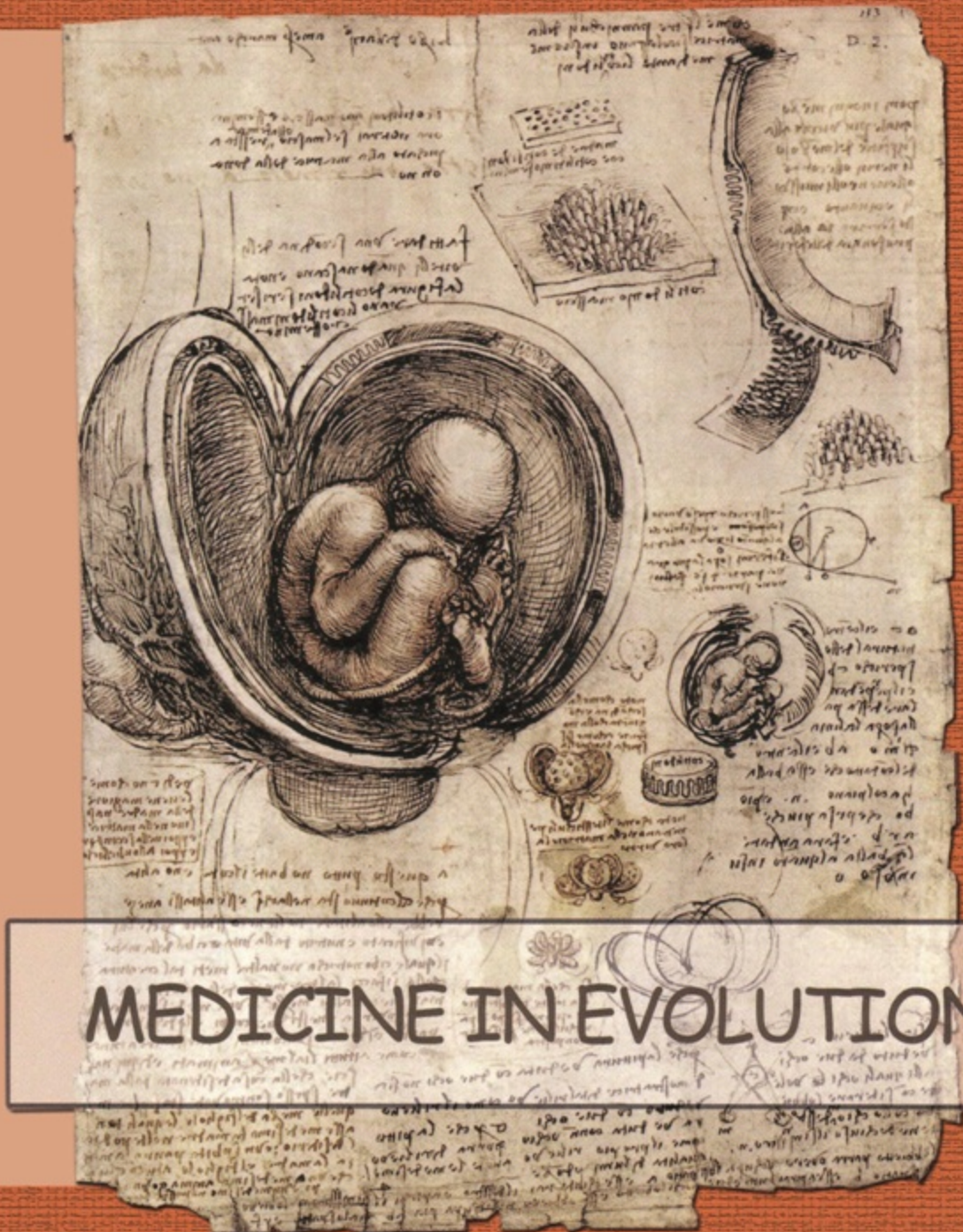


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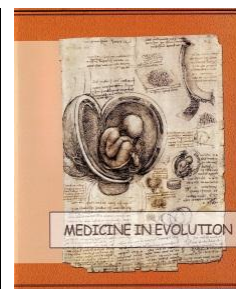
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CONTENTS

ARTICLES



Petrescu R., Valea A., Terzea D., Dumitrascu A., Albu S.E., Carsote M.

Laparoscopic right adrenalectomy and cholecistectomy: from endocrine decision to surgical procedure

473

Colta R.C., Stoicanescu C., Ognean M.L., Baraganescu O., Nicolae M., Colta R., Zgârcea C., Botea I., Georgescu R.

The pattern of development dysplasia of the prematurely newborn

478

Ardeleanu E., Dorobanțu M., Lighezan D., Lighezan R., Darabonț R., Gurgus D., Țilea I., Cezar D., Codreanu G., Varga A.

Diagnostic role of home blood pressure monitoring in primary care

487

Ulmeanu R., Muntean R.A., Valea A., Carsote M.

Glucocorticoid-induced osteoporosis after three decades of self-medication for asthma

494

Iorgescu A.C., Herlea V., Mustafa E.S., Pechianu C., Sajin M., Dumitru A., Tampa M., Georgescu S.R., Popescu I.

Morphological, immunohistochemical and prognostic analysis of gastrointestinal stromal tumors with gastric and small intestine origin

498

Enatescu V.-R., Papava I., Enatescu V., Bredicean C., Manea M.

A cross-sectional study on clinical and personality features associated with chronic medical comorbidity in recurrent depressive disorder inpatients

509

Anghelescu V., Neculae I., Zurac S., Dincă O., Vlădan C., Bucur A.

Comparative histomorphometric study regarding the in vivo bone healing efficacy of anorganic bovine bone, β -tricalcium phosphate and bioactive glasses on rabbit tibia model

523

Nijim B., Vlasceanu D., Dincă O., Bucur M.B., Vlădan C., Bucur A.

Finite element analysis of an implant- artificial cortical tissue structure

530

Ibric Cioranu S., Smarandache A., Sabau D., Ibric Cioranu V.

The use of iliac crest blocks in atrophic maxilla

535

Buzatu R., Boloș C.O., Călniceanu H., Vâlceanu S.A., Onisei D.

Aesthetic improvement of Emax crowns with nanoceramic posts

540

Szuhanek C., Golban D., Schiller E., Jianu R.

Orthodontic treatment in canine impaction - A case report

544

<i>Savencu C.E., Porojan L., Borțun C.M.</i>	
Internal and marginal adaptation of anatomic and uniform thickness metal frameworks fabricated with two CAD/CAM technologies: milling and Selective Laser Melting- in vitro study	548
<i>Saleh K.A.R., Dinu L.C., Stanciu R., Stanciu D., Temelcea A.</i>	
Microbial colonization in orthodontic mini-implants	554
<i>Răducanu A.M., Feraru I.-V., Suciu I., Ionescu E.</i>	
Drug prescription in paediatric dentistry: a retrospective study	560
<i>Pricop M., Rivis M., Urechescu H.</i>	
Extraoral vs. intraoral approach in surgical treatment of mandible subcondylar fracture - case reports and review of the literature	567
<i>Bolos O.C., Vâlceanu A.S., Buzatu R., Bolos A.</i>	
Preliminary photographic documentation in esthetic dentistry	572
<i>Levai M.C., Rusu L.C., Podariu A.C., Tofan S.A., Anculia R.C., Popovici R.A.</i>	
Communication barriers in the doctor's office or medical organizations	578
<i>Popovici R.A., Podariu A.C., Rusu L.C., Porumb A., Todor L., Motoc O., Levai M.C.</i>	
Leadership in dental health services	585
<i>Cosor O.C., Baibata D.E.S., Iurciuc S., Velmirovici D., Duda-Seiman D., Rada M., Gaita D., Mancas S.</i>	
ERRATA - Cardiovascular risk profile of remote process of coronary dezobstruction	595

Laparoscopic right adrenalectomy and cholecistectomy: from endocrine decision to surgical procedure



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Abstract

Objective. We aim to introduce a rare surgical approach: one time laparoscopic adrenalectomy and cholecistectomy (LAC).

