization D'Agostino-Pearson omnibus normality test was used. To demonstrate the association between two variables, Pearson correlation test (r) was applied, and in order to establish the differences between groups, student's t-test (unpaired) was used. Level of significance, $p<0.05$ was considered statistically significant, while the data illustration was carried out through mean and standard deviation values (mean±SD). For all the statistical tests applied, the confidence interval was 95%.

RESULTS

The two groups were taken in comparison based on the correct training periodization and daily aerobic training application reported through total VO_2 value that does not exceed 93%, associated to 95% of the maximum heart rate value. Following the performed VO_{2max} test over the distance of 2,000 m, we reported a completion time of 368±5.83 s for G1 (93.9±10.1 kg body weight; 193±6.85 cm height; 19.69±2.05 years), and 350±17.1 s within G2 (95.7±8.45 kg body weight; 195±4.89 cm height; 21.58±1.5 years), the results being statistical different (p=0.0001, r=0.3784, CI95%=-28.3 to -8.151). Thus the measured values within G1, regarding VT1 (167.6±1.69 b/min) and VT2 (187.6±1.20 b/min) were statistically different from VT1 (161.6±1.93 b/min), VT2 (183.8±1.63 b/min) reported in G2. As a result, accessing 100% carbohydrate, through muscle glycogen, associated to 1.0 RER, was higher in G1 (174.8±1.88 b/min), than in G2 (171.7±1.96 b/min), however, without identifying a significant statistical difference (p=0.2778).

Following the first phase of the effort, characterized through oxygen debt (RER 1.0) and muscle ATP consumption, we associated ATP re-phosphorylation through glycogen and Fat. Thus, the total period of CHO and Fat contribution during ATP re-phosphorylation, was 51.61±3.52 s in G1, and 71.75±5.06 s in group G2 (p=0.0027, r=0.3291, CI95%=7.733 to 32.53). During this phase, the proportion was 44.12±2.78% Fat, and 57.49±2.67% CHO within G1, while the proportion of Fat was equivalent to 44.91±2.87%, and the proportion of CHO was 55.51±2.87% in G2 (Fig. I).

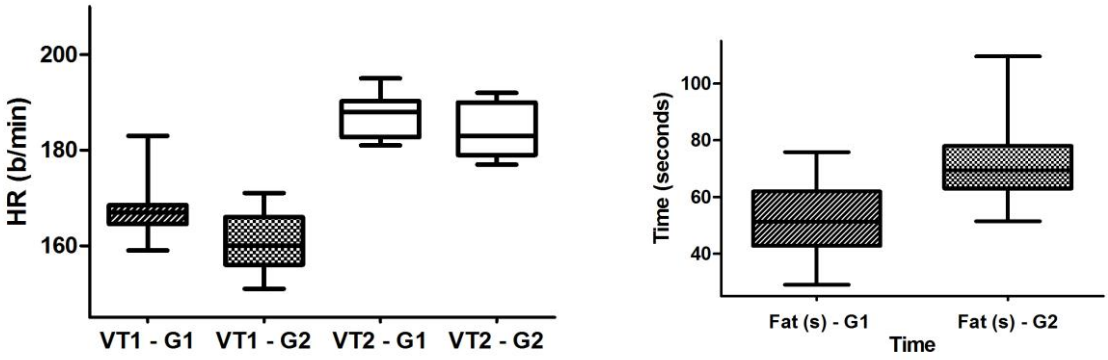

Figure 1. The total time of lipid energy contribution (mean+SD); Ventilator thresholds representation in direct relationship with the heart rate (mean + SD)

The energy consumption resulted in the study groups did not represent statistical differences (p=0.4688), being determined a value of 152.1±3.04 kcal/race in G1, and 148.8±3.15 kcal/race in G2. Pairing was performed in both, carbohydrates distribution (%), and lipids distribution (%/g) as energy resources. Thus, we reported statistically differences in terms of CHO energy contribution (%) during the race (p=0.0064, r=0.2811, CI95%=-4.26 to -0.7822), the amount of CHO reported in grams (p=0.0024, r=0.3369, CI95%=0.1891 to 0.7686), and the contribution of Fat metabolism throughout the effort (%), through p=0.0064, r=0.2811, CI95%=0.7822 to 4.26 (Table I).

Table I. *The distribution of macronutrients and energy through energy substrate*

G1					*G2*				
Kcal	**CHO**		**L**		**Kcal**	**CHO**		**L**	
	%	gr	%	gr		%	gr	%	gr
152.1±3.04	95.01±0.55	37.7±0.86	4.9±0.55	0.84±0.09	148.8±3.15	92.48±0.63	37.1±0.72	7.51±0.63	1.32±0.10

For the following respiratory parameters: Rf (b/min), VE (l/min), VCO2 (ml/min), VE/VCO_2, METS, VT (L) O_2exp (ml) CO_2exp (ml) FeO_2 (%) $FeCO_2$ (%) $PetO_2$ (mmHg) $PetCO_2$ (mmHg), PaO_2 (mmHg), $PaCO_2$ (mmHg), VD/VT, no significant statistical differences were found in the study groups (G1-G2), similar ranges being determined among the monitored parameters during the 2,000 m race simulation. On the other hand, significant statistically differences were obtained between parameters such as: VO2 (ml/min), HR (b/min), VE/VO_2, RER (Table II.).

Table II. *Differences between the groups regarding the respiratory system G1-G2*

Parameteres study			Reported data			
Gr1 Gr2	Mean+SEM	Significant?	*p*	*r*	95% Confidence Interval of the difference	
					Lower	Upper
Rf	57.78±0.95 58.22±2.15	No	0.8428	0.001746	-4.088	4.966
VE	176.2±4.18 179.4±4.83	No	0.6212	0.01079	-9.992	16.38
VO_2	4952±112.7 5475±85.24	*Yes	0.0018	0.3508	215.9	829.1
VCO_2	5576±128.2 5863±103.2	No	0.1072	0.1089	-67.23	642
HR	179.9±1.28 169.4±5.40	*Yes	0.0470	0.1607	-20.77	-0.1507
VE/VO_2	35.73±0.66 33.01±1.06	*Yes	0.0333	0.1822	-5.205	-0.2344
VE/VCO_2	31.85±0.58	No	0.4469	0.02537	-3.098	1.411

Parameteres study			Reported data			
	31±0.97					
METS	15.23±0.40 16.43±0.42	No	0.0546	0.1513	-0.0259	2.424
VT	3.03±0.07 3.09±0.1	No	0.6493	0.009147	-0.2173	0,3418
O_2exp	528±14.07 530±19.79	No	0.9338	0.0003068	-46.9	50.88
CO_2exp	120.1±3.51 124.8±5.98	No	0.4852	0.02141	-8.989	18.37
RER	1.11±0.01 1.06±0.00	*Yes	0.0161	0.2267	-0.1036	-0.01173
FeO_2	17.24±0.08 17.08±0.11	No	0.2631	0.05413	-0.4611	0.1321
$FeCO_2$	4.03±0.07 3.99±0.11	No	0.7898	0.003151	-0.3182	0.2448
$PetO_2$	112.8±0.56 112.9±1.03	No	0.9076	0.0005985	-2.182	2.444
$PetCO_2$	36.01±0.56 36.89±0.92	No	0.4020	0.03072	-1.254	3.017
VD/VT	0.25±0.00 0.24±0.00	No	0.4076	0.03001	-0.03251	0.01368

In G1, significant statistical correlations were identified, thereby increased VT1 (168±6.33 b/min) is associated with increased VT2 (188±4.5 b/min), HR (180±4.82 b/min) and $PetO_2$ (113±2.13 mmHg) while lowering VT1, will be associated with elevated $PetCO_2$ (36±2.11 mmHg) and $PaCO_2$ (37.3±1.79 mmHg). At the same time reducing the aerobic ventilatory threshold, associated with muscle glycogen accession, has been associated with increased $PaCO_2$ value, while the total contribution of CHO, during the 2,000 m race, was higher in association to elevated PaO_2, RER and FeO_2 (17.2±0.32%). Decreased accessing time was associated with decreased VD/VT value (0.25±0.025). Further on, the proportion of carbohydrate used during the race was directly proportional to VO_2 (4956±422 ml/min), VE (176±15.7 l/min), VCO_2 (5576±480 ml/min), O_2 (528±52.7 ml), CO_2 (120±13.2 ml) and VT (3.04±0.29 L) values, while increasing the proportion of lipids (g) used during maximal effort was associated with decreased RER, FeO_2, and PaO_2 values. At the same time, increasing the total use of Fat during effort (4.99±2.07%) was associated with decreased RER, VCO_2, PaO_2 and FeO_2 parameters, inverse association obtained in case of CHO (%), by increasing VCO_2, RER, FeO_2, PaO_2.

In G2, VT1 (161±6.43 b/min) was not significantly correlated with any of the parameters previously mentioned. Increasing VT2 (184±5.42 b/min) was associated with increased aerobic ventilatory threshold (172±6.53 b/min). The total energy provided through muscle glycogen was increased in association to elevated $PetO_2$ (113±3.44 mmHg), PaO_2 (113±2.84 mmHg) and FeO_2 (17.1±0.39%) values, while parameters such as $PetCO_2$ (36.9±3.05 mmHg), $PaCO_2$ (38.1±2.82 mmHg), decreased. However, FeO_2 encountered a directly proportional increase with $PetO_2$, PaO_2, VD/VT (0.24±0.03), while the decrease is related to increased PaO_2, FeO_2, $PetO_2$ values, rising the contribution of Fat during maximal effort. Data reported in Table III.

Table III. *Statistical significance data between the two groups regarding monitored parameters during the 2,000 m race simulation (G1-G2)*

Parameteres		*G1*				*G2*			
		p	*r*	95% Confidence Interval of the difference		*p*	*R*	95% Confidence Interval of the difference	
				Lower	Upper			Lower	Upper
VT1	VT2	0.0133	0.642	0.169	0.875	0.1171	0.5	-0.142	0.846

	HR-CHO	0.0001	0.884	0.665	0.963	0.1142	0.504	-0.138	0.847
	HR	0.0022	0.745	0.355	0.914	0.3050	-0.341	-0.781	0.326
	$PetO_2$	0.0494	0.534	0.00431	0.829	0.8175	-0.0789	-0.692	0.547
	$PetCO_2$	0.0466	-0.539	-0.832	-0.0271	0.6423	-0.158	-0.692	0.488
	$PaCO_2$	0.0417	-0.55	-0.836	-0.0271	0.06071	-0.175	-0.701	0.475
VT2	HR-CHO	0.0133	0.7	0.269	0.897	*0.0032	0.798	0.381	0.945
	HR	0.0001	0.912	0.738	0.972	0.03962	0.285	-0.38	0.756
HR-CHO	$PaCO_2$	0.0443	-0.544	-0.834	-0.019	0.5001	0.228	-0.431	0.728
Muscle Glycogen (s)	RER	0.0336	0.589	0.0556	0.845	0.5749	-0.1904	-0.7094	0.4624
	FeO_2	0.0064	0.689	0.25	0.893	*0.0348	0.6375	0.06083	0.8951
	PaO_2	0.0050	0.703	0.275	0.898	*0.0039	0.7885	0.3577	0.9426
	VD/VT	0.0293	-0.581	-0.85	0.073	0.9720	-0.01202	-0.6076	0.5922
Fat (s)	RER	0.0028	-0.733	-0.91	-0.332	0.4067	-0.279	-0.753	0.386
	FeO_2	0.0088	-0.671	-0.886	-0.218	0.0340	-0.64	-0.896	0.0647
	PaO_2	0.0112	-0.654	-0.879	-0.189	0.0067	-0.759	-0.934	-0.292
Kcal/race	VCO_2	0.0009	0.785	0.437	0.929	0.5706	0.193	-0.461	0.71
	VT	0.0024	0.742	0.349	0.913	0.3712	0.299	-0.366	0.762
	O_2	0.0043	0.712	0.291	0.902	0.3136	0.335	-0.331	0.779
	CO_2	0.0011	0.778	0.421	0.928	0.6305	0.164	-0.484	0.695
	VO_2	0.0001	0.865	0.595	0.953	0.3165	0.333	-0.333	0.778
	VE	0.0294	0.581	0.0728	0.85	0.4630	0.248	-0.414	0.738
CHO/race	VE	0.0208	0.609	0.116	0.861	0.8163	0.0795	-0.546	0.648
	VO_2	0.0001	0.861	0.608	0.955	0.1043	0.518	-0.122	0.852
	VCO_2	0.0004	0.816	0.504	0.94	0.3428	0.317	-0.35	0.77
	VT	0.0033	0.728	0.318	0.907	0.2009	0.418	-0.243	0.814
	O_2	0.0054	0.699	0.267	0.897	0.2116	0.409	-0.253	0.81
	CO_2	0.0014	0.765	0.395	0.922	0.2569	0.374	-0.291	0.796
Fat/race	RER	0.0085	-0.671	-0.886	-0.219	0.3713	-0.299	-0.762	0.366
	FeO_2	0.0078	-0.677	-0.889	-0.229	0.1454	-0.469	-0.834	0.182
	PaO_2	0.0223	-0.604	-0.859	-0.107	0.2887	0.352	-0.314	0.786
Fat%	FeO_2	0.0087	-0.67	-0.886	-0.217	0.1954	-0.423	-0.816	0.238
	RER	0.0141	-0.638	-0.873	-0.162	0.4860	-0.235	-0.732	0.424
	VCO_2	0.0290	-0.582	-0.85	-0.0745	0.8723	-0.0551	-0.634	0.563
	PaO_2	0.0251	-0.594	-0.855	-0.0927	*0.0402	-0.624	-0.891	0.0385
CHO%	VCO_2	0.0290	0.582	0.0745	0.85	0.8723	0.0551	-0.563	0.00303
	RER	0.0141	0.638	0.162	0.873	0.4860	0.235	-0.424	-0.732
	FeO_2	0.0087	0.67	0.21	0.886	0.1954	0.423	-0.238	0.816
	PaO_2	0.0251	0.594	0.0927	0.855	*0.0402	0.624	0.0385	0.891

DISCUSSIONS

The body's ability to retrieve and use oxygen through VO_{2max} value will influence the energy resource used by the body to support physical activity (13), issue that was highlighted in the paper through the relationships identified between VO_2, athlete's energy needs and carbohydrate access during maximal effort. Significant increase in VO_2 value is obtained in terms of aerobic exercise (14) through improvement of the body's ability to use energy resources efficiently during specific effort (15). Such differences were identified between G1 and G2, due to reported oxygen parameters. The anaerobic effort zone, a specific phase in specific rowing activity, is influenced by many factors, secondary to those imposed through the physical effort performed by athletes (16). Among them we can include factors such as gender, muscle mass, muscle fiber type, energy substrate availability, and genetic factors (17).

Increasing aerobic power (VO_{2max}) represents an advantage in aerobe physical activity, however, during a prolonged effort the VO_{2max} fraction is superior as relevance (18) facilitating the use of increased amounts of oxygen during exercise (19) as evidenced in G1 through increased aerobic threshold point. Increasing the consumption of oxygen will impose modifications among the exchange respiratory rate (20), increasing carbohydrate

consumption in association to an elevated RER, or increasing the consumption of fat in association to a low RER, both during rest periods, and effort periods (21), action identified in the study group. Therefore, in G1, elevated RER was associated with increased carbohydrate consumption, while low reported RER in G2 was associated with a higher preponderance of fat, as energy resource, during specific effort. Thus, during 2,000 m race simulation the aerobic energy system contribution is reported between 75-85%, while the anaerobic system will contribute with 25-35% of the total energy demands (22).

The energy systems are divided into three components: energy phosphate degradation, non-oxidative glycolysis and oxidative within phosphates (23). Carbohydrate energy resource will be used during an effort that exceeds 75% of VO_{2max}, representing an important energy source for both non-oxidative glycolysis, and oxidative phosphorylation (24). As a result, aerobic metabolism during rest periods will meet the energy needs of the athlete through a catabolic form of aerobic energy resource, associated with low oxygen needs. The energy system based on lactic acid represents the glycolytic pathway by which ATP is formed in muscle, based on an incomplete anaerobic glucose degradation mechanism in 2 moles of lactate (25). When a low amount of oxygen is involved in ATP synthesis the energy system based on lactic acid will continue to operate and generate energy. However, hydrolyzing phosphocreatine does not depend on the presence of oxygen in significant quantities, so the process of ATP re-synthesis can take place (26) but it will be mentioned that reducing the level of phosphocreatine in the body, will reduce the possibility of ATP re-synthesis (27) being facilitated the access of carbohydrates from muscle glycogen (G1). As a result, fat production in the mitochondria, carbohydrate production, the glycolytic system contribution and phosphate system, struggle to improve ATP re-synthesis, during activity that can benefit from such an energy source (28). During specific effort, although it is activated in the beginning of the activity, it will become a primary energy source only after muscle phosphate degradation (29). As highlighted in the paper, energy intake and the energetic resource used will be dictated by the body's energy demands, stimulating increase or decrease contribution of various energy systems

As a result, aerobic energy system, in efficiency terms, will be directly proportional to VO_2 value. Thus, during maximal effort, glycolysis rate will increase to over 50% of the value reported during rest periods. A decreased pH will inhibit the glycolytic enzymes, being associated a reduction in ATP synthesis (30-31) changing the muscle contraction ability, and energy systems contribution (G1/G2). At the same time, the start of the effort, characterized by oxygen debt, will increase CO_2 production, reducing the amount of O_2 alveolar level, association conducted with increased consumption of CHO during effort (G1). Thus, during effort, $PaCO_2$, $PetCO_2$ will be associated with the respiratory rate, due to CO_2, whose value will not reach a maximum stationary level (32). Sustaining an anaerobic effort, following the transition of aerobic exercise, specific in rowing and competitive actions, will impose an increase in lactic acid concentration, $PetO_2$, and a decrease in $PetCO_2$ value (33) being associated the importance of aerobic system in order to support the effort despite of a significant increase in lactate concentration (34). Basically, during an effort that exceeds the aerobic ventilatory threshold, excess CO_2 production will support VE, and $PetCO_2$ at constant values, differences being reported regarding the VE, VO_2 correlations above the anaerobic ventilatory threshold (35-37).

CONCLUSIONS

Starting with VO_2 value, O_2 consumption, CO_2 production, a drop in $PetCO_2$ as well as FeO_2, all the parameters will associate the consumption of macronutrients, divided into non-protein elements such as carbohydrates and lipids. Improving aerobic capacity, in terms of increasing carbohydrate contribution during limited period of activity will be associated with an increased efficiency of the energy system through oxygen debt, production of ATP, re-

phosphorylation and muscle glycogen access, in order to insure optimal energy distribution during 2,000 m race.

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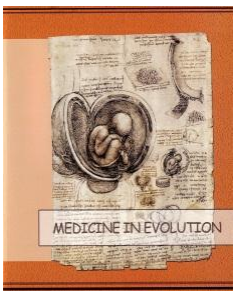
The influence of kindergartens with extended schedule budget on the amount of macronutrients consumption among preschoolers



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Abstract

Aim: The purpose of the paper is to analyze the budget influence on the amount of macronutrients contained by the children's diet enrolled in kindergartens with extended schedule.

Material and method: A analytical, restrospectie observational study was conducted during the period February-April 2016 in Tîrgu Mureş, Romania. 10 menus were used, from each kindergarten, in 2 consecutive weeks, respectively from 15 to 26 February 2016.

Results: The allocated budget for the menus varied between 6 and 12 RON, with an average of 8.06±1.82, a coefficient of variation of 22.59% and a median of 7.75. The analysis of the energy value of the menus, highlights an increased consumption of proteins, lipids and carbohydrates, while the increase budget value represented a significant factor of influence.

Conclusions: The increased budget allocated for the kindergartens' menus leads to an increase amount of macronutrient intake, along with an increases of the proportion of lipids in the total number of calories and a reduction of proteins and carbohydrates intake.

Keywords: kindergarten, nutrition, budget, children

INTRODUCTION

The main goal of the educational institutions, in creating the menus is to ensure that the caloric and macronutrient needs of the children are covered, being in accordance with the legal regulations; the secondary goal is to do this without exceeding the imposed budget for food. In Romania, at the moment, the exact amount allocated for food in schools and other educational institutions is not clearly specified in any of the existing laws, so the amount differs from institution to insitution.

Although the budget limitations are a stress factor for the team which creates the menus, healthy food and balanced menus can be purchased, at the individual/household level, at lower prices than other unhealthy alternatives [1-2]. In some areas like Victoria, Nova Scotia, Port Vila, this is questionable because the prices are significantly influenced by the area of residence (high food prices used in metropolitan areas decrease progressively towards rural areas), people who have a low income having a considerably lower access to healthy products [3-8].

An important issue is the spending of the budget on more expensive food, that has a a high caloric density, in the detriment of vegetables and fruits, although according to researchers, vegetable products can be purchased at cheaper prices [9].

Scientific studies, conducted worldwide, show an increase in body weight due to poor economic status in people who work for private companies or institutions of the state [10-11]. Thus, adapting the budget spending to achieve not only the quantitative requirements, but also the qualitative ones, will be an important second step, following the one through which appropriate daily ration for children are thoroughly regulated. [12].

Aim

The purpose of the paper is to analyze the influence of the food budget value on the amount of macronutrients included in the diet of children enrolled in kindergartens with extended schedule.

Hypothesis

The increase of the amount allocated for food leads to an increase in the quantity of food offered to children, the total macronutrient intake exceeding the needs of the children.

MATERIAL AND METHODS

An analytical, restrospective, observational study was conducted during February-April 2016 in Tîrgu Mureş, Romania. To test the hypothesis a detailed analysis was performed, on the menus, in 8 kindergartens with extended schedule situated in all the key areas of the city. 10 menus were used for each kindergarten, from 2 consecutive weeks, respectively from 15 to 26 February 2016.

The macronutrient needs of the preshcoolers were established according to the laws in Romania, more specifically Bill No. 123 of 27 May 2008 and Order No. 1563 of 12 September 2008 [13]. In spite of existing different recommendations for different age groups, there is a lack of portion differentiation acording to age in all the analyzed kindergartens; therefore, the average values of the Ministry of Health's requirements were used as comparison.

The menus and exact quantities of food products (as represented in the stock records) were provided by the managers of the institutions, same as the signed participation agreement and confidentiality agreement. For confidentiality reasons, for each institution, we have randomly assigned an alpha numeric code, from G1 to G8.

The data was statistically analyzed using GraphPad Prism 7.0 software. The statistical analysis includes descriptive statistics: minimum-maximum values, average value, median,

standard deviations and differences between means. To establish the association between two items, the Pearson correlation was applied, with p values smaller than 0.05 being considered to be significant. The confidence intervals used in all tests applied was 95%.

RESULTS

The allocated budget for the menus was between 6 and 12 RON, with an average of 8.06±1.82,a coefficient of variation of 22.59% and a median of 7.75. RON represents the National Romanian Currency, and according to the Romanian National Bank (BNR), in 18.05.2016, 1 euro (€) was equivalent to 4.4955 RON while 1 dolar ($) was equivalent to 3.9871 RON.

Table I presents the data obtained from the analysis of the kindergartens` menus, next to the ones set by law and considered to be the normal values. The amounts of macronutrients (proteins, fats and carbohydrates) are expressed in grams and as a percentage of the total number of calories consumed during the educational program. The numbers recorded in the table are the mean values obtained after the analysis. „R" represents the quantities recommended for consumption in kindergartens with extended schedule, supposedly equivalent to 75% of the dailly requirements. „T" represents the total energy intake while in kindergarten, equivalent to 2 main meals and 2 snacks.

Table I. *Descriptive statistics of the values obtained after the analysis of the menus*

	Calories		**Proteins**			**Lipids**			**Carbohydrates**		
	Mean	% from R	Mean	% from R	% from T	Mean	% from R	% from T	Mean	% from R	% from T
G1	1711.87	147.26	55.32	130.54	13.25	66.05	149.91	35.88	210.93	145.91	50.51
G2	1570.76	135.12	48.21	113.75	12.58	49.61	112.60	29.37	235.82	163.12	61.55
G3	1440.90	123.95	46.49	109.71	13.23	53.63	121.72	34.61	187.13	129.44	53.24
G4	1599.75	137.61	50.46	119.07	12.93	56.09	127.30	32.60	215.08	148.77	55.12
G5	1829.42	157.37	52.33	123.47	11.73	67.44	153.05	34.28	247.10	170.92	55.37
G6	1776.26	152.80	51.26	120.96	11.83	64.10	145.48	33.56	242.81	167.96	56.04
G7	1661.96	142.96	53.23	125.61	13.13	62.61	142.09	35.03	215.41	149.01	53.14
G8	2338.02	201.12	66.26	156.34	11.62	100.68	228.50	40.04	276.76	191.44	48.53

Figure 1 represents the exact values of macronutrient intake calculated through the menus; analysis, in comparison to the minimum-maximum values set by the Ministry of Health, for preschoolers, for 75% of the day. It is obvious that the reallity clearly exceeds the theoretical limitation imposed by law; also a high variation can be observed in the macronutrient and food intake, between kindergartens but also between the proposed values, on different days, for the same institution.

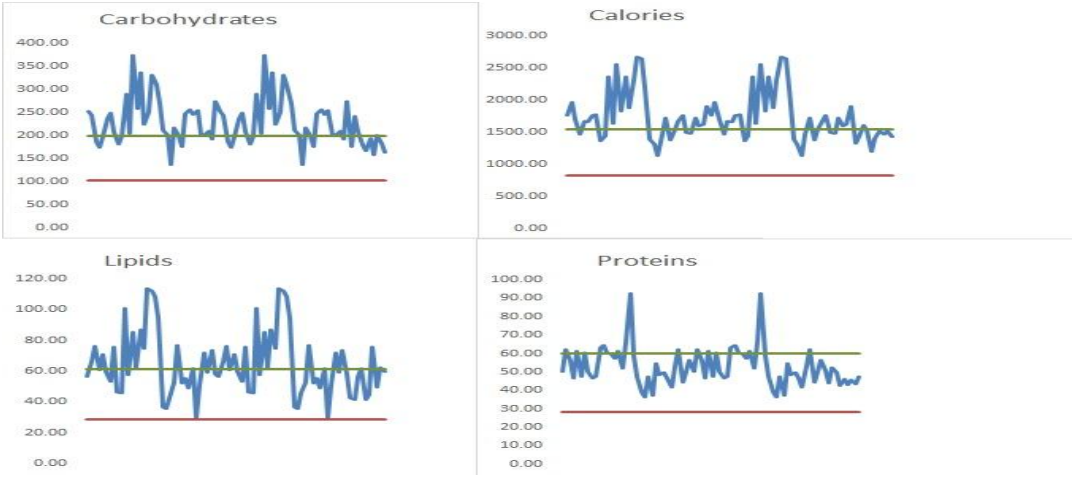

Figure 1. Actual values compared to the recommended minimum and maximum values

In order to establish the influence of the budget allocated for the menu, tests were applied either to establish the link between the budget and the amount of macronutrients, expressed in grams, or the link between the budget and the percentage of macronutrients in the total amount of calories consumed within the institutions. Table II shows the results of these tests.

Table II. Correlation between the budget and the quantity of macronutrients

	p value	Significant?	r	95% CI	R squared
Proteins	<0.0001	yes	0.45	0.255 to 0.609	0.202
Lipids	<0.0001	yes	0.609	0.449 to 0.731	0.371
Carbohydrates	0.0006	yes	0.376	0.171 to 0.55	0.142
Calories	<0.0001	yes	0.567	0.397 to 0.7	0.322
% of Proteins	0.036	yes	-0.234	-0.431 to -0.014	0.054
% of Lipids	0.002	yes	0.33	0.119 to 0.512	0.109
% of Carbohydrates	0.014	yes	-0.272	-0.464 to -0.055	0.074

After the analysis of the data for each of the institutions it can be observed that there are significant differences between them in relation from the standpoint of all macronutrient categories and caloric level. The F value obtained after the mean values differentiation was: 12.24 (R^2=0.538) for proteins, 19.74 (R^2=0.652) for fats, 9.18 (R^2=0.466) for carbohydrates and 20.94 (R^2=0.666) for overall calories. All the p values obtained in this set of tests are smaller than 0.0001.

DISCUSSIONS

During the analysis of the menus it was observed that the macronutrient intake significantly exceedes the recommendations, the biggest differences being recorded in case of carbohydrates. It should also be noted that the amount of carbohydrates consumed in kindergarteners is directly influenced by the budget, the association being significant (p=0.0006), which increases the risk for child obesity due to adipocyte hyperplasia [14-15]. The link between the budget and the quantity of carbohydrates shows that the increase of the amount assigned for food is accompanied by an increase in the percentage of carbohydrates in the diet. The proportions of carbohydrates in the total calories intake, is significantly influenced by the budget (p=0.014). This time the connection is reversed, respectively, when the budget increases, the proportion of carbohydrates decreases, therefore the distribution of macronutrients can not continue to comply with the legal nutritional recommendations.

The budget is shown to be a strong factor of influence in case of lipids (fats) as well; the connection respectively, a budget increase is also observed to be accompanied by an increase in the amount of fats in the diet. However there is the suspicion that the adiposity is inversly related with fat consumption, the excess of dietary lipids not being directly associated with obesity [16].

In terms of the caloric value of the menus, an increase in the level of protein consumption was observed, the increases of the budget being a significant factor of influence. Same as in the case of carbohydrates, in case of proteins it was observed an influence +- for the percentage from the energy, thus, there was a decrease in the percentage of proteins in the case of kindergartens with a bigger budget. According to Carvalho et al, an increase in the amount on proteins consumed from sources like red and/or processed meat does not only contribute to the impairment of health in individuals, but also to an increase of CO_2 equivalents, the contribution of such an individual to the total quantity of CO_2 produced, being the same as the contribution of a car that travels 5.379 km [17].

The situation is a vicious circle: with the availability of a larger budget, the quality of the menu decreases while the amount of calories consumed increases, leading to a weight

excess among children and, subsequently, an increase in the budget allocated to health problems [18-19]. In case of small budgets, as Mizumoto et al also state, the amount of products consumed decreases or we have an often consumption of caloric-dense foods with a low nutritional value, the effect on the body being felt as malnutrition [20,21].

Although the increase of the budget should provide the possibility of purchasing healthier products, such products being regularly sold at a higher price on the food market [22], the effect is the opposite, namely, an increase of the total energy values, based on an excess of calories from proteic and non-proteic sources, situation also observed in preschool institution from other geographical areas [23-25].

Another negative influence is the change in the percentages of macronutrients, namely an increase in the proportion of lipids and a decrease of the level of proteins and carbohydrates. This distribution is causing a reduction in the DRD2 (dopamine D2 receptor) binding density in the rostral caudate putamen and an increasing of the expression of DRD4 mRNA (dopamine D4 receptor, messenger ribonucleic acid) in ventromedical nucleus of the hypothalamus and lateral ventral septal nucleus, toghether with an increase of tyrosine hyroxyl mRNA in the VTA (ventral tegmental area) and locus caeruleus, leading to an increase in weight due to the increase of total body fat and visceral fat [26-28].

CONCLUSIONS

The budget allocated for the menus in the kindergartens with extended schedule is a significant factor of influence for the amount of macronutrients consumed. Increasing the budget allocated for the menus increases the intake of all macronutrients (grams), along with an increase of the proportion of lipids (%) in the total number of calories consumed and a reduction in the intake of protein and carbohydrates (%).

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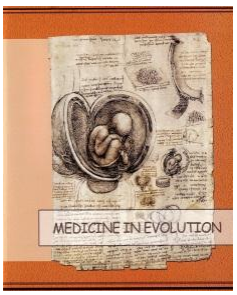
Current approaches in rheumatoid arthritis biomarkers



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Abstract

With the development of medicine, the need to treat patients early in the onset of the condition became obvious, as shown in multiple studies carried out, early treatment offers the most effective results. The problem arises, however, in the diagnosis phase, when selecting patients that require rapid therapeutic intervention. This deadlock occurs due to insufficient resources in the process of diagnosis. Currently, if patients do not accomplish anamnesis criteria for the diagnosis of rheumatoid arthritis (RA), being still in an early stage of the disease, they can remain deprivated of treatment until RA affects the joints, impaired of which damages are irreversible.

Along with known rheumatoid factor (RF), always used in RA diagnosis, the presence of citrullinated proteins antibodies (ACPA) and carbamylated protein antibodies (anti-CARP) provides essential answers in early detection of RA.

Biomarkers allow early detection, evaluation and prediction of disease severity, selecting and monitoring treatment response.

Keywords: Rheumatoid arthritis, ACPA, Anti Carp, MBDA, Biomarkers.

INTRODUCTION

Due to the lack of clinical tests effective treatment has been often hindered. On the basis of diagnosing RA in Romania are currently EULAR classification criteria developed in 1987, RF and C-reactive protein (CRP). The sensitivity of these criteria is too low, however, insufficient for accurate and fast diagnosis of RA. In addition, in 2010 were developed updateded criteria based on the existence of at least one affected joint, which included a set of antibodies against anti-citrullinated proteins (ACPA) showing very high specificity in RA besides the classic RF, the new criteria analyzes ESR- the acute phase reactants and timing of symptoms. If the obtained score is higher than 6, RA is considered present.

Although the association between HLA and RA is not yet fully elucidated, it is assumed that the presence of the antigen and type of immune activation leads to the formation of antibodies which are important in the onset RA. Among environmental factors, smoking is the most pronounced risk, with a greater effect in anti-CCP positive patients.

Due to the fact that at present the diagnosis is made on the basis of joint or bone erosions at which time the optimal treatment window is likely missed the diagnosis and therapeutic intervention is often delayed, resulting in tissue damage.

The possibility of using biomarkers in the diagnosis and treatment of RA, makes the classical image of massive erosion, deformity and disability to be reduced significantly down to total avoidance in a large proportion of patients.

Many patients with early RA and especially those who suffer from arthralgia or nonspecific arthritis may experience spontaneous remission, while other patients may progress to fulminant RA. It is essential therefore the use of specific and sensitive clinical tests through which we can identify and select appropriate early therapy. (Krabben A, 2012)

Biomarkers and target therapy - Biomarkers can be: histological, clinical imaging parameters, specific molecules or molecular models.

The most valuable in clinical decision making are considered to be molecular biomarkers, as they highlight the changes taking place at the onset of disease or response to treatment. Molecular biomarkers include genomics, proteomics and biomarkers lipidomic. (Padyukov L 2004)

Targeted therapy (layered) involves matching a patient with a specific treatment wich is most likely to be effective and safe based on the similarities between patients " disease signature " and a right group with previous positive response to the therapeutic agent.

The instruments of this process are of course biomarkers, representing the individual and serving as indicators of organs activity, pathogenic processes, or treatment response.

The point is that by analyzing biomarkers for groups of patients, a condition can be layered into distinct subsets showing differential results and answers for specific therapy. (MR Trusheim, 2007)

Anti-citrullinated protein antibodies (ACPA) - In the last two decades, it has been shown that antibodies with the highest specificity for RA proteins are antibodies directed against epitopes containing citrulline. These antibodies are called anti-citrullinated proteins (ACPA) and were presented for the first time as anti-perinuclear factor (AFP). ACPA recognize the amino acid citrulline included in the structure of a protein. Citrulline is an encoded amino acid, generated by a posttranslational enzyme modification mediated by protein arginine-arginine deiminase (PAD). This change occurs during a variety of biological processes like inflammation.

ACPA may be present in different forms, including IgG, IgA, IgM and IgE and recognizes a variety of citrullinated antigens: α-enolase, vimentin (also known as Sa antigen), fibrinogen, type II collagen. (RL Nienhuis, 1964)

ACPA isotype distribution does not appear to expand significantly in the progression of unspecific arthritis to RA, indicating that most of the expansion isotype ACPA occurs

before the onset of arthritis. Moreover, the ACPA multiple isotypes have been shown to be present up to nine years before the clinical onset of RA.

Regarding treatment, according to the results database of biomarkers, patients could receive different treatment strategies, therefore, conditions ACPA-positive and negative-should be treated differently. (Willemze A, 2012)

Usually between 50 and 70% of patients with RA are ACPA positive. (Nishimura K, 2007) patients with RA AACP-positive and AACP-negative presents a very similar clinical picture in the early phase of the disease , during subsequent disease is different: extra-articular manifestations are clearly associated with AACP status. AACP-positive is associated with an increased risk of developing lung diseases or coronary heart disease, joints present more destructive damage, developing early erosions compared to AACP-negative patients. Thus, due to more severe course of the disease, positive ACPA patients require a more aggressive treatment regimen than AACP-negative patients.It is obvious that RA AACP-positive and AACP- negative are two different entities of the disease, with different results and different treatment responses. (van der Helm-van Mil AH, 2005)

Carbamylated protein antibodies (Anti-Carp)- The immune response resulting from changes in post transitional is considered to be a key feature in the pathogenesis RA. ACPA recognize proteins only after enzymatic conversion of arginine to citrulline by PAD enzymes. In addition to citrullination appear other post-translational modifications. Therefore, it is possible that the proteins were subjected to another type of post-translational modification to also be recognized by antibodies. One of these other post-translational changes is the process of carbamylation. Mediated by cyanate this chemical reaction transforms lysine into homocitrulline. Cyanate, necessary for such carbamylation is naturally present in the body and is in equilibrium with urea. Imbalances can occur in inflammation, kidney failure or smokers by a mechanism dependent on myeloperoxidase. It is known that the level of myeloperoxidase in patients with rheumatoid is increased. Thus it is likely that in the inflamed synovial tissue carbamylation takes place. Post-translational modified amino acids like citrulline and homocitrulline have very similar structures. The only structural difference between citrulline and homocitrulline is the length: homocitrulline has an extra methyl group. (Willemze A, 2012)

Relevant is that these anti-carP protein antibodies are present not only in ACPA-positive patients, but also in patients with ACPA-negative RA.

When analyzing the clinical status in patients with RA, it was observed that the presence of anti-carP is associated with a higher rate of joint damage. This phenomenon was particularly observed in the subgroup ACPA-negative patients. Identification of anti-carP this group is clinically useful because these patients were difficult to diagnose because no prognostic marker was available. These observations suggest that the population of RA patients is more heterogeneous than it was originally thought, and probably besides highlighting positive ACPA RA, an anti-carP-positive result could be an additional specificity to the disease. Anti-carP antibodies have also been detected in patients with arthralgia, presenting positive values of RF and / or ACPA without being clinically enrolled with arthritis. The fact that these anti-carP antibodies are detectable years before the clinical diagnosis of RA, makes their use a possiblilty in early diagnosis of the condition, thus avoiding joint damage. (JH Humphreys, 2015)

Biomarkers used to indicate the disease activity score of RA- Disease activity score is defined as an index used to evaluate patients disease activity and acute phase response, by including the number of swollen and tender joints.

Many studies have suggested that frequent measurement and subsequent control disease activity is associated strictly with satisfactory clinical results. In everyday clinical practice, however, it is often impossible to schedule patient visits monthly to assess disease

activity. As such, a set of biomarkers to replace the clinical assessment of disease activity is necessary. (Hirata S L. W., 2015)

For this purpose, it has been developed a new algorithm to determine the activity of the disease based on the multi-biomarker disease activity scores (MBDA) by measuring 12 biomarkers in serum (serum amyloid (SAA), interleukin-6 (IL-6), tumor necrosis factor - receptor type I (TNF-RI), vascular endothelial growth factor a (VEGF-A), matrix metalloproteinase-1 or collegenase 1 (MMP-1), human cartilage glycoprotein (YKL 40), matrix metalloproteinase-3 or stromelysin-1 (MMP-3), epidermal growth factor (EGF), vascular cell adhesion molecule-1 (VCAM-1), leptin, resistin, and C-reactive protein (CRP)). This MBDA score was significantly associated with disease activity as measured conventionally. (Hirata S D. L., 2013)

PURPOSE

The aim is to emphasize the importance of achieving individualized therapies by identifying patients who will require early aggressive intervention, and at the same time to prevent this kind of treatment in patients who do not require such an approach.

The focus on the discovery of biomarkers and their development will reveal indicators of changes that can improve RA diagnosis and prognosis, thus allowing the implementation of therapy with an easy monitoring.

MATERIAL

In conducting this review we examined besides scientific literature, 7 articles focused on biomarkers, their action and their importance in the diagnosis and treatment of RA. From these studies we have selected 4 representative studies matching the aim of this review, respectively, early diagnosis, the possibility of avoiding irreversible joint damage and monitoring the medication response.

METHOD

A study made in Leiden, analyzed the serum of 2,086 arthritis patients who experienced at least one affected joint and symptoms existing not more than 2 years. It was analised the presence of anti-carP antibodies, anti-CCP2 and IgM-RF. The study met the ACR 2010 / EULAR criteria. The control sample was taken from healthy residents of Leiden area. The anti carP antibodies were detected in 26% of patients and 2% in healthy individuals. Anti-carP antibodies sensitivity detection in patients with RA was 44% and specificity of 89% was reached to the same population.Also relevant are the results obtained in ACPA negative patients, which showed anti-carP sensitivity and specificity of 12% and respective 91% of patients. (Jing S, 2015)

Another study, conducted in Norfolk, England, focused on the premise that the presence of anti-carP antibodies predict long-term disability in patients with inflammatory type arthritis.

The study included 1995 patients to which the PCR, FR, ACPA and anti-carP antibodies were tested. 1310 patients were female. The presence of anti-carP antibodies was significantly associated with an elevated disease activity score or an advanced degree of disability, especially relevant in ACPA-negative patients. 23% of patients presented positive anti-carP antibodies, while 5% presented just positive anti-carP antibodies. This study showed that the presence of anti-carP antibodies in the serum of patients indicate a more pronounced disability, much more aggressive in early stages of the disease, persistent compared to negative anti-carP antibodies patients. (JH Humphreys, 2015)

A total of 125 patients with RA were included in a Behandel Strategieën study. Serum samples and clinical data were available from 179 visits, 91 at baseline and 88 in the first year. In each serum sample 12 biomarkers were measured by quantitative multiplex immunological tests and concentrations were used as a starting point for a prespecified algorithm to calculate MBDA scores. MBDA scores had significant correlations with DAS28 score and with simplified disease activity index. Changes in MBDA occurred between baseline and evaluation one year later, correlated with changes in DAS28.An essential requirement for an index of disease activity is it's ability to evaluate changes in disease activity of patients in time. (Hirata S D. L., 2013)

An observational study conducted in Japan targeting the relationship between clinical response of patients with RA treated with TNF-alpha inhibitors using a disease activity score through combination of biomarkers included 147 patients diagnosed with RA. Conditions of engagement to the study involves a biological treatment duration of at least one year during the study with serological sampling at the beginning respectively at 52 weeks after initiation of therapy. Eligible patients received treatment with either biological adalimumab, etanercept, or infliximab alone, if it was possible or in combination with methotrexate. 378 serum samples were collected from 147 patients. MBDA score was generated with the same algorithm used in the Vectra DA test. Results showed the response to treatment in 56% of patients. MBDA initial score was 64, and after 52 weeks it decreased to an average of 34-37% of all patients included in the research. Thus the MBDA score decrease observed was of 42%. In short, MBDA score reflected the clinical disease activity and response to treatment with TNF inhibitors in patients with RA. It showed a similar behavior in patients treated with adalimumab, etanercept, or infliximab. MBDA score performance was assessed during biological treatment with TNF-alpha and determine its ability to constantly track disease progression related to treatment response for patient groups with different biological treatment. MBDA scores changes from baseline to 52 weeks were significantly correlated with DAS28-ESR changes and DAS28-PCR for all 147 patients. (Hirata L. W., 2015)

DISCUSSIONS

From all data is highlighted the need of biomarkers in the diagnosis and treatment of RA. Targeted therapy plays an important role in modern medicine due to genetic uniqueness of patients on the one hand, and from the heterogeneity of disease on the other. The fact that both ACPA and Anti-carP antibodies are present in the serum of patients with RA for many years before the onset of the disease constitutes a useful information in early diagnosis of the condition, allowing the possibility of avoiding joint damage.

Also, tracking the specificity of the disease by the appearance of ACPA positive or negative patients, as well as detection of Anti-carP antibodies positive patients among ACPA negative can lead to the optimization of treatment strategies and monitoring of disease taking into account the potential of Anti-carP antibodies to predict the joint damage and aggressiveness of RA. Finally, tracking of the disease activity score (MBDA), together with DAS28 score in patients response to treatment, by default in disease progression, provides important data in approaching treatment schemes and clinical decisions regarding RA.

CONCLUSIONS

In both terms of prognosis and tracking of patients layering biomarkers are part of the disease, therefore of targeted therapy with the potential to expand clinical management of patients with RA.

Presence of several antibodies present in the serum of patients still undiagnosed with RA shows the imminence of the disease, thus providing the opportunity for diagnosis as soon

as possible in the disease process, also, monitoring treatment response trough disease activity scores by using a combination of acute phase biomarkers constitutes a useful monitoring base.