Cases presentation. This is a 61-year female with a right adrenal incidentaloma (and gallbladder stones) which increased after 2 years to 4 cm. After LAC, pathological report confirmed a adrenocortical adenoma while more than 10 stones were found. The second case is a 52-year female with chronic thyroiditis and renal microlithiasis. A right adrenal incidentaloma of 2 cm was discovered at abdominal ultrasound together with a cholecyst stone. One year later, chromogranin A increased to 8 times above normal limits and computer tomography showed stationary gallbladder stone but an enlargement of adrenal mass to 3.15 cm with a second new tumour at the same level of 1.49 cm (both with low pre-contrast density). After LAC, a single benign cortical adenoma was confirmed.

Conclusion. Adrenal tumour and gallbladder stones may be laparoscopic removed by performing simultaneous adrenalectomy and cholecistectomy; this involves a pre-operative inter-disciplinary approach and a skilled surgical team.

Keywords: adrenal tumour, adrenalectomy, cholecistectomy, gallbladder stones

INTRODUCTION

Currently, laparoscopic surgery represents the golden standard of approach regarding both adrenal tumours and cholecistectomy performed for instance, for gallbladder stones. (1) The indication of surgery is usually done after an endocrine assessment of the adrenal mass is done in association with the data provided by imagery scan as computer tomography or magnetic resonance imagery. (2) The adrenal lesion leads to surgery if the tumour displays a secretor pattern or it is very large or if the suspicion of malignancy is presented (in selected cases open procedure might seem safer though), etc. (2) A so-called adrenal "incidentaloma" usually is sent for remove in cases with increased dimensions during follow-up, meaning sometimes years after the first accidental tumour identification. (3) Simultaneously with adrenalectomy, a second organ might be approached if an indication of a secondary surgery is necessary in order to avoid an additional procedure as nephrectomy or splenectomy. (4) However, this complex one time intervention is very rarely done in daily practice depending on medical indication and, especially, on surgeon's skills. (4) We aim to introduce two adult cases with a rare surgical approach: one time laparoscopic adrenalectomy and cholecistectomy. They were diagnosed and treated in different endocrine and surgical centres from Romania. For the two included cases reports the informed written consent was signed by each patient.

CASE PRESENTATION

Case 1

This is a 61-year old non-smoking female who was recently admitted for a routine endocrine check-up after having the following medical and surgical history. As she came from an endemic area, she was known with multi-nodular goitre with associated hypothyroidism which required daily oral levothyroxine substitution with regular TSH (Thyroid Stimulating Hormone) assays to provide adequate replacement since 2000. She also associated high blood pressure, menopausal osteopenia, and high uric acid under therapy. In 2006, she was accidentally found with a right adrenal tumour of 2 centimetre (cm) after having a routine abdominal ultrasound. The endocrine panel of investigations was normal for adrenal function. Two years later, the tumour size increased more than 50% up to almost 4 cm maximum diameter. While performing imagery, a gallbladder stone was also found (without significant clinical correspondent). Due to changes of dimensions, the adrenal mass had an indication to be removed while the gallbladder aspect at assays recommended surgery. Simultaneous laparoscopic adrenalectomy was combined with cholecistectomy with a rapid recovery after intervention. The pathological report confirmed a adrenocortical adenoma while more than 10 stones were found at the level of gallbladder. No adrenal replacement therapy was necessary post-operative. One year later, ACTH (Adrenocorticotrophic Hormone) continued to be normal (of 31 pg/mL, normal levels between 3 and 66 pg/mL) without any anomaly at abdominal ultrasound. The cardio-metabolic complications did not ameliorate after surgery, due to their non-endocrine (essential) type of aetiology and the patient continued specific medication for lowering arterial hypertension, high cholesterol and uric acid up to 2016 when she was recently evaluated.

Case 2

This is the case of a 52-year old non-smoking female known with chronic thyroiditis with normal thyroid function having a history of renal microlithiasis. For this matter, she had an abdominal ultrasound scan done in 2011 which also revealed a gallbladder stone and a right adrenal tumour (of 2 cm diameter at computer tomography). The hormonal assays were

normal, suggestive for an adrenal incidentaloma. Follow-up was recommended at that moment, and one year later the patient was re-evaluated. The biochemistry work-up was normal as well as hormonal panel except for a consistent elevation of serum chromogranin A (about 8 times above the upper normal limit. **(Table 1)** The patient intermittently accused mild pain at the level of right hypocondrium region. The computer tomography showed stationary aspect of gallbladder stone area and increased dimensions of the right adrenal mass to 2.13 by 3.15 by 2.87 cm involving a solid lesion at the lateral adrenal level, of oval well defined shape with spontaneous density of -12 HU (Hounsfield Units) but also apparently a second solid tumour at median area of the same gland of round-oval well defined shaped (of 1.49 by 1.49 by 1.05 cm) displaying similar density with the other mass. Both right adrenal tumours had a density corresponding to arterial time between 16 and 29 HU, respective between 16 and 23 HU for venous time and a late enhancement to 12 HU. **(Figure 1A)** Based on tumour increase as well as abnormal chromogranin A, adrenalectomy was considered useful and gallbladder removal seemed rational due to clinical and imagery aspects. Right adrenal laparoscopic surgery also associated laparoscopic cholecistectomy with a rapid recovery of the patient and post-operative normal adrenal function. The pathological examination showed a benign adenoma of the adrenal cortex corresponding to both masses that were identified at pre-operative computer tomography scanning. **(Table 1)** One year later, the patient continued to feel well while the imagery showed no abnormal finding. **(Figure 1)**

Table 1. This is the endocrine profile on a menopausal female patient with an adrenal incidentaloma which increased in size during follow-up

Parameter	Patient's value		Norma limits	Units	
	Before surgery				
Baseline morning plasma cortisol	12.53		6.2-19.4	µg/dL	
Morning plasma cortisol after 1 mg dexametasone overnight suppression test	1.27		<1.8	µg/dL	
ACTH (Adrenocorticotrophic Hormone)	12.66		1 3-66	pg/mL	
Chromogranin A	834		2 20-125	3	NG/ML
Plasma metanephrines	10		4 10-90	5	PG/ML
6 PLASMA NORMETANEPRINES	7 20		8 20-200	9	PG/ML
10 DHEA	12 5.19		13 1.3-9.8	14	NG/ML
11 (DEHYDROEPIANDROSTERON)					
Six months after laparoscopic right adrenalectomy					
Baseline morning plasma cortisol	11.77		6.2-19.4	µg/dL	
ACTH (Adrenocorticotrophic Hormone)	23.08		15 3-66	pg/mL	
Chromogranin A	70		16 20-125	17	NG/ML

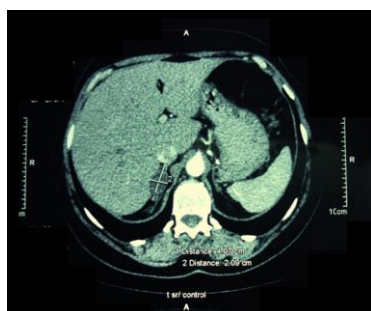


Figure 1A1.

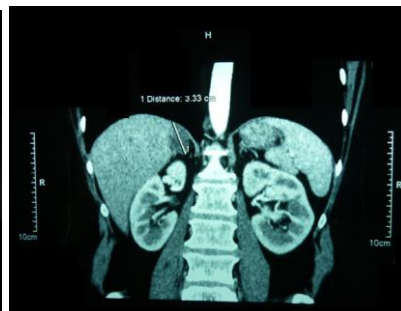


Figure 1A2.



Figure 1B.

Figure 1. Computed tomography: A: right adrenal tumour on adult female (AI: transversal section, respective A2 coronale plane); B: aspect one year after right adrenalectomy and cholecistectomy on an adult female.

DISCUSSIONS

The two cases we introduced are remarkable for the procedure that combines anterior laparoscopic approach of right adrenal and cholecyst remove. A few reports from literature include this particular topic. (5) Both female patients, although diagnosed with adrenal incidentaloma, had an indication of surgery after increase dimensions during follow-up for at least 12 months. A recently launched guideline by European Society of Endocrinology clearly indicates the context of sending such patients to surgery. (6) The second case also had an elevation of chromogranin A marker which might suggest a neuroendocrine component or an intense proliferative aspect but its specificity is rather low especially in cases where a pheochromocytoma was excluded. (7,8) The same mentioned case had a computer tomography with a complex analysis including details of tumour density, respective the exact frame of HU values before and after intravenous contrast substance administration. This is recommended in each case of assaying an adrenal incidentaloma knowing the fact that low density before contrast administration is tidily correlated with a benign behaviour. (6,9) Another predictor of potential malignancy is a tumour larger than the cut-off of 4 cm (or 6 cm, depending on study), a limit that was reached on both cases (considering both tumours described at computer tomography on second case) but not at first diagnosis of adrenal lesion. (6) However, the histological report confirmed a corticoadrenal adenoma in each case. Interestingly, the younger subject had a computer tomography description as having two adrenal masses but, in fact, as post-operative revealed, these were different arms of the same tumour. In challenging cases a selective imagery tool as positron emission tomography/computed tomography (PET/CT) might help the adequate identification of adrenal lesion but some cost issues should be taken into consideration. (6,10,11,12) We also mention the value of multi-disciplinary evaluation including endocrine and gastroenterological assessment to establish the indication of adrenalectomy by the same time with cholecistectomy.

CONCLUSIONS

Adrenal tumour and gallbladder stones may be laparoscopic removed by performing simultaneous adrenalectomy and cholecistectomy; this involves a pre-operative interdisciplinary approach and a skilled surgical team.

Acknowledgement

We thank each the medical teams and the patients who agreed to introduce their medical cases.

Conflict of interest

Nothing to declare

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The pattern of development dysplasia of the prematurely newborn



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Abstract

Objectives: Given that there is still no health program nationally implemented for active and early diagnosis of DDH, the authors attempted through a multicenter study to determine whether hip dysplasia in premature differs from DDH in neonates at term.

Material and Methods: Between 02nd April 2013 - 08th February 2015, 63 preterm and 771 normal weight newborns at term were ultrasound scanned, then staged according to Graf classification. Newborns and infants with birth weight between 2000-2500g underwent ultrasound in the first days after birth. In premature infants who required care, ultrasound screening was postponed. Cases detected with physiologically immature hip or DDH (IIc, III, D, IV) were reassessed at regular intervals and treated conservatively.

Results: It was established that in both case of premature and newborns at term with DDH, multiple variables constitute a predictive model. Although the two mathematical models contain the same variables, both positive (47.6% vs 38.2%) and negative (absence of DDH - 97.6% vs 75%) predictive value for DDH are greater for premature.

In terms of incidence, stage II was more frequent in newborns at term (43.7% vs 30.1%), but stage IIc-IV had the same incidence (1.8% in term and 1, 5% for preterm newborns).

Recovery from stages IIc-IV, was obtained after an average of 95 days for newborns at term and 130 days for preterm newborns. But if we take in consideration the corrected age, the difference is insignificant (95 days vs. 97 days $p > 0.05$).

Conclusions: DDH detection screening for premature infants should be performed as early as maternity. The recovery period in case of early treatment for premature is identical to newborns at term.

Keywords: congenital hip dislocation, perinatal risk factors, incidence, screening, DDH, premature

INTRODUCTION

Hip dysplasia has a multifactorial etiology and still has not been fully elucidated. Hip dysplasia does not just affects the child and family but it is also a big public health problem. Early detection of DDH is extremely important in order to provide the appropriate and definitive treatment.

Objectives

Given that there is still no health program nationally implemented for active diagnosis and early discovery of DDH, the authors attempted through a multicenter study to determine whether hip dysplasia in premature newborns differs from DDH in neonates at term.

MATERIAL AND METHODS

Between 02 April 2013 and 08 February 2015 using ultrasound scan, 63 premature newborns and 771 newborns at term were graded in accordance with Graf staging. Newborns at term and premature infants with the birth weight between 2000 grams and 2500 grams underwent ultrasound scan in the early days post birth. The scan was postponed for premature infants who required care, giving us the chance to obtain a series of evolving spontaneous hip cases. The cases found with physiologically immature hip or DDS (IIc, III, D, IV) were reassessed at regular intervals using ultrasound scan and treated conservatively. We proceeded to compare the mathematical models created by SPSS for premature infants with DDH against newborns at term with DDH. It was compared as well, the stages obtained at future revaluations.

RESULTS AND DISCUSSIONS

Using logistic regression, it was established that in the cases of premature with DDH and at term newborns with DDH as well, the following variables constitute a predictive model: female genre, birth weight, caesarean section delivery, breech presentation, first pregnancy, mother's age, and in addition, to preterm infants, postnatal age of the first ultrasound. Although the two mathematical models contain the same variables, the positive predictive value both to find immature hip (IIa) or DDH at the first assessment, and negative predictive value (absence DDH or persistence of immature type) (97.6% vs 74.1%) it is higher on premature new born group (47.6% vs 39.9%) . In additional, these factors have different importance for premature: female gender is a risk factor for new at term (OR 1.72 vs 0.74), cesarean section delivery is a protective factor more important in infants at term (OR 0.72 vs 0.53), younger mothers is an important risk factor for newborns at term (OR 1.02 vs 0.93), and also breech presentation is increases the risk significantly for newborns at term (OR 2.29 vs 0.8).