In conclusion,by using biomarkers is possible to manage both the onset RA and treatment response.

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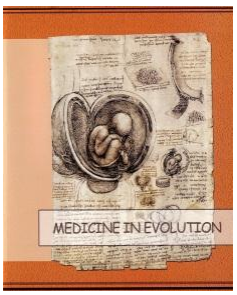
Assessment of the relationship between vehicle driving speed and alcohol and drugs consumption patterns in young adults of Timis county, Romania



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Abstract

The present research aimed to assess the relationship between vehicle driving speed and alcohol and drugs consumption patterns such as binge drinking, drug consumption and mixed alcohol and drugs consumption in young people of Timis County, Romania. A transversal population study was applied to the study group including 1605 young people aged between 18-20 years, 51.4% pupils and 48.6% students, girls being significantly better represented, i.e. 53.8% of pupils and 61.6% of students. Of the young people who drive, 28.8% of boys and 15.2% of girls frequently or always exceed the legally allowed speed limit. According to the pattern of alcohol and/or drug consumption during the last 30 days, 15.6% practice binge drinking, 3.0% consume drugs and 4.3% practice binge drinking together with drug consumption. The frequency of speeding over the legally allowed limit is more frequently reported in boys, with no association to the pattern of alcohol and/or drugs consumption.

Keywords: young people, driving speed, alcohol, and drugs consumption

INTRODUCTION

High speed driving is the most frequent way of breaking traffic rules done by young male drivers and it contributes to almost one third of road accidents. Young adults lacking driving experience, with high levels of 0.05 g alcohol/dl blood are at 2.5 times higher risk to be involved in accidents as compared to older, more experienced drivers [1,2].

A number of risk factors have been identified to increase the probability for certain individuals to be involved in traffic accidents. Some risks are increased among young traffic participants, including pedestrians and drivers, but also among passengers in cars and on motorcycles. High speed driving, alcohol and drugs consumption before driving qualify as factors which influence risk exposure, involvement in, as well as severity of, accidents [3].

Young drivers need counselling for safe driving, while laws banning driving under the influence of alcohol and drugs must be strictly applied. Road safety legal provisions regarding alcohol consumption, speed limits and the elaboration of protocols for granting drivers licenses in a gradual manner, with increasing of privileges in time, might considerably reduce the risk of accidents. Increased access to reliable and safe public transportation may reduce traffic accidents among young people [3,4].

Our study aimed to assess the relationship between the driving speed of a vehicle and consumption patterns represented by binge drinking, drugs consumption and mixed alcohol and drugs consumption in young subjects of Timis County, Romania.

MATERIAL AND METHODS

The study included a group of 1605 young subjects aged between 18 and 20 years, of whom 51.4% (825) were pupils, and the remaining 780 were students (Table 1). Boys represent 46.2% (381) of pupils and 38.4% (299) of students. We found significant differences between the two genders in the two subgroups, girls being significantly better represented among students as compared to pupils, $\chi^2(1)=10.11$, $p=0.001$, OR=1.38, IC 95%=(1.132; 1.685).

The age structure analysis reveals: 72.5% (598) of pupils and 0.8% (6) of students were 18 years old, 25.5% (210) of pupils and 36.0% (281) of students are 19 years old, and 2.1% (17) of pupils and 63.2% (493) of students are aged 20 years. We found no difference between gender distribution depending on age in the subgroup of pupils, $p=0.358$, and in the subgroup of students, $p=0.521$.

Of the total number of participants, 29.5% (463) declare they possess a driver's license, with significantly different proportions between the subgroups, $\chi2(1)=94.45$, $p<0.001$, OR=3.04, IC 95%=(2.419; 3.822): 18.5% (149) of pupils declare to possess a driver's license, while in students the percent is 40.9% (314). Boys possess a driver's license significantly more frequently than girls, both in pupils, $\chi2\ (1)=16.27$, $p<0.001$, OR=2.09, IC 95%=(1.456; 3.016), as well as in students, $\chi2(1)=52.66$, $p<0.001$, OR=3.01, IC 95%=(2.229; 4.082).

Table 1. *Distribution of pupils and students according to gender, age and driver's license possession*

Parameters		Group					
		Pupils		Students		Total	
		Number	%	Number	%	Number	%
Gender	M	381	46.2	299	38.4	680	42.4
	F	444	53.8	480	61.6	923	57.6
	Total	825	100.0	779	100.0	1603	100.0
Age	18	598	72.5	6	0.8	604	37.6
	19	210	25.%	281	36.0	491	30.6
	20	17	2.1	493	63.2	510	31.8
	Total	825	100.0	780	100.0	1605	100.0
Driver's license	Yes	149	18.5	314	40.9	463	29.5
	No	655	81.5	454	59.1	1109	70.5
	Total	804	100.0	768	100.0	1572	100.0

The working method was the transversal population study based upon the CORT 2004 Questionnaire regarding health risk behaviours in adolescents and young people [5]. The questionnaire was validated by the Ethics Committee of the „Victor Babeş" University of Medicine and Pharmacy Timişoara.

The study was approved by university teaching institutions in Timis County.

Young subjects were included in the study only after freely expressed informed consent was obtained from every participant, according to individual rights.

Data were processed using PASW 18 (SPSS18) 2010. The threshold for statistical significance was set at $p<0.05$, except for situations when the Bonferroni correction was applied. For ordinal data comparison we used the Mann-Whitney and Kruskal-Wallis tests. The Chi-square test was used in tables with ordinal/nominal data. We also used logarithmic regression for predicting various association patterns between risk behaviours.

RESULTS

Driving speed in young subjects

Regarding the driving speed of the participants in our study, 21.6% (66) of boys and 33.2% (68) of girls only drive within legal limits and 41.5% (151) of boys and 51.7% (106) of girls only rarely exceed the legal speed limit. The driving speed limit is exceeded frequently or always by 28.8% (88) of boys and by 15.2% (31) of girls.

As compared to girls, boys more frequently report exceeding the driving speed limit, U=25262, z=-3.99, p<0.001, r=0.18, with a low size difference between the two subgroups. When comparing pupils with students we found no differences regarding the driving speed, p=0.323 (Figure 1).

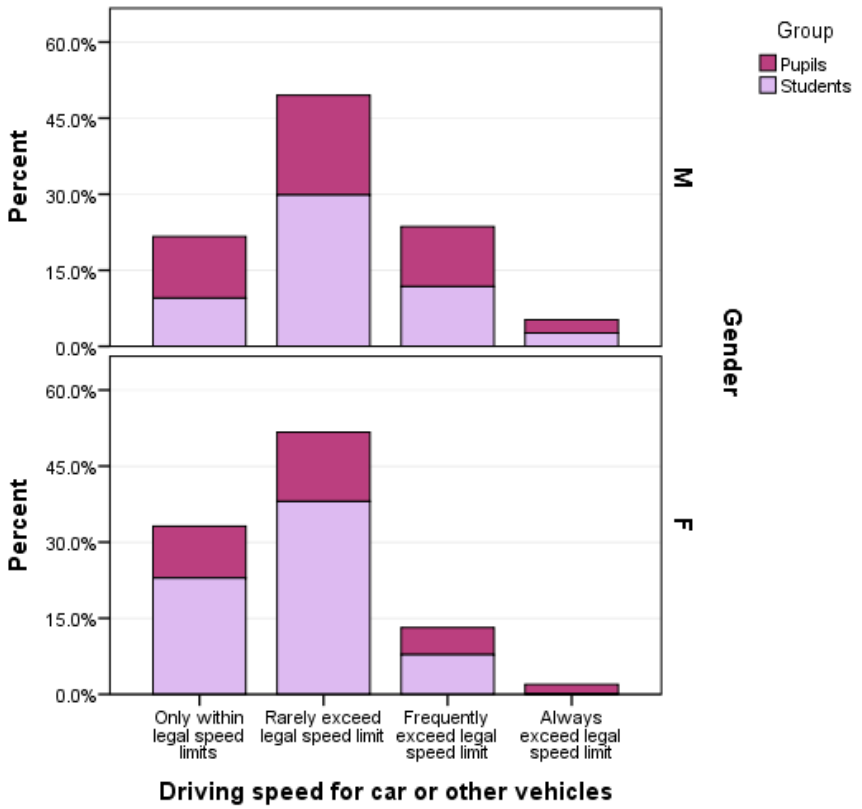

Figure 1. Percent distribution of participants according to driving speed and gender, in the studied subgroups

Driving speed and consumption patterns of alcohol, drugs, alcohol associated with drugs in young people

Based upon the alcohol and/or drugs consumption patterns during the last 30 days, we classified 77.0% (1223) of participants as non-consumers, 15.6% (250) as binge drinkers, 3.0% (47) as drug consumers, and 4.3% (68) as binge drinkers and drug consumers. Boys declare themselves consumers in all the 3 patterns significantly more frequently than girls, the size of the difference between genders being small to medium in the case of binge drinking, and small in the case of drugs and mixed drugs and alcohol consumption, respectively.

Depending on the consumption pattern, we found the legal driving speed limit is exceeded frequently or always by 5.1% (7) of non-consumers, 4.4% (3) of binge drinkers, by none of the drugs consumers and by 21.7% (5) of those practicing mixed consumption. In girls, the driving speed limit is exceeded frequently or always by 3.5% (4) of non-consumers, exclusively. In order to detect associations, if any, between the driving speed and consumption pattern, we applied the Kruskal-Wallis test and found no association in boys, p=0.598, and also none in girls, p=0.385 (Figure 2).

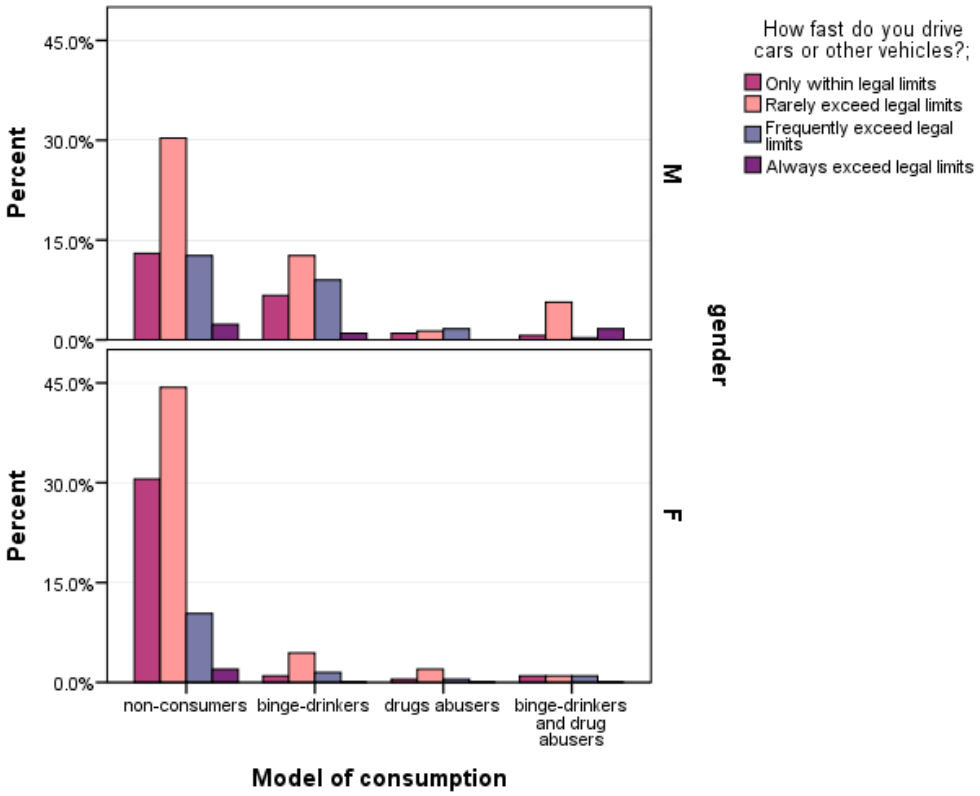

Figure 2. Percent distribution of participants according to driving speed of cars or other vehicles and consumption patterns, on genders

DISCUSSIONS

In our study, boys admit they exceed driving speed limits more frequently than girls: 28.8% of boys frequently or always exceed legal speed limits, as compared to 15.2% of girls. Driving within legal speed limits is declared by 63.1% of boys and by 84.9% of girls.

Using data collected from young people possessing driver's licenses and driving, we did not find a significant contribution to association with driving speed.

According to Zuckerman [6], sensation seeking is "an attribute defined by requiring varied, novel, intense and complex experiences, as well as the wish to accept physical, social, legal and financial risks for the sake of such experiences". Individuals seeking such sensations tend to be engaged in behaviours increasing the amount of stimulation they experience.

Activities by which they reach the preferred degree of excitement vary depending on the size of the associated risk. Sensations seekers accept a risk as a potential effect of obtaining this excitement, but they do not look for the risk *per se.* The personality trait, more pronounced in the male gender, involving sensation seeking during driving, is manifest by behaviours such as high speed driving and not wearing the seat belt.

In a review investigating the mortality risk of pedestrians depending on the speed of the car, Rosen et al [7] found a linear relation between the two parameters. Studies conducted after 2000 tried to take into account potential confounders and demonstrated a gradually increasing risk depending on the speed of the vehicle.

In a study [8] conducted between July 2005 and December 2007 investigating car incidents followed by victims, involving young drivers aged between 15-18 years, the most frequent causes detected were driving errors, representing 95.6% of all causes, the rest being environment or vehicle related. Inadequate surveillance, maladjustment of speed to road and traffic conditions, and attention distractions account for about 50% of all incidents.

Aiming to examine potential differences between self-reported high risk driving behaviours in binge drinker adolescents and a control group, the authors [9] found that binge drinkers engaged in high risk behaviours, such as excessive speed and mobile phone conversations during driving. Binge drinkers get more traffic fines, are involved in more accidents or near misses than the control group. In binge drinkers, fast driving was the most frequent behaviour associated to traffic accidents.

During stimulation following the consumption of 4 drinks, the speed of consumption of the 4 drinks was correlated to the average driving speed, to the duration of exceeding the legal speed limit, to the number of collisions and the driving confidence level [10].

Understanding the risks for young drivers is important in order to plan adequate programmes to reduce traffic related deaths and incidents in this age group. Most interventions decreasing the risk of traffic incidents among the general population will implicitly reduce their occurrence among young subjects. Additionally, the experience of high income countries shows that sustained efforts to implement adequate interventions, specifically tailored for children, adolescents and young adults may succeed in reducing the number of deaths and injuries [3].

CONCLUSIONS

Exceeding the legal speed driving limit is more often reported in boys than in girls.

Excessive speed driving is not associated to behaviour patterns of binge drinking, drugs consumption, mixed drugs and inadequate alcohol consumption.

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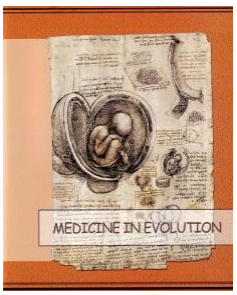
Clinical features in toxic coma in children



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Abstract

Toxic coma is a medical emergency, especially in a Pediatric Emergency Departament, requiring rapid and precise evaluation. Key objectives in evaluation and management of coma in children are: detecting severity characteristics, depth of coma, specific clinical signs and symptoms, etiological and differential diagnostic and also intialising supportive therapy and specific treatment.[1]

Materials and Methods : This is a retrospective study, were we analyzed all pacients diagnosed with coma presented in the ER Children's Hospital "Grigore Alexandrescu" in a nine year period of time: 2003 - 2011. We focused on toxic coma. We also included a prospective component related to tracking certain signs and symptoms associated with toxic coma to diagnose and initiate appropriate therapy as early as possible.

Results : In this nine year study 2003 - 2011 were included 750 comatose patients. We found that toxicants represent the main cause of coma in children. There were 445 pacients diagnosed with toxic coma, representing 59.3 % and 305 cases of non-toxic coma, 40.7 % of all coma cases presented in ER. Etiology of toxic coma in children is dominated by alcohol and abuse substances, followed by neurologic medication. Clinical manifestation were more frequent and more severe as the coma degree increases.

Conclusion: Correlating clinical manifestations in patients with altered neurologic status of toxic cause and toxicants has an important role in practice because it helps us recognize the frequency of association of coma complications such as: aspiration syndrome, arrhythmias and seizures.

Keywords: coma, clinical signs, poisoning, triage, emergency

INTRODUCTION

Toxic coma are neurologic emergencies that require immediate evaluation and therapeutic intervention; therefore, knowing that the first hour is crucial, it is necessary to use specific algorithms (protocols).The first evaluation of the comatose child and first therapeutic measures are initiated in the same time, as soon as possible. Therefore, these children require stabilization of vital functions, because at this stage is difficult to identify etiology.[2,3]

Poisoning is a dynamic condition and may have unpredictable evolution, especially in children. Consciousness and the patient's ability to maintain a patent airway and proper ventilation can change rapidly, so it is important to anticipate the action of involved toxic.[4,5]

Objective

Objesctive: to identify rapidly etiology of toxic coma in children, to appreciate severity of coma, to detect elements of gravity based on associated clinical signs and symptoms, to establish and initiate the effective treatment.

METHODS

This is a retrospective study, were we analyzed all pacients diagnosed with coma presented in the ER Children's Hospital "Grigore Alexandrescu" Bucharest in a nine year period of time: 2003 - 2011. We focused on toxic coma. We also included a prospective component related to tracking certain signs and symptoms associated with toxic coma to diagnose and initiate appropriate therapy as early as possible.

To assess the depth of coma we used Reed scale, with 4 degrees.

There were included in degree 1 of coma patients with disartria, reaction at pain stimuli and reflexe responses present. Patients with 2 degree coma are unresponsive at verbal stimulation and pain stimuli and also have reflexe responses present. In 3 degree coma were included patients unresponsive to verbal or pain stimulation, but had diminished reflexes and vital functions present. Non reactive and unstable patients were included in 4 degree of coma – deep coma.[6]

Blood pressure, respiratory rate and pulse rate in children are specific for different age groups. Therefore, reports were made using reference values for age groups. [7]

RESULTS

In this nine year study 2003 - 2011 were included 750 comatose patients; they were addmited in Pediatric Emergency Department of the " Grigore Alexandrescu" Clinical Hospital for Children. We found that toxicants represent the main cause of coma in children. There were 445 pacients diagnosed with toxic coma, representing 59.3 % and 305 cases of non-toxic coma, 40.7 % of all coma cases presented in ER.

Table 1. *Poisoning cases / coma / deaths between 2003-2011*

YEAR	POISONINGS CASES	TOXIC COMA	% TOXIC COMA	DEATHS	% DEATHS IN TOXIC COMA
2003	663	20	**3,01%**	2	10%
2004	615	42	6,82%	3	7,14%
2005	529	32	6,04%	3	9,37%
2006	570	37	6,49%	**5**	**13,5%**
2007	518	45	8,68%	1	2,22%
2008	634	58	9,10%	2	3,44%

YEAR	POISONINGS CASES	TOXIC COMA	% TOXIC COMA	DEATHS	% DEATHS IN TOXIC COMA
2009	726	62	8,50%	2	3,22%
2010	718	71	9,80%	3	4,22%
2011	**788**	**78**	**9,89%**	2	2,56%
TOTAL	5761	445	7,72%	23	5,16%

Table 2. *Etiology of toxic coma in children*

ETIOLOGY	Frequency	Percent	Cumulative Percent
ETHANOL / ABUSE SUBSTANCES	213	47.9	47.9
CNS ACTING DRUGS	67	15.1	62.9
UNKNOWN	57	12.8	75.7
NONPHARMACOLOGYCAL SUBSTANCES	47	10.6	86.3
MULTIPLE DROG POISONING	35	7.9	94.2
DENTOCALMIN (LIDOCAINE, MENTHOL, PHENOL SOLUTION)	21	4.7	98.9
ISONIAZID	5	1.1	100.0
Total	445	100.0	

It is noted that the etiology of toxic coma in children is dominated by alcohol and abuse substances: 47.9 %, followed by poisoning with drugs acting on the central nervous system: 15.1% . Coma caused by non-pharmacological substances represents 10.6 % of total toxic coma in children. We also found multidrug poisoning in 7.9% of the etiology. A number of 57 toxic remained unknown origin, representing 12.8% . I mentioned separately: Dentocalmin wich is a drug - combination of lidocaine, menthol, phenol, generating severe poisoning - all accidental, and those with isoniazide, commonly used in medical practice in tuberculosis treatment, all suicidal attempt.

Table 3. *Corelations between clinical findings and the depth of coma*

CLINICAL SINGS AND SYMPTOMS IN TOXIC COMA		COMA DEGREE							
		1		2		3		4	
		Nr	%	Nr	%	Nr	%	Nr	%
VOMITING	NO	86	19.3%	54	12.1%	18	4.0%	3	0.7%
	YES	99	22.2%	145	32.6%	34	7.6%	6	1.3%
ASPIRATION SYNDROME	NO	182	40.9%	196	44.0%	51	11.5%	5	1.1%
	YES	3	0.7%	3	0.7%	1	0.2%	4	0.9%
ARRHYTHMIAS	NO	180	40.5%	186	41.9%	30	6.8%	4	0.9%
	YES	4	0.9%	13	2.9%	22	5.0%	5	1.1%
EXTREMITIES	NORMAL	121	27.2%	51	11.5%	0	0.0%	0	0.0%
	COLD, MARBLE, CYANOTIC	63	14.2%	148	33.3%	52	11.7%	9	2.0%
CAPILLARY REFILL TIME	< 3 SEC	163	36.6%	116	26.1%	3	0.7%	0	0.0%
	> 3 SEC	22	4.9%	83	18.7%	49	11.0%	9	2.0%
TEMPERATURE	NORMAL	176	39.6%	174	39.1%	37	8.3%	7	1.6%
	HYPERTHERMIA	2	0.4%	2	0.4%	1	0.2%	0	0.0%
	HYPOTHERMIA	7	1.6%	23	5.2%	14	3.1%	2	0.4%
PUPILAR SIZE	NORMAL	160	36.0%	151	33.9%	19	4.3%	3	0.7%
	MYDRIASIS	11	2.5%	28	6.3%	16	3.6%	5	1.1%
	MIOZIS	14	3.1%	20	4.5%	17	3.8%	1	0.2%
SEIZURES	NO	178	40.0%	163	36.6%	32	7.2%	3	0.7%
	YES	6	1.3%	33	7.4%	16	3.6%	4	0.9%
	CONVULSIVE STATUS	1	0.2%	3	0.7%	4	0.9%	2	0.4%

Establishing different associations between these features enabled us to correlate coma scale degrees and clinical manifestation.

Degree 1 coma was correlated with :

- Vomiting : 46,5 % cases

- Aspiration syndrome :1,6% cases
- Arrhythmias : 2,1% cases
- Cold, marbled, cyanotic extremities : 34% cases
- Capillary refill time over 3 seconds 11,9% cases
- Hypothermia: 3,8% cases and hyperthermia 1%
- Miosis: 7,5% and mydriasis 5,9% cases
- Seizure: 3,2% and convulsive status: 0,5% cases

Degree 2 coma was correlated with:

- vomiting : 72,8% cases
- aspiration syndrome : 1,5% cases
- arrhythmias : 6,5% cases
- cold, marbled, cyanotic extremities : 74, 3% cases
- capillary refill time over 3 seconds : 41% cases
- hypothermia : 11,5 % and hyperthermia : 1% cases
- miosis : 10% and mydriasis 14% cases
- seizure : 16% and convulsive status 1,5 % cases

Degree 3 coma was correlated with :

- vomiting : 65 % cases
- aspiration syndrome : 1,9 % cases
- arrhytmias: 42 % cases
- cold, marbled, cyanotic extremities : 74, 3 % cases
- capillary refill time over 3 seconds
- hypothermia : 11,5 % and hyperthermia : 1 % cases
- miosis : 10 % and mydriasis 14 % cases
- seizure : 16 % and convulsive status: 7.6 % cases

Degree 4 coma was correlated with :

- vomiting : 65 % cases
- aspiration syndrome : 1,9 % cases
- arrhythmias: 42 % cases
- cold, marbled cyanotic extremities : 74, 3 % cases
- capillary refill time over 3 seconds :100% cases
- hypothermia : 11,5 % and hyperthermia : 1 % cases
- miosis : 10 % and mydriasis 14 % cases
- seizure : 16 % and convulsive status :22,2% cases

We can resume that clinical manifestation described above were more frequent and more severe as the coma degree increases. Life threatening symptoms like arrhythmias and seizure or even convulsive status and aspiration syndrome were present in 55,5 % , 44, 4%,22,2 % and respectively 44,4 % of cases in coma scale 4 to 2,1 %, 3,2 % 0,5 % and 1,6 % of cases in degree 1 coma.

A big challenge was to establish a significant correlation between clinical signs and etiology of toxic coma as is showed in the next table..

Table 4. *Association between coma and other clinical signs according to etiology*

Clinical signs associated to toxic coma		**ETIOLOGY**													
		CNS DRUGS		ALCHOOL/ABUSE SUBSTANCES		NONPHARMACOLOGICAL SUBSTANCES		IZONIASIDE		DENTO-CALMIN (LIDOCAIN SOL)		MULTIDRUG		UNKNWON	
		NR	%	NR	%	NR	%	NR	%	NR	%	NR	%	NR	%
VOMITING	NO	32	7.2%	75	16.9%	3	0.7%	1	0.2%	17	3.8%	10	2.2%	23	5.2%
	YES	35	7.9%	138	31.0%	44	9.9%	4	0.9%	4	0.9%	25	5.6%	34	7.6%
ASPIRATION	NO	66	14.8%	211	47.4%	39	8.8%	5	1.1%	21	4.7%	35	7.9%	57	12.8%

SYNDROME	YES	1	0.2%	2	0.4%	8	1.8%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
ARRHYTHMIAS	NO	54	12.2%	211	47.5%	33	7.4%	5	1.1%	9	2.0%	34	7.7%	54	12.2%
	YES	13	2.9%	2	0.5%	13	2.9%	0	0.0%	12	2.7%	1	0.2%	3	0.7%
EXTREMITIES	NORMAL	26	5.8%	103	23.1%	7	1.6%	1	0.2%	0	0.0%	11	2.5%	24	5.4%
	COLD, CYANOTIC , MARBLED	41	9.2%	110	24.7%	39	8.8%	4	0.9%	21	4.7%	24	5.4%	33	7.4%
CAPILLARY REFILL TIME	< 3 SEC	39	8.8%	160	36.0%	12	2.7%	1	0.2%	5	1.1%	21	4.7%	44	9.9%
	> 3 SEC	28	6.3%	53	11.9%	35	7.9%	4	0.9%	16	3.6%	14	3.1%	13	2.9%
TEMPERATURE	NORMAL	63	14.2%	177	39.8%	44	9.9%	4	0.9%	21	4.7%	31	7.0%	54	12.1%
	HYPERTHERMIA	1	0.2%	1	0.2%	1	0.2%	1	0.2%	0	0.0%	0	0.0%	1	0.2%
	HYPOTHERMIA	3	0.7%	35	7.9%	2	0.4%	0	0.0%	0	0.0%	4	0.9%	2	0.4%
PUPILAR DIAMETER	NOR-MAL	27	6.1%	192	43.1%	31	7.0%	2	0.4%	13	2.9%	29	6.5%	39	8.8%
	MYDRIASIS	23	5.2%	17	3.8%	1	0.2%	3	0.7%	8	1.8%	1	0.2%	7	1.6%
	MYOSIS	17	3.8%	4	0.9%	15	3.4%	0	0.0%	0	0.0%	5	1.1%	11	2.5%
SEIZURES	ABSENT	55	12.4%	205	46.1%	28	6.3%	1	0.2%	6	1.3%	31	7.0%	50	11.2%
	PRESENT	12	2.7%	8	1.8%	16	3.6%	2	0.4%	10	2.2%	4	0.9%	7	1.6%
	CONVULSIVE STATUS	0	0.0%	0	0.0%	3	0.7%	2	0.4%	5	1.1%	0	0.0%	0	0.0%

Significant conclusions were drawn after correlating clinical manifestations in patients with altered neurologic status of toxic cause and toxicants.

Vomiting was present in 93,6 % cases of toxic coma produced by non-pharmacological substances: in 80 % cases of isoniazid related coma, in 71 % cases of multidrug related coma, in 64,7 % cases of alcohol and abuse substances induced coma, in 52,2 % cases of toxic coma by neurological medication and in 19 % cases of Dentocalmin induced coma. Vomiting was present in 59,6 % cases of unknown etiology coma..

Aspiration syndrome was present in 24,7% of toxic coma cases. Regarding coma scale, we observed that in 3 cases coma degree was 1 and , in 1 case coma degree was 3 and in 4 cases coma degree was 4. Differences were observed when we related coma to etiology. Aspiration syndrome was present in 8 cases of non-pharmacological substances toxic coma, a total of 17 % , also in 2 cases of poisoning with alcohol and abuse substances (0,9 %) and one case of coma was related to CNS drugs poisoning (1,49%). Aspiration syndrome was not associated with coma in multidrug, isoniazid, Dentocalmin or unknown substances poisoning.

Coma associated with arrhythmias represented 9,8 % of total cases. Distribution according to coma etiology was as follows: 19,4 % cases of coma in CNS drugs poisoning associated arrhythmias and only 0.9 % cases of alcoholic and abuse substances coma associated arrhythmias. Non-pharmacological substances poisoning associated coma and arrhythmias in 27,6 % cases. Dentocalmin produced severe poisoning features manifested not only with altered mental status but also with arrhythmias in 57, 1% cases.

Hypothermia was recorded in 10.3 % cases of coma. Most cases of hypothermia were associated with alcohol poisoning: 16, 4% in all coma cases. Also 4.4 % of patients with coma induced by CNS drugs were hypothermic at presentation.

In 25 % cases of CNS drugs poisoning coma, miosis was present, and in 34 % cases mydriasis, so a total of 59 % cases of coma associated pupillary diameter abnormality.

Seizures were present in 13,2 % cases of toxic coma. 17,9% cases of coma by CNS drugs associated seizures and 3.75 % cases of alcohol and abuse substances coma associated seizures. Non- pharmacological substances poisoning coma associated seizures in 34 % of cases, and in 6 % of cases convulsive status. Two out of five cases of isoniazid poisoning developed seizures (40 %) and other two developed convulsive status resulting a total of 80% of cases with paroxistic manifestation. Seizures in Dentocalmin poisoning were present in 47,6 % cases and convulsive status was recorded in 23,8 % cases (a total of 71,4 %). Association between multidrug poisoning and seizures was noticed in 11,4 % cases and in 12,2 % cases of unknown toxicant poisoning.

Clinical examination of patients at presentation revealed : normal aspect extremities in 38,6 % cases, cold, marbled, cyanotic extremities in 61,4 % cases and capillary refill time was normal in 62,7 % cases and prolonged in 37,3 % cases. Regulation of extremities blood flow is realized by central and peripheral mechanisms: hypoventilation (respiratory toxic drugs) or unventilated pulmonary areas (hydrocarbon aspiration pneumonia), cutaneous vasoconstriction (hypothermia or increased peripheral vascular resistence due to poisoning), decreased oxygen transportation mechanism (nitrites poisoning) and is impaired in poisonings complicated with shock.

This statistical analyze has an important role in practice because it helps us recognize the frequency of association of coma complications such as: aspiration syndrome, arrhythmias and seizures.

CONCLUSIONS

- Etiology of toxic coma in children is dominated by alcohol and abuse substances in 47,9% cases, followed by neurologic medication in 15,1 % of cases. Coma induced by non-pharmacological substances represents a total of 10,6 % cases, but has a higher severity and mortality rate. 7,9 % cases of toxic coma had multidrug etiology. A number of 57 cases remain of unknown toxicant etiology, poisoning substance could not be identified in a total of 12,8 % cases.
- Clinical manifestations associated with toxic coma were more frequent and more severe as the degree of mental status alteration was increasing. Life threatening events like arrhythmias, seizures and convulsive status or aspiration syndrome were present in 55,5 % cases, 44,4 % cases , 22,2 % cases and respectively in 44, 4 % cases of 4 degree Reed coma scale and 2,1 %, 3,2 %, 0,5 % and 0.6 % of cases in 1 degree Reed coma scale.
- Correlating clinical manifestations in patients with altered neurologic status of toxic cause and toxicants has an important role in practice because it helps us recognize the frequency of association of coma complications such as: aspiration syndrome, arrhythmias and seizures.

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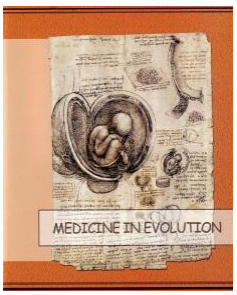
Particularities of consumption for sweets and soft-drinks in adolescents aged 11 to 18 years from Timisoara, Romania



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Abstract

Aim. To investigate particularities of consumption of sweets and soft drinks by teenagers from Timisoara, Romania.

Methods. The work group consisted of 243 pupils: 37.9% were in gymnasium and 62.1% in high-school; 56.4% girls and 43.6% boys; their ages were between 11 and 18 years. The working method was the cross-population study, as a case study.

Results. Daily consumption of sweets is declared by 51.2% of children aged 11 to 14 years and by 36.5% of those aged 15 to 18 years, whereas for soft drinks the percentage is of 33.7% for those aged 11 to 14 years and 29.4% for ages 15 to 18, with no difference between genders and group ages in respect to the consumption frequency. The factors that contribute significantly to daily consumption in relationship with the decision to lose or maintain weight are the age group and the decision to lose weight. Pupils who wish to lose weight consume sweets 2.03 times more rarely than the others. Tested variables do not influence the decision to consume soft drinks daily.

Conclusion. High percents of the respondents in this study consume sugar added soft drinks and sweets. The consumption of sweets is perceived as a factor that influence body weight and is lower among those who wish to lose weight, but the children and adolescents do not perceive the soft drinks as a menace to their weight.

Keywords: teenagers, consumption of sweets and soft drinks

INTRODUCTION

Obesity in children became a major public health concern [1] because of its long-term consequences. One possible reason for the lack of success of interventions in this area may be the lack of identification of overweight determinants.

We propose a study on the particularities of sweets and soft-drinks consumption patterns in adolescents from Timişoara, Romania. Romania is a developing country and is undergoing major socioeconomic change. The environment of the children and adolescents today is very different from the environment of the present adults during their growing up process. The availability of foods and their marketing is completely different because of the transition from a traditional society to a more consumerist type society. One group of foods that is more present now in the alimentation of children and adolescents than it was 10 or 20 years ago is represented by the soft drinks containing sugar and the highly processed sweets.

The increase in body weight and obesity are the result of cumulated effects of some small modifications of daily energetic balance. Many components of diet may directly or indirectly modify this balance, and many epidemiological studies and clinical trials investigated the role that diet factors play in obesity control and prevention. The relative influence of major nutrient groups (fats, carbohydrates and proteins) on fat accumulation in the organism is not clear. Only recently large epidemiological studies were launched in order to investigate the consumption of food groups and alimentary patterns related to long-term weight gain. A good example is represented by recent prospective studies suggesting that a high consumption of sugar containing soft drinks results in weight gain [2].

During the last decades a paralel was registered between dramatic increase of high-caloric sweetener consumption in soft drinks and highly procesed sweets and the obesity epidemic. The source of existing data is mainly the USA [3]. More studies [4-6] reported a significant pozitive association between sweet soft-drinks consumption and the increase of overweight and obesity case numbers in children.

A review [7] demonstrates that the largest part of past epidemiological research validates the idea that obesity is linked to consumption of cheap foods. Highly –procesed cereals, sugar and fats that are added in cheap foods have good taste and are conveniant. A commune report of the World Health Organization and Food and Agriculture Organization concluded that agressive marketing for fast-food products and for those with high energetic density (sweets, soft-drinks) represents a probable causal factor for weight-gain and obesity in children [8].

MATERIAL AND METHODS

Material

The work group consisted of 243 pupils from a school in Timisoara: 37.9% were in gymnasium and 62.1% in high school; 56.4% were girls and 43.6% boys, the two groups were homogenous from the point of view of gender distribution, p=0.248; their ages were between 11 and 18 years, average age was 15.04 years with a standard deviation of 2.124.

Method

The working method was the cross-sectional population study, as a case study, based on the CORT 2004 questionnaire regarding health risk behaviours in adolescents and young people. The questionnaire was validated by the Ethics Committee of the "Victor Babes" University of Medicine and Pharmacy Timisoara.

The study was conducted with written approval of the university. The pupils were included in the study only after the freely expressed consent of each participant of the study while also observing their individual rights.

Data processing and interpretation uses modern methods of advanced medical statistics with the aid of the PASW 18 (SPSS 18) 2010 software. The statistical significance p value was set at $p<0.05$, except for the situations where the Bonferroni correction was applied – in these cases the accepted p value was specified in the text. To compare ordinal data, we have used the Mann-Whitney and Kruskal-Wallis tests. The chi square test was used for ordinal/nominal data. The logarithmic regression test was used as well.

RESULTS

Sweets consumption frequency

Daily sweets consumption is indicated by 51.2% of the pupils aged 11 to 14 years and by 37.5% of the pupils aged 15 to 18 years, these cases being more frequent among girls. 1.1% of gymnasium pupils and 4.2% of high school pupils indicated that they never consume sweets.

In the case of the age group between 11 to 14 years we have not identified differences between genders as related to sweets consumption frequency, $p=0.373$. In the case of the age group between 15 and 18 years, no difference between genders were identified as related to sweets consumption frequency, $p=0.850$. No difference in the sweets consumption frequency was identified neither between the two age groups, nor between boys ($p=0.605$) and girls ($p=0.078$).

Sweetened soft drinks consumption frequency

Consumption of sweetened soft drinks has been reported by 90% of the pupils aged 11 to 14 years and by 86.7% of the pupils aged 15 to 18 years. The 1-3 times per week consumption model is present at 33.7% of gymnasium pupils and 39.2% of high school pupils, cases of girls being more frequent. Daily consumption of sweetened soft drinks is the pattern encountered at 33.7% of gymnasium pupils and at 29.4% of high school pupils, cases of girls being more frequent than cases of boys.

As for the age group between 11 and 14 years, no differences between genders were found in relation with the commercially available soft drinks consumption, $p=0.378$. In the age group between 15 and 18 years we have found no difference between genders in relation with the commercially available soft drinks consumption, $p=0.283$. No difference of soft drinks consumption frequency we identified neither between the two age groups, nor between boys ($p=0.866$) and girls ($p=0.143$).

Determinant factors of the decision to consume sweets daily in connection with the desire to lose weight or to maintain it (Table 1)

We have applied logistic regression in order to demonstrate the influence of gender, age group, BMI and the desire to lose weight on the decision of consuming sweets daily and we have found that the model that includes these four predictors is statistically significant $\chi^2=11.14$, $p=0.025$, this indicating the fact that the model can distinguish between the respondents which have eaten sweets daily and those who have eaten sweets more rarely. The model explains between 4.8% and 6.5% of the variation of the decision to eat sweets daily and classifies correctly 61.5% of the cases.

Only two independent variables contribute significantly to the model, namely age group and the desire to lose weight (Table 1). The age group between 15 and 18 years has an OR (odds ratio) of 2.03, cases of children who eat sweets daily being 2.03 more frequent in the case of high school pupils as compared to gymnasium pupils. Cases of pupils who eat sweets

daily are 2.03 more rare among those who have expressed their desire to lose weight as compared to the others, with different options of evolution in near future. BMI value (p=0.500) and gender (p=0.068) do not contribute to the decision of eating sweets daily.

Table 1. *Factors included in the prediction model of the decision to consume sweets daily for the purpose of losing weight or maintaining it*

	B	SE	p	OR	95% of IC for OR	
					Inferior	
Group (1)	,709	,297	,017	2,032	1,135	3,639
Gender (1)	,539	,295	,068	1,714	,961	3,056
BMI	,032	,047	,500	1,032	,942	1,131
Want to lose weight	,708	,334	,034	2,030	1,055	3,905
Constant	-1,938	1,166	,097	,144	,000	,000

Legend: (1) = first category that was taken as reference for categorical variables included in the model; B= β quotient; SE = standard error of the β quotient; p= p value; OR= odds ratio

Determinant factors of the decision to consume soft drinks daily in relationship with the desire to lose weight or to maintain it

We have applied logistic regression to demonstrate the influence of gender, age group, BMI and of the desire to lose weight, to the decision of consuming soft drinks daily and we have found that the decision of consuming soft drinks daily is not influenced by the tested variables, p=0.312.

DISCUSSIONS

In the age group 11 – 14 years, over half of the respondents declare daily consumption of sweets. The percent is lower for the pupils in the age group 15 – 18 years. For the children, the most important thing when they have to make alimentary choice is represented by the food's taste. Studies on consumers showed that some sensorial characteristics of foods are important for the alimentary choices. Different preferences may lead to developing alimentary patterns, which, in turn, may be linked to effects on the health status. There is evidence that such alimentary patterns are developed early during childhood and adolescence and are carried into adulthood [9].

The epidemiologic European IDEFICS Study addressed alimentary, social and environmental determinants of health status in children. This study showed the majority of children prefer foods added with aromatic substances for sweet, fat and salted tastes [10]. In the same study, indifferent to the country of residence, age, sex, parental education and parental IMC, overweight and obesity in children was positively associated with the child's preference for foods with added fats and for the apple juice containing added sugar. The children preferring the apple juice containing sugar have 50% more chances to be overweight or obese compared to the children preferring the natural juice. The predisposition to consuming foods with high content of fats and sugar is associated with watching TV long periods of time, witch, in its turn, is an indicator more prevalent in overweight and obese children. The cited study concludes that it is plausible that alimentary preferences of children are modeled by cultural, behavioral and environmental factors, including exposure to television and other media [10].

Results of a recent study [11] on a representative sample in the USA suggest publicity on television for soft-drinks and fast food is associated with high consumption of these kinds of foods among children in the elementary schools. Exposure to 100 TV commercials to soft drinks containing sugar in the 2002-2004 time intervals was associated with an increase of 9.4% of children's consumption of soft drinks in 2004.

Other studies [12] on the same subject concluded that even if the TV publicity is subject to regulation, the children in Great Britain are exposed to a considerable number of TV commercials for foods. These are mainly for foods rich in fats, salt and sugar, which are targeted specially to children, using known entertainment characters and themes. Such commercials were proved to induce significant increase of consumption, especially in overweight and obese children, or the increased preference for carbohydrates and fat in children exposed to television publicity.

90% of the pupils aged 11 to 14 years and 86.7% of those aged 15 to 18 years reported consumption of soft drinks containing sugar. The high percent of consumers is alarming taking into consideration how frequent these soft drinks are incriminated for the high rise in body weight by recent studies. Malik and collaborators [13] propose as an explanation of the association between the consumption of sweetened beverages and weight gain, low satiety and the incomplete compensating reduction in the calorie intake to the energy intake in next meals, following consumption of liquid calories. Consumption of sweetened beverages also increases rapidly the concentrations of glucose and insulin in the blood which, together with high quantities that are often eaten, contribute to a diet with high glycaemic load, stimulate appetite and promote weight gaining, and was proven to induce tolerance to glucose and resistance to insulin.

The sweet beverage intake among children has increased during the last decades, thus increasing the calorie intake of sugar to the diet [14]. In theory, on the one side, children's metabolism cannot reduce food consumption in order to compensate the calorie intake from sweetened beverages and, at the same time, sweeteners contribute to weight gaining due to their influence on lipogenesis, insulin emission or leptin production [15, 16]. Results of prospective cohort studies performed on children and teenagers have shown that there is a positive relationship between the consumption of sugar sweetened beverages and weight gaining/obesity [17, 18]. Nevertheless, a recent meta-analysis and other longitudinal studies have concluded that the association between consumption of sugar sweetened beverages and BMI or weight gaining is not fully convincing, based on actual scientific proof [19, 20].

CONCLUSIONS

Over half the pupils 11 to 14 years old and 36.5% of those 15 to 18 years old consume sweets daily without differences between sexes and between the two age groups of the frequency of consumption for sweets. Very high percents of the children and adolescents consume soft drinks containing sugar. Only 9%, respectively 13.3% of the pupils never consume this type of beverages.

The present study established high rates of consumption for sweets and soft drinks containing sugar for a sample of children and adolescents in Timisoara, Romania. The consumption of sweets is perceived as a factor that influence body weight and is lower among those who wish to lose weight, but the children and adolescents do not perceive the soft drinks as a menace to their weight.This study represents a starting point for future educational programs aiming the amelioration of the health status and to reduce the risk for obesity in the children and adolescents.

Conflict of interests

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

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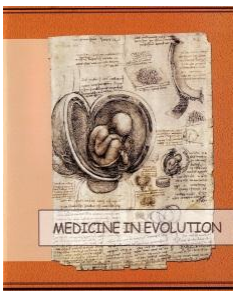
Cardiovascular risk profile of remote process of coronary dezobstruction



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Abstract

Aim: Assessment of modifiable target risk factors of the myocardial revascularized patient standards set by European guide of secondary prevention.