In terms of incidence, stage II was more frequent found in the newborns at term group (42.6% vs 30.1%), but stage IIc-IV had the same incidence (1.8% in term vs 1, 5% for preterm infants). Stage IIa was more often found in the right hip (79.3%) in the at term neonate group. In the preterm new born, IIa stage was more often found at the level of left hip (78.9%).

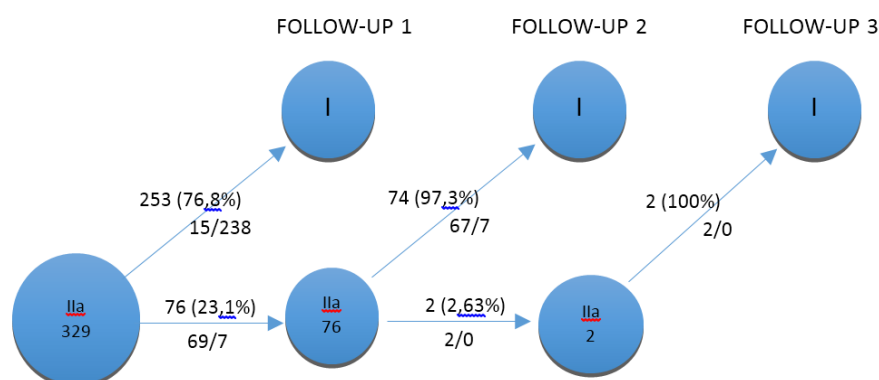


Figure 1. Evolution of type IIa of the newborns at term, discovered in maternity using the ultrasound scan. The first evaluation was conducted at 3.23 ± 1.67 days. The first follow-up was conducted after 4-6 weeks post delivery ($41.27 \text{ zile} \pm 3.28$), the second evaluation at 12 weeks ($77.3 \pm 13.6 \text{ zile}$) and the third assessment 18 weeks (127.5 ± 3.53 days). The report under the arrow of evolution, is the number of subjects with treatment / without treatment

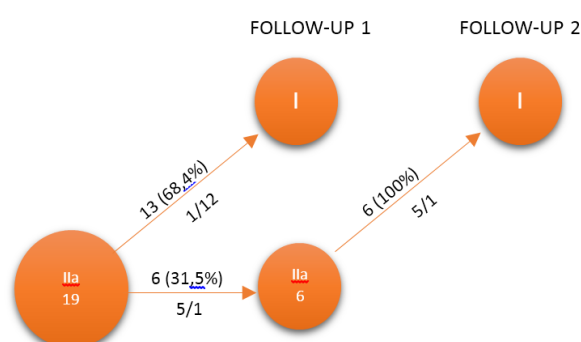


Figure 2. The evolution of type IIa of the premature new born. The first evaluation was performed at $14 \pm 11 \text{ zile}$ postnatally. First follow up was conducted at 46.84 ± 8.64 days (approx 6 weeks and a half postnatally). Second follow up was done at 86.5 ± 15.5 days (12 weeks and 3 days after birth)

Stage IIa.

The first assessment was carried out in maternity. For newborns at term, it occurred in the 3rd postnatal day. For premature the average period for the first evaluation in maternity was $14 \pm 11 \text{ zile}$. Premature infants with stage IIa, had a mean birth weight of $2122 \pm 325 \text{ g}$ and gestational age of 34 ± 1.9 weeks. The first control for both at term infants and for preterm infants staged with IIa was conducted at 6 weeks post birth (for preterm at 4 weeks corrected age). On the first follow up, a significantly higher percentage from the preterm group, persists type IIa (31.5% of preterm infants vs 23.1% of at term infants). At the second follow up preterm infants did not record immature hips comparing with newborns at term, in which we found several cases of persistence at 12 weeks.

Stage IIc.

In newborns group with normal weight, 12 cases were detected in stage IIc (1.55%). Right hip - 6 cases, left hip - 4 cases; bilateral - 2 cases. After 3 months of treatment orthopedic (Pavlik harness), 83% (10 cases) have reached maturity. At 18 weeks one case has reached maturity, while another case was ongoing maturation (IIb).

In the preterm group it was discovered a case with IIc stage (the 14th day) and after 117 days under treatment with the Pavlik harness, the hip became mature. This case did not present to the 6 weeks and 3 months follow up so we do not know intermediate stages. Overall, the absolute duration to achieve the mature stage, seems to be equal to the newborns at term.

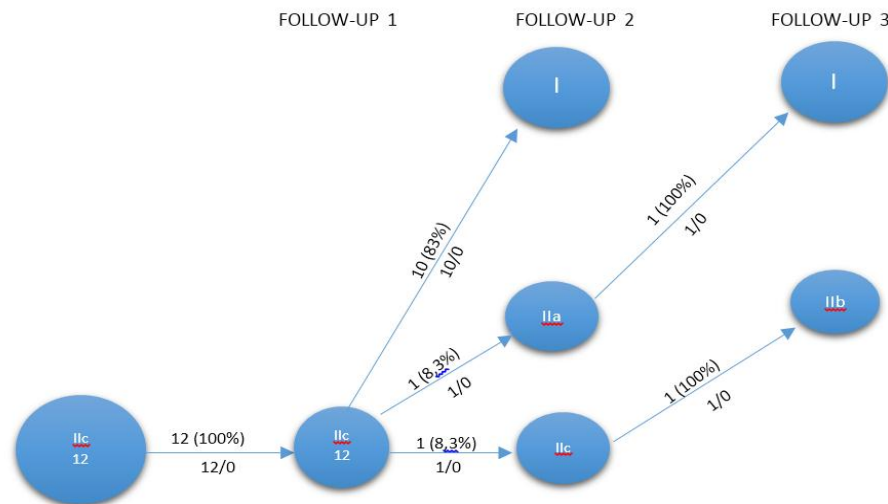


Figure 3. Evolution of the stage IIc of new borns with normal weight. The first assessment - in maternity, age 4 ± 1.3 days. First Follow-up - at 41.75 ± 0.86 days postnatally (6 weeks). Second follow-up - at 87.58 ± 12.73 days (12 and a half weeks). Third follow-up - at $125 \pm 21,21$ zile (aproximaty 18 weeks)

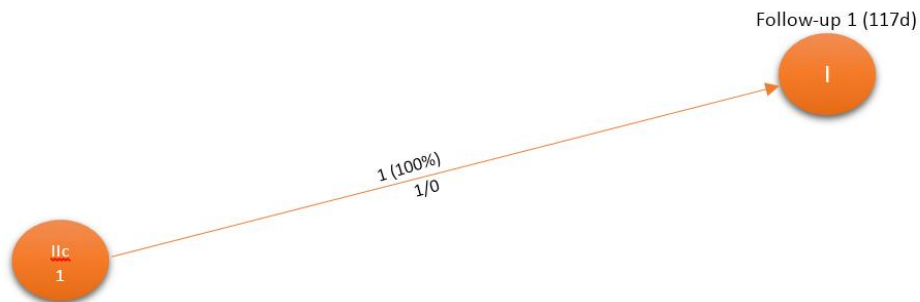


Figure 4. Evolution of the premature with stage IIc. One case detected in maternity at 14th day post birth ,underwent the Pavlik harness treatment.He returned to first follow-up at the postnatal age of 117 days (17 weeks) and found with type I

Type D and IIIa.

Regarding the type IIIa and type D it was diagnosed only one case for each type, and both of them were in the group of the newborns at term. The patient with type D was fully treated using Pavlik harness for 17 weeks. In the case of the patient with type IIIa he was treated as well with Pavlik harness but in his situation he was fully recovered after 13 weeks.

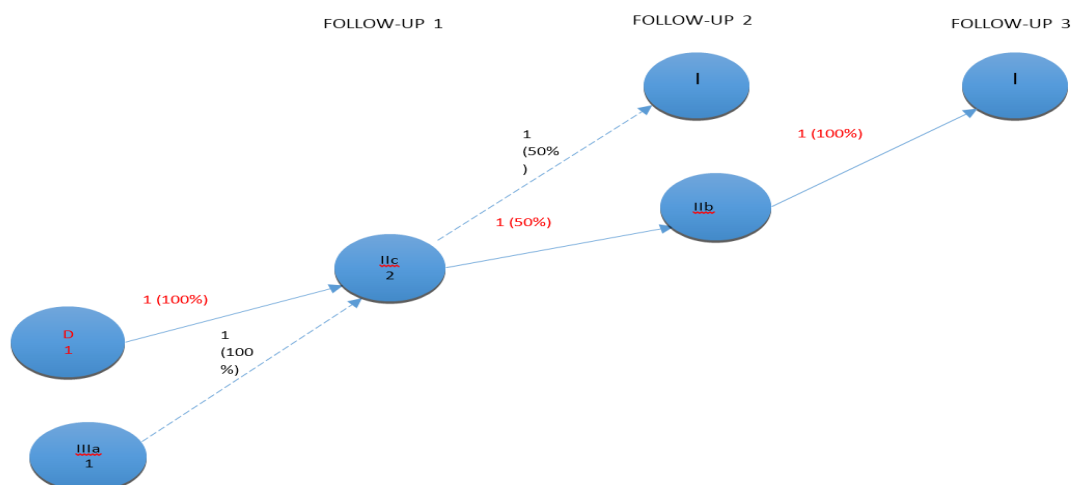


Figure 5. Evolution and type D and type IIIa in neonates at term

The recovery period of type IIc-IV, was obtained after an average of 95 days for newborns at term and 130 days for premature newborns. But if we take in consideration the corrected age, the difference is insignificant (95 days vs. 97 days, $p > 0.05$).

Kaplan-Meier analysis shows significant differences between developments in the two groups (term and preterm).

Initially we have considered the necessary time for achieving full maturation of the hip, making an exception of prematurity corrected age. The exclusion factor was the mature hip, proven with ultrasound. It was not taken in consideration the type or the treatment applied, because for both groups the decision and the treatment was based on the same principles. Log Rank, Breslow and Tarone-Ware indicates highly significant differences ($p < 0.001$) between Kaplan Meier curves.

Table 1. Mean and median time estimated for maturation of the hips in the groups of term and preterm newborns. Time was expressed in days

GA category	Mean(a)				Median			
	Estimates	Std. Error	95% Confidence Interval		Estimates	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
Preterm	74,342	5,131	64,286	84,398	65,000	4,462	56,255	73,745
Term	48,837	,940	46,996	50,679	42,000	,428	41,160	42,840
Overall	50,090	,943	48,243	51,937	42,000	,407	41,202	42,798

a Estimation is limited to the largest survival time if it is censored.

GA - gravitational age

Table 2. Static comparison indicators of maturation time for newborns at term and preterm (time rang - chronological age)

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	23,158	1	,000
Breslow (Generalized Wilcoxon)	28,809	1	,000
Tarone-Ware	28,821	1	,000

Test of equality of survival distributions for the different levels of GA category.

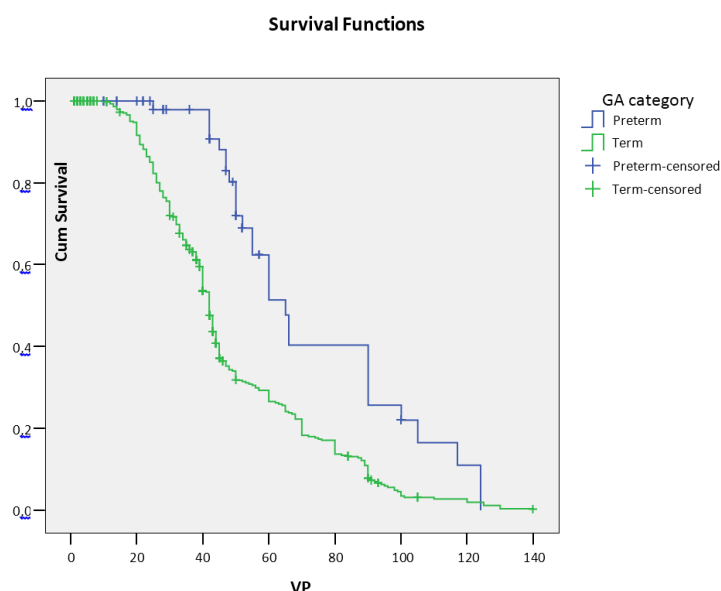


Chart 1. Kaplan-Meier comparison chart for the relationship between the likelihood of maturation in a unit time in the two groups. Green category - the group of term newborns, blue category - preterm infants. There is a tendency to reach maturity faster for green category (in term). Horizontal - time in days. *

The same analysis of comparing the probability of hip maturation per unit of time, was carried out in the two groups, but in premature infants, chronological age has been replaced with corrected age. Because of the negative time values, all the assessments thru ultrasound scan, before the age of 37 weeks corrected age (CA), were excluded from the calculation automatically. In this way, the only remaining assessments were the ones over 37 weeks corrected age (CA). It was more logical to compare the values of the resulted cases with the values of newborns at term. Another reason is the fact that in the obtained chart there is a constant evolving "plateau" for premature newborns in the first 60 days. The results indicate in this case as well, a faster maturation curve for newborns at term, and even if the differences is not so obvious to preterm group, they are still significant.

Table 3. The average and median estimated time for hip maturation in the group of newborns at term and preterm (the chronological age of premature infants being substituted with the corrected age). Time was expressed in days

VG Category	Mean(a)				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
Preterm	58,187	5,689	47,035	69,338	52,000	5,958	40,322	63,678
Term	48,837	,940	46,996	50,679	42,000	,428	41,160	42,840
Overall	49,238	,932	47,411	51,064	42,000	,419	41,178	42,822

Table 4. Log Rank and Tarone-Ware is below the importance threshold (0.10), and indicates significant differences between time events (temporal landmark for premature - corrected age)

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	3,105	1	,078
Breslow (Generalized Wilcoxon)	1,615	1	,204
Tarone-Ware	2,735	1	,098

Test of Equality of survival distributions for the different levels of GA category

Although the Breslow test shows insignificant differences, the Tarone-Ware test is statistically significant and it has more importance. In the Breslow test the time points are related with the number of cases of risk at every moment, and in the Tarone test the time points are related by the square root of the number of cases of risk at every moment.