Material and Method: We included patients coronary miocardic revascularized in EUROASPIRE IV study analyzed –romanian arm.The assessment of traditional risk factors; achieve lipid targets, autoevaluation-exercise activity, events rate occurred and whether the prescription pharmacology secondary prevention indication or not as secondary prevention guideline.

Results: Analyze of biological risk factors in the study group was 43% remain hypertensive, 5% achieve a target LDLc, 37% remain with diabetes, 42% were obese, 17.3% remain smokers, 40.7% perceive autoevaluation of capacity efort. Events rate occurred when T2 was 7.9% for restenosis at a median time estimated at 4.33 years. The prescription was under pharmacological secondary prevention guide.

Conclusions: Coronary remote patient dezobstruction process still pose a important lipid risk.Asociation of obesity and new diabetes cases increase the risk for metabolic assessment of the atherogenic process.

Keywords: cardiovascular risk, myocardial revascularization, secondary preventio

INTRODUCTION

Despite progress in diagnosis and treatment of cardiovascular risk factors, cardiovascular disease is a major cause of disability and loss of quality of life and remains the main cause of overall mortality in the world. (1).

The same situation in our land. Romania has an increased prevalence of cardiovascular risk factors, which is why it was included in the category of European countries with high risk for cardiovascular events (2).

Interest to reduce cardiovascular risk of revascularized coronary lead the development of multiple studies research aspect; all concluded that patients miocardic revascularized are at cardiovascular very high risk and that the atherosclerotic recorded a progression both in the coronary arteries and to the grafts is detreminat and persistent cardiovascular risk factors, genetic, psychosocial and environmental (3, 4).

These factors and their relationship to risk for cardiovascular events fatal / non-fatal were well raised during numerous studies (EUROASPIRE, PERCRO-DOC survey, PROJECT IMPACT NICE) (3,5,6,7)

The major challenge remains medical slowing atherosclerosis among these patients. How? The answer is found in cardiovascular prevention guidelines. Changing the targets set in the last decade for classic risk factors as variations Australian / American / European (8,9,10) conclude the individualization programs for cardiovascular recovery.

The European model which has proposed to analyze the results of implementing a healthy lifestyle, management of risk factors of drug therapies used in patients with coronary revascularization and taking measures to reduce morbidity and mortality of cardiovascular remains study EUROASPIRE, held since 1996, 2016 shows that EUROAPIRE arm RESULTS OF IV (4).

Romanian arm of EUROAPIRE IV aims to analyze the assessment of cardiovascular traditional risk factors; if the lipid target is reached; that is revascularized myocardial patient perception regarding physical activity performed; events rate occurred and if the cardiovascular risk profile of dezobstruction process remote or not influenced by pharmacological indication presccription.

Objective

The aim of the present study focused on the outcome of implementing the standards set by European guide of secondary prevention targets appreciated by evaluating obtain modifiable risk factors that define the risk profile of the revascularized coronary infarction.

MATERIAL AND METHODS

Transversal retrospective study conducted in the Institute of Cardiovascular Diseases Timisoara on revascularized coronary consecutive patients from romanian arm of the EUROASPIRE IV study.

Inclusion criteria followed the protocol EUROASPIRE IV. They included coronary revascularization with PTCA (Percutaneous transluminal coronary angioplasty) and CABG (coronary artery bypass grafting) in <6 months - <36 months from the dezobstruction process.

Evaluation of patients was conducted at three different times:

T0- the moment of inclusion into study – dezobstruction process baseline

T1- time of the interview at> 6 months <3 years, according to the study protocol were invited to complete the questionnaire validated, were examined clinically and blood was collected for biological tests.

T2 -postprocedural <3 years> 5 years, which were quantified fatal /nonfatal cardiovascular events.

We defined biological risk factors: age and sex, and hypertension - personal history of hypertension and antihypertensive therapy or blood pressure> 140/90 mm Hg or> 140/80 mmHg in diabetics; Hypercholesterolemia - Hypercholesterolemia personal history and lipid-lowering therapy or serum total cholesterol> 175 mg / dL, diabetes - diagnosed diabetes or anti diabetic therapy (diet and / or oral antidiabetic drugs, insulin) (10, 11)

Units smoker - people who smoked more than one cigarette / day in the last 6 months or determination of CO in exhaled air to be ≥ 10 p.p.m. (10).

Obesity - body mass index (BMI)> 30 kg / m2, calculated by formula:

$$BMI = G / T2$$

Physical activity was assessed by questionnaire method. Self-evaluation tests involved physical activity at least 20 minutes ≥ 3 times / week (10). Metabolic equivalent was determined from the formula.

Consumption / mx metabolic equivalent (METmx)

$$METS\ y = x\ ml / min / 3.5$$

Note: 1 METS = 3.5 ml / kg / min

We defined category of cardiovascular events occurred after the dezobstruction process and we quantified the following events: cardiovascular death, death and non-cardiovascular restenosis, stroke / cases of accidents TIA, electrostimulation by pacemaker, hospitalization for new bypass, hospitalization for new stent , hospitalization for heart failure and new diagnosis of diabetes.

I analyzed prescribing pharmacological indication on secondary prevention of coronary heart disease in the two moments of evaluation: T0 and T1.

Statistical analysis

Statistical analysis was performed using SPSS Statistics 17.0 software. Included were 31 statistical variables: numerical,nominal and categorical ratings. It looked percent, mean ± standard deviation of the batch. Statistical significance was taken to a value of p less than 0.05 for the 95% range. Variable time was calculated from the date of coronary revascularization patient until event detection as present or absent.

RESULTS

Of the 375 coronary included in the study, remain eligible coronary revascularization 341: mean age 61 ± 21 years, significantly predominantly male (71.3% men).

Profile of biological factors are shown in Table no. 1. postprocedure was characterized by significant increase in mean total cholesterol (CT) at the time T1 (p = 0.001). Mean HDLc dropped significantly at the time T1 (47.42 ± 16.96 vs 59.24 ± 35.78, p = 0.01).

There were no statistically significant differences regarding primary target (LDLc) and secondary target (non-HDLc), (p = NS)., secondary prevention programs in coronary heart disease. In terms of hemodynamic reducing systolic blood pressure values under medication was significantly improved in T1 moment (39.58 vs 28.15).

As for the variables responsible for achieving targets for cardiovascular risk reduction we achieved the following results at the time T1:

- 5% reach the target LDLc,
- 65% to achieve the target non HDLc,
- 43% get tensional control recommended
- The incidence of diabetes at time T1 increases by 37%

- Obesity in the lot at the time T1 occurs in 42% of which 48% had central obesity (Table no. 2).

Table 1. Evaluation and biological risk factors and TA at the T0 and T1 time

RISK FACT.		Mom. T0	Mom. T1	p
CT *	mg/dl	194.55±56.51	175.55±45.69	0.001
LDL c*	mg/dl	106.80±41.32	99.76±33.42	0.08
HDLc*	mg/dl	59.24±35.78	47.421±16.96	0.001
nonHDL c*	mg/dl	135.32±44.95	128.13±40.94	0.06
TG *	mg/dl	142.22±75.35	134.35±71.19	0.04
Pac with LDL > 80 **	mg/dl	74.19	69.50	
Pac. with non-HDL > 130 **	mg/dl	35.29	39.29	
TAS *	mmHg	157±25	154.68±21.63	NS
TAD*	mmHg	103±13	100.80±12.26	NS
Pac. with TAS ≥140**	mmHg	39.58	28.15	
Glicemia a jeun*	mg/dl	112.49±31.62	122.60±52.44	0.017
Pac . with diabet zaharat**	mg/dl	33	37	

* media ±DS
** % lot

Smoking was highlighted in a lower proportion of 12.3% in T1 time after dezobstruction time, 47% among patients clearly aware of the risk to which they were subjected (Table no. 2).

Self-assessment exercise capacity perceived revascularized coronary highlights the possibility to develop physical activity than 6 METS for 40.7% of the sample population (table no. 2).

Table 2. Assessment of physical capacity, BMI and smoking behavior at the time T1

Physical activity METS		%
Low*	**1-2**	**33.43**
Moderate*	**3-6**	**26.39**
High *	**>6**	**40.17**
BMI		%
<25		**7.33**
25-30		**22.58**
>30		**19.64**
SMOKE ATITUDE		%
Non smoker		**35.48**
Old smoker		**47.21**
Smoker		**17.30**

The time in which study participants developed a event had a non-gaussian distribution.

The median time to occurrence of one of the events analyzed was estimated at 4.33 years (3.93- 4.72 years).

Rates of cardiovascular events at T2 was 7.9% for a median survival time of 4.33 years.

Most common events were: heart failure rehospitalization , heart restenosis, indication of new coronary artery bypass (table no. 3)

Table 3. Evaluation of cardiovascular events occurred after myocardial revascularization surgery

n= 341	Cardiovascular Events							
Patients %								
Death CV **0%**	Death nonCV **4%**	Restenosis **3 %**	AVC/AIT **1 %**	Pacemaker implant **3%**	New by-pass **5%**	New stent **3 %**	Hearth failure hospitalization **5 %**	New diabetes **3%**

Pharmacological prescription recommended by the European guidelines for secondary prevention was respected with the following remarks :

- The percentage of coronary indication for antiplatelet medication (monotherapy or bi-therapy) increased by 24.5% when compared to T0,
- was registred a significant increase in the prescription of ACE inhibitors with 46.05%
- Calcium channel blockers was pescribed with 20.53% when compared to T0 T1,
- Almost all patients had an indication statin both at the time T0 (99.99%) and at the time T1 with the following statement: maximum dose of statin was prescribed at the time T0 to 60.41% of revascularized , at the time T1 only 45.16 of coronary have had maximum statin indication (fig. no. 1).

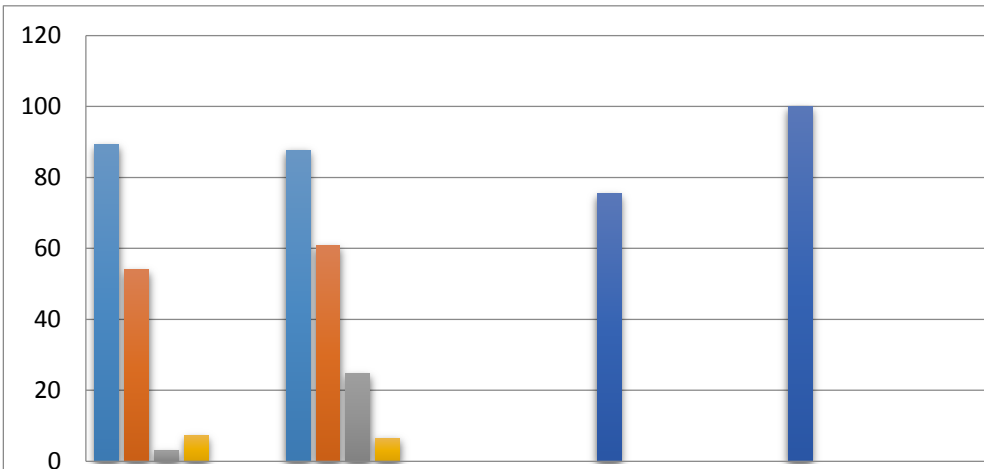

Figure 1. Evaluation of the T0-T1 indication pharmacological after myocardial revascularization surgery

DISCUSSIONS

The present study clearly demonstrates the presence of a high cardiovascular risk profile in 4.33 years postprocedural.

In our study the lipid risk parametres were under control although patients received statin therapy indication.

Though the maximum dose of the statin used for nearly half of the batch at the time T1 benefit was achieved only nonHDLc. We believe that this is why the following events occurred rate was necessary indication for revascularization with coronary bypass.

Randomized, controlled trials have brought substantial evidence showing that the risk of lipid can be reduced by controlling lipid profile target values according to the guide secondary prevention among patients revascularized afalti the maximum dose postprocedure, if it would achieve annual screening of LDLc and nonHDLc to have a marked decrease in the net benefits frequency and complication post procedural extension to 2 years (12,13).

Regarding parameter risk lipid in this group of patients revascularized, a meta-analysis of numerous studies show that the presence of this parameter risk lipid (LDLc) recorded 70% more cardiovascular events fatal / non-fatal and that there is the associated in time with diabetes developer mellitus type 2 (3,4,14).

Another relevant aspect of our study aims hemodynamic profile, optimal blood pressure reduction in medication did not lead to increased risk of fatal cardiovascular hemodynamic externalized through events / non-fatal. Instead metabolic risk was high not only component of hypercholesterolemia but also in the increased incidence of diabetes. This force us to more direct sanctions on making lifestyle change.

The benefit that brings good control of blood pressure is evidenced by a recent meta-analysis showing that 10 mmHg reduction in SBP to reduce by about a partime a recurrent coronary event and stroke risk by about 30% (15).

It is well known that diabetic patients undergoing interventional revascularization are at increased risk of MACE. Pilar Mazon-Ramos et al examines patients revascularized interventional and diabetic, showing that those pacients are at high risk of death at one year revscularizare (16).

Another study emphasizes that patients with coronary interventional or surgical revascularization or with diabetes demonstrated that those undergoing surgical revascularization had a significantly lower mortality rate ($p = 0.002$) than those undergoing interventional revascularization (17).

What we observed in our study, following myocardial revascularization, most patients report an increase in physical activity levels.

Guidelines for prevention of cardiovascular disease says that participation in regular physical activity is associated with a decrease in cardiovascular mortality. Regular physical activity is linked to a reduced risk of cardiovascular events fatal / non-fatal (18).

Revascularized patients physical activity is considered as a very important component at the cardiac rehabilitation programs (10).

A meta-analysis that included mostly middle-aged men most of whom had coronary bypass or percutaneous transluminal coronary angioplasty showed a reduction of about 30% of total mortality for a period of at least 3 months in patients revascularized coronary who conducted regular physical activity. (19).

On smokers we can say that in our study group almost half of those who smoked before the event revascularization, quit smoke at the time of evaluation.

A meta-analysis on stopping smoking on coronary patients showed a decrease of 46% relative risk of coronary mortality and a 36% reduce the mortality from any cause (20).

Yet despite these proven benefits and the fact that three quarters of the smokers were advised to stop smoking and only one quarter have followed the recommendations. (3,4,10) . This situation is found worldwide and communicated according to studies. All smokers and especially postrevascularized patients need professional help in order to quit smoking (4.10).

In their study, Mucha. et al., demonstrated that bypass aorto-coronary revascularized patients and who continued to smoke after intreventieon of myocardial revascularization, have an increased risk of death and a higher rate of new revascularization process compared those who stopped smoking (20).

On body mass index of patients to our study, most patients were presented at control were overweight, which demonstrates an increased prevalence of obesity among coronary certificates, valued at the dezobstruction vascular time distance.

Another study comes to us strengthen results warning that in their study most patients come to achieve myocardial revascularization they were overweight and that there were no statistical significance during following between the deceased and the survivors in terms of average value of body mass index. (21)

To a large extent, the results of our study that we conducted on the cardiovascular risk profile of the patient coronary revascularized are in line with previous surveys conducted in Europe that have demonstrated poor control of cardiovascular risk factors and therefore , the high prevalence of cardiovascular disease recurrence therapy.

CONCLUSIONS

Coronary remote patient at dezobstruction process shows another important lipid risk.The association of obesity and newly diagnosed cases of diabetes defining increased risk for metabolic evolution pro-atherogenic process. Preventive measures must be reconsidered and individualized, so that to assure the vascular protection efficiency.

Limits of the study

The study presents the results in a population of coronary revascularization selected by inclusion criteria so that results are addressed in this sample.

Comparing arm our data published in EuroAspire IV validates the quality of our study.

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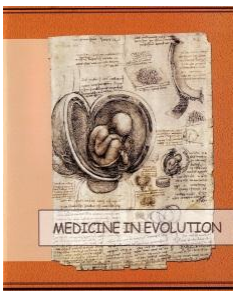
Complete cervical resection of large mediastinal goiter - Case report



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Abstract

We present the case of a female, age 75 years, with a mediastinal multinodular goiter, ¾ of the goiter volume was intra-thoracic, with an extension to the superior mediastinum, then posteriorly towards the aortic arch and trachea, downwards to the tracheal bifurcation, with dyspnea as the primary symptom. The goiter was hyperfunctional with lowered TSH, and normal FT3 and FT4. Clinical examination discovered that left lobe was larger, imobile with swallowing, firm consistency. CT scan showed the extension of the goiter into the aortopulmonary window, with a further retrotracheal extension. The patient underwent near total thyroidectomy through cervical incision alone, without sternotomy or toracotomy. Main reason for performing a near total thyrodectomy was the adhesions between the left lobe and the left recurrent laringeal nerve. Dissection started with the superior pole of the left lobe and continued to the inferior aspect of the lobe with traction upon the intrathoracic goiter and succesive freeing of its volume. There were no postoperative complications and the drainage tube was removed on the postoperative day 6th; the patient was discharged on the 8th postoperative day. We showed that cervical goiters with intrathoracic extension could be managed through a cervical approach, even if the intrathoracic volume is important. Majority of these cases have blood supply coming from the cervical region, not from the thorax, making this procedure possible.

Keywords: goiter, mediastinal goiter, tyroid, thyroidectomy

INTRODUCTION

Surgical treatment of the thyroid goiter is an actual debate in the medical literature. The surgical approach of thoracic goiters has a special place in these debates. Through the anatomical reports that the thyroid goiters have with intramediastinal organs, the surgical treatment poses remarkable problems. Therefore, the surgical approach must be adapted particulary in each case, the final aim being a total thyroidectomy and also preventing intraoperative incidents and postoperative complications, especially those due to aberrant vascularisation. Taking into account the fact that, in most cases, the retrosternal goiter extends in two surgical areas (neck and thorax), it requires a complex team including a general and a thoracic surgeons. However, the unanimous oppinion of the authors is that these goiters need to undergo surgery in specialised centers, with experienced surgeons [1].

The nomenclature of the retrosternal goiters (plunging, intrathoracic, mediastinal) is still an unsolved problem. Due to the different evaluation factors of these goiters, an author identified at least 6 different definitions in the literature [2]. This diversity explains the fact that the authors reported an incidence of 2% to 19% of these goiters amidst all the reported thyroidectomies [3]. Still, the giant thyroid goiters represent 5,8% of all the mediastinal masses [4].

From 1940, Wakeley şi Mulvani, suggested a classification of retrosternal goiters based on size and the mediastinal location [5]. This classification is still used. There are 3 types of goiters:

Type 1: goiters with the inferior pole at the level of the aortic arch.

Type 2: goiters with the inferior pole under the aortic arch, in the inferior mediastinum.

Type 3: large intrathoracic goiters, possibly with superior vena cava syndrome.

CASE REPORT

A female patient, 75 years old, with no family history of thyroid pathology, was clinically diagnosed with palpable cervical goiter, especially in the left lobe, imobile with deglutition. The general practitioner required a thoracic X-ray which showed enlargement of the superior mediastinum. The patient was admitted at the Endocrinology Clinic in Timisoara for evaluation and further investigations. Medical past history included: hysterectomy for uterine fibroma in 1961, hip prosthesis in 2007, right knee arthrosis.

Her clinical exam at hospital admission showed: inspiratory dyspnea, nonproductive persistent cough, hypersthenic constitution (IMC=28,7 kg/m^2), normally coloured skin and mucosa, post prosthetic scar at the left hip, normal cardio-pulmonay sounds, HR=75beats/min, BP=125/85 mmHg, normal peripheral arterial pulse, normal dygestive system. At the palpation of the cervical area we found a multinodular goiter, especially at the left lobe, firm consistency, painless, imobile with deglutition.

Thyroid ultrasound has revelead a left thyroid lobe with retrosternal extension, which cannot be measured entirely. Hormonal dosage highlighted subclinical hyperthyroid status, with suppresed TSH, FT3 and FT4 being in normal limits. The blood tests revealed mild hypercholesterolemy, urinary infection treated according to the urinary antibiogram and right hip osteopenia treated with Vigantolleten 1000 IU, 1 tablet/day.

The CT scan of the thorax pointed out the enlargement of the superior and middle mediastinum, secondary to the hypertrophy of the thyroid gland, mainly of the left lobe, with the inferior pole at the level of the aortopulmonary window. Trachea was diverted to the right side secondary to the local mass effect (figures 1 and 2). Posterior to the left thyroid lobe there was a nodular lession with a diameter of 25 mm and heterogenous structure.

Figure 1. CT scan of the thorax – enlarged left lobe with trachea diverted to the right

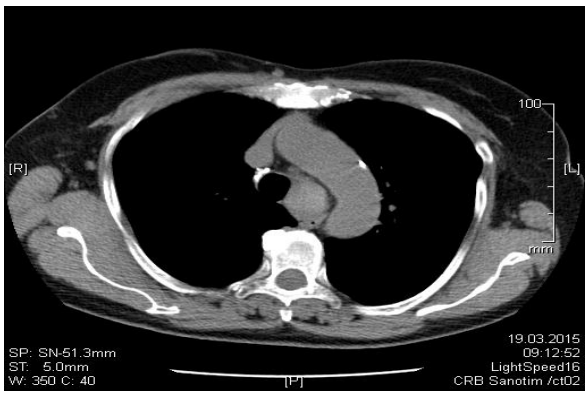

Figure 2. Left tyroid lobe had an extension posterior to the aortic arch down to the bifurcation of the trachea

Considering the compressive phenomena, the pacient has been transfered to the Second Surgical Clinic Timisoara for surgical treatment. After a preoperative meeting between the general surgeon, the anesthesiologist and the thoracic surgeon, the decision was made to begin the surgery with classical cervical approach, with the thoracic surgeon present and available in to the operating theather in case that sternotomy was required. Because of the fact that most of the goiter was located into the anterior mediastinum, thoracotomy was unlikely to be needed.

The surgery started with general anesthesia, followed by intubation using videolaryngoscope. Arcuated cervicotomy was performed at the base of the neck and after the bilateral sectioning of the subhyoidian muscles, acces was gained into the thyroid gland lodge. The right thyroid lobe had an increased volume (12/6/6 cm), with multiple nodules, with adhession to the trachea and the right recurent nerve, without exceding at the lower end the superior edge of the right clavicle. Total right lobectomy was performed without any difficulty.

The left thyroid lobe appeared to be increased of volume with a cervical portion of 16/10/6 cm, but with an intrathoracic extension, with a volume impossible to determine palpatory. The cervical part of the lobe was freed and the superior thyroid vessels were ligated, then dissection continued downwards to the level of the manubrium and the clavicle. Using mild traction cranially upon the left lobe, the rest of it was freed using ligatures of the lobe's attachements. As this maneuver continues, the intrathoracic part externalises gradually to the point when all of the left lobe was in the suprasternal cervical area (figure 3). The inferior thyroid vessels had a normal anatomical origin. The middle third of the left thyroid lobe presented a retrotracheal extension, with fibrous adhessions to the laryngeal recurrent nerve, leading to an intracapsular excision at this level. The thyroid lobe was extended posteriorly of the aortic arch down to the tracheal bifurcation and also into the posterior mediastinum. A drainage is left to the left lateral tracheal remaining cavity. Only the superior left parathyroid gland has been found and preserved.

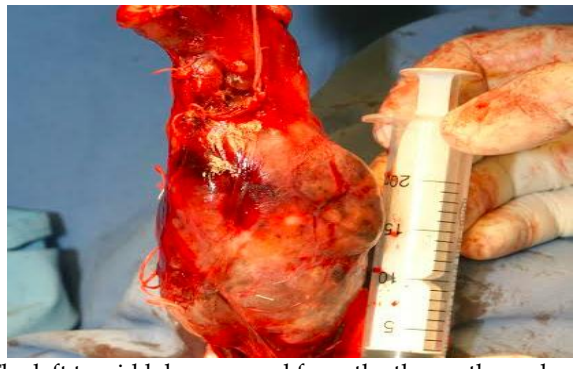

Figure 3. The left tyroid lobe removed from the thorax through cervicotomy

Postoperative course was uneventful, without dysphonia or tranzitory hypocalcemia. Considering the intubation difficulties the pacient received medium doses of intravenous Dexamethasone. The drainage tube has been removed on the 6th postoperative day, and the pacient was dismissed from the hospital on the 8th postoperative day. Histopathological exam did not revel any malignant lessions and the pacient started replacement hormone therapy with Euthyrox.

DISCUSSIONS

Mediastinal goiters are more frequent in women over 50 years old. In a study performed on 137 cases, Wei Du reported a number of 111 women and only 26 men, with an average age of 47,8 years [6]. In another study performed in 127 pacients with mediastinal goiters, there were 89 women and 38 men, with an average age of 62 [7].

Surgical treatment of a mediastinal goiter is based on the goiter type. In the third type goiters, sternotomy or thoracotomy are the only approaches possible, while in type 1 goiters, cervical approach is obvious. Choosing the proper approach is more difficult in type 2 goiters, especially the large ones extending to the superior mediastin. The case we presented was a type 2 goiter, approximately 75% of the gland's volume beeing located intrathoracic, extending posteriorly to the aortic arch and downwards to the tracheal bifurcation. In these cases, preoperative examinations are needed to provide information regarding the size of the goiter and the anatomical modifications of the mediastinum [8].

With these goiters, the question is always about the necesity of sternotomy or thoracotomy. One case, pretty much similar with the one we have presented, had been treated by some authors using posterior right thoracotomy [9], while others had performed thyroidectomy by cervicotomy [10]. Another case of retrosternal goiter, extending into the posterior mediastinum and retrotracheally, has been cured by cervicotomy followed by right thoracotomy [11].

On a series of 130 cases with intathoracic masses, Horvath has performed total thyroidectomy through cervicotomy in 106 cases: in the other cases cervicotomy with sternotomy was performed except for one case in which he performed cervicotomy with thoracotomy [8]. Nankee has conducted a study regarding all the goiters exceeding the superior opening line of the thorax. At this cases he had to perform 7 (5,5%) sternotomies on a series of 127 pacients [7]. In a series of 93 retrosternal goiters, one team from Maroco had performed sternotomy only in 4 (4,3%) cases [12].

Some authors have tried to identify clinical and imagistic data which could indicate the necesity for sternotomy or thoracotomy. Analizing 165 articles with this subject, McKenzie noticed that the thyroid tissue density was the most important risk factor for sternotomy, able to increase this risk up to 47 times [13]. Other risk factors to consider would be the long history of the retrosternal goiter, its size and position in the posterior mediastinum. Most of the authors admit that even if it is not always possible to predict whether sternotomy or thoracotomy will be compulsatory to perform, the CTscan gives information that allows an appreciation of the need for thoracotomy, guiding the surgeon how to perform this thoracotomy [14].

Despite all of this data, we must consider that over 90% of all the retrosternal goiters can undergo surgery with cervical approach [15]. In this given situations, through disection, step by step, of the periglandular plan, with the ligation of the superior and inferior thyroid vessels, the gradual goiter mobilisation will be possible, followed by its traction from the mediastinum up to the cervical region and complete excision by cervical approach only. The case we have presented is an exemple of this type of goiter. The surgery has been performed without any incidents or significant haemorrhage, without postoperatory dysphonia or tranzitory hypocalcemia.

Still, there are situation when the goiter located in the mediastinum has retrotracheal positions, sometimes with compressive effects over the great vessels, which will require thoracotomy. In this cases the recomendation is to remove the maximum possible of the goiter volume through a cervical approach, after which the cervical wound will be closed and right or left thoracothomy will be performed depending on the position of the mediastinal goiter [11]. In this situations we recommend a colaboration with the thoracic surgeon, which has to be present into the operating theather if the sternotomy or thoracotomy are required.

As a conclusion, the case we have presented proves the fact that even the pacients with large mediastinal goiter can undergo succesfull gland removal surgery through cervicothomy.

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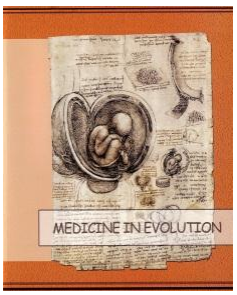
Eating behavior evaluation in Prader Willi Romanian patients



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Abstract

Introduction. Prader Willi syndrome (PWS) is a rare genetic disease, caused by a mutation of chromosome 15 or by uniparental disomy. It is the most frequent cause of genetic obesity, with a large clinical variability. Hyperphagia is a life-threatening symptom in PWS patients.

Aim. Our study aims to evaluate eating behavior in Romanian patients clinically and genetically diagnosed with PWS, to highlight the differences between male and female patients with PWS and to evaluate the correlation between the patients' weight and height and specific questions.

Material and methods. 11 patients, 4 girls and 7 boys, ranged in age from 2.1 to 30 years, were evaluated. All of them have a positive diagnosis of PWS. We applied a Hyperphagia quiz with 13 questions, divided into three groups. The items was rated from 1- not a problem to 5- severe problem.

Results. We identified significant differences for the mean of all answers for Hyperphagia behavior, between male and female- the female patients recorded higher values. For Hyperphagia Severity, we found higher values of answers in female. The obtained results highlighted a direct, significant and strong correlation between weight and BMI with Hyperphagia Behavior. A medium correlation was proved for Hyperphagia Severity.

Discussions. The insignificant differences were more frequent in our study. The small number of included patients could be a reason for those results.

Conclusions. In our study, the applied questionnaire did not seem to identify significant differences between male and female PWS patients regarding eating behavior. An important finding was more intense features in patients with a delayed diagnosis. Larger studies will offer the possibility to evaluate the differences of the specific symptoms in PWS between female and male patients and a better understanding of factors that interfere with those symptoms.

Keywords: Prader Willi Syndrom, Hyperphagia, questionnaire, eating behavior, food

INTRODUCTION

Prader Willi syndrome (PWS) is a rare genetic disease, the most common form of genetic obesity, caused by a mutation of paternal copy of 15q11.2-13, by a deletion of the specific region or by uniparental disomy [1, 2]. It affects approximately 1 from 1:10,000 to 1:30,000 newborns, male and female, and the prevalence is different according to geographic area [3, 4]. Clinically, PWS is characterized by a wide variability; the main important clinical signs are connected to eating behavior.

Disease specific features appear from utero with decreased fetal movement. At birth, the baby presents neonatal hypotonia, he cannot eat and needs enteral and parenteral nutrition. The development is slower than in other children. Usually, after the age of 3, the child starts to gain weight and the main cause is the hyperphagia, the absence of satiety. The patients have morbid obesity and its associated health problems. The cardio-respiratory diseases, secondary to obesity, are the most important causes of death in PWS patients, especially adults [5].

Hyperphagia is a very important symptom in PWS patients. Even if it is a life-threatening feature, it was not very well evaluated and understood by researchers [6].

In 2011, in a comprehensive article, Miller et al, highlighted the hyperphagia stages in PWS [7]. They described 5 stages and 2 sub- stages. The stage 0 is characterized by decreased fetal movements in utero and growth restriction; during stage 1, the patients are hypotonic-sub-phase 1a is considered between birth and 15 month of life and is marked by feeding difficulties compared sub-phase 1b (age 5-15 months) when patients have a constant growth and normal weight. Stage 2 has also 2 sub- phases. It is characterized by weight gain without a change in appetite (2a) or with a higher interest for food. Hyperphagia and lack of satiety appear in phase 3 (median age of onset was appreciated at 8 years). Phase 4 appears in some adults which became able to feel full.

There were different approaches used to evaluate hyperphagia. The use of questionnaires completed by parents or care providers is one of the easiest way to evaluate eating behavior [8].

The presented study used a Hyperphagia questionnaire with important items to evaluate the symptoms severity. It was completed by patients parents and was related to age, sex, weight, height and body mass index (BMI).

Aim

The study aims to evaluate eating behavior in Romanian patients clinically and genetically diagnosed with PWS and to highlight the differences between male and female patients and also the correlation between the patients weight, height and BMI and specific questions.

MATERIAL AND METHODS

We included 11 patients, 4 girls and 7 boys, ranged in age from 2.1 to 30 years [mean 15.8± 9.85 years). All girls and 2 boys were obese, with a mean BMI 50.61 kg/m2 and SD 4.51. All patients had a positive clinical score for PWS and a molecular confirmation of this diagnosis; three patients, boys, had an early diagnosis, in their first year of life and the parents could implement a specific diet, in order to prevent a specific PWS weight increase. The patients were divided into groups - male and female

Table 1 presents patients' characteristics.

Table 1. PWS patients characteristics

	Girls		Boys	
	Mean	SD**	Mean	SD
Age	25.37	6.36	10.37	6.77
Weight	112.75	16.31	67.61	58.33
Height	150.37	5.9	134.85	40.97
BMI*	49.88	4.95	29.18	16.53
- number of normal weight	-		4	
- number of overweight	-		1	
- number of obese	-		-	
- number of extremely obese	4		2	

*BMI- body mass index; ** SD- standard deviation

We applied the hyperphagia quiz [6], 13 questions divided into three groups: Hyperphagic Behavior (5 questions), Hyperphagic Drive (4 questions), Hyperphagic Severity (2 questions). The severity was evaluated "based on the definition of symptom-related impairment as operationalized by the American Psychiatric Association". The answers was rated from 1- not a problem to 5- severe problem (table 2).

Table 2. Hyperphagia quiz subgroups

Hyperphagic Behavior	**Hyperphagic Drive**	**Hyperphagic Severity**
How often does your child try to bargain or manipulate to get more food at meals?	How upset does your child generally become when denied a desired food?	Outside of normal meal times, how much time does your child spend talking about food or engaged in food-related behaviors?
How often does your child forage through the trash for food?	Once your child has food on their mind, how easy is it for you or others to re-direct your child away from food to other things?	To what extent to food-related thoughts, talk, or behavior interfere with your child's normal daily routines, self-care, school, or work?
How often does your child get up at night to food seek?	How persistent is your child in asking or looking for food after being told "no" or "no more"?	
How often does your child try to steal food (that you are aware of?)	What happened when others try to stop your child from talking about food or engaging in food-related behaviors?	
How clever or fast is your child in obtaining food?		

We calculated the mean for each question and we compared the results using a non-parametric statistical test, the Mann-Whitney U test [9]. We evaluated the answers for the quiz three groups. We considered a significance level of 0.05.

We also evaluated the correlation between weight, height and eating behavior. We applied Spearman's rank correlation coefficient with a significance level of 0.01 and 0.05. The height influence was evaluated using BMI [10].

In the end, we applied Cronbach Alpha coefficient [11] to test the quiz groups consistency (with a significance level alpha=0.7) and Kaiser-Meyer-Olkin method to appreciate the sampling adequacy.

Ethical considerations

All participants were informed about the study aim and protocol, the risks and benefits of the study. We explained to each one the nature of questions.

The study respects the Helsinki Declaration regarding confidentiality of data collected.

Their parents answered to included questions and they gave us the permission to publish the results.

RESULTS

Two questions were excluded from the statistical analysis (the age of onset of hyperphagia and variability in the drive for food).

The mean and standard deviation for each question are presented in figure 1.

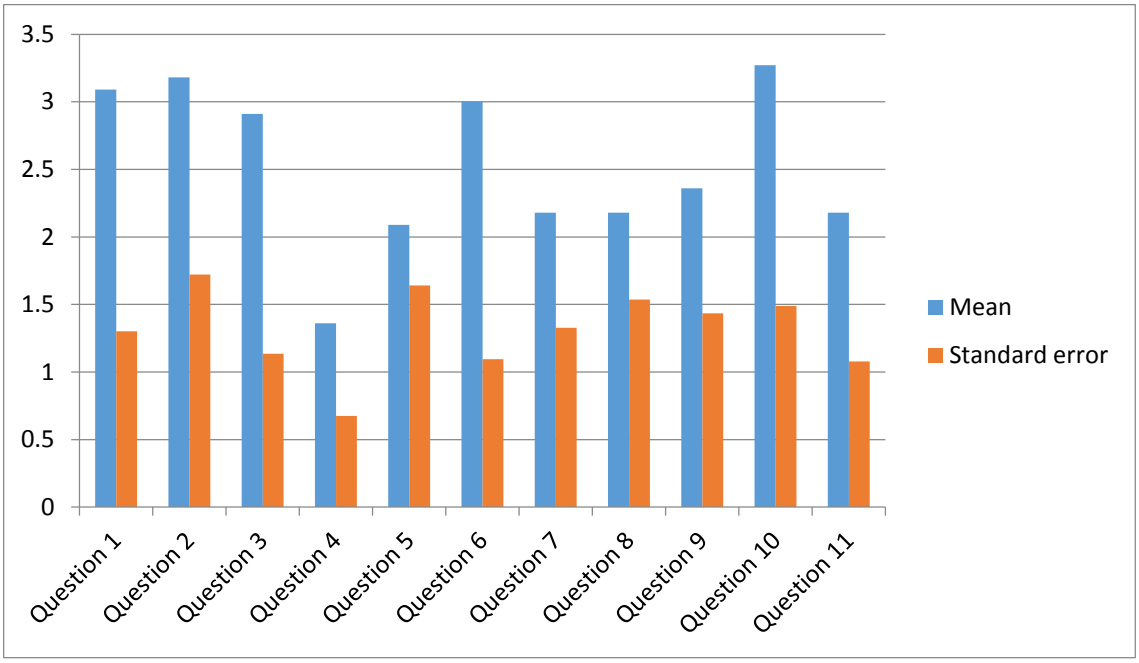

Figure 1. Mean and standard deviation

We created the two groups: males with 7 patients and females (4).

We did not identified significance differences between the two groups when we evaluated separately the answers for each question. The cumulate answers highlighted a higher mean value in female subjects compared with males (p-value= 0.035).

Table 3. Differences between males and females

Question	Gender	Number of participants	Mean Rank	Psign.
Q1	Male	7	5,00	0,176 ns
	Female	4	7,75	
Q2	Male	7	4,93	0,142 ns
	Female	4	7,88	
Q3	Male	7	5,14	0,240 ns
	Female	4	7,50	
Q4	Male	7	5,21	0,185 ns
	Female	4	7,38	
Q5	Male	7	4,93	0,099 ns
	Female	4	7,88	
Q6	Male	7	5,29	0,319 ns
	Female	4	7,25	
Q7	Male	7	4,57	0,047 s
	Female	4	8,50	
Q8	Male	7	4,64	0,057 ns
	Female	4	8,38	
Q9	Male	7	5,19	0,328 ns
	Female	4	7,20	
Q10	Male	7	4,93	0,134 ns
	Female	4	7,88	
Q11	Male	7	5,86	0,842 ns
	Female	4	6,25	

*Mean Rank- the mean from patients answers for each question
Psign- p-value
ns – insignificant difference
s - significant difference

The cumulative mean for each quiz group highlighted significant differences (p-value 0.035) between males and females in Hyperphagic Behaviour (table 4).

Table 4. Cumulative answer differences between males and females

Group	Gender	Number of participants	Mean Rank	$P_{sign.}$
Hyperphagic behaviour	Male	7	4,50	0,035 s
	Female	4	8,63	
Hyperphagic Drive	Male	7	5.32	0,294 ns
	Female	4	7.38	
Hyperphgic Severity	Male	7	4.93	0,148 ns
	Female	4	7.88	

The evaluation of correlation between patients weight and the mean of answers for included questions into Hyperphagic Behavior subgroup had as result a Spearman correlation coefficient $\rho=0,835$, $p=0,001$ and significance level $\alpha=0,01$- it revealed a direct, strong and significant correlation.

There also was a direct, strong and significant correlation between BMI and Hyperphagic Behavior (Spearman correlation coefficient $\rho=0,903$, $p<0,001$ and significance level $\alpha=0,001$).

For our included subject, we identified a Spearman correlation coefficient $\rho=0,524$, $p=0,048$ (significance level $\alpha=0,05$) between the patients weight and the mean of Q7 and Q11 (Hyperphagic Severity) answers.

Between BMI and this subgroup answers (Hyperphagic Severity) was a Spearman correlation coefficient $\rho=0,548$ and $p=0,039$ (significance level $\alpha=0,05$).

The age of hyperphagia unset was variable, from 1 to 10 years old. 45% of our patients had somewhere between 1 and 3 years old when they "first showed an increased interest in food".

45% from the patients parents declared that "child's preoccupation or interest in food" is usually the same, with no variation. We get only one answer ranged 5 on this question- child's preoccupation or interest in food goes up and down all the time. This came from a male patient, aged 17 years old, with 120kilograms weight, 157 centimeters height and BMI 48.78 kg/cm2.

The Cronbach's alpha coefficient for intern consistency was different for each quiz group; for Hyperphagic Behavior 0.880, for Hyperphagic Drive 0.888 and 0.398 for Hyperphagic Severity.

86% (85.83%) of quiz variation is given by the first group (Hyperphagic Behavior) while the third group contribution is insignificant (5.57)- Kaiser-Meyer-Olkin method.

DISCUSSIONS

The present study evaluated important items in severity and range of hyperphagia.

The answers were different between males and females but we did not identify significant differences. When we considered the entire subgroup, Hyperphagia Behavior, the differences between them were statistically significant- the female group had more severe specific symptoms for this area, they tried to manipulate, to steal or to forage through the trash for food more often compared with male patients. This could be explained on the one hand by their age (female had an older age than male) because the lack of satiety worsens

with age in PWS; on the other hand it could be more severe in female patients, no matter the age.

Hyperphagic behavior questions had a strong and significant correlation with patients weight and height- patients with an increased weight and BMI had a higher correlation coefficient than the others. There also was a direct, significant and medium correlation with Hyperphagic severity. For our cohort, the food was more important and interferes with normal daily routines for obese patients. PWS female patients spent more time "talking about food or engaged in food-related behaviors" than males (p-value for question 7= 0.047) according to our results.

Evaluating the group consistency, we noticed that the third group (Hyperphagic Severity) had consistency problems (alpha< 0.7).

The insignificant differences were more frequent in our study. The small number of included patients could be a reason for those results. Larger studies will offer the possibility to evaluate the differences of the specific symptoms in PWS between female and male patients and a better understanding of factors that interfere with those symptoms. A national record of PWS patients would be very useful in this direction.

A larg study from E. Dykens et al used the same quiz in 153 persons (55% men and 45% women) with PWS. They succeeded to enroll a large number of participants, patients with a rare disease which is an achievement and frames this study into one of the most important studies for this area. The data analysis was performed comparing different groups of patients according to their age [6].

The Children's Eating Behavior Inventory is another type of hyperphagia questionnaire used especially in patients with anorexia or bulimia. It was applied in PWS patients but unfortunately it does not include questions for important eating behavior abnormalities which are typical in PWS- steeling food, getting up at night to seek food, "foraging through the trash for food" [12].

Russell and Oliver elaborated a 16-items questionnaire- Food-Related Problems Questionnaire (FRPQ). It was addressed to PWS patients but there are some important limitations. Some questions require a verbal answer from PWS patients and this implies important biases because of incapacity of some PWS patients to express themself or the answers could be influenced by different factors. It does not evaluate the severity of symptoms and the "items and domains were derived from focus groups with parents, and items were not subjected to statistical analyses that confirmed these classifications" [6,13].

Some studies placed patients with PWS in rooms with different types of food, some of them were contaminated, and the investigators evaluated their eating behavior and food-seeking behavior [14, 15].

Strengths and limitations

The presented study evaluated patients with a rare disease (PWS). Although, it included a small cohort (11 patients), they were characterized by a large clinical variability that highlighted the eating behavior problems in PWS. They also had very different diagnosis ages, a very important predictive factor of quality of life in those patients. We identified the repercussions of a delayed diagnosis and the importance of an easier accessibility to genetic counseling.

We could not obtain all needed information about the patients and their medical history because most of them did not have the medical papers and did not know exactly what to answer about the IQ or other similar questions. The rare diseases area is relatively new in Romania and this could be the reason why some patients were diagnosed only after the age of 20's with a very aggressive eating behavior.

CONCLUSIONS

In our study, the applied questionnaire did not seem to identify significant differences between male and female PWS patients regarding eating behavior. An important finding was more intense features in patients with a delayed diagnosis highlighted once again the importance of awareness and acknowledges in rare diseases area amongst medical staff and normal population also. It could be very useful to applied this quiz in larger cohort and correlate it with genetic cause of disease and other specific features.

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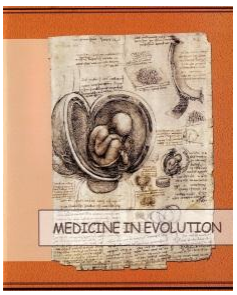
Acromegaly profile on menopausal women after 36 months of medical therapy with somatostatin analogues



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Abstract

Acromegaly is mostly caused by a pituitary adenoma- related growth hormone excess. The use of somatostatin analogues as octreotide LAR is widely recognised but their availably depends on each country protocol and their efficacy varies. A series of three subjects diagnosed with acromegaly and secondary amenorrhea is followed for 36 months. The first six months they were treated with octreotide LAR 20 mg per month then one patient increased to 30 mg and another after one year. Both of them were further diagnosed with diabetes mellitus and have active disease two months after stopping the medication. The third subject (who previously undergone only pituitary radiotherapy) achieved diseases control after three years of octreotide LAR 20 mg. We found no gallstones in the patients. Follicle -stimulant hormone was suggestive for central ovarian insufficiency in two cases. Based on our observations after three years of monthly octreotide LAR in menopausal women the disease was still active two months after stopping the drug in cases to whom the dose increase was necessary during first 24 months; new cases of diabetes mellitus were discovered in the situations with inadequate disease control.

Keywords: acromegaly, menopause, octreotide

INTRODUCTION

Acromegaly represents a complex endocrine disorder caused by growth hormone excess which is mostly secreted by a pituitary adenoma [1,2,3]. The cardiovascular, bone, and potential oncologic anomalies are caused by somatotrope hormone itself but also by Insulin Growth Factor 1 (IGF1) which is produced at hepatic level due to growth hormone stimulation [1,23]. The metabolic disturbances as high blood pressure, hyperlypemia, diabetes mellitus, cardiomyopathy, ischemic heart disease are similar to the metabolic syndrome except for the cause: the excess of both GH and IGF1 [3,4,5]. The management of the underlying tumour varies from pituitary surgery or radiotherapy to medical treatment which is focused on somatostatin analogues as octreotide or lanreotide, growth hormone receptors blockers as pegvisomant, and dopamine analogues as cabergoline [2]. Usually, the macroadenoma remission ratio after surgery is lower than seen in microadenomas (less than 50%) thus the need for medical therapy. [3,6]. The combination of different therapeutically options allows control disease in a majority of cases with improvement of baseline complications [3,6]. The use of somatostatin analogues is widely recognised. The molecule mimics somatostatin which is a cyclic hormone with peptide formula displaying into the human body inhibitory effects on pituitary hormones as GH or pancreatic hormones as insulin [7]. Five types of somatostatin receptors are described and the pharmacological products as octreotide or pasireotide have different affinity on different types [7,8]. They are long-acting somatostatin analogues with different clinical applications as acromegaly and carcinoid tumours (octreotide, lanreotide), Cushing's disease (pasireotide) [7,8]. Compare to octreotide and lanreotide which are highly selective for type 2 receptors, pasireotide has increased affinity for type 1, 2, 3, and 5 and no effect on type 4 [8,9]. Overall, current pharmacotherapy options induces biochemical control of GH and IGF1 excess, and, potentially, the tumour size control also not all the cases have an optimal expected response [10]. The lack of medical therapy efficacy is explained by poor compliance, therapy resistance, drug side effects as worsening the glucose metabolism profile or gallbladder stones on somatostatin analogues [11]. We aim to introduce three females cases series analyze, patients who were diagnosed with acromegaly and associated secondary amenorrhea, focusing on GH and IGF1 pattern under long-term therapy with octreotide LAR as well as the gonadal function.

CASES SERIES

In each case, acromegaly was confirmed based in 75-grams oral glucose loading tolerance test (OGTT) providing a nadir GH (ELISA kit) level more than 1 ng/mL during the test and Insulin Growth Factor 1 (IGF1) levels above the normal limit for age and sex. All patients had the medical history analyzed, the imagery confirmation based on computed tomography (CT) or magnetic resonance imagery (MRI). The study was conducted by starting the octreotide therapy in a single tertiary centre of endocrinology, between 2009 and 2014; regardless the females have previous presentations at different endocrinology, gynaecology, neurosurgery centres. The entire three patients were first confirmed with pituitary condition while they had secondary amenorrhea, and they were followed for more than 36 months. First six months, octreotide LAR was offered to each patient 20 miligrams (mg) by intramuscular injection every 28 days. A first evaluation of GH and IGF1 is done after three months. Six months from baseline the hormonal panel was re-done: fasting IGF1 and GH within OGTT if the patient is not diabetic or, in case of uncontrolled diabetes mellitus, 24-hour GH profile (at least four assays within 24 hours and the mean GH should be above 2.5 ng/mL to confirm active disease). If the control of acromegaly was not adequate, a higher dose of octreotide LAR may as 30 mg every 28 days was offered. After the first 36 months of therapy an octreotide free interval of 2 months afterwards the tests was performed again in

order to check the acromegaly status. If the pituitary tumour was still active, the somatostatin analogue was re-introduced. **(Fig.1**) Also during OGTT the diagnosis of diabetes mellitus may be established by 2 hours blood glucose of ≥ 200 mg/dL [12]. The endocrine and imagery changes as well as side effects under medication are registered and analyzed. All the patients gave their consent. The patients were aged between 51 and 68 years (at baseline when introducing therapy with octreotide LAR). Patient 1 was found acromegalic at age of 42. Typical clinical features as well as central hypogonadism were presented. She had selective pituitary surgery and radiotherapy done (12,000 R azi). **(Table 1)** Later on, at age of 68, the disease was still active and 12 months after a 20 mg dose of octreotide LAR the GH nadir was not adequately suppressed so she continued with monthly 30 mg. After 36, respective 2 months of octreotide LAR, free drug interval, GH and IGF1 secretions were high and a dose of 30 mg was further recommended. **(Table 2)** No gallbladder stone was found but diabetes mellitus was found after 1 year of octreotide LAR 20 mg per month. **(Table 3)** Patient number 2 was confirmed with GH producing adenoma at age of 45 displaying specific clinical characteristics. She had both pituitary surgery and radiotherapy done and residual active disease was continued for 6 years when monthly octreotide LAR was started. **(Table 1)** After first 6 months of therapy the dose was increased to 30 mg per month and later 2 months free of therapy after the first 36 months the acromegaly was still active so 40 mg per months were recommended. **(Table 2)** She had diabetes mellitus diagnosed after the first 30 months of therapy when she was treated with 30 mg per month of octreotide LAR**. (Table 3)** Patient number 3 had GH secreting tumour confirmed at age of 51. No surgery was performed but pituitary radiotherapy was applied with secondary persistent disease. **(Table 1)** 6 years later (at age of 57) octreotide LAR was started with a general improvement of GH and IGF1 values after 36 months of therapy. **(Table 2)** At the end of 2 months (when octreotid LAR was stopped) the diseases was remitted. No side effects were seen regarding gallbladder, neither glucose profile. **(Table 3).**

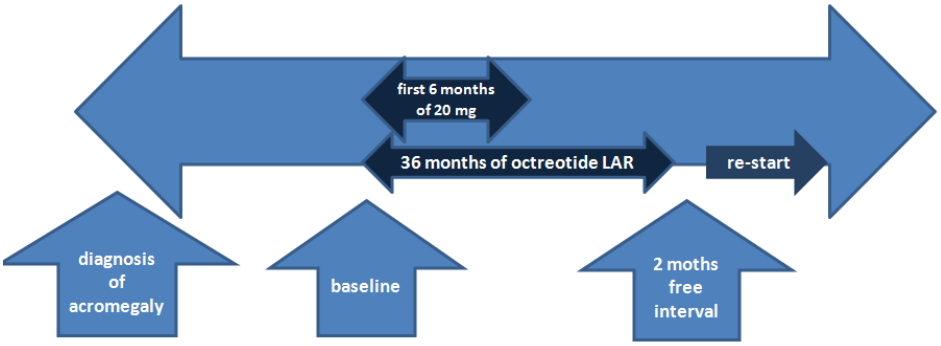

Figure 1. Octreotide LAR protocol from baseline, the first 6 months under monthly 20 mg and then 20 or 30 mg per months; after then a 2 months free interval is required and in case of persistent acromegaly re-administration is necessary

Table 1. Medical history of the patients at baseline (when octreotide LAR was started)

	patient 1	patient 2	patient 2
diagnosis before baseline of therapy (years)	-26	-6	-6
tumour size (macro/microadenoma)	macro	macro	macro
pituitary surgery	yes	yes	no
pituitary radiotherapy	yes	yes	yes
high blood pressure	yes	yes	yes
visual field defects	yes	no	no

Table 2. The octreotide LAR regimes during the 36 months of therapy and after 2 more months of stopping the drug (last column). The values of fasting blood glucose and 2 hours after 75-g (grams) OGTT; the fasting values of IGF1 (normal levels between 44 and 240 ng/mL); the value of Growth Hormone (GH) in OGTT (first value and nadir)

	parameters	baseline	3 months	6 months	12 months	24 months	36 months	36+2 months
patient 1	octreotid LAR monthly dose (mg)	20	20	20	30	30	30	30
	fasting blood glucose (mg/dL)	66	72	62	98	90	91	99
	2-h glucose (OGTT) (mg/dL)	175	186	178	234	233	223	255
	IGF1 (ng/mL)	601	199	191	247	108	211	266
	nadir GH in OGTT (ng/mL)	3.52	1.9	1.93	1.65	0.8	1.6	3.03
	fasting GH (ng/mL)	5.63	2.52	2.03	1.89	1.02	2.6	3.12
patient 2	octreotid LAR monthly dose	20	20	30	30	30	30	40
	fasting blood glucose (mg/dL)	94	128	104	128	96	98	99
	2-h glucose (OGTT) (mg/dL)	97	138	138	138	173	200	201
	IGF1 (ng/mL)	775	308	435	570	753	320	416
	nadir GH in OGTT (ng/mL)	7.76	15	11.1	6.4	2.83	1.8	2.2
	fasting GH (ng/mL)	11.2	20.9	13.1	8.33	4.18	3.6	5.37
patient 3	octreotid LAR monthly dose	20	20	20	20	20	20	stop
	fasting blood glucose (mg/dL)	93	87	71	87	70	96	85
	2-h glucose (OGTT) (mg/dL)	62	60	61	67	76	69	56
	IGF1 (ng/mL)	838	495	240	666	122	104	211
	nadir GH in OGTT (ng/mL)	24.3	8.9	1.93	5.1	0.8	0.34	0.72
	fasting GH (ng/mL)	15.8	9.7	2.96	5.08	0.93	0.37	0.86

Table 3. The endocrine parameters after 36 months of octreotide LAR (*) and the side effects (#)

	Patient 1	Patient 2	Patient 3	Normal levels
FSH*(Follicle Stimulant Hormone) (UI/mL)	29	60	26	>40mUI/mL suggestive for menopause
Prolactin* (ng/mL)	9	7	38	1.3-20 ng/mL
FreeT4* (pmol/l)	1.7	1.1	1.32	
Morning plasma cortisol* (µg/dL)	11.4	16.8	11.7	5-25 µg/dL
Tumour maximum diameter changes* (mm)	17→24	10→4	18→cystic transformation	
Visual fields defects*	yes	no	no	Stationary from baseline
Diabetes mellitus # (DM)	yes	yes	no	
The dose of octreotide LAR at the moment of DM diagnosis (mg/month) #	20	30	no	
The interval of octreotide LAR therapy when DM was diagnosed #	9	30		

DISCUSSIONS

Several key points are related to the mentioned cases. Clinical phenotype included secondary amenorrhea from diagnosis of acromegaly. Three years after octreotide was started, only in case 1 and 3 central hypogonadism component was confirmed based on Follicle -stimulant hormone (FSH) values; the patient number 2 had FSH adequate for menopausal status in a subject with intact central gonadotropes function. Generally, GH secreting tumours involve lack of menses because of secondary ovarian failure due the pituitary mass effects and/or hyperprolactinemia [13]. Whether hypogonadism represents a particular contributor to the metabolic impairment or the disease control under medication is still difficult to establish.

On the other hand, the therapy with analogue of somatostatin was followed for at least three years in each patient and after two months of octreotide LAR free interval, the drug was re-started. The period of time to be recommended is prolonged. Despite the good cost efficient profile for octreotide LAR if the tumour remission is not registered (for instance, the

case number 2) a second decision in acromegaly management is necessary as re-intervention or adding pegvisomant, apart from increasing the doses of somatostatin analogue [14]. Overall, the studied patients registered an improvement of GH and IGF1 levels: in patient number 1 adequate nadir of GH was seen after 24 months and IGF1 normalization after three months of octreotide LAR. In patient number 2, there was a 30% decrease of IGF1 after three years but GH was never less than 1 ng/mL in OGTT during the first three years. Subject number 3 had controlled levels of GH after two years and IGF1 levels although fluctuating were normal after six months of octreotide LAR 20 mg per months. A real life study published in 2015 revealed that the outcome in acromegaly is correlated with less than 36% of the patients that actually obtain the targeted GH and IGF1 values when octreotide LAR is started [15].Yet, general data agree that the drug is effective in controlling the symptoms, the hormonal excess, and eventually the tumour mass in acromegaly and it represents an elegant option especially in subjects that are not cured by surgery (as patients number 1 and 2 were) or in the window to reveal the radiotherapy efficacy (as subject number 3) [16]. The side effects we analysed are the gallbladder stones that were not registered at ultrasound at any patient although a high percent is reported in many studies because of the billiary effects of somatostatin [17]. Diabetes mellitus was discovered in two subjects based on 2-hours glucose levels on OGTT. The anomaly is caused by the somatostatin blocking effect on insulin (which is the major hypoglycemic hormone) while GH (which acts a hyperglycemiant agent) is reduced thus some improvement in glucose profile might be seen [18].

CONCLUSIONS

Based on our observations after three years of monthly octreotide LAR in menopausal women the disease was still active tho months after stopping the drug in cases when increasing the dose was necessary during first 24 months; new cases of diabetes mellitus were discovered in the situations with inadequate disease control.

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Conflict of interest

None.

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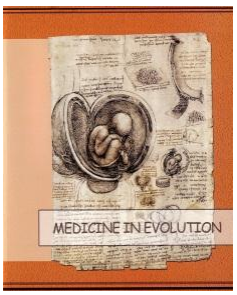
Sarcoid-like reaction and amyloid deposition in the pelvic lymph nodes from a patient with endometrial carcinoma – A case report and extensive review of literature



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Abstract

Sarcoidosis is a chronic inflammatory disease of unknown etiology commonly affecting young adults, which is defined by a widespread development of non-caseous epithelioid granulomas in multiple organs, especially the lungs. We report the case of a 67-year-old postmenopausal woman presenting with a well-differentiated (G1) endometrial endometrioid carcinoma and several non-confluent and non-caseous epithelioid granulomas and localized amyloid deposits, scattered in several pelvic lymph nodes, in the absence of any metastases. The diagnosis of systemic sarcoidosis was excluded based on the clinical profile, imaging and pulmonary function tests as well as the histopathological aspects of the granulomas and immunophenotyping of the lymphocytes. All histopathological findings were consistent with the notion of sarcoid-like reaction. The association with localized amyloidosis piques the interest whether this is the result of a long-term immunological defense mechanism against the concurrent endometrial malignancy or if it is merely a coincidence.

Keywords: sarcoid reaction, amyloid, endometrial carcinoma

INTRODUCTION

Sarcoidosis, which in Latin translates as "meaty chunk-like lesions" [1] is a multisystemic chronic inflammatory disease of unknown etiology commonly affecting the lungs and lymphatic system. Its histopathologic hallmark is represented by the widespread development of variable-sized non-caseous epithelioid granulomas within multiple organs, including the lungs, eyes, skin, nerves, bones and heart [2]. Virtually all cases of sarcoidosis involve the respiratory tract to some extent, pulmonary sarcoidosis being one of the most frequent causes of interstitial lung disease [3]. Cancer-associated sarcoidosis is a relatively common entity which is frequently described in the [4-6] scientific literature. There are also several case reports of cancer-associated non-caseous epithelioid granulomas which do not fulfill the diagnostic criteria for systemic sarcoidosis, but present with similar clinical and histological features. Many authors refer to these findings as sarcoid-like reactions. The real incidence of their association with malignancy is difficult to determine because the scientific literature contains mostly case reports, which usually aid in generating hypotheses rather than establishing evidence-based facts [7]. However, most cancer-associated sarcoid-like reactions are reported in patients with lung cancer or lymphoma [8-10].

In the gynecologic field, the scientific literature contains multiple case reports of sarcoidosis or localized lymph node amyloidosis associated with uterine cancer. However, we were unable to find any reports or descriptions of sarcoid-like reactions consecutive or subsequent to endometrial malignancy. To our knowledge, this case may represent the first report of sarcoid-like reaction and amyloid deposition associated with endometrial carcinoma.

MATERIAL AND METHODS

Here, we report the case of a 67-year-old postmenopausal woman presenting to our clinic with abnormal genital bleeding and dull lower abdominal pain. Computer tomography of the pelvic region revealed an intrauterine tumor mass and several enlarged pelvic lymph nodes with short-axis diameters ranging between 0.8 and 1.4 cm.

The patient underwent endometrial biopsy, which revealed a well differentiated endometrial endometrioid carcinoma, followed by radical hysterectomy with bilateral salpingo-oophorectomy. Histopathological processing, staining and examination of the specimen were performed in the Department of Pathology of the University Emergency Hospital in Bucharest Romania. We must mention that the therapeutic management did not involve any type of preoperative chemo- or radiotherapy.

RESULTS

Histopathological examination of standard stained slides from the hysterectomy specimen revealed a FIGO Stage IB well differentiated (G1) endometrial endometrioid carcinoma. Interestingly, upon microscopic examination of the internal and external iliac lymph nodes, we identified several small, scattered, non-confluent and non-caseous epithelioid granulomas, composed of irregularly distributed epithelioid cells, lymphocytes, macrophages and rare multinucleated giant cells. There was no evidence of asteroid bodies, Schaumann bodies, eosinophils, necrosis or malignancy. Immunohistochemical staining for pan B-cell markers CD19 (mouse monoclonal antibody, isotype IgG1, dilution 1:100, provided by Biocare Medical, catalog number CM 310 A) CD20 (mouse monoclonal antibody, isotype IgG2a/kappa, clone L26, dilution 1:100, provided by Biocare Medical, catalog number CM 004 A) and CD22 (mouse monoclonal antibody, isotype IgG1, clone FPC1, dilution 1:100, provided by Biocare Medical, catalog number CM 169 B) revealed diffuse positivity within

the granulomas and intense perigranulomatous immunopositive reaction. Immunostaining for AE1/AE3 pan-cytokeratin (mouse monoclonal antibody, isotype IgG1, clone AE1/AE3, dilution 1:50, provided by Biocare Medical, catalog number CM 011 A) was negative. Moreover, the granulomatous structures were diffusely positive with Congo Red staining (provided by DiaPath, code 010214), showing apple green birefringence in polarized light and dull pink proteinaceous material with van Gieson staining (provided by DiaPath, code 010218). These findings are consistent with the diagnosis of sarcoid-like reaction with amyloid deposition.

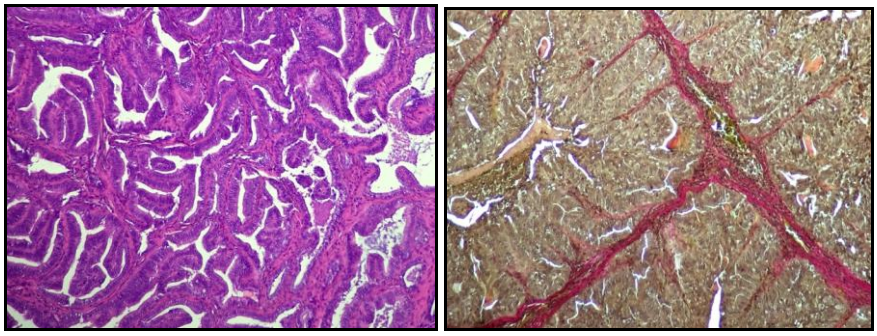

Figure 1&2. Microscopic appearance of endometrial endometrioid carcinoma showing crowded villoglandular structures with architectural and cytologic atypia, separated by thin strands of mostly acellular, desmoplastic stroma (right: H.E., 100x, left: van Gieson, 100x)

After the unexpected discovery revealed in the pelvic lymph nodes, all tumor slides have been thoroughly reviewed in search of similar features, yet we were unable to identify any intra- or peritumoral area with amyloid deposits or epithelioid granulomas.

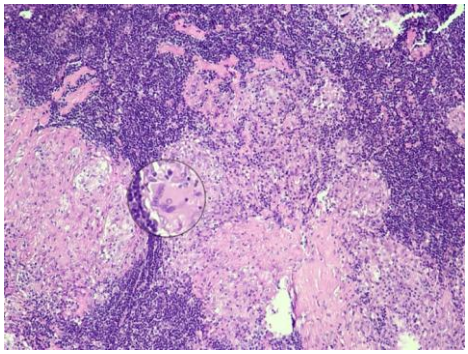

Figure 3. Microphotograph of a pelvic lymph node composed of non-confluent and non-caseous epithelioid granulomas with irregularly distributed epithelioid cells, lymphocytes, macrophages and rare multinucleated giant cells (H.E., 100x)

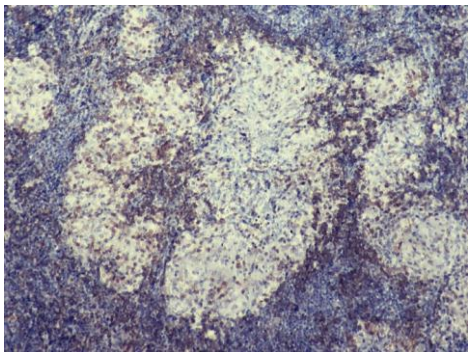

Figure 4. Immunostaining for CD20, revealing diffuse positivity within the granulomas with a more intense perigranulomatous immunopositive reaction (CD20 immunohistochemical staining, DAB cromogen, 100x)

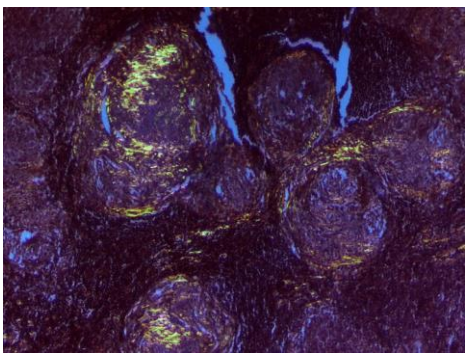

Figure 5. Microphotograph of a pelvic lymph node with amyloid deposits, confirmed by apple-green birefringence in polarized light (Congo Red stain, 40x)

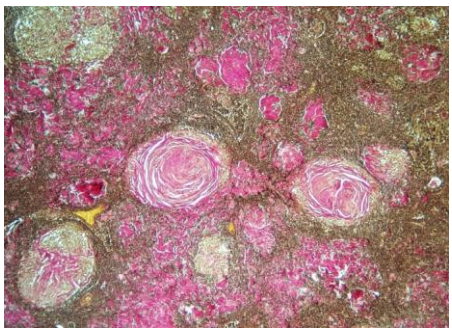

Figure 6. Microphotograph of a pelvic lymph node showing epithelioid granulomas with pink collagenous material (van Gieson stain, 40x)

The diagnostic possibilities of systemic sarcoidosis and/or tuberculosis were excluded due to extensive examination specific for these diseases. Special stains (Ziehl-Neelsen) for acid-fast bacilli and fungi were negative. Tuberculin test results were also negative. Chest X-ray showed no signs of hilar lymphadenopathy, micronodular opacities or consolidation. Six months after surgery, a repeated CT-scan of the pelvic region revealed spontaneous resolution of all previously noted nodules.

DISCUSSIONS

Sarcoidosis also known as Besnier-Boek-Schaumann disease is a systemic disease of unknown etiology which affects mostly young individuals, regardless of race, sex or age [3]. Establishing the diagnosis of sarcoidosis requires compatible clinical and imagistic findings (bilateral enlargement of the hilar nodes and pulmonary infiltrate with perivascular distribution) as well as the histopathologic identification of non-caseating epithelioid granulomas in at least two organs, with exclusion of all known causes of granulomatous disease. Therefore, sarcoidosis remains a diagnosis of exclusion, which requires extensive clinical data [11].

Non-caseating epithelioid granulomas are not pathognomonic for systemic sarcoidosis and may be occasionally identified in regional lymph nodes with an underlying pathology [1], without any clinical evidence of sarcoidosis. This finding is referred to as "epithelioid granuloma", "tuberculoid granuloma", "pseudotuberculous reaction", "sarcoid-like reaction", "sarcoid reaction" [8] or simply “sarcoidal” and it has been reported in association with various diseases such as: carcinoma (of the uterus, breast, lung and stomach) [8,12-14], toxoplasmosis, fungal infection, tuberculosis, atypical mycobacterial disease, pneumoconiosis, immunocompromised status (Crohn's disease, primary biliary cirrhosis and Sjögren's syndrome), extrinsic allergic inflammatory alveolitis (farmer's lung) and anticancer chemotherapy, as well as in association with various chemicals (beryllium, zirconium, silicon, starch granules and pine pollen) [1,15]. Similar to sarcoidosis, sarcoid-like reactions are usually asymptomatic and self-limiting, treatment being rarely required [16].

Sarcoidosis was first observed in 1869 by the British physician Jonathan Hutchinson who considered it a variant of mumps and described it as a "livid papillary psoriasis" in a patient with “peculiar patches of dark purplish color on his extremities” [17]. The condition was later described by Boeck [18] in 1899 on 24 patients with “benign miliary lupoids” and by Wolbach [19] in 1911 on 5 patients with “widely distributed miliary-sized lesions of granulomatous character”. However, its association with cancer was not recognized until 1917, when Herxheimer [20] described sarcoid-like granulomas in patients with carcinomas of the breast, rectum and cystic duct. Further research performed throughout the first decades of the 1900s eventually allowed Nickerson in 1937 to establish a clear distinction between localized development of sarcoidal granulomas and sarcoidosis – a multisystemic disease with various symptoms and serum abnormalities [21], which was later acknowledged as a tumor-related histologic change, termed "sarcoid reaction". Further studies performed by Brincker [22] in the early 1990s divided these conditions in two main categories, based on the presence or absence of B cells within the granulomas. He observed that B-cell-negative granulomas occurred in sarcoidosis and mycobacterial infections while the B-cell-positive ones were associated with malignant tumors, toxoplasmosis and other granulomatous lesions of unknown significance [23].

Although its physiopathology has not been elucidated yet, the sarcoid-like reaction can be defined as a granulomatous lymphadenitis resulting from a long-term immunological defense mechanism of persistently stimulated lymph nodes against metabolites and breakdown products of malignant tumors [24-25]. At molecular level, the induction and evolution of granuloma formation results from a complex interplay between different cell populations, cytokines, and chemokines.

Sarcoid reactions have been reported in association with various types of primary tumors, either in the vicinity of the tumor itself, or within the regional lymph nodes draining that particular tumor, even in the absence of any metastases. According to a thorough review of literature, sarcoid-like reactions have been described in lymphomas [12], lung cancer [26], gastric cancer [27], breast cancer [28], testicular cancer [29], renal cell carcinoma [30] and leiomyosarcoma [31]. Statistical studies reveal that sarcoid-like reactions appear 4 times more often in regional lymph nodes without metastases than in metastatic ones. Also, the presence of sarcoid-like reactions in advanced-stage cancers appears to be associated with a more favorable overall prognosis [32-33].

It is also worth taking into consideration the interplay between sarcoid-like reactions and immunodeficiency. A recent report from the ophthalmology service of the Hospital of Avicenne in France, described two cases of malignancy associated with sarcoid-like reactions of the lung which occurred a few months to few years after the patients were diagnosed with immunodeficiency [34]. In our case, no immunologic tests were performed in order to evaluate the immunologic status of the patient, but there was no clinical suspicion of immunodeficiency.

The combination between sarcoidosis or sarcoid-reaction and amyloidosis has rarely been described [35-37] in the scientific literature. Case reports of sarcoidosis associated with AA amyloidosis suggest that the sarcoid-related inflammatory process is very likely to be involved in the pathogenesis of amyloidosis. However, there is no consensus on whether there is a relation between sarcoid reactions and AL amyloidosis or if their coexistence is merely a coincidence. In this paper we discuss the case of a peritumoral lymph node sarcoid-like reaction accompanied by localized amyloid deposition.

Amyloidosis is defined by its precursor protein and can be classified as acquired or hereditary and as local or systemic [38-39]. The acquired forms of amyloidosis are: primary amyloidosis (AL type, systemic), local nodular amyloidosis, secondary amyloidosis (AA type, systemic and reactive) and senile systemic amyloidosis. Primary (AL) amyloidosis is associated with plasma cell disorders (multiple myeloma), the abnormal protein being derived from immunoglobulin light chains (AL amyloid) or, less commonly, immunoglobulin heavy chains (AH amyloid). Local nodular amyloidosis primarily affects the skin, respiratory and urogenital tract, the abnormal protein being derived from immunoglobulin light chains as well. Secondary (AA) amyloidosis is associated with various forms of cancer and inflammatory conditions, including chronic infections (osteomyelitis, leprosy, bronchiectasis), rheumatoid arthritis and Crohn's disease, the abnormal protein being derived from serum amyloid A protein (SAA protein), a normal serum acute phase reactant and a novel marker for endometrial carcinoma [40]. Approximately 25% of elderly individuals present senile systemic amyloidosis, characterized by clinically silent systemic deposits, which are usually widespread in the myocardium, resulting in life-threatening cardiac dysfunction. Various forms of autosomal dominant hereditary amyloidosis have also been described [3].

The physiopathology of lymph node amyloidosis is usually correlated with an underlying clonal lymphoproliferative disorder such as lymphoplasmocytic lymphoma, marginal zone lymphoma, chronic lymphocytic leukemia [41-44] or an IgM monoclonal paraproteinemia [45-48]. An extensive study on lymph node amyloidosis performed in a single institution revealed that localized lymph node amyloid deposition is associated either with a peritumoral distribution, defined as amyloid restricted to sites of detectable lymphoma or localized, defined as lymph node amyloidosis without lymphoma or a circulating monoclonal protein.

CONCLUSIONS

In cancer patients, lymph node enlargement due to sarcoidosis or sarcoid-like reactions could mimic advanced-stage metastatic disease, eventually leading to an incorrect

therapeutic management. Preoperative differential diagnosis between metastasis, sarcoidosis and sarcoid reaction based on non-invasive imagistic investigations is impossible or unreliable. Therefore, histopathological examination is mandatory in order to distinguish between these diseases. The association with localized amyloidosis seen in our case piques the interest whether this is the result of a long-term immunological defense mechanism against the concurrent endometrial malignancy or if it is merely a coincidence.

Conflict of interests

None to declare.

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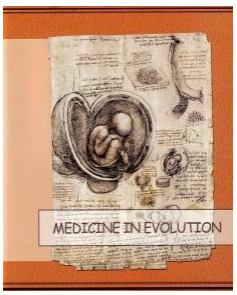
Anthropometric measurements of the orbit. A study on 332 orbital cavities using dry skulls



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Abstract

The orbit is one of the most complex and variable anatomic structures; hence the assessment of orbital dimensions in the normal population is essential not only from an anthropologic point of view but also for the surgical management of different diseases. The objective of the study was to measure important orbital dimensions in dried skulls using a digital Vernier Caliper and define the effects of gender on orbital anthropometry.

Materials and methods: We measured orbital width, height, depth, length of the medial and lateral wall, biorbital and interorbital diameter and orbital index in 166 adult skulls (332 orbital cavities) and compared right and left sides and male to female.

Results: The mean orbital index was 83.28 ±5.46. The population belongs to the mesoseme category. The orbital height, width, biorbital and interorbital widths, length of the medial and lateral walls were higher in males than in females and the differences were statistically significant ($p<0.001$). Orbital depths were comparatively evaluated between gender groups and no statistically significant difference was found. No differences were found between the orbital index of male and female orbits.

Conclusions: The study revealed important differences of most orbital dimensions between genders but it also provides an important baseline of anthropometric data for multidisciplinary clinical and surgical use.

Keywords: direct measurements, orbital dimensions, Vernier Caliper, orbital index, mesoseme

INTRODUCTION

The orbit is one of the most complex structures of the human skull. The interest for measuring the diameters and volume of this highly variable and complicated anatomic structure started more than a century ago and there is still no standardized method approved worldwide. Measurements of the orbit are vital given the multitude of pathology involving this anatomic region. Traumatic orbital fractures, congenital diseases, intraorbital tumors, inflammatory diseases are frequent and this explains the multidisciplinary interest in correctly measuring and quantifying the orbital contents [1]. Knowledge of the anatomy, gender and racial variations of the human orbit are essential in diagnosing, evaluating and treating patients [2].

Anthropometry is a technique of quantitatively expressing the form of the human body and skeleton [3].

In 1875, Paul Broca described the orbital index by measuring orbital height and width in order to evaluate the orbital size and shape as a quantity [3]. Patnaik et al. [4] calculated the orbital index and showed the relation between width and height of the orbit. He defined 3 orbital categories: *megaseme (large)* — the orbital index is 89 or higher; it is found in the yellow race except the Eskimos [3]; *mesoseme (medium)* — the orbital index ranges between 89 and 83 and it is found in the Caucasian race [3]; *microseme (small)* — the orbital index is 83 or lower; this type is found in the black race [3].

The purpose of this study was to research the anthropometric variation of the orbit in the normal population using direct measurements of different orbital diameters.

MATERIAL AND METHODS

In order to achieve our goal we examined a total of 166 preserved adult human skulls (n=166) from the collection of Craniology of the "Fr. I Rainer" Institute for Anthropology in Bucharest, Romania.

Measurements were performed manually by a single investigator using a digital Vernier Caliper (*Fig. 1*). Standard anatomical points were determined and used for the measurement of the orbital width, height, biorbital and interorbital diameter, depth, length of the lateral and medial wall and the orbital index.

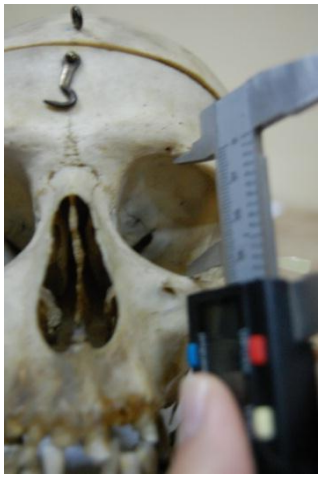

Figure 1. Direct measurement of the orbital height using the digital Vernier Caliper

Orbital height - the maximum distance between the superior and inferior orbital margins.

Orbital width: distance between the midpoint of the medial margin of the orbit to the midpoint on the lateral margin of the orbit.

Orbital index - orbital height/orbital widthX100.

Biorbital width **-** distance between left and right midpoint of the orbital lateral margin.

Interorbital width **-** distance between the midpoint of the medial margin of the left and right orbits

Orbital depth **-** distance between the optic foramen and the midpoint of the line defining the orbital width

Length of the lateral wall - distance between the optic foramen and the midpoint of the lateral margin.

Length of the medial wall - distance between the optic foramen and the midpoint of the medial margin (on the anterior lacrimal crest).

All measurements were recorded and expressed as Means ± Standard Deviation and range (min value- max value). For all the statistical analyses we used the SPSS 20.0 version software. To evaluate the gender differences between the groups we used the Mann-Whitney U-test. $P<0.05$ was considered significant.

RESULTS

From the 166 preserved human skulls 86 (51.8%) were female and 80 (48.2%) male. The average age of the group was 44.57 (±16). For the female group the average age was 44.84 (±17.55) (18-85) and for the male group it was 44.29 (± 14.30) (23-82).

The heights and widths of the orbits were as follows: mean right orbital width 40.0 ± 2.01 mm and mean height 33.3± 2.53 mm; mean left orbital width 39.7 ± 1.77 mm and mean height 32.98 ± 2.28 mm. When left and right orbital heights and widths were comparatively evaluated between gender groups, left and right orbital widths and heights were higher in males (mean right orbital width 40.73 ± 1.90 mm and mean height 33.92± 2.68 mm; mean left orbital width 40.38± 1.63 mm and mean height 33.48± 2.28 mm) then in females (mean right orbital width 39.32 ± 1.88 mm and mean height 32.86± 2.29 mm; mean left orbital width 39.12 ± 1.68 mm and mean height 32.52 ± 2.20 mm) and the difference was statistically significant ($p < 0.001$).

The orbital index (orbital height/orbital width × 100) on the right side is 84.49 ± 5.66 and on the left side 83.06 ± 5.27. The orbital index in the male group was 83.33 ± 5.97 for the right orbit and 82.96 ± 5.61 for the left orbit and in the female group it was 83.65 ± 5.38 on the right side and 83.16 ± 4.96 on the left side. When orbital indexes were comparatively evaluated between gender groups, no statistically significant difference was found ($p > 0.05$) (*see Table I*).

Table I. *Dispersion of orbital height, width and orbital index according to genders and right/left sides*

	Right Orbit			Left orbit			
Gender	Height	width	Orbital Index	Height	Width	Orbital index	Total
Female	32.8698 (2.2907)	39.3255 (1.8828)	83.65 (5.38)	32.5278 (2.2036)	39.1273 (1.6817)	83.16 (4.96)	86
Male	33.9266 (2.6881)	40.7336 (1.9039)	83.33 (5.97)	33.4826 (2.2805)	40.3870 (1.6347)	82.96 (5.61)	80
Total	33.3791 (2.5384)	40.004 (2.0149)	84.49 (5.66)	32.988 (2.2849)	39.7344 (1.7705)	83.06 (5.27)	166

The depths and lengths of the medial and lateral walls were as follows: mean right orbital depth 43.42 ± 2.45 mm, mean right orbital length of the medial wall 45.15± 2.33, and

mean right orbital length of the lateral wall 45.89± 2.57; the mean left orbital depth was 43.01± 2.39, mean left orbital length of the medial wall 45.33± 2.32, and mean left orbital length of the lateral wall 45.49± 2.55 mm. When left and right orbital depths were comparatively evaluated between gender groups, no statistically significant difference was found (p=0.9, p>0.05). When lengths of the right and left medial and lateral wall were comparatively evaluated between gender groups they were higher in males (mean right orbital length of the medial wall 45.82 ±2.30, and 46.87 ±2.68 of the lateral wall and mean left orbital length of the medial wall 46.09±2.33, and 46.53 ±2.55 of the lateral wall) then in females (mean right orbital length of the medial wall 44.53 ±2.19, and 44.97 ±2.09 of the lateral wall and mean left orbital length of the medial wall 44.62±2.09, and 44.52±2.14 of the lateral wall) and the difference was statistically significant (p < 0.001) (*see Table II*).

Table II. *Dispersion of orbital depth, lenght of medial and lateral walls according to genders and right/left sides*

	Right orbit			Left orbit			
Gender	Depth	Length of the medial wall	Length of the lateral wall	Depth	Length of the medial wall	Length of the lateral wall	Total
Female	43.4677 (2.2263)	44.5312 (2.1978)	44.9749 (2.0912)	42.9127 (2.2184)	44.6230 (2.0965)	44.5284 (2.1450)	86
Male	43.3721 (2.6895)	45.8238 (2.3010)	46.8764 (2.6835)	43.1294 (2.5809)	46.0935 (2.3348)	46.53 (2.5577)	80
Total	43.4216 (2.4533)	45.1541 (2.3330)	45.8913 (2.5708)	43.0171 (2.3950)	45.3317 (2.3275)	45.493 (2.5512)	166

The average biorbital width was 94.76± 4.52 mm, and the interorbital width was 15.02 ± 2.88 mm. When the biorbital and interorbital widths were evaluated comparatively between gender groups, they were found higher in males (97.27 ± 4.01 and 16.15 ± 2.69) than in females (92.42 ±3.63 and 13.96 ±2.66) and the difference was statistically significant (p < 0.001) (*see Table III*).

Table III. *Dispersion of biorbital and interorbital width according to genders*

Gender	Biorbital width	Interorbital width	Total
Female	92.4222 (3.6313)	13.9694 (2.6626)	86
Male	97.2771 (4.0160)	16.1565 (2.6939)	80
Total	94.7619 (4.5206)	15.0234 (2.8859)	166

DISCUSSIONS

Our current study revealed important anthropometric differences of the orbit between genders. The average orbital index of the whole group was 83.28 ±5.46 (83.40 ±5.17 in the female group, and 83.14 ±15.78 in the male group). These results place the group in the mesoseme category. The orbital index in the male group was 83.33 ± 5.97 for the right orbit and 82.96 ± 5.61 for the left orbit and in the female group it was 83.65 ± 5.38 on the right side and 83.16 ± 4.96 on the left side. We found that the orbital height and width were higher in males than in females and the differences were statistically significant (p<0.001). When orbital indexes were comparatively evaluated between gender groups, no statistically significant difference was found (p > 0.05).

In our study we also measured the sagittal diameters of the orbit (depth, length of the lateral and medial walls) which we consider to be among the most important in the management of surgical pathologies. The depths of the right and left orbits were 43.42 ± 2.45

mm and 43.01± 2.39. Interestingly when compared between gender groups, no statistically significant difference was found (p=0.9).

The length of the medial and lateral walls for the right and left eye were 45.15± 2.33, 45.89± 2.57, 45.33± 2.32 and 45.49± 2.55 mm. When they were comparatively evaluated between gender groups all the diameters were higher in the males than the females and the differences were statistically significant (p<0.001).

An interesting result is that even though most of the distances measured were higher in males than females (orbital width, height, lengths of the lateral and medial walls) there was no difference between genders when the mean depth of the orbit was calculated. This result was similar to the one obtained by Karampatakis et. al. in a study published in 1997 [5].

Too few anthropometric studies have included the sagittal diameters of the orbit but knowledge of these measurements could improve surgical safety and accuracy of different interventions, like retrobulbar anesthesia.

Katsev et al studied the needle path length in retrobulbar anesthesia on 120 human orbits and found the distance from the inferior temporal orbital rim to the optic foramen to be between 42 and 54 mm concluding that 11% of the population is at risk for perforation of the optic nerve when the common 38 mm needle is used. He recommends placing the needle less than 31 mm behind the orbital rim [6].

Karampatakis studied the orbital depth in relation to retrobulbar anesthesia in 50 adult skulls. He found the distance from the inferolateral orbital rim to the optic foramen varied from 4.4 to 5.7 cm in males (mean 5.024±0.272) and from 4.5 to 5.5 cm in females (mean 4.9± 0.204). Similar to our study he found no difference between males and females (p>0.05). He concluded that individuals with shallow orbits are more susceptible to optic nerve injury than those with deep orbits [5].

Chang et al studied 71 pediatric patients (4 months-17.8 years) and performed quantitative measurements of the orbital depth, biparietal and nasion-occipital distances and found a very strong linear correlation between these distances with a correlation coefficient of 0.83 (p<0.0001). They also found a strong nonlinear exponential correlation between age and depth of the orbit (0.88 p<0.0001). They concluded this information could improve surgical safety in pediatric patients [7].

In our study the average biorbital width was 94.76± 4.52 mm, and the interorbital width was 15.02 ± 2.88 mm. When the biorbital and interorbital widths were evaluated comparatively between gender groups, they were found higher in males (97.27 ± 4.01 and 16.15 ± 2.69) than in females (92.42 ±3.63 and 13.96 ±2.66) and the difference was statistically significant (p < 0.001). In a similar study Gosavi et al [8] found a biorbital distance of 95.65 ± 3.48 mm and interorbital distance of 19.49 ± 3.35 mm and compared it to other studies. They suggested the biorbital diameter determines the width of the upper face and the differences in interorbital and biorbital diameters need to be considered during facial cosmetic surgery, nasal bridge reconstruction and also in the design of spectacle bridges, frames and protective equipment for the eye. In the French population [9] the biorbital-interorbital distances were 98.97 and 19.81 mm.

In the present study we found that the orbital height, width, biorbital and interorbital widths, length of the medial and lateral walls were higher in males than in females and the differences were statistically significant (p<0.001). We found no statistically significant difference between gender groups when the depths of the orbits were evaluated (p=0.9, p>0.05). When orbital indexes were comparatively evaluated between gender groups, no statistically significant difference was found (p > 0.05).

The orbital index was presented by Broca in 1875 and based on the different values obtained three categories of orbits have been described for the human populations. Cassidy (1913) attributed the megaseme (orbital index over 89) to the yellow races (except for the

Eskimos) and the microseme (orbital index 83 or less) to the black races. The third category, mesoseme (between 83 and 89) was attributed to the white races. [10].

The orbital index determines the shape of the face. The populations with larger indexes will have round orbital openings (width and height almost equal) and narrow faces. In microseme populations the width is larger than the height and the orbital opening is rectangular.

More recent studies found a great variation of the orbital index with gender, age, race, regions within the same race and also period of evolution making it even more difficult to estimate the dimensions of the orbit within a population by just using this classification. A study on the orbital dimensions of the Malawi population found an orbital index of 95.15±4.56 (90.63-99.75) placing it in the megaseme category, contrary to the Casidy classification. Ukoha et. al. [2] studied a Nigerian population and described it as megaseme. Fawehinmi [11] also found an orbital index of 89.21 in the Nigerian population studied. In another study in Port Hacourt Nigeria, Fawehinmi et al studied a population that was also in the megaseme category. Studies in different regions of China performed by Black (1928) [12], Harrower (1928) and Hisaschi (1982) [13] found all three categories of orbits in the Chinese population proving once again the high regional variability within the same race. [14].