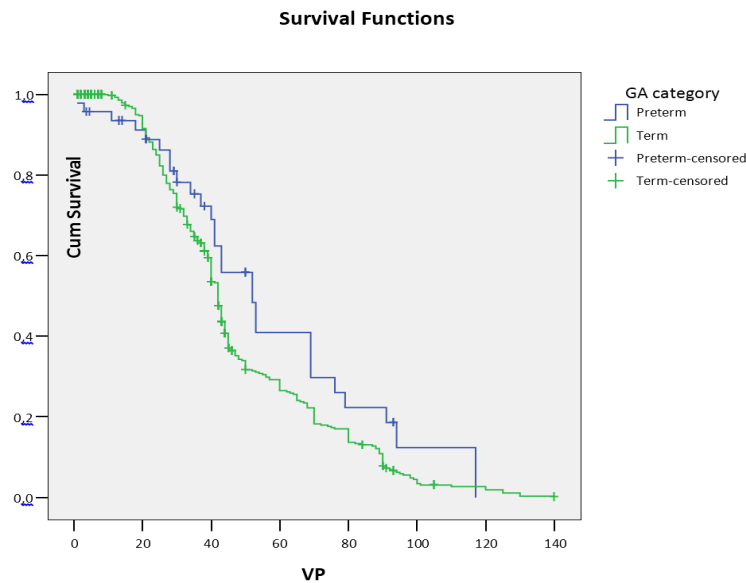


Chart 2. The Kaplan-Meier comparative chart for the relationship between the likelihood of hip maturation time unit in the two studied groups. For premature was used in calculating the corrected age. Green category - the group of newborns at term, blue category - the preterm infants. There is a tendency to reach maturity faster for green category (newborns at term).
Horizontal - time expressed in days

Carefully analyzing Chart 2, when for the premature was used the corrected age for calculation it is noted that the two curves are very close during the first 40 days. For this reason, we proceeded in analyzing the premature newborns with a corrected age up to 40 days versus the newborns at term with the same age group (0-40 days) and we analyzed separately the Kaplan-Meier curves.

For this interval we have not found significant differences in the evolution of the two groups. After this time point of 40 days, the premature newborns maintain the same and constant evolution slope in contrast with the newborns at term who have a very steep slope development.

Table 5. Mean time (for newborns at term the actual age in days, and for preterm newborns the corrected age) for the first 40 days

VG category	Mean(a)				Median			
	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
Preterm	29,973	2,519	25,036	34,911	34,000	4,733	24,724	43,276
Term	29,425	,387	28,666	30,184	30,000	,592	28,839	31,161
Overall	29,459	,382	28,710	30,208	30,000	,568	28,887	31,113

a Estimation is limited to the largest survival time if it is censored.

Table 6. The significance test is above the cutoff value (0.10)

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	,475	1	,491
Breslow (Generalized Wilcoxon)	,072	1	,788
Tarone-Ware	,116	1	,734

Test of equality of survival distributions for the different levels of GA category

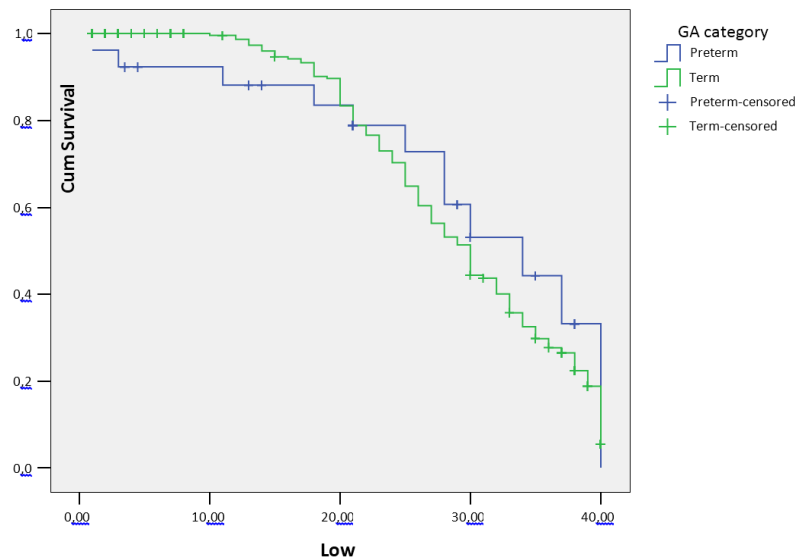


Chart 3. Kaplan-Meier comparative curves between the likelihood of curing unit time in the two groups for the first 40 days interval. For premature was used the corrected age. Green category - the group of newborns at term, blue category - the preterm infants. For this period of time, the evolution is very similar for all the subjects. Horizontal - time in days

CONCLUSIONS

Although it is the same disease, the pattern of the disease in premature newborns is distinguishable from newborns at term. The same predisposing factors appear to prematurely as well but have greater significance for the newborns at term when acting in isolation. Actually the presence of risk factors is less predictive for the disease, while their absence is more predictive for the absence of the disease.

The incidence of the immature or dysplastic hip is higher in premature newborns and the evolution is slow till 40 days corrected age, and even if it is detected and treated during this period, the rate of maturation seems not to be influenced very much.

In the case of the premature newborns it is expected that follow-up period to be longer with more frequent assessments which greatly raises the costs of recovery.

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None.

Disclosures

None.

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Diagnostic role of home blood pressure monitoring in primary care



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Abstract

The aim of the study was the evaluation of the utility and value of home blood pressure monitoring (HBPM) in primary care offices of Timiș County. From 2314 annual examinations at the GPs (visit 1), office blood pressure monitoring (OBPM) detected 255 (11.01%) subjects with newly diagnosed hypertension (HT). At visit 2, involving 200 cases with grade I and II hypertension (HT), repeated OBPM detected normal BP in 18 cases (9%) and in 182 (91%) high BP values. HBPM confirmed in 128 cases (84.76%) sustained HT and in 23 (15.24%) white-coat HT (WCHT). Average OBPM in sustained HT was for SBP 159.97 mmHg (SD $\pm$ 10.13), 95% CI: 1.84 (158.13–161.81 mmHg) and for DBP 94.59 mmHg (SD $\pm$ 5.62), 95% CI: 1.03 (93.56–95.62 mmHg). In WCHT average office SBP was 160.85 (SD $\pm$ 6.31), 95% CI: 2.46 (158.39–163.31 mmHg) and average DBP was 96.61 (SD $\pm$ 4.55), 95% CI: 1.78 (94.83–98.39 mmHg). Average HBPM in sustained HT patients was for SBP 143.27 mmHg (SD $\pm$ 7.20), 95% CI: 1.31 (141.96–144.58 mmHg) and for DBP 86.83 mmHg (SD $\pm$ 4.97), 95% CI: 0.90 (85.91–87.75 mmHg). In WCHT average home SBP was 129.91 mmHg (SD $\pm$ 5.80), 95% CI: 2.27 (127.63–132.19 mmHg) and average home DBP was 79.42 mmHg (SD $\pm$ 4.81), 95% CI: 1.89 (77.53–81.31 mmHg). Conclusions. HBPM enables a quick and accurate diagnosis of sustained and WCHT, proving a great potential to be widely used by family doctors in Timiș County.

Keywords: hypertension-home blood pressure monitoring-primary care

INTRODUCTION

As demonstrated by the SEPHAR III Study¹, hypertension has a prevalence of 44% in the adult Romanian population, having a major contribution to cardiovascular morbidity and mortality. Its diagnosis and management must be improved at the primary care level by developing strategies based on international guidelines².

The standard method for blood pressure (BP) measurement is represented by readings taken by a general practitioner (GP) or nurse in an office setting, using the auscultatory technique with aneroid sphygmomanometers and the oscillometric technique with semiautomatic devices. These measurements are mostly used by GPs for the management of hypertension. The disadvantages of OBPM is that it gives often inadequate information about a patient's true BP. As recommended by the guidelines, the confirmation of the diagnosis of HT requires three, sometimes even more OBPMs, with BP values ≥ 140 /and or 90 mmHg.

An increasing trend exists to supplement OBPM with out-of-office measurements. Of the two methods of out-of-office measurements, home blood pressure monitoring has the greatest potential to become routine in primary care. International hypertension guidelines propose after OBPM, out-of-office BP measurements with ambulatory blood pressure monitoring (ABPM) and HBPM^{2,3}. These 2 methods have many advantages over OBPM: they eliminate office-induced BP increase, minimise observer errors, have greater accuracy through many repeated measurements, provide a BP profile over a long period (days and weeks with HBPM or 24h with ABPM, including night-time)⁴. HBPM and ABPM must coexist and that they are complementary tools, providing common, but also different information about the BP status⁵.

ABPM has still a limited availability in family medicine, due to its costs, lack of reimbursement and inconvenience for some patients. HBPM requires reliable validated and accurate devices and correct reporting of data. Cut-off values for diagnosis of HT are average readings equal or higher than of 135/85 mmHg^{6,7}. An increasing number of Romanian patients are using for checking their BP at home different BP monitors, some of which may be inaccurate. Medical recommendations for monitor use are missing often and patients are not always well instructed by their GPs. Doctors have to verify patient's measurement technique and the accuracy of the BP measurement devices^{8,9}.

The objectives of the study were to evaluate in primary care settings OBPM and HBPM in a newly diagnosed hypertensive population and to determine the role of these methods for improving and accelerating the diagnosis of sustained hypertension and that of WCHT.

MATERIAL AND METHODS

We have done a prospective observational study using a primary practice population from 10 family medicine offices of Timiș County, which involved 10 GP and 8 residents. The study took place between January and December 2015 and was approved by the local ethics committee.

Selection of the subjects was made with the occasion of the annual clinical evaluation (visit 1). Patients were eligible under the following conditions: (1) if they presented newly office HT grade I or II (systolic BP (SBP) ≥ 140 and ≤ 179 mmHg or diastolic BP (DBP) ≥ 90 and ≤ 109 mmHg), (2) they were adults, (3) they accepted to perform the HBPM protocol.

Exclusion criteria were: severe HT, when treatment was immediately started, presence of cardiovascular diseases and target organ damage, presence of diabetes mellitus, atrial fibrillation or frequent ectopic beats and anxious patients. All enrolled participants gave their written informed consent.

The medical team was instructed to use the 2013 ESH/ESC (European Society of Hypertension/European Society of Cardiology) guidelines recommendations for HT measurement through the C.O.M.B.A.T course (Romanian National Course on the Management of Hypertensive Patient) organised by the Romanian Hypertension Society¹⁰.

OBPM were performed in seated position, after at least 5 minutes of rest, with the back supported, legs uncrossed, cuff positioned at the heart level and after adjusting cuff size to the arm circumference, more than 30 minutes without smoking or drinking coffee. If the two BP values were different, repeated measurements were done. Automated validated sphygmomanometers (OMRON HEM 7251G) were used by all GPs.

HBPM consisted of 7 days duplicate morning and evening BP measurements. The first-day readings were discarded and the remaining measurements averaged. HBPM was taken in a quiet room, with the patient in a seated position, back and arm supported, readings taken with 1 minute pause between. Home readings were made with different types of validated oscillometric monitors. All devices fulfilled the standards of the British Hypertension Society.

BP levels for definition of office HT were SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg. For HBPM were accepted SBP ≥ 135 mmHg and/or DBP ≥ 85 mmHg for diagnosis of HT. Normal BP was diagnosed when both OBPM and HBPM had normal values. Office hypertension was appreciated as elevated OBPM, taken at the visits 1 and 2. Sustained HT was diagnosed by elevated repeated OBPM (at both visits) and by elevated HBPM. WCHT was defined by elevated OBPM at both office visits, but normal HBPM.

The study included 3 visits at the GPs. Visit 1 at the annual medical examination, detected newly elevated OBPM. A medical history, anthropometric data and a clinical examination were then performed. In those with hypertension, a second visit was made for repeating OBPM within 7-14 days. After the second confirmation of high OBPM, the patients underwent HBPM. Investigations for risk factors assessment and target organ damage detection were performed. At visit 3, the GPs compared data of OBPM and HBPM and the diagnosis of sustained HT or WCHT was elaborated.

Statistical analysis:

Data were presented as frequencies and percentages for qualitative variables and as mean $\pm$ SD for quantitative variables. Differences between groups of variables were assessed with the Pearson χ^2 for qualitative variables and the Student t test for quantitative data. The independent variables with a $p < 0.05$, were considered as having statistical significance. All the statistical analyses were performed using the software Stata 9.2.

RESULTS

At visit 1, from a number of 2314 adult examinations, OBPM detected 255 (11.01%) subjects with newly diagnosed office hypertension. The population with newly office hypertension had the following characteristics: male gender 125 (49.02%), female 130 (50.98%) and a mean age of 57.1 years, SD ± 13.43 , 95% CI: 2.19 (54.22 – 58.68 years).

The age groups were represented by: 18-24 years group (8 subjects 3.14%), 25-34 years group (5 subjects, 1.96%), 35-44 years group (31 subjects, 12.16%), 45-54 years group (71 subjects, 27.84%), 55-64 years group (66 subjects, 25.88%) and over 65 years 74 subjects (29.02%).

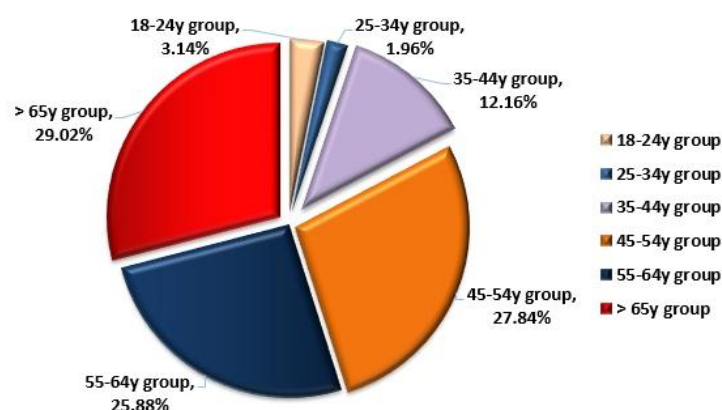


Figure 1. Age groups of the study population

Of the 255 subjects with newly detected office HT, 110 subjects (43.13%) were living in rural environment and 145 subjects (56.87%) in urban environment. A sedentary life style was present in 156 cases (61.17%). Body mass index was normal in 41 subjects (16.08%), overweight being present in 94 cases (36.86%). Obesity class I was present in 55 subjects (21.57%) and class II obesity in 65 cases (25.49%).