Studies on different populations in Japan (Kanto and Kinki region) classified the group as microseme (79.26-80.33). Measurements on prehistoric men in Japan found orbital indices of 65.2-66.7 and in the Neolithic men of 76.39-75.11, thus proving the evolution has a major role in the facial skeleton development. Although facial skeleton is genetically determined it can be modified before (in utero) or after birth in response to environmental and epigenetic factors like climate or masticatory function [15].

Our results are similar to other studies [16, 17] which found that the orbital height, width, biorbital-interorbital widths were higher in males than in females but opposite to our findings the orbital index was also higher in males than in females. Hussmann et al [2] found the orbital index higher in females than in males. In our study we found no statistically significant difference between gender groups when orbital indexes were compared ($p > 0.05$).

A study similar to ours was conducted in India on 64 skulls using a digital Vernier Caliper to measure the orbital height, width, biorbital and interorbital distance and the orbital index. The mean orbital height was 32.31 ± 2.52 mm. The mean orbital width was observed as 39.46 ± 2.57 mm. hence the Orbital index was calculated as 81.88 mm. The studied population was classified as microseme. The mean biorbital distance was 95.65 ± 3.48 mm (range – 88.5 – 102.5 mm) and the mean interorbital distance was 19.49 ± 3.35 mm (range – 11.8 – 27.6 mm) [8].

The growing need for anthropometric studies of the orbit within the local population is due to the great complexity and variability of this anatomic region. Knowledge of its anatomy is of vital importance in different pathologies and specialties (ophthalmology, ENT, oral and maxillofacial surgery and neurosurgery) both in diagnosing and treating patients.

CONCLUSIONS

The orbit is one of the most complex anatomic regions of the human body and the understanding of its anatomy is essential and vital in many surgical specialties like ophthalmology, ENT, maxillofacial surgery and neurosurgery. Its variability with gender, race and ethnicity also makes it important in forensic medicine. To our knowledge this is the first study on the orbital dimensions of a population from Romania and due to the large number of cases we were able to have very statistically relevant results. The study revealed important differences of most orbital dimensions between genders but it also provides an important baseline of anthropometric data for multidisciplinary clinical and surgical use.

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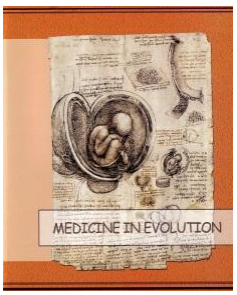
Lice and history



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Abstract

Lice are members of the *Phthiraptera* order, insecta class. Humans can only be parasitized by three species of lice, all of them belonging to the *Anoplura* suborder: *pediculus humanus humanus* (the human body louse), *pediculus humanus capitis* (the human head lice) and *pthirus pubis* (the human pubic or crab louse). The current article aims to look over the role of lice in evolutionary history, antiquity and archaeology and to explain how lice might have had a role in the outcome of several wars.

Keywords: lice, pediculus humanus, history

INTRODUCTION

Lice are members of the *Phthiraptera* order, insecta class. They are obligate ectoparasites of birds and mammals. The order *Phthiraptera* is divided into two groups, sucking lice and chewing lice, and four suborders: *Anoplura, Amblycera*, *Ischnocera* and *Rhynchophthirina*. *Anoplura* suborder belongs to the sucking lice group and the others belong to the chewing lice group. Sucking lice feed exclusively on blood while chewing lice feed on epidermal structures like hair and feathers. Both lice groups have the same ancestral origin and were separated approximately 100-150 million years ago, in the late Jurassic to early Cretaceous period. Currently, more than 550 species of sucking lice and 4400 species of chewing lice are described [1-3].

Humans can only be parasitized by three species of lice, all of them belonging to the *Anoplura* suborder: *pediculus humanus humanus* (the human body louse), *pediculus humanus capitis* (the human head lice) and *pthirus pubis* (the human pubic or crab louse). The body louse and the head louse belong to the *Pediculidae* family. Morphologically, they are very similar and can even interbreed. They are related to *Pediculus schaeffi*, the chimpanzee louse. The pubic louse belongs to the *Pthiridae* family. It is morphologically different from the head and body lice and it is very similar to *Pthirus gorillae*, the gorilla louse, which is in fact its ancestor. It is not exactly known how humans acquired pubic lice from gorillas. They are indeed primarily transmitted through sexual intercourse but this might not have been the case in this particular situation. It is therefore believed that archaic humans lived among gorillas and shared nesting sites or even fed on gorillas, a transfer between species thus being possible [2, 4].

LICE AND EVOLUTIONARY HISTORY

Lice complete their life cycle on their hosts. They are extremely host-specific and can evolve together with the organism they parasitize. There is much debate around the evolution of modern *Homo sapiens* from his archaic ancestors. Fossils are intensely studied but the poor quality of the material and the very old age often prevent liberation of sequenceable DNA. Therefore, lice, and other parasites, have been used to study human evolutionary history. The molecular examination of *pediculus humanus* showed two ancient louse lineages. The first one has a worldwide distribution and shows a population expansion 100,000 years ago, concurrent with the out-of-Africa population expansion of *homo sapiens*. The second one diverged from the first one 1.18 million years ago and remained isolated in the New World. It is still very difficult to explain why both louse lineages occur in modern *homo sapiens* but direct physical contact between *homo sapiens* and *homo erectus* during periods of overlap might explain the process [4-7].

Human migrations are also intensely studied. The study of lice from Europe and North America, Canada, Honduras and Asia reinforces the theory that the first people in Central America originated in Asia. Lice in North America are of European lineage while lice in Honduras show the influence of both European colonisation and Native Americans [8].

Lice were also used to determine the origin of clothing. Studies show that the body louse emerged from the head louse 72,000 ± 42,000 years ago. It is believed that the differentiation occurred when modern humans started wearing clothes frequently. The appearance of body lice around the time of human migrations from Africa also supports this hypothesis, as clothes might have allowed humans to colonize areas with lower temperatures. If the theory is correct, clothing appeared quite late in human evolution [8, 9].

LICE IN ANTIQUITY

Lice have been long known to humans. Aristotle (384-322 BC) described lice and the *lousy disease*, which he believed was an affliction determined by wild lice, in one of his works, "History of animals". He believed that lice were insects which lived on the juices of living flesh and that they were generated out of the flesh of animals. He also described that when the eruption determined by these insects was opened, lice jumped out [10, 11]. Diodorus Siculus, a Greek historian, described cases of phthiriasis he had seen in a North-African tribe, in a similar fashion [11, 12]. Galen also believed that lice were formed in the skin, probably as a result of warmth and moisture. Due to the proverb "Plato's lice", some people believe that the philosopher died of phthiriasis. That is most likely not true and the proverb was probably meant to suggest that Plato had poor standards of hygiene [13]. The great Greek historian Herodotus (484-425 BC) also mentions lice in his work as a cause of death of Pheretima, the tyrant queen of Cyrenaica. According to him, her body was "seething with worms while she was still alive". Pliny the Elder believed that lice were formed in the blood and ate up the flesh of the patient [11, 14, 15].

Al Gahiz, an Arabian zoologist, described several insects. He believed that lice had the same colours as one's hair and that if that person changes his hair, the louse will change its colour. He also believed that lice infest any clothing except those of lepers [16].

Lice are also mentioned in the Bible. According to the Book of Exodus (8:16-17) God inflicted ten calamities upon Egypt in order to convince the Pharaoh to release the Israelites from slavery and let them go with Moses. Lice were the third plague and they affected all the people and animals in Egypt [17].

Phthiriasis was considered by many a punishment for sins and several tyrants from legends and classical history were said to have died of this terrible illness. After the 1850's however, many scholars became sceptical. In 1865 the famous dermatology professor, Ferdinand von Hebra strongly reacted against the existence of the lousy disease, as described from antiquity to that time, based on this professional experience and the extensive study of the medical literature [15].

LICE IN ARCHAEOLOGY

Several lice and louse eggs were discovered after studying mummies from all over the world. The oldest intact louse egg was found on hair which was dated to 8000 years BC and was discovered in northeast Brazil. The authors suggest that lice arrived in the New World together with the first human colonists. Nits and eggs of head lice dating between 4000 BC and 500 AD were also found in Arica, northern Chile. Head lice eggs were also discovered in a young Inca prince who was probably sacrificed in Chile to the God of Sun between 1480 and 1540 AD [18-21].

Pubic lice were also discovered in pubic hair of a 2000 year old mummy from Chile and in the clothes of a 1000 year old mummy from Peru. These findings are very important because they prove that pubic lice were present in the New World in antiquity and were not brought here from the Old World after Columbus discovered America, as initially believed [22, 22].

In North America, lice were found in Indian mummies, in agricultural sites of United States and in Mexico. The oldest nits in Asia date to 7000 BC and were found in the Nahal Hemar cave in Israel. Other lice were found in China in a 3800 year old mummy from the Loulan period [20, 23].

Mummies in Europe and Africa also presented lice and nits. Lice were therefore found in mummies from the Roman period, Iceland, Greenland and Egypt. The study of the mummy of Ferdinand II of Aragon (1467-1496) proved that the king of Naples was infested with both head lice and pubic lice. High concentrations of mercury were also found in his

hair. Since there is evidence that mercury was used to treat pediculosis in that time, the metal was probably applied externally for therapeutic purposes [20, 23, 24].

Lice were discovered in hair combs excavated in Judean and Negev desserts and dating from the first century BC to the eighth century AD. Some of the combs had two sides: one side for straightening the hair and the other side for delousing. The presence of high numbers of lice and eggs in the combs shows that the inhabitants knew the disease and had an effective means of delousing [23].

LICE CHANGING HISTORY

Lice have changed the course of history by influencing the outcome of several wars. In order to explain how that might happen, we must first discuss the disorders which can be transmitted by lice.

Head lice are more frequent in children from families with low socio-economic status. Pediculosis capitis is very contagious and manifests as scalp pruritus. Body lice on the other hand are less frequent and represent a real public health concern. Their prevalence significantly rises during wars. Pediculosis corporis manifests as generalized pruritus associated with scratching. Pubic lice are considered a sexually transmitted disease and manifests as pubic itching and maculae coeruleae. Of all, only body lice are vectors for infectious diseases and can transmit epidemic typhus, relapsing fever and trench fever. However, studies show that in people with head lice and poor hygiene head lice can differentiate into body lice [25, 26].

Lice as vectors for infectious diseases

Epidemic typhus is caused by *Rickettsia prowazeki*, a bacteria which lives in the faeces of infected lice. Lice become infected by feeding on people with typhus. Humans get infected after the bacteria enters the bloodstream through open sores, skin erosions or after scratching. Since *R. prowazeki* can survive in dried faeces for about 60 days, the particles can be inhaled or enter the conjunctiva and therefore affect even people who are not infested with lice. Clinically, affected people get fever, malaise, muscle aches, a reddish-blue rash, delirium and headaches. In severe cases, it can lead to coma, hypotension and death. In 1909 Charles Nicolle discovered that lice were responsible for the transmission of typhus, after he was accidentally infected and survived. In 1928 he was awarded the Noble prize for his discovery and his work with typhus. Howard Ricketts and Stanislaus von Prowazek, other researchers working with typhus, were not as lucky as Nicolle and did not survive their infection. To recognize their merits, the bacteria was named after them [1, 27-29].

Relapsing fever is determined by the spirochete *Borrelia recurrentis*. Since humans are the only reservoir for this bacteria, lice get infected after feeding on people with the spirochete in the bloodstream. Humans get infected after lice are crushed during scratching. It clinically manifests with high fever, fatigue, anorexia, dizziness, skin and mucosal haemorrhaging, enlarged liver, renal and neurological involvement [1, 26].

Trench fever is caused by *Bartonella quitana*, a gram-negative bacteria and is also known as the five-day fever. It is usually transmitted by infected lice but the bacteria was also found in cat fleas. It manifests with fever, headaches, dizziness, shin pain and nausea. In some cases it may be asymptomatic. Fatal cases were not described. It is called trench fever because it affected troops engaging in trench warfare during World War I [1, 26].

The role of lice in history

Lice had an important role in history. During the Middle Ages, in Sweden, a louse was responsible for choosing the mayor of Hurdenburg for the next year. Therefore, all eligible elders sat around a table and spread their beards. The louse was placed in the middle of the

table. The elder in whose beard the louse climbed was chosen mayor. In other countries lice were fashion setters. They were an important reason why noble people started wearing wigs in the sixteenth century. Since shaving the hair was an effective method of getting rid of lice, wearing wigs became very fashionable in that time. Wigs had the advantage that they could be washed or boiled. Unfortunately, in time people forgot why they wore wigs in the first place. Those became very elaborate and high maintenance and were as infested with lice as hair was [30-32].

Lice also decided the course of several wars. In the spring of 1812 general Napoleon Bonaparte was marching to Moscow in front of *Grande Armée*, a great army of approximately 600 000 soldiers, with 440 000 frontline troops. His army outnumbered by far the Russian army. During their retreat, the Russians had destroyed most of Poland and the French had difficulties acquiring water and food. French soldiers therefore plundered the Russians and Polish living in the countryside. These areas were very poor and the people were infested with lice, bugs and fleas. Napoleon's soldiers were quickly affected by those bugs and many developed "war fever" or typhus, a severe bacterial infection transmitted by lice. This disease killed more soldiers than the battles did. As a result, in the autumn of 1812 the French army started the 1000 mile retreat with only 95 000 soldiers. During the retreat, many others died. Napoleon blamed the defeat on the cold weather. In fact, the disease transmitted by lice played a more important role [33-35].

The Crimean War (1853-1856) involved the Russians on one side and the French, British, Ottoman-Turkish and Sardinians, on the other side. Soldiers from both armies were affected by louse-borne typhus, dysentery and cholera. During this war, approximately 200,000 French soldiers died. Of those, 50,000 died due to wounds received in battles while the other 150,000 were hospitalized for typhus. Typhus however was not solely responsible for those casualties. The horrifying sanitary conditions helped the spread of other infectious diseases like cholera, dysentery and typhoid fever. The return of infested soldiers from war determined the outbreak of typhus epidemics, especially affecting people from poor, overcrowded areas, who lacked personal cleanliness. Florence Nightingale, the founder of modern nursing, had a very important role in organizing the Allied military hospitals. Her special concern for sanitation significantly reduced the death rate in military hospitals from 45% to 2% [31, 36-39].

The American Civil War (1861-1865) was fought between the North (Federals) and the South (Confederates). Lice were a universal problem and affected both armies. Unlike Europe however, those lice did not carry typhus and were therefore not responsible for many deaths. At first those infested were embarrassed by their situation and tried to hide it. After a while however, lice became a means of entertainment. Lice races and lice fights were very common among soldiers from both armies. Metal plates were therefore heated using a candle and lice were placed in the middle of the plates. The louse that first got off the plate was declared winner and his host won money, tobacco or alcohol. The Federals called lice "greybacks". This was the same name they used for the Confederates [31, 40].

Lice also affected the course of World War I (1914-1918). Austria declared war on Serbia after the Archduke Ferdinand was killed in 1914. Serbia was very vulnerable because the war with Turkey had only just finished. Hospitals were destroyed and lice and microbes were spreading throughout the country and affecting the population and the prisoners of war. In a very short time, approximately 200,000 Serbs and half of the prisoners of war died of typhus. Being aware of the epidemics which had occurred in Serbia and afraid of the possible consequences, the Central Powers no longer invaded this territory. Their attack in a key moment of the war was delayed by six months and, in the end, they were defeated.

Another important aspect about lice and typhus during World War I was that the Western Front was not affected by those while the Eastern Front was fighting serious epidemics. The explanation is simple: at that time Nicolle had discovered that lice were

responsible for transmitting typhus and the Western countries quickly realized the importance of hygiene and started delousing all soldiers returning from the frontlines [41, 42].

The Russian Civil War (1917-1923) between the Bolshevik party and the anti-socialist factions led to the rise of the Soviet Union. The country was weakened by famine and poverty and refugees were spreading lice throughout the nation. During this war, approximately 30 million people were diagnosed with typhus and 3 million people died. Lenin, the leader of the Bolshevik party, is supposed to have said: "Either socialism will defeat the louse, or the louse will defeat socialism" [31, 35, 41].

During the Second World War (1939-1945) lice and typhus were no longer a problem as DDT (dichlorodiphenyltrichloroethane) was discovered and used directly on soldiers and their clothing to prevent infestations [43].

CONCLUSIONS

Lice are obligate ectoparasites of birds and mammals which complete their life-cycle on their host. They are generally perceived in the general population as nothing more than a sign of poor hygiene. When it comes to history however, they proved their importance in the study of population expansions, human migrations or the origin of clothing. They were trend-setters and were involved in political issues. Lice, as vectors for infectious diseases, influenced the outcome of several wars. DDT put an end to the terrors that lice helped spread.

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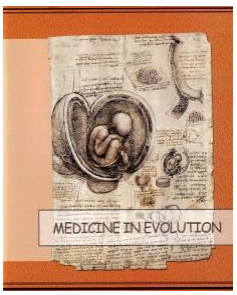
Historical legislative governing doctor-patient relationship



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Abstract

One of the most important rights of the patient is ***the right to medical information,*** the patient having the right to be informed about his health state, the proposed medical intervention, potential risks of each procedure, and on diagnostic and prognostic data. The accurate, complete, and accessible patient's information, relative to its level of understanding, regarding the state of health and the consequences of granting or refusing the medical service is a prerequisite to a valid consent expressed of requesting another medical opinion or refusal to receive certain medical services. In this respect, to protect the most important human right, the right to a healthier life, were adopted several laws which create an institutional framework to regulate the relationship between patient and the medical staff, with the rights that the patient has from the health care system to benefit from the highest quality care that society has at one time. The professional medical quality is sometimes diminished by violating the professional ethics, but in most cases, the lack of financial resources and necessary materials, with the consequence of non-practising the full potential available in the medical profession. As it follows that, inevitably the question arises to what extent the state fulfills its specific obligations pertaining to health insurance and thereby quality of life.

Keywords: medical System, the patients rights, professional ethics, public health, quality of life

HISTORICAL LEGISLATIVE GOVERNING DOCTOR-PATIENT RELATIONSHIP, PATIENTS' RIGHTS AND OBLIGATIONS

With a long history, dating back to the ethical principles of Hippocrates from a constitutional level principle, this fundamental value enshrined in **1948, when by art. 25 of the Basic Law, has provided expressly that "the State bears the public health care through the establishment and development of health services".** In art. 20 par. 2, 1965 Constitution imposed a duty on the State to ensure "health assistance through its institutions". From this point of view, we can say that the current Basic Law is superior by guaranteeing this right and by assuming the state obligations. In art. 33 par.1 of the current Constitution provides that "**The right to shield the health is guaranteed"** and the provisions of par. 2, `**The state is obliged to take measures for ensuring hygiene and public health.**

Special laws designed in the field, also have known a diversification and an improvement of regulations. Therefore, by Law no. 984 of 11 April 1927 for organizing the House Health, this institution was established alongside the Ministry of Health and Social Welfare, with the main tasks of studying the public health and Social Welfare issues, to centralize and manage all funds depending on the Ministry.

According to the Decree no. 212 of 13 May 1953 on the regulation of the medical doctor profession, that may be practised in private clinics or in government service.

In the same period, the provisions of Decree no. 246 of 29 May 1958 on the regulation of addressing medical assistance and medicines, the medical service recipients were divided into two categories: first category includes people receiving care and free medicines, and the second category includes persons who were beneficiating by certain price cut in costs of healthcare and drugs.

Art. 34 of the Romanian Constitution guarantees the right of Romanian citizen to health, the Romanian State undertaking to take all necessary measures for ensuring the public health.

In this respect, to protect the most important human right, the right to a healthy life, the Romanian legislature adopted **Patient rights law no. 46/2003**, regulatory document wherethrough creates an institutional framework which aims to familiarize the patient and the medical staff with the rights that the patient has in the system of health care in order to receive care of the highest quality, that the company has at a certain time. [1.2,3,4]

When adopting this law were envisaged to promote the principles of patients' rights in the European states of the World Health Organization, principles adopted as a result of the WHO European Consultation on Patients' Rights held in Amsterdam in 1994. To outline these principles of patients' rights in Europe were considered:

- Universal Declaration of Human Rights (1948), European Convention on Human Rights and Fundamental Freedoms (1950), European Social Charter (1961), International Covenant on Civil and Political Rights (1966), International Covenant on Economic, Social and Cultural Rights (1966).
- Principles that I made reference earlier concern: patient's right to respect for his person as a human being, right to self-determination, the right to physical and mental integrity, the right to the security of his own person, the right to be respected for his own privacy, the right to have its own moral and cultural values, the patient's right to the respect of religious and philosophical beliefs, the right of the "**health**" protection, through appropriate preventive measures.

In art. 2 of the Law on patient rights, the patients have the right to health care of the highest quality that the society has, according to the human financial and material resources, the rule of law enshrining a right to which corresponds implicitly correlative obligation of the Romanian state to take all necessary political, social, fiscal and legislative measures, to ensure quality health care.

Art. 3 of the law states the patient's right to be respected as a human person, without any discrimination, by discrimination in the legal sense, understanding the distinction between persons in similar situations based on race, sex, ethnicity, national or social origin, religious, political or personal antipathy.

One of the most important patient rights is ***right to medical information*** regulated in chapter II of the law, according to these legal norms, the patient having the right to be informed about his health, the proposed medical intervention, potential risks of each procedure, and on diagnostic and prognostic data. The patient also has: *the right to decide* if he wants to be informed, if the information submitted would cause suffering, *the right to ask explicitly* not to be informed or to choose another person to be informed in his place.

The accurate, complete and accessible patient's information, relative to its level of understanding, regarding the state of health and the consequences of granting or refusing the medical service is a prerequisite to a valid consent expressed, of requesting another medical opinion or refusal to receive certain medical services.

Compliance with this fundamental right has a special impact on another aspect, indispensable for carrying nursing acts: **patient consent.** According to art. 13 of Law no. 46/2003, the patient has the right to refuse or withhold the medical intervention taking the responsibility for its decision in writing, with the corresponding obligation of medical professionals to explain the consequences of refusing or stopping the patient's medical acts. [4]

Consent must be free and uncorrupted in order to take effect. Vices of consent under civil law are represented by error, fraud (action done in bad faith, cunning) and violence.

- *The error* is the false representation of reality in order to obtain the approval, the false representation failing which the patient would not have consented to perform a medical act.
- *The fraud (cunning)* is the vice of consent that consists in misleading anyone by cunning or by bad faith in order to obtain his consent.
- *The violence* as well as fault consent, consists in threatening a person with an evil which produces a fear that causes to give the consent that otherwise would not have given.

Even if these vices of consent are rare in practice, we have considered their explicit necessary due to major importance that has the patient's consent to exercising a medical act.

But there are exceptional circumstances, when the legislature considered that the patient's interest is above his consent:

- if the patient requires a medical emergency intervention, the legal representative's consent is no longer necessary.
- where the healthcare providers consider that the intervention is in the interest of the patient and the legal representative refuses to give **the consent** the decisions denied to an arbitration panel, specialized committee made up of three doctors if there are hospitalized patients or two doctors for outpatients.

Art. 26 of the Romanian Constitution enshrines the principle that public authorities ***respect and protect the intimate, family and private life of Romanian citizens.*** Respecting this fundamental principle, Chapter IV of Law no. 46/2003 governing *the right to confidentiality and privacy of patient's life*. According to art. 21 and art. 22 of the law, all the information according on the patient's condition, the investigation results, diagnosis, prognosis, treatment, personal data is confidential even after death, theoe could be provided only if the patient consents or unless the law requires expressly . Only in the exceptional situation where the information is necessary for other accredited healthcare providers involved in patient's care, giving consent for the provision of such information is no longer compulsory. Given the importance of this patient's right, the legislator considered that the violation of this right constitutes, in relation to the seriousness of the offense, an offense regulated as such **art. 196 of the Criminal Code** according to which the act consisting of

disclosure without the right input data of the one to whom they have been entrusted or who has knowledge by virtue of profession or position, if this act is liable to harm a person, is an offense and can be punishable by imprisonment from three months to two years or with criminal fine. Since the legislator established **patient rights** to treatment and medical care for preventing possible abuses, **art. 29 of Law no. 46/2003** regulates the obligation of providers that if they are forced to resort to selecting patients for certain types of treatment that are available in limited number, the selection is based solely on medical criteria. par.2 of art. 29 of the Law prescribe that the Ministry of Health and Family that within 30 days of the entry into force of the law, respectively until the end of March 2003 to develop the medical criteria for selecting the patients for certain types of treatment. However, it seems that this initiative likewise praiseworthy, remained at the level of legal provision as the only selection criteria developed by order of the Minister of Health were those in patients with chronic viral hepatitis and those with cirrhosis, criteria regularly updated which today are contained in Order no. 658/2006 concerning on the eligibility criteria for inclusion in antiviral treatment and choice of regimen in patients with viral hepatitis B, C and D, and in patients with liver cirrhosis.

As for other types of treatment have not been published until now no such selection criteria, the question is what are the criteria to be considered in common practice and what is the degree of objectivity with which this patient selection is made. By adopting a special law exclusively regarding patient rights, it can be seen that the legislator, has sought to confer for the patient the safety and trust in the medical and health services that it provides. Moreover, to ensure that violation of these rights do not occur, through special laws have been enacted also the obligations of the medical staff towards the patients with appropriate violation sanctions.

It must be emphasized the fact that the patient should be aware that it has not only rights but also correlative **obligations**, some of these obligations being governed by the legal rules. So, **art. 38 of Law no. 95/2006** paying attention to the health reform requires for the Romanian citizens and any other persons living in Romania to:

- obey the measures of preventing and combating the communicable diseases,
- fully respect the rules of hygiene and public health,
- provide the requested information
- enforce the measures set on establishing conditions for disease prevention and health promotion for the individual and population.

At the same time, art. 219 of Law no. 95/2006 on healthcare reform lists the obligations that the insured patients have in their health insurance system to benefit from the rights conferred by law:

- to join the list of a family doctor;
- to notify your family doctor whenever there are changes in their health status;
- to submit to regular and preventive controls determined by the framework contract;
- to announce within 15 days the family doctor and home insurance on identity data changes or changes related to their enrollment in a class of policyholders;
- to strictly follow the treatment and doctor's instructions;
- to have a civilized conduct towards the healthcare worforce;
- to pay the contribution due fund and the amount of co-payment, as determined by the framework contract;
- to submit to the health care providers the attesting documents as insured.

For certain situations, the Romanian legislator took into account the seriousness of the consequences of breaching the patient's obligations, for which he was assigned as **offense** to forestall any act of combating diseases, of venereal contamination and transmission of acquired immunodeficiency syndrome and avoiding medical treatment.

For the purposes of the Criminal Code offense to forestall disease control, provided by art. 308, consists of non-compliance measures for the prevention and combating of disease, whether it has resulted in the spread of disease, and shall be punished with imprisonment from one month to two years or a fine, and the offense of venereal contamination and the transmission of the immunodeficiency acquired syndrome governed by art. 309, is the transmission of a venereal disease or immunodeficiency syndrome acquired through sexual intercourse of any kind with a person of the opposite sex or the same sex or through acts of sexual perversion by a person who knows he is suffering from such a disease, penalty set by the legislator as imprisonment of one to five years for venereal contamination and imprisonment from five to fifteen years when transmitting AIDS. As a safety measure, para. 3 of art. 309 establishes the defendant obligation to medical treatment, as imperatively be taken by the court, flight from this safety constituting an offense punishable by imprisonment from three months to one year or a fine.

Even if Law no.46/2003 there is no separate chapter regarding to the patient's obligations, they must always have in mind a principle enshrined in art. 57 of the Fundamental Law of Romania, being that both Romanian citizens and foreign citizens and stateless persons shall exercise their constitutional rights and freedoms in good faith, without infringing upon the rights and liberties of others, so without committing an abuse of justice. Therefore, the patient must exercise their legal rights in such a manner as to maintain a balance between his rights and the duties towards the medical and to other peers of his, because only so the health system can work correctly in the Romanian society and the patient can really enjoy his rights.

Information confidentiality

When referring to liability, the legislator comes to the fore about patient privacy and medical act, after referring to all other rights enumerated in the law. The legislator's option can be based on their seriousness, increased frequency compared to other violations or procedural aspects, in that it can be proved easily.

The right to confidentiality is at the same time, a form of protection for the patient's life privacy and guaranteed by obligating the healthcare providers to keep the professional secrecy. Headquarters is the material provision **art. Penal Code 196**according to which constitutes the offense of confidential disclosure and shall be punished with imprisonment from 3 months to 2 years or with a fine, deed consisting in disclosure without right to some data, by the one to whom they were entrusted, or of which he became aware in the profession virtue or function, if the act is likely to harm a person**.** Acts of this nature are rare, but there is an abundance of similar regulations in the sense that in apparently different forms through a standard reference, each regulatory document resumes also the text criminality content.

Art. 79 para. 1 Criminal Procedure Code "*Listening to the person bound to secrecy professional"*. The person bound to professional secrecy (the medical note) can not be heard as a witness on the facts and circumstances of which he has knowledge in the exercise of profession, without the consent of the person to which it is bound to secrecy (consent is given in writing). Thus, the same right to confidentiality, with the correlative obligation of professional secrecy, under penalty of criminal law rules, enshrined in. [1.2]

- art. 78 para. - (1) of Law no. 3/1978, meaning that "*documents, data and medical information obtained by the health personnel in the exercise of their duties, constitues a professional secrecy, disclosure is prohibited*"
- art. 30 para. - (2) of Law no. 100/1998 on public health nurse which provides that "*confidentiality of information relating to individuals is mandatory for all employees who have access to them through the work they carry out, directly or indirectly*"
- art. 17 of Law no. 307/2004 regarding the practice of nurse, establishment, organization and functioning of Nurses in Romania, in that "*nurse is bound by*

professional secrecy and patient-related information, obtained from or related to the exercise of his profession, can not be shared with another person outside the medical team, unless expressly provided by the law".

Consent to medical intervention

Free and uncorrupted needed of consent obtained from the patient, prior to rendering medical service, is an expression of the freedom of every person to have about the limits and forms of existence, within the rules of general interest.

Consent is implied when the patient requires medical service. Sometimes, due to particular circumstances in which the patient is, you need written consent from the patient or from the family members, situations that different laws govern them thoroughly.

The law on organ procurement and transplantation, establises the freedom of consent for both the donor and the recipient. According to art. 5 written consent is required, free, prior and expressly obtained from donor; consent on which it can return, and according to art. 11 transplants of tissues and organs can be performed only with the written consent of the recipient.

The right to medical information

The right to medical information, as enshrined by the legislator in favor of the patient, is at the same time an obligation of health providers services. Accurate information, complete and accessible for the patient, relative to its level of understanding of health state and the consequences of granting or refusing the medical service, assembles the preseume of a valid consent expressed, request and another medical opinion, or rather the refusal to receive such services.

This right and also corresponding obligation results from Art. 70-76 of Law no. 3/1978, as well as some special regulations. Thus, according to Art. 5 paragraph. 3 of Law no. 2/1998, concerning the collection and human organs transplantation and tissues is mandatory "*donor information on potential risks and consequences on the physical, mental, family and professional consequences of that removal is mandatory*". [1]

The right to be respected as a human

The relationship between doctor and patient is particularized and by human coordinate dimension, driven throughout the health system. Being vulnerable patient's personality must enjoy extra protection and respect from the medical staff. From this perspective, the legislator expressle established, also the patient's right to be respected as a human obligation arising mainly from the Code of Professional Ethics and the general legal norms.

According to art. 3 paragraphs. - (1) of Law no. 74/1995, on exercising the medical profession, the establishment, organization and functioning of the College of Doctors in Romania, in the practice, the physician must prove "*availability, honesty, devotion and respect for the human being*"and according to art. 15 of Law no. 307/2004, in the practice, the nurse respects human dignity and the principles of ethics, demonstrating professionalism and moral responsibility, always acting in the interest of the patient, patient's family and community. "[3]

According to art. 3 of Law no. 46/2003, [4] patient has the right to be respected as a human person, without any discrimination. Even in the absence of express consecration, the law on patient rights by the Criminal Code with the other fundamental attributes, honor and dignity is protected.

Right to the health care of the highest quality

Right to health care the highest quality is established through a multitude of regulations. In this regard, according to Art. 117 of Law no. 3/1978, "all citizens are entitled to general medical and emergency assistance," according to art. 1, paragraph 2 of Law no. 100/1998, "public health assistance is guaranteed by the state", and according to art. 2 of Law no. 46/2003, "patients have a right to health care of the highest quality". [5, 2, 11]

The issue is whether, and to what extent, patients can fully and effectively exploit this right enshrined in a form so generous.

The professional medical quality is sometimes diminished by violating the professional ethics [6,7], but in most cases, the lack of financial resources and necessary materials, with the consequence of non-practising the full potential available in the medical profession. As it follows that, inevitably the question arises to what extent the state fulfills its specific obligations pertaining to health insurance and thereby quality of life [8, 9].

Will Law on the Rights of patients be followed by a law on the rights of healthcare providers? [10, 12] Perhaps the answer is negative**.** This being so, it follows that in this contractual rights and reciprocal obligations, the legislator intended to establish more rights for the patients and more obligations for the medical staff. This is because, appealing to health services, patients value their right [13, 14], while rendering these services, providers fulfill their professional, ethical and moral obligation.

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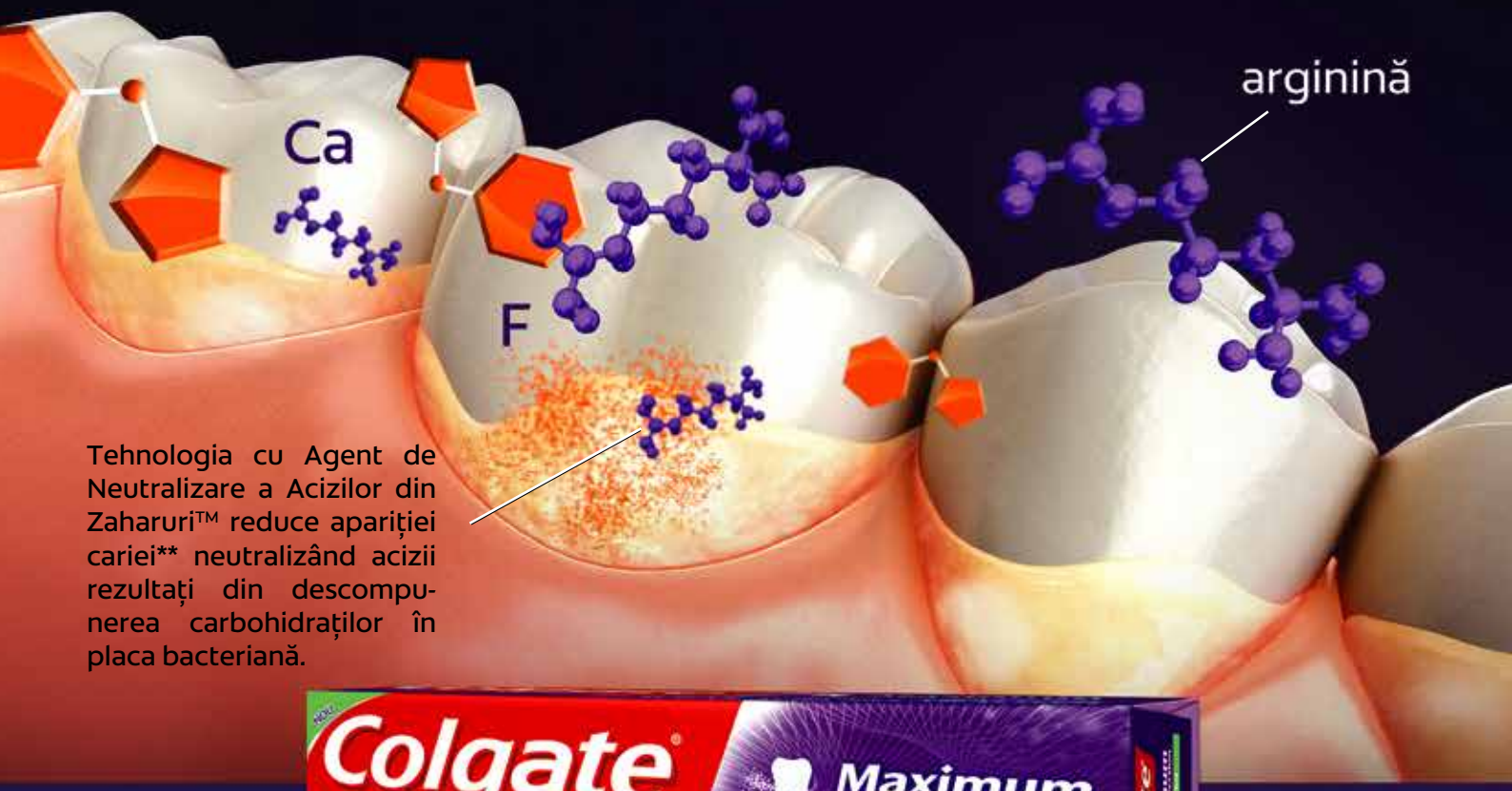

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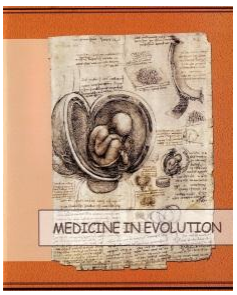
Autologous bone blocks in oral rehabilitation. Case review



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Abstract

Oral rehabilitation has changed dramatically in the last years through the ever increasing use of dental implants. Although more and more patients are demanding implant supported prosthesis for the rehabilitation of their edentulous spans, in many cases dentists feel reluctant in placing the implants due the decreased bone volume. There are many tehnics but autologous bone in granulate form or as a block remains the gold standard for the reconstruction of the atrophied jaws.

Keywords: Autologous bone, bone atrophy, dental implant, oral rehabilitation

INTRODUCTION

Since their introduction six decades ago dental implants have change for the better the life of patients. A major problem in the dentists' every day use is the lack of adequate bone support needed for implant stabilization. Although there are many solutions in the market such as: short and narrow implants, tilted implants, cortical and zygomatic implants, there are cases where even these solutions don't seem to work. Often in these cases the patients are sent to the maxillofacial surgeon office to restore the missing bone volume. The surgeon has to ensure a proper bone volume for a good prognosis of dental implants. There are many surgical procedures with a well established protocol. There are also many bone substitutes: xenograft or allogenous in both particulate and blocks form. But there is only one material that can ensure a good volume both in quantity and in quality: autologous bone graft (1). It can be obtained as particulate chips with the use of special burs or cut as a block which will be fixed with osteosynthesis screws. It does not necessitate any other material for protection and it brings the largest quantity of bone proliferative cells than any other material (2).

CASE REPORT

Patient R. D., aged 40, was sent to our office by her current dentist regarding the rehabilitation of the lower left dental segment.

Clinical exam

At presentation there was an edentulous span from 36 to 38, multiple fixed prosthesis in the lower jaw (46-48, 35) and in the upper jaw 14-16 and 24-27 (porcelain fused to metal restorations). There were no cavities. There was a periodontal involvement as there were multiple recessions at the premolar areas. The teeth were generally well aligned and there are some dental spaces (Figure 1A). The occlusion was neutral, but there was temporomandibular joint (TMJ) dysfunction with later deviation of the jaw during open movement. The mouth opening was slightly reduced. The TMJ dysfunction was caused by unilateral mastication due to the missing lower left molars.

Patient history

The patient reported that sometimes there was tenderness after prolonged mouth opening and there were times when clicking and popping noises could be heard in the left TMJ.

The patient informed the medical team that multiple dental implants were delivered in the jaw a few years ago.

The medical status revealed the patient had an appendectomy in childhood and a caesarean section few years ago. The patient did not take any treatment.

Radiographic exam

The x-ray panoramic exam showed 2 implants fixed in her right jaw (45,46) and one had a bone loss that ranged to 50% of the implant surface, there were numerous endodontic treatments some of them incorrect and the second lower left premolar had a severe periodontal involved and was proposed for extraction. There was also a huge defect in the lower left first molar region (Figure 1B).

The cone beam computer tomography (CBCT) showed the 3D extent of the defect of the leftl jaw: there was a good bony width in the area of tooth 36 but considering the height there were actually a few mm of bone coronal to the inferior alveolar nerve (1-2mm). The second premolar was not restorable from a periodontal perspective, completely missing 2 bony walls (Figure 1 C, D).

Figure 1. A. Initial intraoral status (April 2015). B. Panoramic radiograph showing the bone defect in the lower left mandible. C,D Tomography scans showing limited residual bone in the molar and premolar area left lower quadrant

Treatment and evolution

A decision was made to place a bone graft simultaneous with the lower left premolar extraction. In this particular case due to the extent of the defect a bone block harvested intraoral was proposed to the patient. After 4 months 2 implants would be placed and after another 4 months the dental prosthesis would be set.

Under local anesthesia (articaine 4%) a crestal incision was performed ranging from tooth 34 to 38 and vertical releasing incisions at the level of tooth 34 and at the ramus. A full trapezoidal mucoperiostal flap was raised and the bone defect was visualized clinically. The surgical extraction was performed atraumatically using the piezosurgery device. The bone block was harvested from the retromolar area with the piezosurgery unit in order to minimize the bony trauma. The dimensions of the block were 13mm by 10 mm. 2 osteosynthesis screws were delivered to secure the graft at the positions of the future implants corresponding to teeth 35 and 36 (Figure 2). After periostal release the flap was repositioned in such way to cover the graft entirely. The suture (Polytetrafluoroethylene PTFE) was a horizontal mattress with interrupted knots. The sutures were removed 10 days after. The healing went uneventful.

After 4 months the patient performed a CBCT scan that showed proper bone formation (10-11 mm height in 36 and 35 sites) adequate for placing 2 dental implants (Figure 3B, C). Under local anesthesia the graft was uncovered and 2 dental implants (3,6/10 mm) were placed, that were left to heal for another 4 months (Figure 3A). At the end of the healing phase the implants were uncovered and porcelain fused to metal restoration was delivered to the patient (Figure 4).

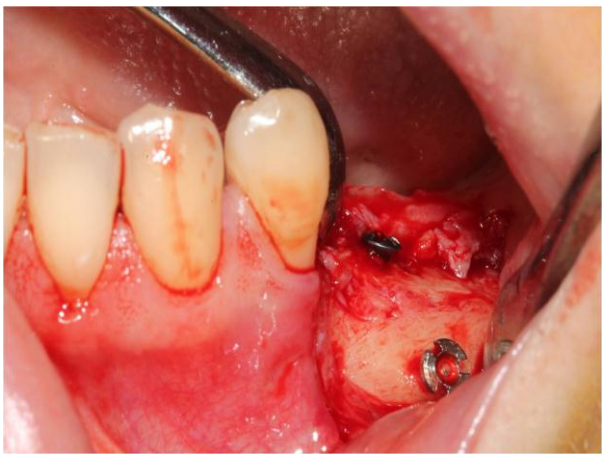

Figure 2. Intraoperative photo showing the bone block fixed into the defect with 2 screws (July 2015)

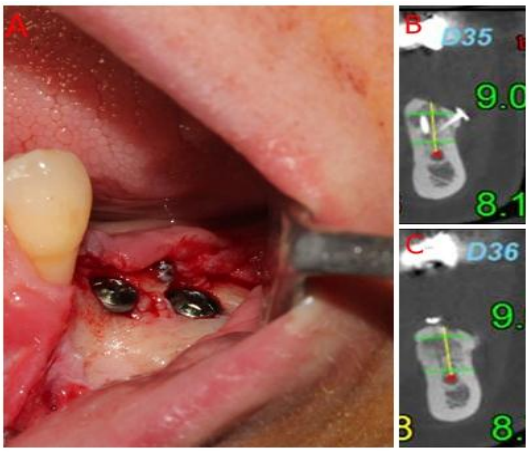

Figure 3. A. 2 dental implants placed into the healed graft (Nov 2015). B,C Tomography scans showing adequate amount of bone in the premolar and molar sites of the left jaw

Figure 4. Final prosthesis (April 2016). Intraoral view

DISCUSSIONS

In the present case a serious bone defect was surgically managed with the use of an autologous bone block and later implant fixtures placement. Due the rich of bone cells and growth factors an adequate bone volume was obtained with a high bone quality.

In similar defects a variety of procedures and materials are available. The defect can be restored using natural or synthetic bone substitutes. The disadvantage is the high cost of these materials and the lack of a good constant result. Also there is a less percentage of viable bone at the end of the healing phase. The allograft or xenograft material requires an extended healing time (8-10 months) in comparison with the autologous which is mandatory to be uncovered after 4 months (3). Also these types of materials require graft covering with collagen membranes but the autologous bone block does not need any kind of protection for the soft tissue.

The main disadvantage of autologous bone harvesting is the second site morbidity and some operative discomfort due to a prolonged procedure (4). The edema and bone trauma can be highly reduced with the help of piezosurgery units versus conventional rotary instruments (burs, saws). This piezo machine cuts the bone in a unique fashion and reduces bleeding at the cutting site (5).

The donor site for a 2 or3 teeth defect is ideally the oral cavity especially the retromolara area, the *linea oblicua externa* or the chin for the mandible. There are a few dedicated maxillary regions such as the hard palate, the zygomatic buttress or the tuberoses, but the upper jaw sites have a bigger percentage of spongious bone then cortical.

Larger defects can be treated by autologous bone but the donor site must be extra orally for a proper bone volume. The typical sites are the Ilium and the *calvaria* regions (6). This kind of procedure requires general anesthesia and the use of good operatory room.

The intimate contact and fixation of the graft is crucial for graft stability and a good prognosis. The bone blocks must be fixed with titanium screws in respect to the osteosynthesis principles of the maxillofacial trauma.

Another complication is wound dehiscence which can lead to graft failure. The moment of time in which dehiscence occur is thus critical. Early dehiscence leads to graft failure, thus the mucoperiostal flap must fully and passively cover the block without any tensions. The sutures should be tailored to ensure a good fit of the flap.

There are some reports regarding inferior alveolar nerve disesthesia after block harvesting but with accurate CBCT planning these chances are significantly decreased (7).

The graft undertakes a remodeling procedure by the body thus is imperative for the block to be placed in an over corrective manner so the final bone volume after the healing will insure a proper support for the dental implants.

The crestal bone resorption around the neck of the implants is a common phenomena even in implants placed in natural bone so there is some bone remodeling at the neck of the implants but that will not lead to implant failure (8).

CONCLUSIONS

The use of autologous bone blocks is considered to be the gold standard in implant preprosthetic treatment. There is a shorter healing phase comparative with other methods. The facial edema due to donor site morbidity can be severely decreased with the use of piezosonic surgery. The amount of viable bone is significant greater than with any other synthetic or natural material.

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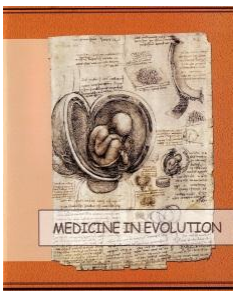
Vacuum formed invisible appliances for the correction of mild sagittal discrepancies



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Abstract

Adult orthodontics is an increasing field nowadays that demands esthetic alternatives to conventional treatment Moderate and mild malocclusions can be treated with the use of invisible appliances such as vacuum formed devices made on an in-office set-up. Small sagittal dental discrepancies can be corrected with the use of plastic aligners with attachments for elastic wear. Minor distalization in class II patients can be achieved through-out a series of aligners before class II elastics can compensate the dental protrusion and improve anchorage. This approach can be satisfactory for adult patients with small orthodontic problems due to less social impact of their dental appliances.

Keywords: *invisible appliances, vacuum formed devices, class II elastics*

INTRODUCTION

When treating a dental class II patient, the correction of the sagittal discrepancy can be corrected in different ways: molar distalization, extractions and class II elastics. Since distalization more than 3 mm is impossible with the use of aligners and extraction cases are out of the question or at least controversial even with the use of more complex systems (such as Invisalign or Clear Aligner),[1] class II elastics can be used for minor dental corrections (< 2 mm of antero-posterior movement). In order to correct the OJ and the incisor flaring, small buttons can be added to the upper and lower vacuumformed devices. This alternative is comfortable and esthetic for adult patients when it comes to finishing, after a previous conventional treatment with braces, or even as a primary treatment for minor malocclusions. [2]

Study objectives

Our study objective is to emphasize the role of the vacuumformed plastic appliances for the correction of minor sagittal discrepancies. Other tooth movements can also be done with the use of an in office set-up : minor rotations or minor angulation problems.

MATERIAL AND METHODS

We evaluated a few clinical cases with antero-posterior orthodontic problems. Vacuum formed appliances were provided to the patients and plastic buttons were added to the appliances. The vacuum formed appliances are fabricated from a plastic material (polyethylene) in order to provide stability, retention, comfort and esthetics [3] and the attachments are manufactured by a dental technician or orthodontist with the use of some special pliers: the accent pliers (Clear Aligner). The PETg material used for the manufacturing of the aligners consists of special foils with different thickness: 0,5 mm, 0,625 mm and 0,75 mm and the pliers are provided by Clear Aligner (Clear Collection tray).

These pliers are often used to enhance biomechanics with vacuum formed appliances. Different attachments can be made with the use of the pliers: vertical or horizontal, round, square or other shapes. Such attachments can increase the contact point between the teeth and the aligners or they can create force couples for more complex tooth movements: rotations, incisor torque, etc. [4] More specific procedures like class elastics or elastic chain (for space closure) require more simple attachments. The procedure is very simple due to the ergonomic design of the pliers. Heating the pliers will create a minor impression in the vacuum formed appliance. Although good results were obtained with this technique, heating the pliers is not always recommended because of possible side effects of the aligners or unwanted plastic deformation. [5]

To support all of the above, some cases were selected.

The first case refers to a young patient with a slightly increased overjet and minor angulation problems in the lower arch (lower incisors). Vacuum formed appliances were manufactured, after an in office set-up (fig. 1, 2). The next step will consist of another set of aligners (upper and lower) with small buttons (round attachments) for elastic wear.

Figure 1. The dental set-up prepared for the manufacturing of the aligners

Figure 2. The first set of the vacuum formed aligners

The aligners are made out of foils with different thickness : 0,5 mm, 0,625 mm, 0,75 mm and 1 mm (the last one is used as a retention appliance). The next set will be provided to the patient after the desired dental corrections are obtained. The case is still in progress.

The second case is a typical example of elastic wear for the correction of a minor sagittal discrepancy. The upper and lower aligners include small round attachments for class II elastics. A small acrylic tooth was included in the lower aligner to maintain the space before a prosthetic solution will be implemented. (fig. 3, 4)

Figure 3. The lower vacuumformed appliance with the small attachment for class II elastics

Figure 4. The lower set-up : other dental corrections were made in the frontal area and an acrylic tooth was added (for space maintenance)

RESULTS AND DISCUSSIONS

With the development of new procedures and techniques regarding aligners, in office appliances gained more popularity due to new ways of replacing direct bonding attachments, for more complex tooth movements or elastic wear, with direct plastic attachments. Progressively increasing the thickness of the vacuum formed appliances, from a 0,5 mm foil to a 0,75 mm foil, light forces can be used, since they induce physiologic responses and provide more comfort for the orthodontic patients. [6,7]

CONCLUSIONS

Vacuum formed appliances made directly in the dental office, provide a more rapid solution for the patients who seek orthodontic treatment for minor malocclusions. Even if dental alignment is achieved with the use of aligners, sagittal discrepancies can only be corrected through-out the use of attachments and elastics, without being forced to implement more radical and inesthetic solutions. Rapid solutions and esthetic results can be obtained with just a pressure forming machine, PETg foils, special pliers and cooperative patients for good treatment outcomes. [8]

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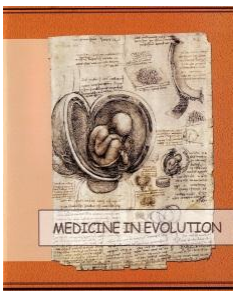
Clinical and statistical correlations between haematological disorders and lesions of the oral cavity



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Abstract

Oral manifestations of haematological disorders are entities that have great impact on the clinical evolution and the complex therapy of these disorders, early detection in the oral cavity having prognostic significance.

Objectives: This research study aimed to investigate the incidence of bleeding disorders and their manifestations in the oral cavity in relation to the type of haematological disease.

Material and method: The study was conducted in a group of 185 patients with malignant haematological disorders hospitalized to the Haematology Department of the Internal Medicine Clinic I, County Hospital, Tirgu Mures during 2012-2015.

Results: There are many types of haematological disorders, from simple to benign forms of thrombocytopenic purpura, found in 2.16% of cases up to severe forms of malignant non-Hodgkin's lymphoma- 15.13%, multiple myeloma- 8.64% and megaloblastic anemia in 10.81% of cases.

Discussions: In our study, the most common oral manifestations were represented by spontaneous gingival bleeding in a percentage similar to the studies conducted in Australia

Conclusions:Dentists have an important role in the diagnosis, prevention and treatment of oro-dental diseases in patients with bleeding disorders.

Keywords: Oral, manifestation, haematological, bleeding

INTRODUCTION

Oral manifestations of haematological disorders are entities that have great impact on the clinical evolution and the complex therapy of these disorders, early detection in the oral cavity having prognostic significance. Being familiar with the clinical and laboratory aspects of blood dyscrasias helps the dentist to establish a correct diagnosis of the lesions of the oral cavity and to adopt appropriate local and general therapeutic conduct, thus minimizing the occurrence of unexpected complications associated to dental therapy [1].

The increasing number of hemopathies of various causes and advanced studies in this area fully motivate the research of this issue from the dentist's point of view. Hence the dentist by being in contact with a large number of patients is able to detect characteristic lesions in the early stages of these diseases. The treatment of oro-dental diseases can be delayed or minimally invasive solutions can be adopted according to the underlying haematological disease [2].

Objectives

This research study aimed to investigate the incidence of bleeding disorders and their manifestations in the oral cavity in relation to the type of haematological disease, clinical stage, age and gender.

MATERIAL AND METHODS

The retrospective study was conducted in a group of 185 patients (97 males and 88 females) with malignant haematological disorders hospitalized to the Haematology Department of the Internal Medicine Clinic I, County Hospital, Tirgu Mures during 2012-2015. The patients were grouped into two age groups: 25-40 years old and 40-60 years old. In the first subgroup we evaluated 40 male and 42 female patients, while in the second group: 57 male and 48 female patients. We used the patient's observation sheets to analyze the following parameters for each of them:

- histological diagnostic, pathogenic evolutionary factors and complications
- haemorrhages, systemic manifestations
- manifestations in the oral cavity

Oral examination was performed with classic instruments in the dental office of the Emergency County Hospital, Tirgu Mures: mirror and dental probe. This evaluation was performed by examining the patient's skin and other mucous membranes and according to the type of the haematological disease. The statistical analysis of the obtained data was performed with the chi square test.

RESULTS

There are many types of haematological disorders, from simple to benign forms of thrombocytopenic purpura, found in 2.16% of cases up to severe forms of malignant non-Hodgkin's lymphoma- 15.13%, multiple myeloma- 8.64% and megaloblastic anemia in 10.81% of cases. (Table 1)

Table 1. Haematological disorders encountered in the study group of patients

No.	**Disease**	**Patients**	
		No.	**Percent %**
1	Acute lymphoblastic leukemia	8	4,32%
2	Acute myeloid leukemia	15	8,10%
3	Chronic lymphocytic leukemia	18	9,72%
4	Non-Hodgkin malignant lymphoma	28	15,13%

5	Hodgkin lymphoma	12	6,48%
6	Multiple myeloma	16	8,64%
7	Chronic myelogenous leukemia	16	8.64%
8	Immune thrombocytopenic purpura	4	2,16%
9	Hypersplenism	26	14,05%
10	Megaloblastic anemia	20	10,81%
11	Myelodysplastic syndrome	7	3,78%
12	Hemophilia	9	4,86%
13	Bone marrow aplasia	6	3,24%
14	**Total**	185	100%

If we analyze the incidence of the disease by gender and age groups, the results show a higher rate of leukemia in women in the age group of 25-40 years old and in males a higher incidence of malignant non-Hodgkin and Hodgkin lymphomas in the age group of 40 -60 years old. (Table 2)

Table 2. The incidence of haematological diseases by gender and age

No.	**Disease**	**Patients**		**p-value**
		Number	%	
1	Acute lymphoblastic leukemia	5 women, 3 men	4,32%	0.7205
2	Acute myeloid leukemia	9 women, 6 men	8,10%	0.5916
3	Chronic lymphocytic leukemia	10 women , 8 men	9,72%	0.8049
4	Non-Hodgkin malignant lymphoma	11 women, 17 men	15,13%	0.2248
5	Hodgkin lymphoma	5 women, 7 men	6,48%	0.5669
6	Multiple myeloma	9 women, 7 men	8,64%	0.7946
7	Chronic myelogenous leukemia	10 women, 6 men	8.64%	0.4337
8	Immune thrombocytopenic purpura	3 women, 1 man	2,16%	0.6209
9	Hypersplenism	10 women, 16 men	14,05%	0.2112
10	Megaloblastic anemia	11 women, 9 men	10,81%	0.8135
11	Myelodysplastic syndrome	5 women, 2 men	3,78%	0.4441
12	Hemophilia	3 women, 6 men	4,86%	0.5017
13	Bone marrow aplasia	2 women, 4 men	3,24%	0.4441
14	**Total**	185	100%	

By analyzing the most common haematological disorders we can observe that malignant haemopathies show the greatest value among all studied cases. Thus acute leukemia with a 12.42% is found in a myeloblastic form in 8.1% of cases while the lymphoblastic one in 4.32% of cases (Fig.1).

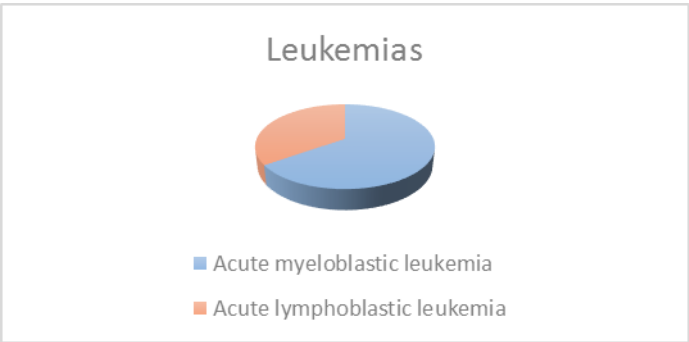

Figure 1. The incidence of leukemia

Leukemia is a disease with increased risk, with multiple manifestations in the oral cavity and with an uncertain prognosis, especially at a young age. Leukemias are problems with constant influence on the oral cavity, the dentist being often the first to observe the changes at the level of the gingival, dental and periodontal structures, changes represented by erythema, edema, gingivostomatitis and frequent gingival bleeding. The most frequent oral

manifestation among the studied group was represented by gingival bleeding in both female and male patients, in both age groups. Values are highlighted in the table below. (Table 3)

Table 3. The incidence of oral manifestations

No.	Type of manifestations	Male	Percent	Female	Percent	p-value
10	Gingival bleeding	47	31,12%	12	21,87%	0.3943
11	Purpura on the oral mucosa	7	4,63%	8	7,21%	-
12	Oozing hemorrhage	2	1,32%	7	6,72%	-
13	Oral hematoma	1	0,66%	5	4,18%	-
14	Oral petechiae	8	5,29%	4	12,5%	0.2282
15	Prolonged bleeding after extraction	1	0,66%	-	-	
	Total	**151**		**36**		

In descending order of frequency petechiae appear on the buccal mucosa due to thrombocytopenia and the alteration of clotting factors, which constantly appear in bleeding syndromes. Due to the prolonged evolution of the disease and repeated hospitalizations for treatment or intercurrent diseases at the same patient polymorphous aspects of the bleeding syndrome in simultaneous and / or successive outbursts were reported.

Analyzing patients with severe chronic, potentially malignant, leukemia the most frequent disease appears to be malignant non Hodgkin lymphoma (37.83%), followed by chronic lymphocytic leukemia (24.32%) and multiple myeloma (21.62%) as shown in Table 4.

Table 4. The incidence of leukemia disorders

Nr	Diagnosis	Number of Patients	Percent %
1	Chronic lymphocytic leukemia	18	24,32%
2	Non-Hodgkin malignant lymphoma	28	37,83%
3	Hodgkin malignant lymphoma	12	16,21%
4	Multiple myeloma	16	21,62%
5	**Total**	**74**	**100%**

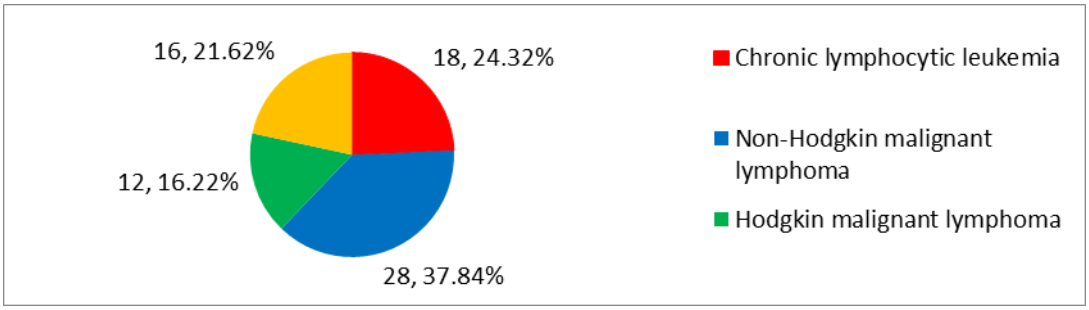

Figure 2. Percentage distribution of leukemic disorders

A total of 18 patients with chronic lymphocytic leukemia were analyzed according to the evolutionary stage of the disease.

No.	Clinical Stage	Number of Patients	Percent%
1	Stage I	2	11,11%
2	Stage II	2	11,11%
3	Stage III	6	33,33%
4	Stage IV	8	44,44%
5	Total	18	100%

At these 18 patients multiple general and oral bleeding manifestations were discovered, their frequency being directly proportional to the evolutionary stage of the disease.

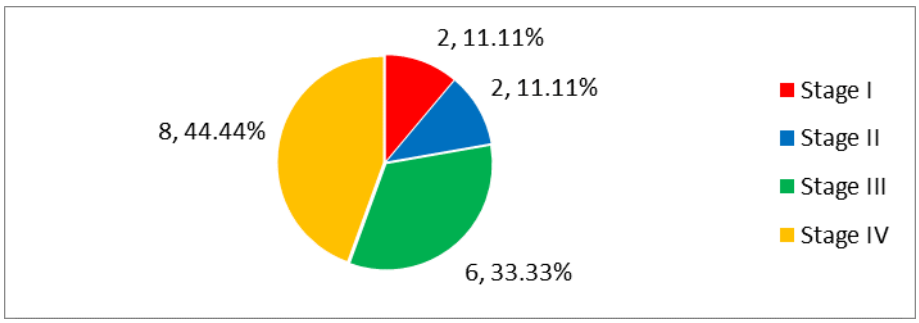

Figure 3. Clinical stage

a. **Stage I** – 26 bleeding manifestations: 15 manifestations of epistaxis (57,69%), 1 manifestation of gastrointestinal bleeding (6,66%), 5 manifestations of hematuria (19,23%) and 5 manifestation of gingival bleeding (19,23%).

b. **Stage II** – 41 bleeding manifestations: 17 manifestations of hematuria (41,46%), 12 manifestations of epistaxis (29,26%), 8 manifestation of gingival bleeding (19,51%), 3 manifestations of superficial ecchymosis and hematomas (7,31%), and 1 manifestation of prolonged bleeding after extraction (2,43%).

c. **Stage III** – 54 bleeding manifestations: 13 manifestations of hematuria (24,07%), 10 manifestations of cutaneous purpura (18,51%), 9 manifestations of epistaxis (16.66%), 7 manifestations of superficial ecchymosis and hematomas (12,96%), 8 manifestations of gingival bleeding (14,81%), 4 manifestations of purpura on the oral mucosa (7,4%), 2 manifestations of digestive bleeding (3,7%), 1 manifestation of hemoptysis and after extraction bleeding (1,85%).

d**. Stage IV** – 132 bleeding manifestations: 27 manifestations of cutaneous purpura (20,45%), 20 manifestations of superficial ecchymosis and hematomas (15,15%), 20 manifestations of hematuria (15,15%), 22 manifestations of gingival bleeding (16,66%), 13 manifestations of epistaxis (9,84%), 10 manifestations of purpura on the oral mucosa (7,57%), 5 manifestations of deep hematomas (5.78%), 2 manifestations of hematoma at the level of the oral cavity (1.51%), 2 manifestations of prolonged bleeding after extraction (1,51%), 1 manifestation of oozing hemorrhage at the level of the buccal mucosa (0,75%), and 10 other common manifestations (7,57%).

After analyzing the presented material it can be concluded that in stages III and IV the number and diversity of the bleeding manifestations have increased compared to those in stages I and II and the percentage of the oral manifestations compared to the common ones has increased as well.

DISCUSSIONS

The high frequency of haematological diseases requires consultation and dental treatment, given that any infection at the level of the oral cavity worsens the prognosis of a haematological disease, especially that of leukemia. In leukemia oral manifestations are frequent especially in the acute and subacute forms and less in the chronic ones. In all forms of leukemia local irritation is considered to be the factor that precipitates oral modifications.

In the clinical picture of acute leukemia changes can be observed not only at the level of the soft oro-maxillo-facial and pharyngeal tissue but also at the level of dental and jawbone structures (serious disorders in developing dental buds in children, often destructive leading to loss of alveolar bone). [3] In adults bone destructions may occur near the apex of the distal mandibular dental roots or resorptions of hard lamina which explains the installation of a pathological mobility of the teeth. [3]

Bleedings may be caused by the rapid decrease in the number of platelets, myelo- and lymphoproliferation of the bone marrow, which develops to the detriment of platelets and

red blood cells. In our study, the most common oral manifestations were represented by spontaneous gingival bleeding in a percentage similar to the studies conducted in Australia [4]

Similar studies on the relationship between the frequency of hyperplastic gingivitis and acute myeloid leukemia were initiated by Babu et al [5]

In our study, the most common oral manifestations were represented by spontaneous gingival bleeding in a percentage similar to the studies conducted in Australia [4]

Similar studies on the relationship between the frequency of hyperplastic gingivitis and acute myeloid leukemia were initiated by Babu et al [5] The complexity of the patient's pathology, determines a rigorous evaluation of the oral cavity and any dental treatment should be initiated in collaboration with the hematologist. Bleeding maneuvers are contraindicated except those imposed by certain emergencies such as fractures or bleeding in the floor of the mouth and severe infections. [6]

CONCLUSIONS

1. Dentists have an important role in the diagnosis, prevention and treatment of oro-dental diseases in patients with bleeding disorders, given the increased risk of infection and bleeding due to underlying disease and radiation therapy and chemotherapy.

2. In chronic lymphocytic leukemia the percentage of the oral manifestations was represented by gingival bleeding in both female and male patients and these signes has increased as well, as stage increase.

3. Inadequate therapeutic conduct regarding dental outbreaks and oral soft tissue injuries, due to a bleeding disorder, in case of weakened immunity may compromise the evolution of specific treatment and can lead to increased morbidity and hospitalization expenses.

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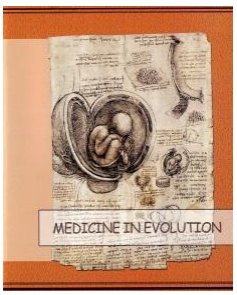
Self medication for oral health issues in children: a cross sectional study



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Abstract

Aim and objectives: The objective of this study was to assess the self-medication pattern for oral health problems in children presenting for the first time at the Paediatric Dentistry Clinic.

Material and methods: The cross sectional study ran for six months and was based on questionnaires distributed to a sample of 466 children and adolescents (mean age 8.21 ± 0.19 years).

Results: The prevalence of children and adolescent patients who received self-medication for oral health problems was 24.5%, significantly influenced by children's age (p=0.023) and parents' education level (p<0.001).

The most common reason for self-medication was toothache (51.7%) and the most frequently administered self-medication were analgesics (43.6%). Most of the persons prescribing the self-medication were members of the family (40.1%) and in most of the cases the outcomes of drugs administration were not as expected, especially in antibiotics (74.6%).

Conclusions: Improving knowledge and understanding of the effects of self-medication can lead to an increase of the rate of its favourable outcomes.

Keywords: self-medication, children, analgesics, antibiotics

INTRODUCTION

Pharmacotherapy, both prescribed and self-administered, is reported being on the rise and plays an important role in the management of oral health issues in adult or paediatric patients [1, 2].

Self-medication is defined as the use of medicines by individuals (or a member of the individuals' family) to treat self-diagnosed conditions or symptoms [3].

The prevalence of self-medication for oral health problems is high and is associated with age, familial status and location. The most frequently self-medicated oral health aspect is toothache [4].

The knowledge of the parents about the proper way of dealing with drugs and potential dangers of self-medication in children is both insufficient and often erroneous [5].

Most of the parents do not know that medicines administration in children shows some special features because the paediatric patient is a growing body reacting differently to the drugs, (need of dose adjustment, choice of the proper route of administration and the need of taking into account the pharmacokinetics and pharmacodynamics particularities of the medicines) [6, 7].

According to some studies, a large part of the self-prescribed antibiotics was either not indicated or were inappropriate in terms of drugs or dosage [8, 9].

That is why the prescription of medications is more challenging today than in the past because of microbial resistance to prescribed antibiotics and drug interactions developed after a previous incorrect self-medication [10].

The objective of this study was to assess the self-medication pattern for oral health problems in children presenting for the first time at the emergency room of the Paediatric Dentistry Clinic because, as far as we know, there are no other studies in Romania related to this matter. The international literature contains, as well, only scarce information on the subject of self-medication in paediatric dentistry patients.

The prevalence of self-medication was evaluated in accordance with some variables like: the reason for self-medication, the duration of self-medication, the effect of self-medication a.s.o.

MATERIALS AND METHODS

This cross sectional study ran for six months (the first six months of 2013) in the Paediatric Dentistry Department, Faculty of Dental Medicine, "Carol Davila", Bucharest.

The research was a pilot study based on data collected from questionnaires addressed to the parents.

A total of 545 questionnaires were initially distributed to all the new patients who presented at the emergency room. Applying the inclusion criteria, presented below, the initial patients sample was reduced to 466, aged between 8 months and 17 years and 9 months, with an average age of 8 years and 2 months (8.21 ± 0.19 years).

The patients' inclusion criteria were:

- patients who were at the first presentation in our clinic,
- patients accompanied by an adult person who supervised the administration of drugs,
- patients whose parents / adult caregivers agreed to complete the questionnaire,
- patients whose parents / adult caregivers completed the questionnaire properly.

Out of the 466 patients was drafted the study group of self-medicated children, comprised of 114 subjects aged between 1 year and 8 months and 17 years and 1 month, with an average age of 8 years and 6 months (8.54±0.37 years).

The questionnaire included two sections:

1. **Personal data of the child and parents:**
   - age (3 age groups for children), gender (girls / boys), living environment (urban / rural). The subjects of the study group were divided into two age groups: group 1 (0-9 years) and group 2 (9-18 years).
   - information about the parent / caregiver (age, gender, degree of education), The subjects of the study group were divided into eight groups by the degree of education of parents: no studies, 4 classes, 8 classes, 10 classes, high school, professional school, faculty, postgraduate studies. For the statistical analysis these categories were reduced to two groups: education below / above the level of high school.
2. **Six questions regarding:**
   - the administration of drugs for oral problems in the recent past (yes/no),
   - the reason of dental medication (toothache, swelling, soft tissue pain – infectious of traumatic),
   - the type of drug that was administrated: general medicines such as antibiotic, pain relievers (non-opioid analgesics, non-steroidal anti-inflammatory analgesics, mild opioid analgesics), topical medicines such as colutory, mouthwashes or herbal medicines both appropriate and harmful such as alcohol, vinegar, garlic,
   - the presentation form of the drug (tablets and other solid types, liquid, suppositories, suspension, syrup), the route of administration (oral, rectal, topical),
   - the duration of medication (when needed, several times a day, less than three days, for 3-6 days, over six days),
   - the effects of the self-medication (complete remission, partial remission, lack of remission, side effects), the person who prescribed the drug (family, dentists, other doctors or pharmacists, friends, mass media etc.). The administration of drugs following the advice of family, friends, mass media, pharmacists etc. was considered self-medication, while the administration of drugs following indications received from dentists and other doctors was considered medical prescription.

Data were statistically analysed using PSPP v.0.8.0 and the graphic illustration of the results was done using Microsoft Excel 2010. Statistical tests (Pearson's chi squared) were performed for a confidence level of 95% ($p \leq 0.05$).

RESULTS

In the initial sample, the frequency of patients who used drugs to treat oral problems was 49.4% n=230 and of those who did not use any medicine was 50.6% n=236. *The number of medicines* used to treat oral problems was 329, resulting in an average of 1.43 medicines per patient.

The prevalence of patients who received *self-medication* was 24.5% (n=114), the prevalence of patients who received prescription-medication was 24.9% (n=116) while 50.6% (n=236) of the patients did not receive any medicines.

The gender distribution of the *self-medicated* patients was the following: 36% (n=41) girls and 64% (n=73) boys. Reported to the initial sample, the frequency of drugs administration was higher in boys (59.6%, n=152) than in girls (37%, n=78) ($p<0.001$).

The age distribution of the self-medicated patients was the following: 0-9 years 58.7% (n=67) and 9-18 years 41.3% (n=47). Reported to the initial sample, the frequency of self-medication was higher in patients in the 9-18 years old age group (28.7%, n=47) compared to those in the 0-9 years old group (22.2%, n=67) ($p=0.023$).

The distribution of the parents/caregivers of the self-medicated patients according to the education level was the following: below high school 65.8% (n=75), above high school 34.2% (n=39). Reported to the initial sample of patients, the frequency of self-medication was

higher in parents with lower education level (33.9%, n=75) than in parents with higher education levels (15.9%, n=39) (p<0.001).

Most of the patients having received self-medication were living in urban areas - 94.7% (n=108) while 5.3% (n=6) were living in rural areas. Reported to the initial sample of patients, the frequency of self-administered drugs was higher in patients from the urban area than in patients from the rural area, although this difference was not statistically significant (p=0.394).

Self-medicated patients received 52.3% (n=172) of the medicines, resulting in an average of 1.51 medicines per patient while *prescription-medicated* patients received 47.7% (n=157) of the medicines, resulting in an average of 1.33 medicines per patient.

The distribution of *the systemic drugs* in self-medicated patients was: pain relievers 43.6% (n=75), antibiotics 32% (n=55) while *the topical drugs* were either beneficial 22.1% (n=38) or harmful 2.3% (n=4).

Only 41.8% (n=23) of the antibiotics (n=55) were represented by penicillins and 65.4% (n=49) of the pain relievers (n=75) were represented by paracetamol.

The distribution of the self-administered medicines according to *the route of administration* was the following: oral route 73.3% (n=126), rectal 2.3% (n=4) and topical 24.4% (n=42).

In patients receiving self-medication, *the pharmaceutical form* of the administered drugs was the following: pills 57.6% (n=99), syrup 7.6% (n=13), suspension 8.1% (n=14), suppository 2.3% (n=4) and topical 24.4% (n=42).

The duration of medicine administration in self-medicated patients according to the type of drug was the following:

- For systemic drugs: painkillers - when needed 18,7%, n=14; less than 3 days 61.3%, n=46; between 3 and 6 days 16%, n=12; more than 6 days: 4% n=3; antibiotics - when needed 9.1%, n=5; less than 3 days 40%, n=22; between 3 and 6 days 45.5%, n=25; more than 6 days: 5.5%, n=3;
- For topical drugs: beneficial – when needed 13.2%, n=5; less than 3 days 31.6%, n=12; between 3 and 6 days 55.3%, n=21; harmful – when needed 75%, n=3; less than 3 days 25%, n=1.

The reasons for administering drugs in self-medicated patients were the following: toothache 51.7%, n=89; swelling 31.4%, n=54; soft tissues pain 16.9%, n=29.

According to the *reason of drugs administration, the types of medicines* received by the self-medicated patients were the following:

- For toothache: painkillers – 56.2% (n=50), antibiotics – 34.8% (n=31), beneficial topical medicines 6.7% (n=6), harmful topical substances 2.2% (n=2);
- For swelling: painkillers - 37% (n=20), antibiotics – 44.4% (n=24), beneficial topical medicines - 18.5% (n=10);
- For soft tissue pain: painkillers - 17.2% (n=5), beneficial topical medicines – 75.9% (n=22), harmful topical substances – 6.9% (n=2).

The distribution of self-medication according to the *person prescribing* it was as follows: family 40.1% (n=69), pharmacists 29.7% (n=51), friends/acquaintances 23.3% (n=40), mass media 7% (n=12).

The outcomes of self-medication were as follows: complete remission 25.6% (n=44), lack of remission 30.2% (n=52) and partial remission 44.2% (n=76). In 3% (n=5) of the children signs/symptoms interpreted as possible side effects were recorded. Harmful effects were recorded in 9.53% (n=4) of the self-administered topical medicines.

The outcomes of self-medication in accordance to the source of the prescription were as follows: pharmacists - complete remission 56.9% (n=29), lack of remission 13.7% (n=7), partial remission 29.4% (n=15); family - complete remission 17.4% (n=12), lack of remission 31.9% (n=22), partial remission 50.7% (n=35); friends/acquaintances - complete remission

7.5% (n=3), lack of remission 50% (n=20), partial remission 42.5% (n=17); mass media - lack of remission 25% (n=3), partial remission 75% (n=9).

The failure of self-medication (represented by the lack of remission or partial remission of symptoms) according to the type of medication was distributed as follows: painkillers – 74.6% (n=56), antibiotics – 74.6% (n=41), beneficial topical medicines – 71% (n=27).

The causes of failure by the type of medicine were as follows: painkillers – inadequate medicine 33.3% (n=25), short administration period 4% (n=3), lack of dental treatment 37.3% (n=28); antibiotics - inadequate medicine 9.1% (n=5), short administration period 47.3% (n=26), lack of dental treatment 18.2% (n=10); topical medicines - inadequate medicine 54.8% (n=23), short administration period 11.9% (n=5), lack of dental treatment 26.2% (n=11).

DISCUSSIONS

Self-medication is a component of health self-care and represents the use of non-prescription medicines by people on their own initiative or on the advice of a pharmacist or a lay person instead of consulting a medical practitioner [2, 11].

The prevalence of self-medication, as reported by WHO, was 80% of the world population, exceeding four billion people. The prevalence of self - medication was reported in USA and Lebanon as 41.6%, in Ghana as 74.5%, in Mali in the pharmacies as 63% and in Saudi patients as 80% [12, 13, 14]. However, other studies revealed a much lower prevalence of self-medication (22% in a population-based study in Czechoslovakia) [5].

In our study almost half of children (49.4%) took medication (self-medication or prescribed) for the treatment of dental problems that means an average of 1.42 medicines per patient.

More than half of the medicines (52.3%) were received by self-medicated patients, with an average of 1.51 medicines per patient compared to an average of 1.33 medicines received by prescription-medicated patients. The prevalence of children and adolescent patients who received self-medication for oral health problems was 24.5% in our study which represents an important value but significantly lower compared with the results of other authors such as Pereira et al. (2012) in Brazil who reported a rate of self–medication among dental students of 43% and among nursing students of 41.6%, Agbor et al. (2011) - 67.8% in young adults in Cameroon, Kalyan et al. (2013) - 62.5% among dental students in South India and Bennadi (2013) - 99% among young patients in Tumkur, India [4, 11, 15] .

The prevalence of self-medication for oral health problems was not significantly associated with gender and living environment result that is in discordance with the findings of Agbor et al. (2011) in Cameroon [4]. Although there was a statistically significant difference in the frequency of drug use according to gender (59.6% of the boys did receive medication compared to only 37% of the girls, $p<0.001$), there were no statistically significant differences concerning the prevalence of self-medication between boys and girls. In disagreement with our study Buck (2007) reported that adolescent girls in Dresden were more prone towards self-medication for general problems than boys [16].

Although the higher prevalence of self-medication in children from urban area was not statistically demonstrated, the result was in concordance with the one obtained by Bennadi (2013) who revealed that among dental patients in Tumkur India that the prevalence of self-medication was 56.6% in town areas and 43.3% in rural areas [17].

A statistically significant association was found between the prevalence of self-medication and the age group, indicating that older children (9-18 years of age) were more frequently self-medicated ($p=0.023$). The prevalence of self-medication in adolescents (28.7%) was slightly lower than the one reported by Buck for general problems (2007), who found a rate of 33.3% [16].

There were also statistically significant differences concerning the frequency of self-medication according to the education level of the parents, indicating that those with a lower

level of education (less than high school) had the tendency to self-medicate their children more often (p<0.001) result that is in disagreement with the study of Bennadi (2013) who observed a trend towards self-medication in educated population as compared to uneducated population [17]. Our results were also in disagreement with the results of Khalid et al. (2013) that indicated that the level of education did not affect the percentage of self-prescribed antibiotic [12].

In our study the most common oral health problem treated by self-medication was toothache (51.7%) result which is in agreement with the findings of Agbor et al. 54.7% (2011) in Cameroon and in disagreement with Kalyan et al. (2013) in South India who found that headache and mouth ulcers were the most common reasons of self-medication [4, 15].

The most commonly used drugs in our study were pain relievers (43.6%), in disagreement with Bennadi (2013) who reported a much higher percentage of pain reliever use of 98% [17]. The second most frequently used drug were antibiotics (32%), result that is higher than the findings of Kalyan (2013) who reported a frequency of antibiotics use of 17% in undergraduate dental students in a private dental teaching hospital from South India and closer to the results of Abid (2012) who reported a 48% rate of antibiotic use. Khalil et al. (2013) reported a higher rate of antibiotics use, 80% [12, 15, 18]. Sharma et al. (2014) reported somewhat similar administration rates of both analgesics 37.7% and antibiotics 36.4% [9].

In our study 65.4% of painkillers were represented by paracetamol and 41.8% of antibiotics were represented by penicillin, results that were in accordance with many other authors who gave different rate values: Souaga (2000), Sweileh (2004), Konate (2005), Tamietti (2012), Khalil et al. (2013) [12, 13, 19, 20, 21, 22]. However, Heard (2008) reported that the most frequently used analgesic was ibuprofen (37%) [19].

In our study we found no aspirin use in children result that is similar with authors as Tamietti et al. (2012) or Souaga et al. (2000) [20, 22].

Nearly three-quarters (73.3%) of patients have taken drugs using the oral route of administration and over half of them preferred pills 57.6% results that are in accordance with Baig et al (2012) who reported that analgesics were administered orally as a rate of 58.8% or in combination with antibiotics as a rate of 13.4% [6, 23].

Most of the persons prescribing the self-medication were members of the family (40.1%), followed by pharmacists (29.7%), which was in agreement with Agbor and Azodo (2011) and Ellul et al. (2008) [4, 24]. While medicines prescribed by pharmacists were effective in 70.6% of cases, drugs prescribed by family members were effective in only 17.4% of cases.

The outcome of the administration of almost three quarters of the total self-prescribed medicines (74.4%) was considered as a failure, the highest rate of failure being recorded for both antibiotics and analgesics (74.6%).

In our study, at the high number of failures were added some side effects (in 3% of cases), fewer than reported by Major et al (1998) (5.6%) and also some harmful effects (in 2.3% of cases) [3, 14].

The duration of systemic drugs administration was incorrect in 40% of the analgesics and almost a half of the antibiotics, which were administered for short periods of time in 46.8% of the cases. Similarly, most of the patients in the study of Khalil et al. (2013) were confused about the period over which the antibiotic should be taken. Most of these patients have taken the antibiotic for just one day. These errors in antibiotic administration may lead to an increased occurrence of microbial resistances [12].

In the present study, only a little over a quarter (26.2%) of topical medications have been properly administrated while 54.8% of them represented a wrong choice.

Analysing the distribution of the types of drugs based on their prescribing reasons one may observe that the pain in pulpitis was managed with no effect in under 4.5 of cases with antibiotics (wrongfully used as analgesics) or with harmful topical drugs (2.2%). Agbor et al.

(2011) reported that a minority of patients took dangerous substances (7.7%) and yet he found a much higher proportion than us [4].

All these serious errors resulted from the lack of or poor knowledge about drugs of the persons who recommended the medicines and about the urgent need of paedodontic treatment [2, 5, 16, 17, 24, 25]. For example, inadequate types of antibiotics were prescribed in 9.1% of cases, in almost one fifth of the self-prescribed medicines the duration of administration was too short (19.8%) and dental treatment was neglected in 23.8% of cases.

The results of this survey may be biased by the fact that they resulted from a small sampling of dental patients and only over a 6-month timeframe. In addition, patients' answers regarding the use of self-prescription medication in the past may have been incomplete or inaccurate.

CONCLUSIONS

The prevalence of children and adolescent patients who received self-medication for oral health problems was important (24.5%) and significantly influenced by the age of the children and the education level of the parents.

The most common reason for self-medication was toothache and the most frequently administered self-medication were analgesics, followed by antibiotics.

Most of the persons prescribing the self-medication were members of the family and in most of the cases the outcomes of drugs administration were not as expected, especially in antibiotics.

Improving knowledge and understanding of the effects of self-medication can lead to an increase of the rate of favourable outcomes.3

Authors' contribution

All authors had an equal contribution to the elaboration of the article.

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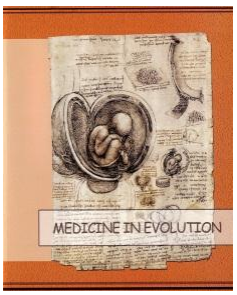
Limitations in prosthetic treatment in dentinogenesis imperfecta type II: a case report



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Abstract

Introduction. Dentinogenesis imperfecta type II is characterized by poor mineralization and abnormal deposition of the dentine, which leads to: color and shape-modification teeth, rapid wear of the enamel, pulpal complications associated with obliterated pulp chambers, VDO reduction. The treatment is usually phased, long-term, based on multidisciplinary approach, influenced by the severity of the clinical manifestations and cooperation with the patient.

Aim. The aim of this article is to describe the dental treatment performed in a 9½ years old boy affected by DI type II, with emphasis on the limits that may occur during treatment.

Case report. To prevent further attrition and pulp complications, as well as restoring vertical dimension of occlusion and functionality, the first treatment phase involved prosthetic rehabilitation with temporary acrylic bridges placed on permanent incisors and Ni-Cr metal crowns applied to permanent first molars. Growth phase not finished, challenging clinical conditions, reduced financial possibilities and modest technical features were the main limitations encountered during treatment.

Conclusion. No matter the limitations, oral rehabilitation must and can be done to improve the quality of life in patients with dentinogenesis imperfecta.

Keywords: dentinogenesis imperfecta type II, prosthetic treatment, acrylic bridge, metal crowns, limitations

INTRODUCTION

Dentinogenesis imperfecta (DI) represents an autosomal dominant disease[17], divided into three types, according to Shields classification (1973)[6,19].

DI type II (isolated, hereditary opalescent dentin "Cap de pont") is as a result of dentin-sialo-fosfoprotein's mutation associated with chromosome 4q12-21[17]. It appears in both dentitions, healthy genders, with an incidence of 1/6000 to 1/8000[1,13,15,16]. Histological it is characterized by poor mineralization and abnormal deposition of dentine, which progressively obliterates the pulp chamber[16]. Clinically, teeth appear with a a variable yellow-brown to blue-gray discoloration[1,13], translucent, opalescent; when subjected to occlusal stress rapid wear of the enamel and dentine leads to pulpal exposure with consecutive reduction of the vertical dimension of occlusion (VDO). Radiographically crowns appear bulbous, with a marked cervical constriction and roots are short and thin, with an increased risk of dentigerous cysts[15,19,,20].

In most cases, dentinogenesis imperfecta requires a multidisciplinary approach, considering the patient's age, cooperation, tooth destruction and pulp root abnormalities[13,14]. In mild to moderate cases, treatment involves restorative methods (dental fillings, bleaching)[19], in more severe cases, fixed (veneers, occlusal onlays, full coverage crowns, implants) and removable (overdentures) prosthetic methods are the treatment of choice[4,24].

Objectives

The aim of this article is to describe the dental treatment performed in a child affected by DI type II, with emphasis on the limits that may occur during treatment.

CASE REPORT

9½ years old boy from Filiaşi, Dolj County, was brought by his mother to the Department of Pediatric Dentistry at the "Carol Davila" Dentistry School, Bucharest, Romania, with the chief complaint of chipping of teeth and abnormal teeth color.

Diagnosis of dentinogenesis imperfecta type II was given on the basis of clinical and radiographic features. The family history suggests that no other member had clinical aspects suggestive for dentinogenesis imperfecta.

Patient was overweight, no bone abnormalities were present and his medical history was not relevant. Oral examination revealed mixed dentition (premolars, inferior canines and second molars in eruption), with a slightly precocious eruption. Clinical features fitted into the typical dentinigenesis imperfecta type II pattern: both dentitions affected, yellow-brown opalescent teeth (Fig. 2); except for the teeth in eruption, all of them presented different grades of abrasion (Fig. 1), but the pulp chambers were not exposed; reduced VDO; low carioactivity). Gingivitis was localized at inferior first molars.

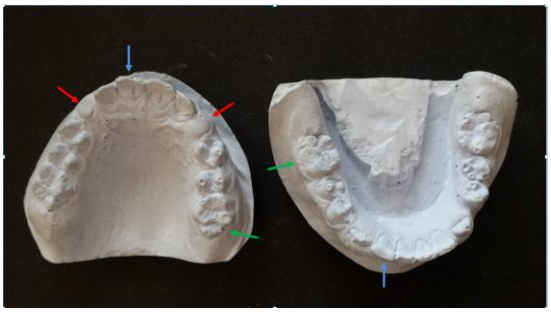

Figure 1. Mixed dentition, teeth with different grades of abrasion (I-blue arrow, II-green arrow, III-red arrow)

Figure 2. Generalized yellow-brown color of the teeth, typical to dentinogenesis imperfecta

Orthopantomograph revealed "tulip-like teeth" (short bulbous crowns, marked cervical constriction) and narrowed pulp chambers due to abnormal dentin deposition, even for un-erupted permanent teeth (Fig. 3). Periapical pathology was not evidenced.

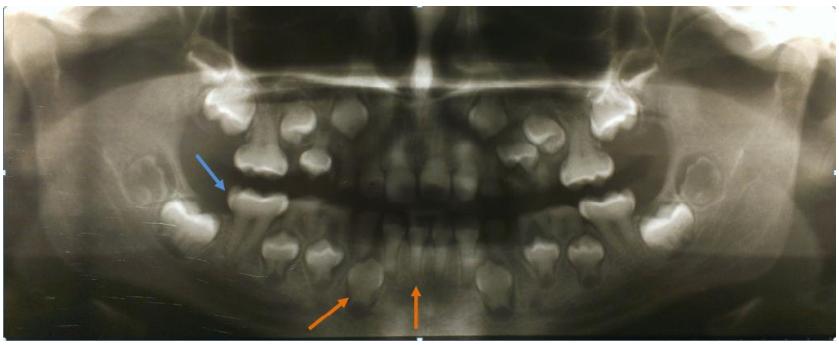

Figure 3. OPG reveals "tulip-like teeth" (blue arrow) and narrowed pulp chambers (orange arrows)

Treatment plan

Because the patient had not finished the growth phase, a two-phased treatment was developed. First phase (temporary, provisional), during mixed dentition, had the aim to: establish a long-term collaboration doctor-patient and limit the psychological implications of the disease; improve oral hygiene and maintain dental health; stop dental wear and preserve vitality; restore vertical dimension of occlusion and facial features. The second phase of the treatment (long-lasting, definitive), established after the eruption of all permanent teeth and complete somatic development, aimed to provide functionality through prosthetic full mouth rehabilitation.

Treatment procedure

The first phase of the treatment started with: behavior management (tell-show-do, straighten positive behavior, non-verbal communication), prophylactic treatment (instruction about oral hygiene, use of fluorides, diet guidance) oral cavity sanitation (scaling and professional cleaning), restorative procedures (metal reinforced/glass-ionomer fluoride-releasing fillings on molars, adhesive sealings on premolars) and orthodontic evaluation (for premolars' de-rotation).

First phase of prosthetic treatment included achieving acrylic bridges on maxillary and mandible permanent incisors and Ni-Cr metal crowns on 6 years old molars. Being the most affected, the inferior incisors were restored first. Using a tapered diamond and air-water cooling, the crowns were slightly reduced and a direct provisional self-curing acrylic bridge (Duracryl, SpofaDental) was cemented (Ketac Cem, 3M ESPE), VDO being increased with 2 mm (Fig. 4).

Figure 4. Direct acrylic bridge on lower inferior incisors

Figure 8. Minim-invasive preparation of the first maxillary incisors

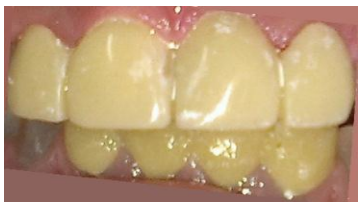

Figure 9. Temporary acrylic bridges on permanent incisors

After 6 months, without using anesthesia, permanent first molars were prepared for indirect Ni-Cr crowns (Fig. 5, 6, 7). A two-steps impression technique with condensation

silicone (Zetaplus Putty + Oranwash L, Zhermack) was performed, after gingival eviction with retraction cords (Ultrapak + Vascostat, Ultradent). Reestablishing the optimal VDO (increased with 1 mm), metallic crowns were temporary cemented (Temp Bond, Kerr). Based on an impression of the slightly prepared maxillary incisors (Fig. 8), an indirect provisional acrylic bridge (Fig. 9) reestablishes correct occlusion in static and dynamic. Both the maxillary bridge and the metal crowns on first molars were cemented with glass-ionomer cement (Ketac Cem, 3M ESPE). An indirect acrylic restoration on lower incisors had to replace the direct bridge, but the patient no longer came to treatment.

Figure 5. Minim-invasive preparation on first molars

Figure 6. Molars on one side - preparations for simultaneous crowning

Figure 7. Indirect Ni-Cr metallic crowns placed on first molars

During first prosthetic phase, prosthetic treatments have been hampered by: an initial uncooperative behavior; difficult acceptance to advices regarding diet; neglected oral hygiene that determined gingivitis and delayed impression; lack of vertical space for the restorations which led to increased VDO; difficulties in assuring retention and color-matching crowns; gagging reflex causing difficulties in impression recordings, countered with local anesthesia in the posterior maxilla; necessity of rare and long treatment sessions due to great distance to the university, time- and money-consuming; guiding treatments according to the patient's limited financial possibilities; conceiving treatment strategies and the use of minimally invasive procedures to preserve tooth vitality and allow normal development of the patient.

DISCUSSIONS

As presented, clinical features of the patient fitted into the typical DI type II pattern described in the literature[15]. Despite the tendency to normal or lower weight, due to poor mastication or general health condition[22], the patient was overweight.

Many challenges were experienced during treatment, among which: patient in growing phase, partially cooperative; severity of clinical manifestations due treatment delay; treatment difficulties caused by the disease itself; limited financial possibilities of the patient; great distance between patient's home and university; limited technology.

To follow general and oral growth and development of the patient, which was the greatest challenge, prosthetic treatment had to be phased in a longer period of time, associated with long-term follow-ups[4,28]. Temporary prosthetic rehabilitation (acrylic and metallic crowns), made up and worn until the end of growth[4], had to: limit dental abrasion, pulpal pathology, associated with difficult endodontic treatment (due pulpal obliteration)[23] or

extractions; reproduce ideal intermaxillary relationships; improve esthetics, assure functionality and create ideal conditions for long-term rehabilitation[23].

Although literature guides that treatment of patients affected by DI should begin as early as possible[8,15,23], in this case delays in dental procedures could not prevent teeth abrasion, VDO reduction and functional problems, transforming the treatment into a complex one[3].

As shown in the literature by *Abukabbos et. al*, treatment of this case of dentinogenesis imperfecta was interdisciplinar[1]. Behavior therapy managed to transform a partially cooperative (Frankl 3) into a totally cooperative patient (Frankl 4)[21], interventions were being conducted without the use of sedation or general anesthesia[27]. Prophylactic treatment was mandatory, especially considering that oral hygiene was poor. As described by *Leal et.al,* restorative procedures on first molars were not successful, due to poor adhesion (poor hybrid layer consecutive dentin malformation)[5,13,15,26].

Crowns are recommended as soon as teeth erupt[17], fixed prosthetic treatments (veneers, occlusal onlays, polycarbonate -, prefabricated stainless steel -, faced-crowns, metal reinforced ceramic or ceramic crowns, pin/root-aggregated or not) being indicated in the literature[2,14,23,29]. Like *Delgado et. al*, acrylic and metallic crowns were adopted considering: minimum dental structures sacrifice; simple, time-saving, low-cost techniques; possibility to be modified to adapt to changing structures[11,12,13]. As well as *Guven* and *Brix*, ceramic[5], zirconia or ceramic fused to metal restorations[13] were to be used as definitive prosthetic restorations, after completion of growth.

Considering the reduced financial possibilities of the patient, limited number of treatment sessions due to patient's home-dental office distance (265 km, 3h 50 min. with train) and limited technical equipment of the university, a direct provisional self-curing acrylic bridge was first made on the lower incisors, to explore patient's reactivity to prosthetic treatment. To establish more resistance and esthetics[10], an indirect acrylic bridge was conducted for upper incisors. Initially, prefabricated crowns were considered, but no match to size, color and teeth morphology[1,24] could be found, unlike *Sapir* or *Abukabbos*. Although it was difficult to perform prosthetic pieces with matching color to adjunct teeth, the patient was esthetically satisfied and an increased self-confidence could be observed. To avoid affecting the teeth vitality, slight reduction of teeth with permanent cooling was considered.

Regarding first molars other problems were encountered: short crowns, marked cervical constrictions and thin, fragile roots created deficiencies in retention and possibility of cervical fractures[9,18], offset by subgingival preparations[4]; second permanent molars in eruption generated difficulties in preparation of the distal face[11]. Resembling *Gibbard*, molars on one side were prepared and crowned as balanced occlusion and low cusp angles, according to the initial shape and size of the crowns, to be provided by the technician[11] (Fig. 6). For a better long-term retention crowns were fixed using long-term cement (Ketac Cem, 3M ESPE) and bridges were used to restore superior incisors, the same as *Bouvier et.al*[4]. Other methods to increase retention could have been used: retention grooves, parapulpal screws, gingivectomy for crown-lengthening[9,11].

Done progressively[7], during few months, first with the lower incisors bridge and second with crowns on molars, the attempt to restore an optimal anthropometric and functional DVO, was successful - no pain or functional problems were reported.

Although towards the end of this dental procedures the collaboration with the child and his mother was good, the treatment had not been finalized and long-term documented, unlike *Bouvier et.al*[4], probably due the complexity and time-extended treatment, distance home-dental office and financial limitations.

CONCLUSIONS

Treatment of patients with DI is complex, long and phased. Early multidisciplinary approach and long-term collaboration doctor-patient lead to functional, esthetic and psychological rehabilitation of the patient.

No matter the limitations (challenging clinical cases, limited financial possibilities, modest technical conditions) oral rehabilitation must and can be done to improve the quality of life of patients with dentinogenesis imperfecta.

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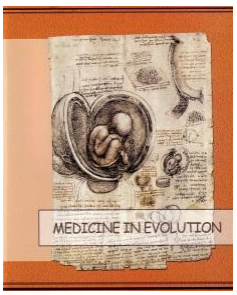
The importance of the digital photography as complementary examination in orthodontics



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Abstract

Digital photography offers precious advantages in the orthodontic field. Because of the fact that during orthodontic treatment, resumption of some images after a certain period of time is most often impossible, only thinking at dental extractions for orthodontic purposes, it should be given a particular importance to the immediate assessment of the image quality achieved. The view according to which digital photography would facilitate achieving great images is partly true. And further processing possibilities of the images are partly erroneously interpreted, which leads to the occurrence of some unprofessional compromises regarding the quality of the initial image. For this reason in the next exposure will be discussed in addition to specific aspects of digital photography also the reasoning underlying the photographic technique and the image composition. We will focus more on the necessary equipment and achieving the standard images, respectively photographic status of the orthodontic patient, wanting to emphasize once again the importance of photography as complementary examination of orthodontic treatment.

Keywords: dental digital photography, orthodontic treatment documentation

THE OBJECT OF THE STUDY

This paper aims to highlight the role of the digital photography as complementary examination in orthodontics, it giving precious advantages in the orthodontic field. Because of the fact that during orthodontic treatment the resumption of some images after a certain time is most of the times impossible, only thinking at dental extractions for orthodontical purpose, it should be given a particular importance to immediate appreciation of the image quality achieved.

MATERIALS AND METHODS

We used the camera Power Shot G Compact 16 set from Canon. It is equipped with flash, objectives and helpful means: retractors of soft tissue and oral mirrors. We will discuss about how to obtain black background and the basic indications of the adjustments, both in frontal images as well as in lateral images. The view according to which digital photography would facilitate achieving great images is partly true. And further processing possibilities of the images are partly erroneously interpreted, which leads to the occurrence of some unprofessional compromises regarding the quality of the initial image. Ne vom axa mai mult pe dotarea necesară şi realizarea imaginilor standard, respectiv a statusului fotografic al pacientului ortodontic. For this reason in the next exposure will be discussed in addition to specific aspects of digital photography also the reasoning underlying the photographic technique and the image composition. We will focus more on the necessary equipment and achieving the standard images, respectively photographic status of the orthodontic patient.

RESULTS AND DISCUSSIONS

The camera

For the majority of digital cameras is about the devices with gaze through the viewfinder, which like the cameras for amateurs can be used in dentistry for recording images with macro setting, but the results obtained are not always the best and they ultimately constitute a compromise solution. The significant disadvantages of these devices are represented on one hand by not overlapping the axes of the viewfinder and of the objective images in the macro zone, meaning the lack of congruence between the viewfinder and the snapshot itself, and on the other hand the macro function, most often made available only through superangulation or halfway through position of the objective, leading thus to a reduced working distance, a deformation in terms of perspective and the unsatisfying illumination [1], Moreover, at the cameras with gaze through the viewfinder is missing the optical viewfinder with the so-called "What you see is what you get" effect, otherwise present at the SLR cameras (SLR = single lens reflex), forcing us to rely when focusing on automatic machine system and also to have limited control over the depth of field.

Another great advantage of SLR devices is naturally represented by the option to change the objective, which, under the given circumstances, allows further use of the objectives already present. And other accessories (flash) can continue to be used alongside digital SLR cameras. Yet, there are many semi-professional devices which after being properly equipped, may become suitable for taking pictures in orthodontics are lighter and more valuable and can be used by the user in and out the dental office (E.g. Nikon Coolpix 5000/ 5700/ 4500/ 995, Minolta Dimage 71, Olympus Medical-D)[1] or Canon PowerShot G16 set with the compact and professional variants.

However who wants to deal on the long term and in the most serious way with photographic documentation, it is better to buy a digital SLR camera. Because digital cameras

with gaze through the viewfinder must also be adapted for use in the dental field, the price difference compared to the SLR cameras is not as significant as it was a few years ago.

When using SLR cameras it is very useful to change the light diffusion screen with a screen with orientation collimator. Quadrilation is almost indispensable for horizontal positioning of the camera and choosing center of the image respectively the vertical median line. This accessory has such a great value that, when choosing the camera it is always taken into account if the device given by the seller presents such a screen [1].

The flash

The discussions about the use of circular or lateral flash in the field of dental photography are still partly controversial [1]. Certainly, at a larger work distance (e.g. overview images), circular flash allows obtaining some placid, without brightness, detail and refinement images, while systems with lateral flash offer more plastic contrasting and bright images. In addition, lateral flashes allow greater variability in the conduction of light and can be used to highlight certain details and textures. Also the color shades of the hard dental substance can be highlighted better. However lateral flash systems have their limitations in the side areas of the arches in these situations, where access and space are limited, circular flashes are more advantageous due to easier handling and uniform and intense light emission in the vicinity of the photographed object. Thereby according to the main use domain, both systems followers are entitled.

Because of the fact that photography in orthodontics surprises structures with strong contrasts, for example the white of the tooth and the red of the gingiva, the possibility of automatic adjusting TTL (= through the lens) of the flash has a great importance, because illumination correction is almost always required. For this reason, manual adjustment of the parameters of illumination should be made by choosing the diaphragm aperture.

Semiprofessional devices with gaze through the viewfinder especially present as light source the LED. This is characterized by low power consumption, enables obtaining shadeless illumination similar to that offered by circular flash, but it prevents the playback of color nuances and of fine surface textures. Since this is a continuous light, the illumination can be verified directly on the camera monitor, and the focus is thus eased. As a compromise solution, for semiprofessional amateurs devices there can be used screens of light diffusion which give the embedded flash the possibility of also being used in the field of macrophotography, thus obtaining acceptable results.

Objectives

Macro objectives with focal length between 50 and 200 mm can be usually used for stomatological photography. A macro objective with a focal length of 100 or 105 mm is however more appropriate for dental photography [1]. Zoom objectives allow rapid modification of photographic perspective, but lead to more difficult obtaining of long-term results due to the fact that it adds a new variable among programming parameters.

Objectives with automatically focus do not facilitate macro photography. However if using them it is recommended to discontinue autofocus function. Focusing is performed better coarse for the beginning by using the adjustment ring, and then finely adjusted by the anterior-posterior movement of the body. Choosing a quality objective has great importance for achieving great images, so it is recommended not to do economy when buying an objective. It is not mandatory to use exclusively camera manufacturer objectives to achieve quality results. The objective should provide a magnification of 1:2 or better 1:1. For greater magnification are usually required accessories such as teleconverter and lenses for macro.

Lenses for macro have the advantage of being lighter, but also valuable, practically not allowing the loss of light. However they shorten the working distance, being able to influence the image quality. Teleconverters extend the focal distance and increase working distance,

absorbing however the light, which helps reducing the depth of field by a decreasing the value of diaphragm aperture.

When using digital SLR cameras it should be considered that COD sensors, respectively CMOS present smaller film format than of the conventional film devices with 35mm. Thus obtaining a factor of extension of the depth of focus of about 1,3 to l,5. This means that at an expanding factor of the depth of focus of l, 5 can be achieved with the objective of 100 mm images similar to those obtained by using the conventional technique with an 150 mm objective. Device-specific expansion factors are mentioned by producers and should be taken into account when choosing the objective. Classical 100 mm objectives represent however an interesting choice for the majority of digital SLR cameras.

Helpful means: Soft tissue retractors

To obtain a good access in the oral cavity, highlighting some structures and appropriate illumination, soft parts retractors are indispensable. Besides the need to ensure a particular patient's comfort, these should not reflect light and be easily individualized, considering working with assistance, unilateral lips and cheeks retractors Mirahold (Fa. Hager & Werken, Duisburg) are the most indicated. With their help or of other similar retractors, lips can be removed in a targeted and dosed way by dental arches and alveolar processes. To avoid for example in the big pictures of the maxillary or mandibular arcade the visibility of the hooks, one of the pairs of retractors can be modified by using a cutter for acrylate and removing the opposite sides of the retractors the lateral extending of the hook up to the level of the handle. With such shortened retractors, soft tissue removal will be more effective.

If working unassisted, complete retractors are recommended, such as Span-dex (Fa. Hager & Werken; Abb. 5) or OptraGate (Fa. Ivoclar Vivadent, Ellwangen) while the Spandex retractor, do not depart sufficiently well the lips from the alveolar process, OptraGate provides a complete picture down to the sac bottoms. Therefore OptraGate allows obtaining better results when working unassisted, being preferred in these situations.

Usually, regardless of model it should used the biggest retractor in order to obtain optimal visibility. Applying cream on the lips and moistening the retractor, the patient will endure easier the maneuver. Many times for the patient it is more comfortable to hold the retractors himself, this way being able to control the maximum tension induced.

Oral mirrors

For the realization of many intraoral photographs mirrors are needed. Obtaining some brilliant photos without double images, requires the use of glass mirrors with the surface treated with rhodium vapor [1]. Mirrors with long handle (as those of the company Filtrop, Balzers, Liechtenstein) have a great advantage, because they allow holding the mirror at distance from the region to be photographed. This facilitates the achievement of imagistic documentation in situations where is also required the presence of other additional instruments in the vicinity of the tooth and avoids the appearance of the image of the fingers of the person holding the mirror.

To avoid fogging the mirror by the patient's breathing, the mirror should be preheated. This is achieved using hot water or a modified heated plate. Besides this the patient is asked to breathe through the nose. The person assisting can also prevent fogging the mirror by slowly and steadily blowing air spray.

Oral mirrors are extremely sensitive and should be handled with care as an optical device, to prevent the damage to the surfaces, which would reduce the quality of images taken.

The black background

When shooting frontal teeth the structures from background may negatively influence the image. Using a black plaque placed behind the dental arch can improve the image quality and attract the viewer's attention on the essential. The black background can be particularly helpful for highlighting the translucency of the incision area. Besides commercial products especially designed for this purpose (BlackGround, Fa. Anaxdent, Stuttgart; Contrastor, Fa. Doctorseyes, Ochsenhausen) can be used black plexiglass plaques (can be found in the construction materials shops) - that will be cropped individually as needed [1].

The use of this background is of course a matter of taste and not a necessary condition to obtain aesthetic images. If however we decide to use a black background, it should be used consistently throughout the series of photos of a case. Further computer processing does not lead to obtaining the same results as when using black background and does not produce the same accentuation on transparencies.

Adjustments: basic indications

Before presenting the concrete parameters intended for shooting certain aspects, we remind a few basic rules to achieve aesthetic clinical images.

It is very important the harmony between the image composition and the anatomical structures. Not overlapping the median lines or occlusion plans photographed crooked can damage the appearance of an image. The appearance in the image of the surrounding structures such as nose, beard, retractor or tongue, may in certain conditions alter the charm of a photo. This should be avoided by effective removal of soft tissues and appropriate selection of the sequence to be photographed.

Of course, also excessive salivation in the areas that will be photographed may produce annoying effects like reflections and uncertainties, but also masking of the surface structures. The presence of soft and hard deposits, as well as dental surfaces colorations and gingivitis may also hinder obtaining appropriate documentation from the qualitative point of view. Therefore, these factors should be removed before beginning shooting, except for cases where the photos are intended to highlight oral hygiene and the periodontal condition of the patient.

Also the structures in the immediate vicinity of the area to be photographed should be viewed critically. So it should be verified, for example, if dental dam is properly adjusted, the wadding roll is still unsoaked with saliva, if the dentinal sawdust was removed or if there should first be treated the neighboring teeth. Fogged mirrors, scratched or dirty lead of course to obtaining unsatisfactory results. Usually it should be working with a diaphragmatic opening as small as possible (high value) to obtain optimum depth of field. Therefore, the camera is programmed on delayed triggering (leads most often to a exposure time fixedly dependent on flash synchronization) and the diaphragmatic opening is adjusted manually depending on the scale of image magnification (between 16 to 40)

During focusing (which should be also manual) it should be considered that motive of the image that should be represented particularly clear. Thus, in frontal images is necessary to adjust the maximum clarity in the area of the canines, to comprise both the anterior teeth as well as the lateral ones in the depth of field. The focus on the frontal teeth would result in an unclear representation of the lateral tooth area. For the same reason, in the case of lateral teeth occlusal photographs the focus should not be made on the cuspidiene tops, but rather on bottoms of the cavities or of fissures, and to get a clear picture at the level of the gingiva as well.

SLR cameras have a function that controls the depth of field. Pressing a button activates the selected diaphragmatic opening so that, looking directly through the viewfinder, to be able to verify the depth of field.

Frontal images

For complete frontal images it should be preferably chosen 2 retractors of lips and cheeks, to be held by an assistant or even by the patient, exerting traction outward and forward, in order to highlight the entire buccal vestibule. The center of the image should be fixed on the mesial contact point of the mandibular and maxillary central incisors, and the central horizontal line will be oriented along the occlusal plane. Also the vertical median line will be carefully targeted corresponding anatomical structures, having as landmark upper and lower lip train and the dental median line. The screen with orientation collimator is practically indispensable in order to obtain an accurate image. The sequence to be photographed should be chosen so that the corners of the photo to be located at the deepest point of the vestibule lateral region, thus enabling a better representation of the entire alveolar process. To capitalize the most optimally the depth of field, focus should be made on the canines. Lips or the components of the retractors should not appear in the picture. It should be avoided any deviation from the sagittal axis as it gives an asymmetric image of the oral corridor[1,2,3].

In the cases where photographic documentation only interest the frontal area, also a representation with a higher multiplication factor is suitable. The lateral edges of the photo will be placed slightly distal from the canines or it is intersecting them at the middle of the vestibular face, while the upper and lower edges located at the level of the fixed gingiva. Otherwise are valid all the features of frontal photography. To register the labial profile and the harmony of frontal dental arch and of the lips, 2 photos can be made, without retractor, presenting the whole area of the lips, with the mouth slightly open and smiling / laughing. We must pay attention to the horizontal orientation of the occlusal plane and the median line. The optical axis should be oriented as perpendicular as possible to the vestibular surface of the upper incisors[1,2,3].

Occlusal images

Occlusal image- maxillary

To obtain occlusal images without the interposition of soft tissue or components of retractors, it is recommended the use of sectioned Mirahold retractors. With their help upper lip can be removed outward and forward by an assistant or by the patient. This maneuver is facilitated by supplementary fixation of the lip in the retractor using the index finger or the thumb. For images of the maxillary arch,the mirror properly chosen as size can be kept and by the patient as well. He is asked to open to a maximum the mouth to ensure a sufficient distance between the mirror and the occlusal surfaces of the maxillary teeth. The mirror will be positioned on the distal mandible teeth, to get an equal distance to the maxillary posterior teeth. The mirror will then be inclined downwards until it reaches the incisal edges of the lower front teeth. Since it cannot always be avoided getting into the image the edges of the mirror, it is important to pay attention to its orientation in the sagittal axis in order to get a symmetrical and harmonious photo. Focusing is performed in the premolar region. Horizontal centerline follows an imaginary line connecting the second premolars and the vertical midline must match the anatomic median line the jaw[1,4,5].

To obtain subsequent occlusal photographs according to reality (for presentations or publications), images must be processed by using a software that creates a vertical mirror image of the arcade recorded. The processed data should be saved under a different name and the software should allow an image processing without quality loss.

Occlusal image- mandible

Achieving the overview images of the mandibular occlusal surfaces is more difficult to achieve than of the maxillary. In this case also will be used shortened retractors and the mirror. For positioning the mirror, the patient is asked to open his mouth to maximum and carry the tip of the tongue to the palace in order to a lead it behind the mirror. The mirror will

be supported on the distal teeth of the jaw and then inclined until it reaches the upper front teeth. Focus will be made in this case also at level of the premolars fissures. Horizontal centerline will be oriented along an imaginary line that connects the second premolars, and the vertical center line will correspond to the anatomic midline of the jaw (lingual frenulum, dental midline) [1,4,5].

In order to obtain subsequent occlusal photos according to reality (for presentations or publications), images must be processed by using a software that creates a vertical mirror image of arcade recorded.

Lateral images

For the lateral images are used elongated mirrors. With a retractor of cheeks (ex. Mirahold if possible of "small" dimension) which moderately departs opposite commissure of the side that we want to photograph and then oral mirror is rotated in the buccal vestibule sideways, the mouth being moderately open. The cheek is then removed from the alveolar process by using the mirror and the patient is asked to close the mouth[1,6].

Horizontal median line should correspond to the occlusal plane. The image to be photographed must be chosen so as to cover both the canine and the distal arch tooth. The upper and lower edge of the photography are corresponding to the fixed gingiva or the bottom of buccal vestibule, the lips and the edges of the mirror will have to not be showing in the frame. The center of the image is located at the tip of the cusp of the second upper premolar or the first molar, this also being the point on which it focuses[1,6].

If working with lateral flash, it is advisable to stop the remote flash or (if possible) to be reduced, thereby obtaining a more uniform illumination.

CONCLUSIONS

Dental photography occupies, after the study of model and dental radiography, the most important place in complementary examinations in orthodontics.

The digital photography offers numerous precious advantages for documenting the clinical stages of an orthodontic treatment: initial, of stage and final. Besides the high capacity of electronic data storage and management of images, as well as multiplication and their light transfer, particularly important is the immediate availability of the images, in this way it can be immediately appreciated the recording quality and depending on the situation the maneuver may be repeated. Because of the fact that in the course of medical therapy resumption at a later stage of treatment of some photographic images it is often impossible, only thinking at tooth extractions in orthodontic purpose, digital photo even appears to have been created for this activity domain. Thus, by choosing the appropriate technical equipment, it is the user himself on which depends obtaining high quality images of the clinical situations.

Before triggering, the photographer should look through the viewfinder and take account of the following:

- horizontal and vertical orientation, as well as the image center to match the respective anatomic landmarks;
- in the image not to appear neighboring areas that could affect the picture (cheek retractors, chin, etc.); photographed sequence to be adapted to the situation (representation of a "single tooth");
- optimal field drying without traces of saliva on the teeth and gingiva;
- lack of dental deposits, healthy gingiva;
- clean work field (with no trace of blood, dentinal sawdust, etc.);
- neighboring teeth to be restored properly ;
- the mirror to be clean;
- diaphragmatic opening to allow sufficient depth of field;

- focus established in the central area of the depth of field domain.

Many times are highlighted among the advantages of digital technology also the possibility of further processing of images. Of course this is an option of unquestionable value, but carries the risk of creating the habit of making compromises related to initial picture quality, relying heavily on the possibility of its further digital processing. Many users overestimate however the possibilities of processing the images using special programs, respectively their capacity to work with complex software, being put in the situation of not achieving the desired result of the original image that in a further step of the treatment , as for example after performing a tooth extraction in orthodontic purposes, will not be able to get it, that tooth leaving the oral cavity forever. For this reason, during the immediate verification of the image quality will be accepted only good picture, without making compromises, in these circumstances the image being repeated as many times it is needed until the result will match our requirements. The basic parameters of photography, such as image composition, appropriate depth of field and illumination clarity, are in the case of digital technology factors dependent of the photographer, new technologies could only facilitate their adjustment.

Therefore, as the different fingerprinting techniques in dentistry can lead to obtaining similar results, precise, also to achieve a perfect picture can be followed several ways. Important is that the user to use a device of superior quality and to process, respectively to use this material every time with great care.

Acknowledgement

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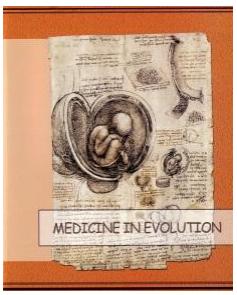
Oro-dental health education in primary classes



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Abstract

The purpose of oro-dental health education for primary students is familiarizing with the dentomaxilary anatomy presented ,meaning their level of understanding of the basic rules of hygiene teeth and the mouth and their familiarity with the dentist and dental office.Our projects have targeted 1007 children in primary schools in the town were taken into the project in Oradea, 614 girls and 393 boys. Our concerns in this area have assumed involvement and motivation of primary school teachers, teachers and students from the Faculty of Medicine and Pharmacy Oradea.The activities were: class activities with students, demonstrations, film screenings, educational visits to dental offices. We believe in the importance of health education for primary students because this period habits are formed and fixed habits, children are responsive and future developments will depend on involving them at this time of life as the patients or future doctors. We consider it important to involve students from specialty dentistry to their training as future professionals.

Keywords: Oral health, dental students, education

INTRODUCTION

Health education is a current priority. After many years in which prophylaxis was regarded as a Cinderella of medicine, came its turn to be put in value. We knows that it is much easier and less expensive to prevent a disease than to treat it.

Dentistry is no exception to this rule and lately dentists are increasingly involved in prevention programs, educational projects prophylactically or events aimed mainly dental prophylaxis.

Furthermore, dental schools have an increasingly important role in this regard, many teachers are involved in educational projects especially in the primary classes. The benefittors of these educational projects are all members involved: pupils, students, teachers and teacher.

Very important in this project is adapting and preparing lessons and teaching by material demonstration to under age children .The results must constantly be monitored, learning concepts should be checked regularly, learning correctly and being well understood, thus they gain respect from the students.

Also, the selection of students participating in these programs must be done rigorously, they should possess knowledge of theoretical and practical prevention methods and posses qualities such as being empathetic, be charismatic, patient, etc. to be fully understood.

It is important and working with both the teacher and the university teacher in primary education .The reluctance in collaboration or in achieving such a project from either side will not lead to expected results.

Objectives

Our objectives are :

O1: Introducing students from primary classes to the dentist and working methods in dental medicine office to reduce their anxiety

O2: skills based dental care to children in primary

O3: Starting Dental Medicine students specialization in work with child patient

MATERIAL AND METHODS

Our projects have targeted children in primary schools in town were taken into project in Oradea. We studied 1,007 children ranging from 614 girls and 393 boys .The project included a visit to part with primary class students, accompanied by staff and some children have visited the Clinic Oradea Faculty of Medicine and Pharmacy, Dental Medicine department.

In the first phase, students accompanied by teachers visited children in classes .The students supported health education classes teeth and the mouth during which they explained the basic rules of dental care, brushing, explained the importance of healthy eating, there were movies screened, exhibits and children were tested to verify proper knowledge of the materials presented.After a period of 6 months, children were retested to verify long-term fixation of the concepts taught.

The second part of the project included visits Clinic Faculty of Medicine and Pharmacy Oradea, Department of Dental Medicine where children had the opportunity to attend dental treatments, to see and to explain the equipment used in the dental office and even play the role of the dentist. Students were also evaluated for change their behavior towards the child after patient involvement in our study.

Our results were listed in tables, based on which they made graphs.

RESULTS

Table 1. Learning the rules of dental care

SEX	Learning the rules of hygiene	Learning the rules of hygiene After 6 months
GIRLS	554 (90.22 %)	471 (76.71 %)
BOYS	200 (50.89 %)	150 (38.16 %)

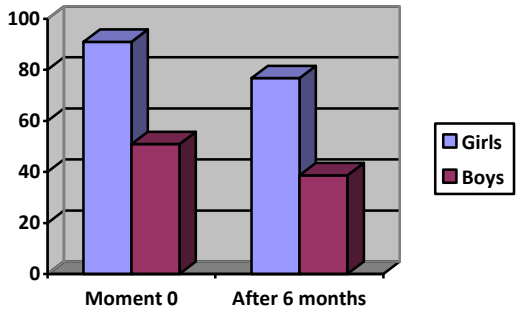

Chart 1. Learning Orodental hygiene rules

Analyzing the table and the graph above we can see that the girls in the percentage of over 90% have acquired the skills and hygiene rules explained percentage is kept quite high and after 6 months. The boys have a lower percent for assimilating the rules and skills, a percentage that falls around the same extent as the girls after 6 months.

Table 2. Anxiety compared to the dentist and dental treatment

SEX	Initial Anxiety	Anxiety at the end of the study
GIRLS	590 (96.09 %)	212 (34.52 %)
BOYS	362 (92.11 %)	72 (18.32 %)

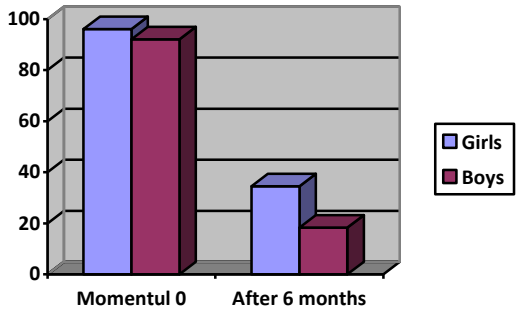

Chart 2. Anxiety compared to the dentist and dental treatment

Analyzing the table and graph of we find that dental anxiety for girls is very high, respectively, over 90% in both groups completed the study, those after 6 months, anxiety decreases in a very high percentage (34% for girls and 18% boys) which is a result beyond our expectations. The result motivates us to continue the study and application to other groups of children.

CONCLUSIONS

• It is undeniable importance of education oro-dental prophylactic starting elementary school age, this age forming habits that will remain the main automatism in life

• Acquiring hygiene rule is higher compared to girls (boys, one explanation could be developing more advanced milestones of girls at this age, the percentage decreasing approximately 20% in both categories after 6 months

• In terms of anxiety to dental treatment, almost to all children had anxiety at baseline, during the second phase percentage decreased significantly (from 95% to 34% girls and 18% boys)

• Regarding the students' behavior, we can say that at the beginning of the study of child behavior was identical to that of adults. At the end of the study, they realized that this behavior and approach must be different, they understood many of the elements of child psychology and they learned new method of approach.

• Because the study was developed in a non-formal setting, it facilitated the creation of a closer link between teacher - student understanding and mutual acceptance, which led to stimulate students to engage in learning.

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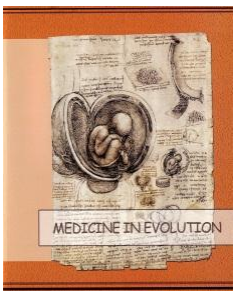
The influence of natural feeding on the development of the dental maxillary apparatus



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Abstract

The objective of the study: The breastfeeding of the infant has an extremely important role concerning the harmonious growth and development of the organism in general and of the dental and maxillary apparatus in particular.

Material and method: This study has the purpose to resume the feeding possibilities of an infant and to show the influence of these possibilities in the harmonious development of the dental and maxillary apparatus.

Results and discussions: Breastfeeding means the feeding of the infant only with breast milk in the first 4-6 months after birth. Breastfeeding is made by the infant through an automatic, inborn, reflex. Beside the rhythmic movements of the mandible, at the natural act of feeding the perioral muscles participate as well. Exclusive formula feeding of the infant and most of all made with inadequate systems will have various negative effects both on the normal development of the dental and maxillary apparatus and on the little child's psychic. The selection of inadequate systems for formula feeding can lead to an imbalance and gradually to the apparition of some dental and maxillary anomalies.

Conclusions: Breastfeeding has the great advantage of ensuring the normal growth of the dental and maxillary apparatus and to influence the harmonious development of all its component elements

Keywords: milk, breastfeeding, formula feeding, dental and maxillary anomalies

PURPOSE OF THE STUDY

The nursling child's natural feeding plays an important part in terms of harmonious growth and development of the body in general and especially the dental-maxillary apparatus.

MATERIAL AND METHODS

The present paper aims at offering an overview of the feeding possibilities of the nursling baby and their influence on the harmonious development of the dental-maxillary apparatus. It is well-known that the new-born's physiological prognathism is present at birth, also known as physiological mandibular retrognathia. In other words, at birth the alveolar ridge of the upper jaw goes beyond the alveolar ridge of the lower jaw by 5-6 mm in sagittal plan, sometimes even more. In the frontal region, the lower alveolar ridge reaches the upper incisive plane and in the lateral region the alveolar ridges touch one another on the entire surface. It is considered that an essential role in the future evolution of inter maxillary relations is represented by the natural breastfeeding of the baby which favours the rhythmical propulsion of the lower jaw and the decrease of the inter maxillary deviation with the reduction of the distance between the two antagonist alveolar ridges. These modifications that appear in the first months after birth are known by the name of the first physiological mesialization of the lower jaw. This way, if this phenomenon has taken place, at the age of 6 months or the age when the temporary teeth eruption start with the eruption of the temporary incisors, in the frontal region of the alveolar ridges will be on a "head to head" relation, a premise for a normal occlusion in sagittal plan of the temporary incisors.

RESULTS AND DISCUSSIONS

Natural feeding is made by the nursling baby through an inborn automatic reflex. Except for the rhythmical propulsion and retropulsion movements, made by the lower jaw, the perioral muscles also participate in the nutrition process. Hence, we observe contractions in the muscles of the cheeks, tongue, mouth, lips, propulsive and retropulsive mandibular muscles, but also elevation and lowering movements of the hyoid bone and head inclination or extension movements. The natural feeding has the great advantage to insure the growth of the dental maxillary apparatus and to influence the development of its component elements. The muscular activity involved in the feeding process causes the balanced and proportional development of the bone elements it is inserted on. The tongue's rhythmical movements influence directly the harmonious development of the palatine vault and nasal cavities. By pressing on the palatine vault, the tongue stimulates the osteogenetic activity within the maxillary's growth centres in this area, namely the incisive-canine suture and the inter-maxillary suture ensuring a correct development in transversal and sagittal plan. The growth of the lower jaw is influenced in the same way. The contraction of the propulsive muscle is followed by the contraction of the antagonist muscles triggering stimuli functioning within the growth serum, especially in the mandibular condyle. The beneficial effects can also be observed in the anatomic structures of the temporal-mandibular joint.

Natural feeding refers to the exclusive breastfeeding in the first 4-6 month of life. Before reaching the state of mature milk, the lactation secretion has different aspects and compositions, according to the nutritional necessities of the new-born in the first days of life. Hence, from the first months of pregnancy until the first five days after birth, the mother's body produces colostrum. It is an opalescent, yellow liquid with a 7.4 pH. It is rich in minerals, vitamins, epithelial or macrophage cells, neutrophils, lymphocytes. Later on, between the sixth and tenth day the transition milk is produced. Only from the tenth day after

birth the milk secretion will be mature. The mature milk has a 6.97 pH, it contains protein, carbon hydrates, lipids, minerals, vitamins and anti-infective protection factors.

The advantages of natural breastfeeding are multiple: maternal milk represents a natural food specific to the infant in the first 4-6 months of life, with a qualitative and quantitative content of nutritious substances perfectly adapted to the needs and metabolism of the breastfeeding baby whose composition changes along the day adapting to the baby's physiological necessities; it is available anytime and anywhere, without the necessity to prepare it; it is a cheap food with an increased content of anti-infective protection factors; it offers anti-allergic protection, since the baby is not exposed to foreign proteins; it prevents the baby's sickness by reducing the risk of digestive infections, it prevents malnutrition, it offers emotional and psychological satisfaction to the nursing baby who feels safe having a tight bond with their mother. Natural feeding has beneficial effects on the mother as well, meaning that it prevents uterine atony, reduces the incidence of breast cancer and genital cancer, offers a natural contraceptive effect.

There are also a few contraindications of the natural breastfeeding related to the mother's and the baby's health state. The maternal causes can represent permanent contraindications, such as certain infections (for example active tuberculosis), systemic diseases (for example unbalanced diabetes mellitus, cardiac insufficiency, haemorrhagic diseases), neurologic diseases, psychosis or the chronic treatment with chemotherapeutic, psychotropic drugs. There are also temporary maternal contraindications related to breast diseases or diseases that required the administration of medicines such as metronidazole, chloramphenicol, tetracycline, sulphonamides. In what regards the causes related to the infant and that prohibits permanently natural breastfeeding, metabolic diseases are quoted more often.

Natural breastfeeding will be offered upon request and ideally until self-weaning. However, due to the increase need of more complex and nutritional substances requested by the growing organism, little by little usually between 6 and 12 months it is considered that it is the proper time to introduce the milk formulas that will progressively substitute maternal milk. In the specialists' opinion, the age of six months is usually also the optimal age to start weaning.

From the point of view of the effect on the development of the dental maxillary apparatus, for the artificial feeding it is recommended to use orthodontic bottle teats, usually made from a sterilization-proof silicone material that imitates the breast anatomy as good as possible. It is also important the number and diameters of the teats' orifices that the milk formula flows through, depending on the child's age. The preferred teats are those that trigger a certain effort in extracting the milk from the bottle so that the rhythmical movements of propulsion of the upper jaw can be performed in order to stimulate its development in relation to the upper jaw.

Although the technological progresses for obtaining devices to imitate the natural feeding as faithfully as possible are more and more advanced; however the bottle feeding causes the adaptation of muscular contractions corresponding to the new conditions. The contraction of the labial muscle will not be as intense because it will not be necessary anymore since the milk will flow on its own through its weight. Hence, in time there can be a hypotony of orbicular muscles which will lead to the appearance of various dental maxillary anomalies through the modification of the growth directions in the sense of more powerful sources through the unbalance created in the „dental corridor" (neutralising area of the forces exerted by the three main antagonist muscle groups, tongue, cheeks and lips muscles which allow the harmonious lining up of the teeth on the arches). The same principle is valid for the cheeks' muscles which in time become hypotonic since they are not used too much for an intraoral pressure necessary to the extraction of milk. In what regards the muscles of the tongue, the hypotony favours the apparition of a deep ogival palatine vault, affecting the floor of the

nasal cavities which is also affected by narrowing, which will hinder the obtaining of an exclusively nasal respiration. The oral respiration will slowly appear, being total non-physiological. Its consequences on the development of the dental maxillary apparatus characterises the dental maxillary anomaly are called the maxillary compression syndrome.

The exclusively artificial feeding and especially the one made improperly from the point of view of the materials used will have various effects both on the normal development of the dental maxillary apparatus and on the psyche of the young child. Hence, an inadequate teat will not allow the child to achieve those complex and rhythmical movements of the lower jaw that allow the mezialization and establishing an optimal relation with the maxilla, representing an etiological factor in the apparition of the dental maxillary anomaly known under the name of functional mandibular retrognathia (Fig. 1).

Figure 1. Maxillary compression syndrome. Functional mandibular retrognathia

By not offering the infant the possibility of satisfying the pleasure to stay at the mother's breast, they can find compensation alternatives, most often with negative effects on the development of the dental-maxillary apparatus, such as the vicious habits of suckling on their thumb, pacifier or textile toys. The consequences of these vicious habits are generally the occlusions - the functional open occlusions type (Fig. 2).

Figure 2. Frontal open occlusion

CONCLUSIONS

The natural feeding has the great advantage to insure the growth of the dental maxillary apparatus and to influence the development of its component elements.

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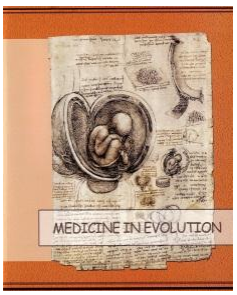
Coronary morphological study of lower wisdom tooth



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Abstract

The study presents aspects related to the morphology of the lower wisdom teeth, monitoring several parameters concerning their crown, in order to determine which are the most commonly found morphological types. For this purpose there were collected the lower wisdom teeth with integral morphology.

Keywords: lower wisdom tooth, coronary morphology, occlusal surface, fissures, cusps

INTRODUCTION

The lower wisdom tooth is neither more nor less studied than the rest of the teeth by the specialized researchers [1]. Teeth have their own phylogenetic and ontogenetic development, with the most various forms and functions, these representing manifestations of adaptation to the surrounding environment [2]. The variations of the morphological characters of the lower wisdom tooth are obvious in the morphological and dimensional variations which may go as far as forms of dwarfism and homodontia [3,4, 5].

Like all paired organs teeth are also asymmetric. Almost all details of relief: ditches, optic pits, ridges, cuspids are also asymmetric. This asymmetry makes it difficult to study dental morphology, but on the other hand, helps us determine accurately the headquarters of the teeth on one of the hemiarcade [6].

The shape and contour of the teeth results from a combination of lines and curved surfaces more or less accentuated. The studies conducted by numerous researchers have led to the conclusion that the form of dental crowns may be compared with various geometric forms: parallelepipeds, prisms, curvatures etc. [7,8,9].

MATERIAL AND METHODS

Wishing to gain personal experience concerning the morphology of the mandibular wisdom tooth and to add the observations obtained to that of our predecessors, we conducted the collection of lower wisdom teeth from patients aged between 17 and 50 years.

In general is about patients which have addressed the dental medical service, directed or on their own initiative, for sufferings related to the three mandibular molars, or for other conditions of the oral cavity at which the clinical and the paraclinical radiological examination highlighted the condition of the lower wisdom teeth.

After each tooth extraction soft parts were removed, respecting the physical and chemical integrity of the hard parts. The teeth were kept for 4-5 days in hydrogen peroxide, after which they were washed under running water and dried at heat, after prior immersion in chloroform. We selected for study 208 lower wisdom teeth. The study aimed to provide data about the shape of the crown and of the occlusal surface of the third mandibular molar.

RESULTS

After studying the shape of the crowns of the mandibular wisdom teeth of the collection we were able to group them after five geometrical shapes compared to which they present the greatest similarity, which in order of frequency are: parallelepiped, equilateral triangle prism, globe (sphere slightly flattened at the poles) cube, pyramid trunk (table I).

Table I. Mandibular third molar crown shape

crown shape	Number	percentage
parallelepiped	198	95,19%
triangular prism	4	1,92%
globe	3	1,44%
cube	2	0,96%
pyramid trunk	1	0.48%

The most elaborate part of any study of dental morphology is the one presenting the occlusal surface of the tooth crown.

If for the crown shape we used the similarity to geometrical bodies for the occlusal face shape we used geometric shapes. For the study we used 171 lower wisdom teeth which presented occlusal surface integrity. The geometrical shapes compared to which they presented the greatest similarity are: trapeze (with the small base distal), rectangle (with large sides mesial and distal), triangle (with the tip distally), parallelogram (with large sides mesial and distal), square, oval (table II).

Table II. Occlusal surface shape of the mandibular third molar

occlusal surface shape	Number	percentage
trapeze	88	51.46%
rectangle	56	32.74%
triangle	13	7.6%
parallelogram	6	3.51%
square	4	2.34%
oval	4	2.34%

Occlusal surface shape is closely related to occlusal morphology within which an important place is occupied by cusps as positive forms of relief. Molars from the collection present 2, 3, 4, 5 or 6 cusps. When three or four cusps are highlighted, two are situated vestibularly, and at the specimens with 5 or 6 cusps, vestibularly are found three. Rarely cusps are well highlighted with clear descriptive elements. They are blunted, without individuality.

There is a huge variety of negative relief of the occlusal surface, especially central fissures, which are generated by the intersection of two main ditches. These were presented under the following forms: ┼ (cruciform); **X**-shaped (scale), **Y** (dryopithecus), or **T**. At 166 lower wisdom teeth was highlighted central fissure (Table III).

Table III. The shape of central fissures

central fissure shape	number	percentage
┼	114	66.68%
Y	34	20.48%
X	13	7.83%
T	5	3.01%

Molars also presents two marginal fissures (mesial and distal) resulting from mesial-distal main ditch encounter with marginal ridges. Inferior wisdom teeth, not being constant bearers of all formations generally valid for the molars group, do not all present the two proximal fissures. At 161 three inferior molars was identified the mesial marginal fissure, forms being shown in Table IV, variant in T not being found in any case.

Table IV. The shape of mesial marginal fissures

mesial fissure shape	number	percentage
┼	11	6.83%
Y	143	88.82%
X	7	4.35%

At 147 inferior wisdom teeth distal marginal fissure was also highlighted (Table V).

Table V. The shape of distal marginal fissures

distal fissure shape	number	percentage
┼	6	4.08%
Y	138	93.88%
X	3	2.04%

While for the central fissure the most common shape is the cruciform one, for proximal fissures Y shape dominates (Figure 1).

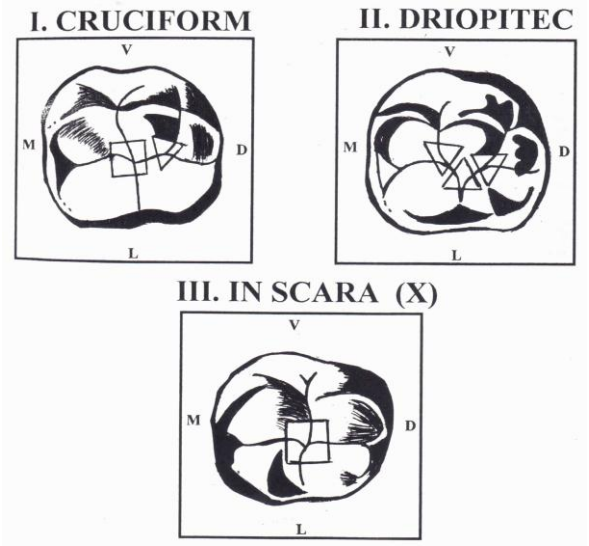

Figure 1. Shapes of the fissures

DISCUSSIONS AND CONCLUSIONS

The dominant form of the dental crown at the lower wisdom tooth is the parallelipipedal one(95,19%). Lower third molar crown may also present shape of triangular prism (1,92%), globe (1,44%), cube (0,96%) or pyramid trunk (0,48%).

Regarding the occlusal surface, the most commonly encountered shape is the trapezoid (51,46%), with the smaller base oriented towards the distal. The rectangle is represented by 32,74%, its larger sides being oriented mesial and distal. Are also encountered forms similar to: triangle with the tip towards distal (7.6%), parallelogram with the large sides mesial and distal (3.51%), square or oval (each 2.34%).

Positive occlusal relief shapes are generally poorly highlighted, cusps being less tall and rarely well individualized. There have been identified at least three cusps, of which two situated vestibularly and maximum five cusps, three vestibular always.

Negative occlusal relief shapes had a huge variety, especially central fissures. The three mandibular molars do not present all occlusal formations specific to molar group. However the central fissures are usually present mainly cruciform (66.68%), and in lower percentages in the shape of X, Y, or T.

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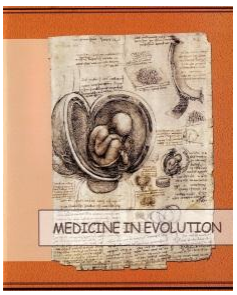
Numerical simulation using finite element analysis of the implant-natural bone assembly



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Abstract

This study emphasizes the tension and deformation in the implant-bone assembly according to three surgical procedures. Comparing the results it seems implant – artificial cortical tissue addition – trabecular tissue – cortical tissue asembly represents the model with the best biomechanical behavior, the influence of the artificial tissue layer offering a better resistance of the functional assembly.

Keywords: finite element analysis, implant, bone

INTRODUCTION

The most important factor for determining the success of impant osseointegration is the state of the peri-implant tissue[1].

Biomechanical conditions directly affect bone remodeling and help to maintain the integrity of the implant; mechanical turmoils plays a major role, resulting in unnecessary costs and treatment time, and even complications that may not be easily cured[2].

Therefore, the potential biomechanical risks of failure need to be evaluated before undertaking such interventions, since the application of necessary precautions may improve the survival of implants.

Finite element analysis is a numerical stress analysis technique that is widely used in medicine to assess biomechanical problems. This method allows application of simulated forces at specific points in the implant-bone assembly and stress analysis[3].

MATERIAL AND METHODS

This study emphasizes the tension and deformation in the implant-bone assembly in the oral cavity.

Three analysis cases will be presented according to the surgical procedure that was used:

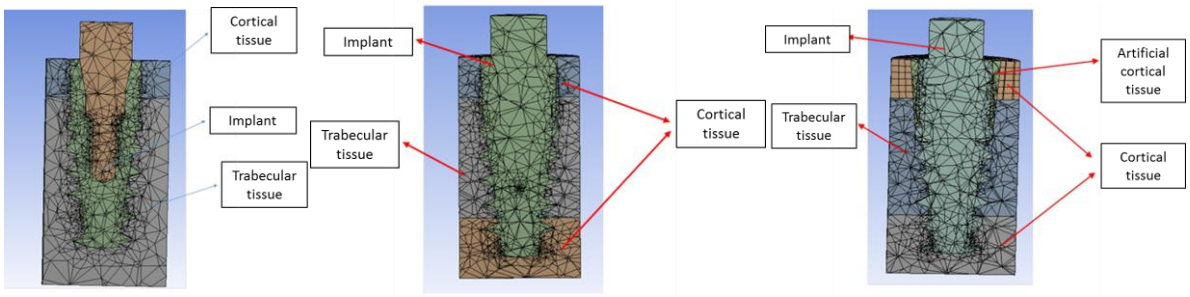

Figure 1. The implant-bone ensemble according to the surgical procedure

The geometrical model was obtained using SolidWorks software and by modeling two bodies which express the morphological configuration in the oral implantation area – the upper body represents the cortical tissue area and the inferior body the trabecular tissue area.

According the fact that the analyzed structure was designed tridimensional, for the discretization it was chosen a finite element tridimensional-solid-type coded as SOLID185, a tetrahedral finite element.

For the numerical simulation it is absolutely necessary to specify the elastic properties (longitudinal elasticity modulus – Young's modulus and the transverse contraction coefficient – Poisson's ratio) for the materials used to obtain a correct physical and mechanical simulation, and their behavior under external load action. After applying properties to the material and choosing the finite element type, the following stage is meshing the analyzed assembly. This process consists in dividing the structure into a finite element mesh with the purpose of obtaining information regarding the mechanical behavior from several points of the structure after numerical simulation, in order to issue valid conclusions on the purpose of the study.

According the scientific literature in the domain regarding the external efforts, it was applied a 300 N force at 30° angle to the longitudinal axes of the implant). In order to obtain the direction of the oriented force and to avoid the appearance of a local effect of concentrated tensions, this force was divided on two directions – a vertical one F_V and a horizontal one F_H. The two forces were applied the following values F_V=Fcos30=259,81 N and F_H=Fsin30=150 N.

In this study, natural bone was considered homogenous; however, in fact, natural bone have widely variable density properties. That simplification was aimed at limiting the computing difficulties associated with performance of our study.

RESULTS

The obtained result will be presented for the three cases at once to emphasize the differences that appear in each case of implantation.

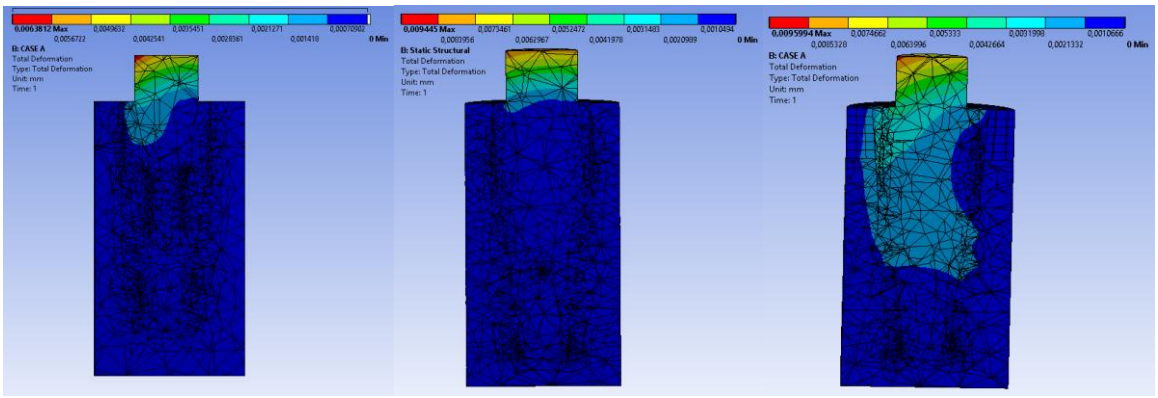

Figure 2. Different colors indicate total displacement around the implant-bone assembly

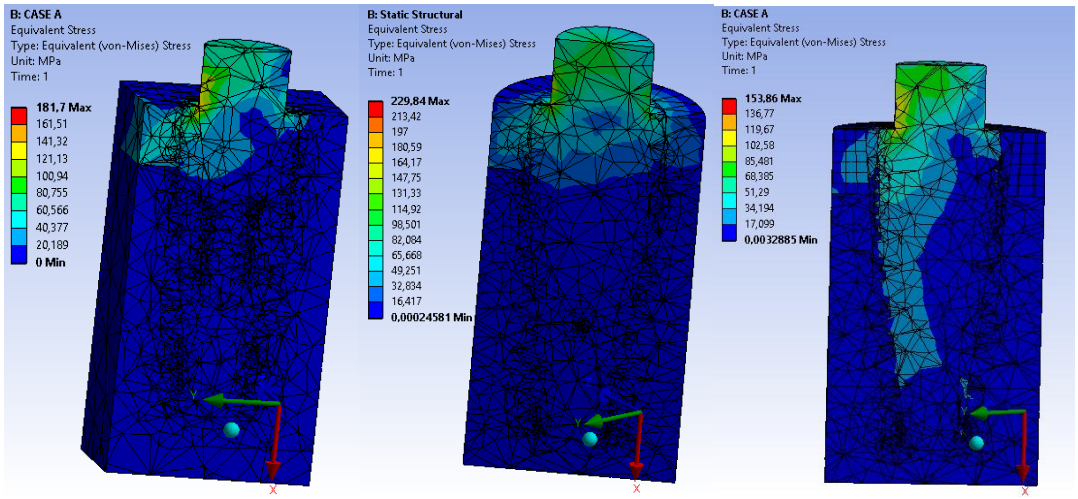

Figure 3. Equivalent stress in the three cases

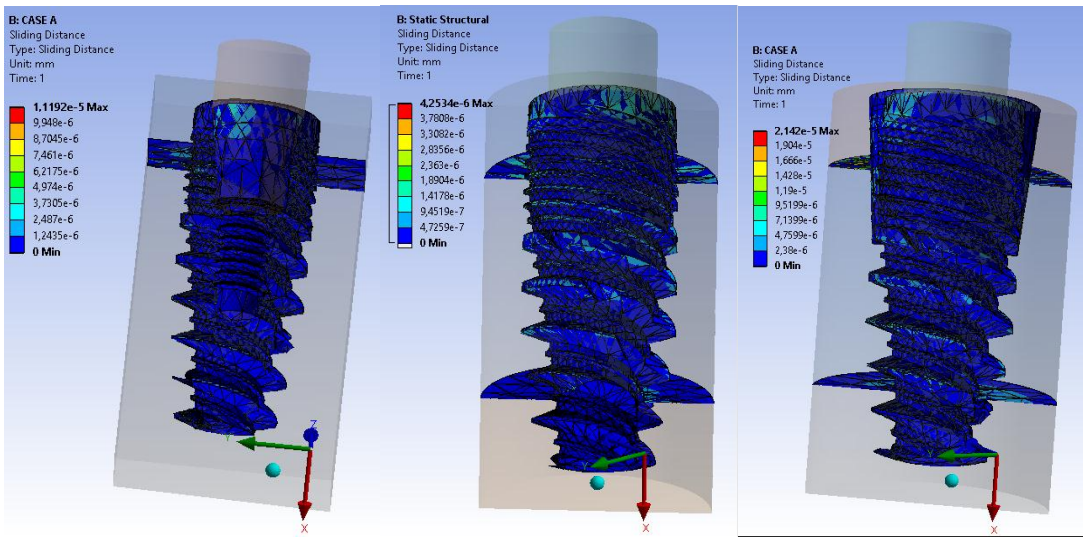

Figure 4. Sliding distance on the contact areas

DISCUSSIONS

By analyzing the results we observe that the values of displacements in the investigated models are small, micron sized. The areas where extreme values appear are found in the upper part of the implant.

In our analysis, the tangential tensions distribution (shear tensions) which appear in the bone tissue-implant assembly shows the slipping phenomena which can occur in the assembly during functioning.

We also observed that tangential tensions are focused more in the implant for Case I and II, and for the third case the tangential tensions distribution are dissipated in the whole implant with very low values; the extreme values are focused as local effects in the upper part of the implant in the jointing area between the metallic implant's components.

The contact pressure area between implant and bone tissue explains the phenomena that can appear in the interface – sliding phenomena, which in practice represents a dangerous situation leading to loosing structural integrity.

However, we should be aware that this study have some critical limitations and assumptions that will clearly affect the applicability of the results in practice. Confirming our results with clinical analysis is essential.

CONCLUSIONS

We can conclude that the equivalent tensions, determined using *von Mises* criteria, are larger in Case II than in Case I and III. From the three cases, the third case offers the best reliability considering the tension state.

Model III represents the model with the best biomechanical behavior, the influence of the artificial tissue layer offering a better resistance of the functional assembly.

The contact pressure which develops in the contact area between bone tissue and implant, in third case is significantly lower than in Cases I and II.

Correlating finite element analysis results with long-term clinical studies may help to validate our model.

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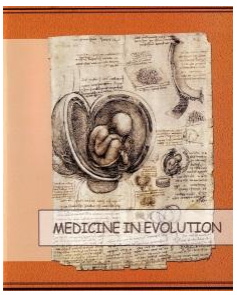
Multidisciplinary management including orthodontics, periodontics and prosthetics in adult patients



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Abstract

The purpose of this article is to show the importance of interdisciplinarity in treating adult patients with complex situations. Three patients (1 male and 2 females) adressed to a specialist for consult because aesthetic and functional problems (masticatory problems). After clinical examination, radiographs were taken and complex diagnosis established. The treatment plan was discussed with every patient and included: orthodontic treatment, periodontal therapy and prosthetic restorations. At the end of the treatment, the patient's main problems were solved and the functional aspects were improved. Nowadays, dentistry should look at a patient like a whole and not to treat a situation individually.

Keywords: orthodontic treatment, gingival recession, multidisciplinarity, adult patient

INTRODUCTION

In the past, most patients who sought orthodontic therapy were children or adolescents. Currently, orthodontists are treating more adult patients because they are more interested in solving aesthetic discrepancies and some of the functional problems. In some offices the percentage of adult patients can be pretty high. On the other hand, this increased number could be due to interrelation between orthodontics and other specialties like periodontics or prosthodontics.

Therefore, the number of patients with periodontal problems that attend orthodontic practices is significantly greater than in the past [1]. It is important that orthodontist can identify specific periodontal problem before orthodontic treatment and determine the correct treatment plan to ameliorate these problems. The periodontal condition is usually present as tooth mobility, migration, spacing, and marginal gingival recession. Particularly in the maxillary anterior region, functional discomfort is usually accompanied by compromised aesthetics [2]. This can result in the development of a median diastema or general spacing of the teeth with or without incisor proclination, rotation or tipping of the premolars and molars and collapse of the posterior occlusion [5]. The primary objective of periodontal therapy is to restore and maintain the health and integrity of the attachment apparatus of the teeth [1]. Orthodontic treatment for realignment of migrated periodontally involved teeth is initiated only after control of the periodontal inflammation has been achieved. A long healing period and radiographic evidence of bone apposition are required before initiation of the orthodontic tooth movement [3,4] This is the reason that all these periodontal conditions have to be co-evaluated by the periodontist and the orthodontist to choose the appropriate orthodontic intervention. This may involve adjunct tooth movement that can facilitate other dental procedures or comprehensive orthodontic treatment to correct a malocclusion [5].

The objective of a preprosthetic orthodontic treatment is to position the teeth in such a way that a treatment with (fixed) dental prostheses is made possible or simplified or to affect the result of this treatment positively. Conceivable preprosthetic orthodontic treatments are: correcting primary orthodontic anomalies, closing or reducing interdental spaces and correcting the migration of teeth [6]. The importance of the combined orthodontic-prosthetic approach of the complex cases was emphasized by numerous authors [1,3,5].

The aim of this paper is to present three clinical cases, treated by a multidisciplinary team.

CASES REPORTS

We will present three therapeutic options for adult patients with complex dental diagnostics.

Case Report 1

I. Anamnesis. The patient, S.A, male, aged 28 years, came in our practice 3 years ago. The patient presented because he was unsatisfied with the aesthetic aspect of his dentition (Fig. 1a). His general medical and dental history were not significant and he had no family history of any oral or dental anomaly.

II. Clinical examination data.

Extraoral examination revealed a slightly protrusive upper lip. Intraoral examination revealed: multiple cavities in posterior teeth, absence of the teeth 35, 36 and 45. There were noticed also some periodontal problems: gingival recession on many teeth, the presence of black triangles in the frontal upper and lower teeth. Analysis of mini and microesthetics revealed crowding of the upper incisors, difference in the mesio-distal diameter of 11 and 21 and a flat smile line. The maxillary midline was shifted 2 mm to the left of the midsagittal

plane. A functional examination shows lateral interferences of posterior teeth and mandibular shift to closure tendency (Figure 1 b-f). Intraoral examination revealed a Class II malocclusion, confirmed by the examination in all the 3 plans:

Sagital plan

Right and left molars: mesially tipped molars with false class III relationship

Canines: bilaterally class II

Incisors: neutral, with the exception of 21

Transversal plan

Neutral relationships posteriorly, 2 mm shift of the lower midline to left.

Vertical plan

Cusp to cusp relationship posteriorly, at the 15, 16 and 26

Normal overbite at the level of the incisors

Figure 1a. Smile view and pre-treatment intraoral potos

Figure 1b-f. Intraoral view of patient case 1.

III. Aditional paraclinical investigations. Cephalometric examination showed a hyperdivergent class I skeletal relationship, with class II tendency (ANB angle 4) (fig 2a). The

panoramic radiograph shows alveolar bone loss in the lower arch, especially where teeth were extracted, with the mesial tipping of the remaining lower molars (fig 2b).

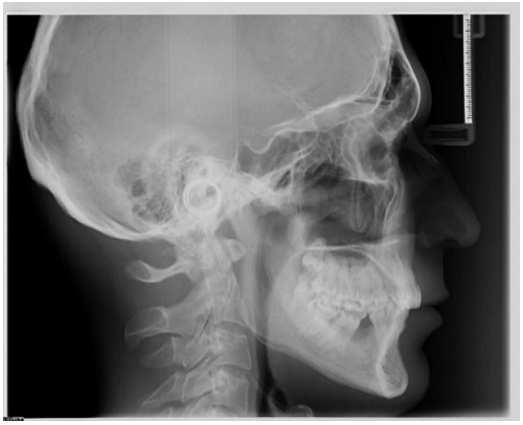

Figure 2a. Pre-treatment cephalometric radiographic image

Figure 2b. Pre-treatment panoramic image

IV. Treatment and evolution. Treatment objectives were primarily dentoalveolar and included: improving smile and aesthetic in the frontal area by correcting midline deviation, aligning and leveling, correcting the canine class II relationships, uprighting the lower molars and reopening the space for bone grafting and prosthetic implant in the left lower quadrant. He received periodontal care with professional cleaning, scaling, root planing, and curettage, in order to improve the periodontal status and the attachment of the gingiva. Therefore upper first premolars were extracted and a transpalatal bar inserted for reinforcement of the anchorage. Maxillary and mandibular .018" preadjusted Roth prescription fixed appliance was also inserted). Initial alignament and leveling were achieved with a sequence of round and rectangular NiTi wires (figure 3 a, b). Proper arch form and coordination was reached through rectangular .016"X.022" inch SS archwires with individual torque control plus finishing details.

Figure 3a,b. Treatment progress: round NiTi archwires placed to complete arch alignment

In approximately 18 months the main objectives were completed, only the uprighting of the lower molars was not fully accomplished (figure 4 a). Insertion of 2 miniimplants to facilitate the molars movement was discussed but the patient refused.

After 22 months of active treatment the fixed appliance was removed, excepting the molar bands on the 37 and 38 and the bracket on 34. This space maintaining was left in place during the bone graft integration and the implant insertion (figure 4 a-e).

Figure 4a-e. Intraoral view after the appliance removal

To improve the esthetics in the frontal area, direct composite reconstructions were performed on the upper incisors. The restorative prosthetic crown on the implant was also inserted (figure 5 a-f).

Figure 5a-f. Final treatment result

Case Report 2

I. Anamnesis. The patient, H.L, female, aged 32 years, looked for specialized dental treatment because there was a space on the left side in the upper arch (figure 6). Her general medical and dental history were not significant. The family history regarding dental anomalies was significant, her father and son having upper lateral incisors anodontia.

Figure 6. Initial smile view of patient case 2

II. Clinical examination data.

Extraoral examination revealed a slightly increased lower face height but with straight profile. Intraoral examination revealed: small upper lateral incisors, the absence of the teeth 14, 23, 25 and 46, and the presence of a prosthetic rehabilitation in the upper first quadrant. There were noticed also some gingival recessions on the lower anterior teeth. The front teeth from the lower arch present a high grade of abrasion and the right central incisors has some irregularities of incisal edge. The maxillary midline was shifted 2 mm to the left of the midsagittal plane and the mandibular midline was shifted 1.5 mm to the right. A functional examination shows lateral interferences of posterior teeth and mandibular shift to closure tendency. Intraoral examination revealed a Class I malocclusion, confirmed by the examination in all the 3 plans (figure 7 a-e):

Sagital plan

Right and left molars: mesially tipped molars with false class II relationship

Canines: left canine neutral, right canine false class II

Incisors: neutral

Transversal plan

Neutral relationships posteriorly, shift of the lower midline to the right

Vertical plan

Neutral posteriorly and normal overbite at the level of the incisors

Figure 7a-e. Pre-treatment intraoral view of patient case 2

III. Aditional paraclinical investigations. Cephalometric examination showed a hyperdivergent class I skeletal relationship. The panoramic radiograph showed impacted 23, and confirmed the absence 14, 25 and 46 are missing (figure 8). Some alveolar bone loss was also seen especially in the lower arch.

Figure 8. Pre-treatment panoramic radiograph of patient case 2

IV. Treatment and evolution. After treatment plan was discussed with the patient, the treatment objectives were established: to facilitate the eruption of the impacted canine, to correct the maxillary dental midline, to regain the space in the region of the mandibulary right molar, to achieve an acceptable occlusion, to restore esthetics by restoring the upper incisors. Retraction of the upper right canine in the extraction space of 14 was decided in order to acomplish the neutral relationship.

Maxillary and mandibular .018" preadjusted Roth prescription fixed appliance was inserted. Initial alignament and leveling were achieved with a sequence of round and

rectangular NiTi wires. Traction of the impacted canine was started after the rectangular, stiff 016″X.022″ inch SS archwires was inserted. Fully eruption and derotation of the canine was acomplished only in 14 months.

In approximately 22 months the objectives were partially completed, the dental midline deviation was improved but not fully corrected (figure 9 a-c).

Figure 9a-c. Clinical situation at the end of orthodontic treatment, patient case 2

After 24 months of active treatment the fixed appliance was removed and the prosthetic rehabilitation began. It included a zirconium crown on the 15, porcelain laminate veneers on the upper incisors. The lower incisors were fixed with a twistflex retainer. After the final stage of prosthetic rehabilitation the patient was satisfied with her aesthetic appearance (figure 10 a, b).

Figure 10a-d. Photos after final frontal restoration, patient case 2

Case Report 3

I. Anamnesis. The patient C.E, 57 years old presented for orthodontic treatment with a periodontally compromised dentition and a large diastema in the maxillary anterior region. The patient's chief complaint was to improve her esthetics (figure 11). Her general medical and dental history were not significant. Periodontal problems in her family history were present..

Figure 11. Initial smile view, patient case 3

II. Clinical examination data. Pre-treatment facial photographs showed a symmetrical facial pattern with convex profile and lip incompetence due to the buccaly tipped upper incisor. Intraoral examination revealed severe diastemas, both in the lower and the upper arch, the absence of 16,17,26, 32, 42, 36, 46 and a severe crowding in the upper left quadrant. A pontic bridge restoration from tooth 14 to tooth 18 were also present. The dentition showed generalized gingival recession with pockets from three to 9 mm and severe mobility af the lower incisors. Radiographic examination revealed generalized moderate and severe bone loss (Figure 2). No signs or symptoms of temporomandibular disorder were noted despite the occlusal dysfunction due to malocclusion.

Intraoral examination revealed a Class I malocclusion, confirmed by the examination in all the 3 plans (Figure 12 a-d):

Sagital plan

Right and left molars: mesially tipped molars

Canines: left and right canine neutral

Incisors: increased overjet

Transversal plan

Neutral relationships posteriorly, left canine in crossbite,

Vertical plan

Neutral posteriorly and normal overbite at the level of the incisors

Figure 12a-d. Pretreatment intraoral view, patient case 3

III. Aditional paraclinical investigations. Lateral cephalometric radiograph (figure13 a,b) showed an excessive proclination of upper and lower frontal teeth and class I skeletal relatioship.

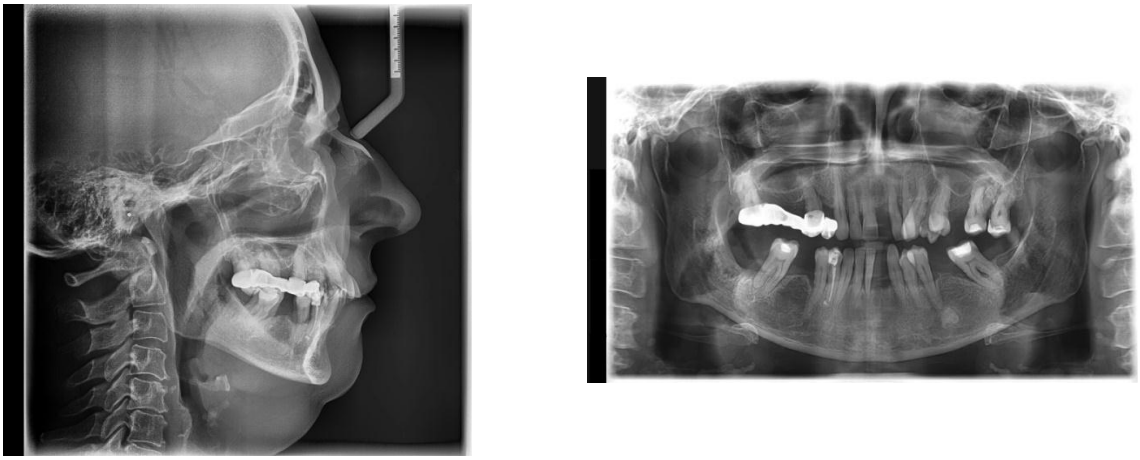

Figure 13a,b. Initial radiographic images

IV. Treatment and evolution. The treatment goals for this patient were to control periodontal disease and to correct the esthetic problem involving the crowding in the upper arch and the maxillary incisors. The treatment objectives also included prosthetic reabilitation of the edentulous spaces. Extraction of the upper left second premolar was decided.

After periodontal treatment (subgingival scaling and root planing) was completed and intensive oral hygiene instructions were given. Clinical signs of gingival inflammation were absent and a gain in clinical attachment levels was noted. Orthodontic fixed appliance was inserted with an initial 0.014 inch NiTi wire for aligning the upper and lower arch (figure 14).

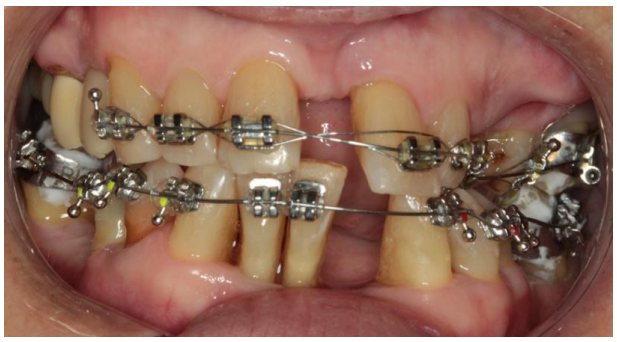

Figure 14. Niti archwires inserted in the 0.018 inch slot Roth prescription appliance

The total treatment time for the orthodontic therapy was 8 months. After removal of the appliance, upper twistflex fixed retainer was bonded and the prosthetic rehabilitation of the lower archwire completed (figure 15-a-d). For financial reasons, the patient refused/ postponed the rehabilitation of the upper arch.

Figure 15a-d. Intraoral photos at the end of the treatment, patient case 3

DISCUSSIONS

This cases reports illustrate the need for a multidisciplinary team approach to care, both at the treatment planning stage and throughout the entire course of treatment. The main objectives in the management of any complex case are: to improve esthetics, to control the periodontal disease and to restore masticatory function. Considerably esthetic improvements were obtained in all three cases, even if not all the treatment objectives were completed (midline discrepancy in case 2 and uprighting left molar in case 1). It is also well known, that in adults patients orthodontic treatment involves significant time, as bone density and characteristics are different from young patients [1].

Orthodontic treatment is recommended in the therapy of severe adult patients, with or without periodontal involment [3]. In cases with severe periodontal disease, like case 3, orthodontic treatment might enhance the possibilities of saving and restoring a deteriorated dentition. Periodontal treatment and the patient's cooperation in oral hygiene were also a key

factor in succes. Good coordination was achieved among all 3 dental specialties throughout the treatment. In cooperation with the patient, a combined treatment plan was agreed to and the patient was reviewed at planned intervals both during active orthodontic treatment and later during retention. The result was both occlusally and periodontally stable, while allowing appropriate access for prosthetic reabilitation. The patient esthetic appearance was improved, which had also a great psihologic impact.

The use of direct and indirect frontal restoration is recommended by many authors [1-5], to improve esthetics and function of the frontal teeth, after the initial orthodontic treatment phase. In case 1, direct composite restorations were done, in order to modify the teeth proportions and to close the embrasures. The disatvantages of the direct composite veneers are poor surface qualities and disscoloration overtime. However, with good patient compliance in oral hygiene and good finishing of the dental material surface, the esthetic result might be prolonged. In case 2 laminate porcelain veneers were used, which have the advantage of a more stable and esthetic results.

In contemporary dentistry, interdisciplinary approach in treatment planning is an important factor achieving well-defined esthetic objectives. Taking into consideration the impact of function, structure, and biology, the clinician will be able to use the various disciplines in dentistry to deliver the highest level of dental care to each patient.

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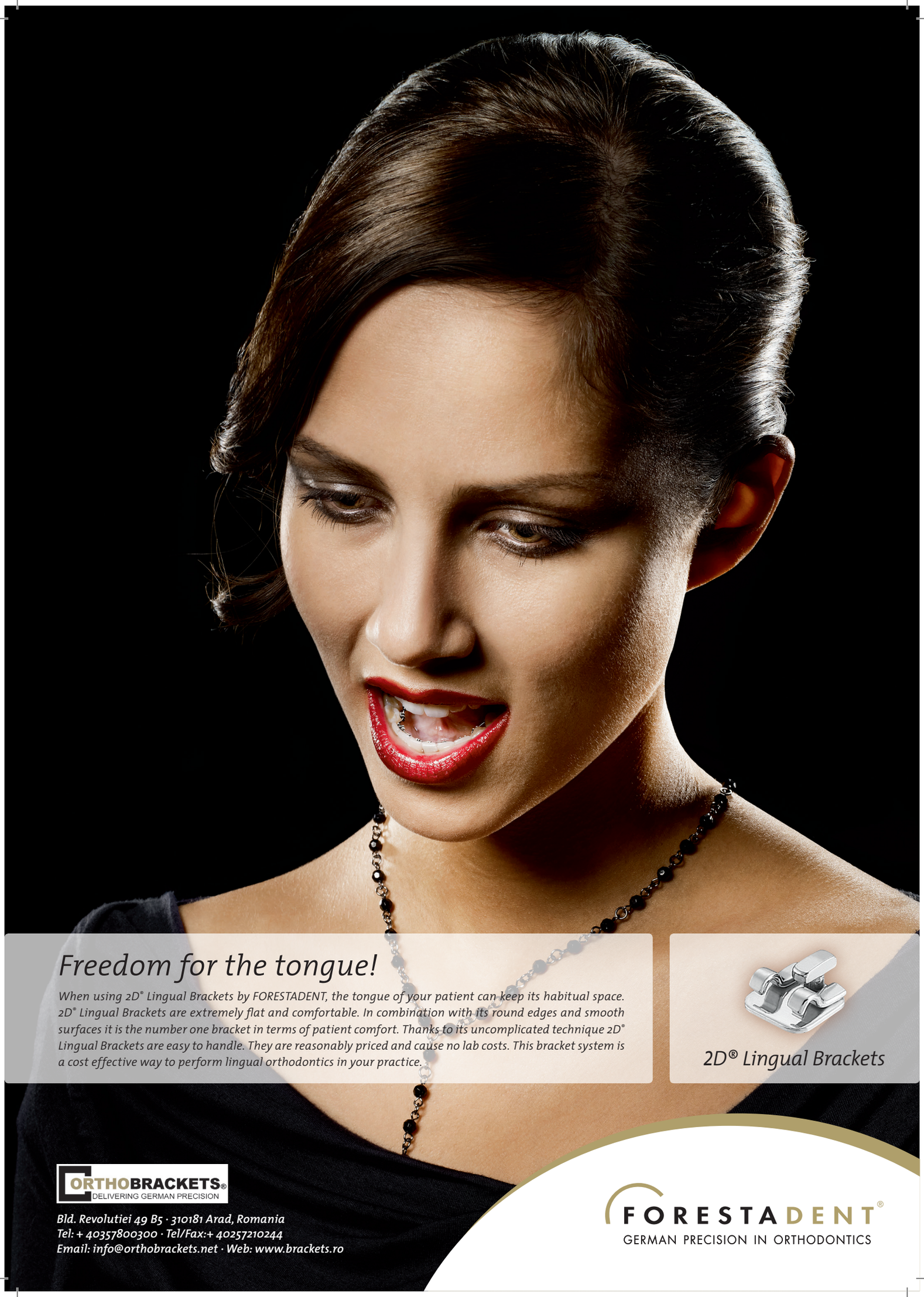
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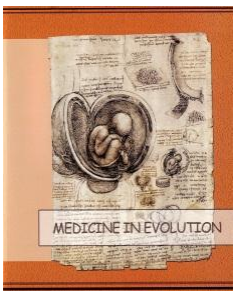
ERRATA - The silent burden of a population: chronic hepatitis C. General population screening/ *Medicine in evolution, No. 2/2016*



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ERRATA

Due to an improper processing in data analysis, in the article entitled ,,The silent burden of a population: chronic hepatitis C. General population screening", from ,,Medicine in evolution" journal, No. 2/2016, an error has occurred.

For a better understanding of the data and a correct interpretation of the outcomes, on the page. 231, the conclusion number 3 will be read as:

,,From the study of mortality from HCV resulted, in 2013, an increase in the number of cases of death from cirrhosis due to HCV infection by 67.9% compared with 1990 and for HCV-induced hepatic cancer, an increase of **291.9%** compared with 1990, which confirms that this silent burden, hepatitis C virus is a disease that kills slowly and surely".

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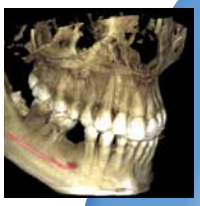

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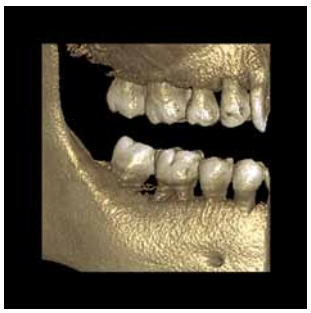

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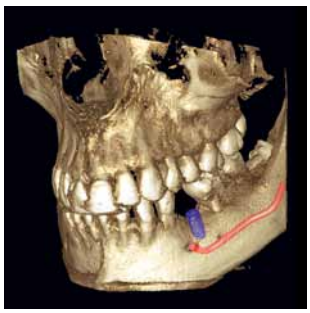

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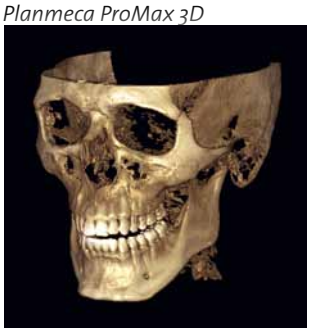

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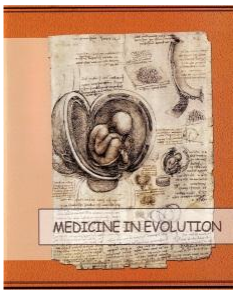

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A numbered list of references must be provided at the end of the paper. The list should be arranged in the order of citation in the text of the publication, assignment or essay, not in alphabetical order(according to the Vancouver rules). List only one reference per reference number. It is very important that you use the correct punctuation and that the order of details in the references is also correct.

- Books - Standard format - #. Author of Part, AA. Title of chapter or part. In: Editor A, Editor B, editors. Title: subtitle of Book. Edition(if not the first). Place of publication: Publisher; Year. p. page numbers.
- Journal Articles - Standard format - #. Author of article AA, Author of article BB, Author of article CC. Title of article. Abbreviated Title of Journal. year; vol(issue):page number(s).
- E-Books - Standard format - #. Author A, Author B. Title of e-book [format]. Place: Publisher; Date of original publication [cited year abbreviated month day]. Available from : Source. URL.
- E-Journals - Standard format - #. Author A, Author B. Title of article. Abbreviated Title of Journal [format]. year [cited year abbreviated month day];vol(no):page numbers[estimated if necessary]. Available from: Database Name (if appropriate). URL.

Internet Documents - Standard format - #. Author A, Author B. Document title. Webpage name [format]. Source/production information; Date of internet publication [cited year month day]. Available from: URL. [Book Antiqua, 10 point, normal, justified alignment].

[1] _____
[2] _____
[3] _____

6.2. CONTENT OF THE PAPER - INDICATIONS FOR CASE REPORTS

Content of the paper for case report will respect indications for original articles.

Themes may be selected from all medical fields. Manuscripts which offer a special gain for daily activity will have priority. The title must be clearly, precisely stated. It may be completed by a subtitle. It is advisable to include in the key words of the title the main message, the special element which may be observed from the case evolution. The content of a case report must be divided into three parts:

Introduction – It must include a maximum of 15 typed rows (half page). Here, the main medical problem is summarized in order to place the case in a specific domain.

Case report – It contains essential specific information on the case. In order to make a logical, chronological and didactical case report the following 5 chapters are needed:

I. Anamnesis;
II. Clinical examination data;
III. Laboratory data;
IV. Additional paraclinical investigations;
V. Treatment and evolution.

Discussions – The reason for the case report must be stated. The report must be patient-centered. Occasional deviations from typical (characteristic) evolutions, nosologically important facts must be presented in such a manner to expose the clinical picture as completely as possible. The case report must not appear as an appendix of a general review. Dimensions of a case report: maximum 6-8 typed pages, 30 rows of 60 characters/page.

6.3. MEASUREMENT UNITS, SYMBOLS, ABREVIATIONS

All measurements must be expressed in International System (IS) units. Abreviations must be fully explained when first used.

6.4. TABLES

Tables are noted with Roman figures and they will have a brief and concise title, concordant with their content.

6.5. ILLUSTRATIONS

Number all illustrations in Arabic figures in a single succession. Apply a label on the back side of every illustration, containing its number and an arrow indicating the upper side. Coloured illustrations may be accepted but it is the choice of the editors, according to particular technical abilities of each journal issue, or it may involve a fee in special cases.

6.6. EXPLANATIONS FOR DRAWINGS AND GRAPHS

Explanation for drawings and graphs must be clear and in readable dimensions, considering the necessary publishing shrinkage.

6.7. PHOTOGRAPHS

Offer glossy, good quality photographs. Any annotation, inscription, etc. must contrast with the ground. Microphotographs must include a scale marker.

6.8. ILLUSTRATION LEGENDS

Include explanations for each used symbol, etc. Identify the printing method for microphotographs.

7. COPIES FOR PUBLISHING

In order to accelerate publishing, the main author will send a set of printed sheets presenting the final version of the paper, as it will appear in the journal. It is really helpful that texts to be also sent on electronic support, diacritic characters mandatory.

8. REJECTION OF PAPERS

If a paper does not meet publishing conditions, whatever these may be, the editors will notify the first author on this fact, without the obligation of returning the material. Original photographs or the whole material will be returned only if the author comes to the editor and takes them.

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