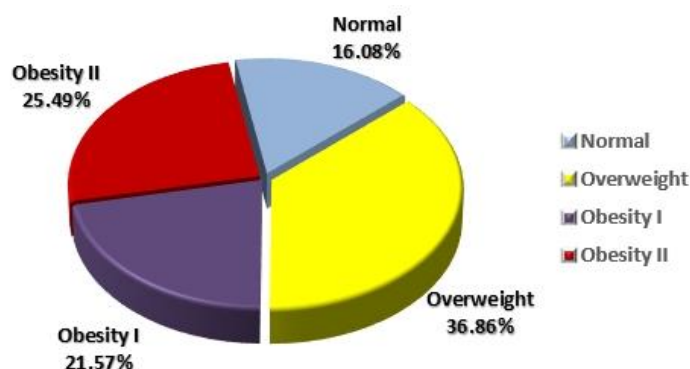


Figure 2. Characteristics concerning body mass index of the study population

There were 54 smokers (21.17%), 82 cases (32.15%) with hypercholesterolemia and 71 cases (27.84%) with hypertriglyceridemia.

Of the 255 newly diagnosed office HT at visit 1, a number of 164 cases (64.31%) were mild HT (grade 1), 58 cases (22.75%) moderate (grade 2) and 33 cases (12.94%) severe HT (grade 3), the last group being excluded from the study, as it started immediate treatment.

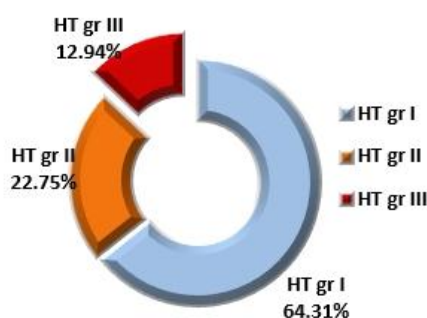


Figure 3. Grade of hypertension

Two weeks after the first visit, the patients were recalled to the second office visit that was attended by 200 patients with mild and moderate office HT. 22 subjects missed visit 2. Repeated OBPM detected in 18 (9%) subjects normal BP values (excluded from the study as

normotensives) and in 182 (91%) subjects elevated OBPM (these were further evaluated by HBPM).

Visit 3 was attended by 151 patients, 12 subjects missed and 19 subjects had unsatisfactory HBPM, being so excluded from the study.

Finally only 151 patients had both OBPM and acceptable HBPM. Based on the results of OBPM and HBPM, the GPs established the final diagnosis of sustained HT in 128 subjects (84.76%) and WCHT in 23 subjects (15.24%). The diagnostic algorithm, starting with OBPM at visit 1, repeated OBPM at visit 2, than evaluation with HBPM and establishment of hypertension type based on OBPM and HBPM is presented in figure 4.

The lowest OBPM obtained during the two office visits was used for comparison between OBPM and HBPM.

In the final study group (151 patients), average OBPM for SBP was 158.67 mmHg (SD $\pm$ 9.45), 95% CI: 1.55 (157.12 – 160.22 mmHg) and average DPB was 93.27 mmHg (SD $\pm$ 5.44), 95% CI: 0.89 (92.38 – 94.16 mmHg).

In the sustained HT group (128 patients) average OBPM for SBP was 159.97 mmHg (SD $\pm$ 10.13), 95% CI: 1.84 (158.13 – 161.81 mmHg) and average DPB was 94.59 mmHg (SD $\pm$ 5.61), 95% CI: 1.03 (93.56 – 95.62 mmHg).

In the WCHT group (23 patients), average OBPM for SBP was 160.85 mmHg (SD $\pm$ 6.32), 95% CI: 2.46 (158.39 – 163.31 mmHg) and average DPB was 96.61 mmHg (SD $\pm$ 4.56), 95% CI: 1.78 (94.83 – 98.39 mmHg). The WCHT group presented the highest OBPM for SBP and DBP.

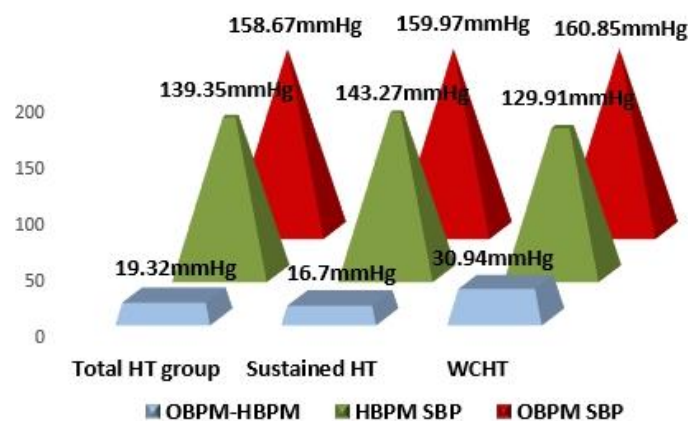


Figure 4. Average SBP with OBPM and HBPM in the study groups and their difference

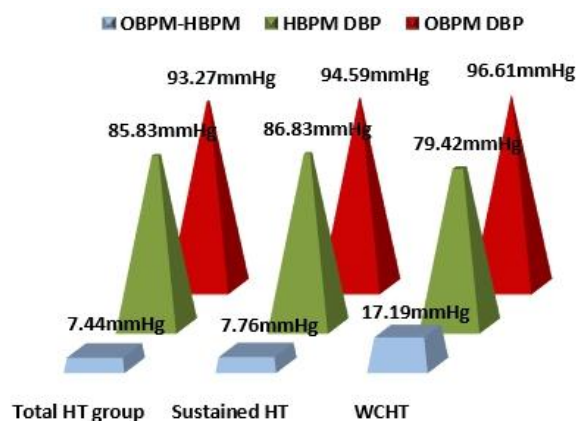


Figure 5. Average DBP with OBPM and HBPM in the study groups and their difference

Average HBPM values were lower than OBPM values. In the sustained HT group average HBPM for SBP was 143.27 mmHg (SD $\pm$ 7.20), 95% CI: 1.31 (141.96 – 144.58 mmHg). Average DBP was 86.83 mmHg (SD $\pm$ 4.96), 95% CI: 0.92 (85.91 – 87.75 mmHg).

In the WCHT group average SBP for HBPM was 129.91 mmHg (SD $\pm$ 5.81), 95% CI: 2.28 (127.63 – 132.19 mmHg) and average DBP was 79.42 mmHg (SD $\pm$ 4.80), 95% CI: 1.89 (77.53 – 81.31 mmHg). The differences between OBPM and HBPM were in all types of hypertension greater for SBP than for DBP. The greatest difference between OBPM and HBPM was noted in WCHT.

DISCUSSIONS

The prevalence of newly diagnosed HT of 11.01% in our study is lower than the national prevalence (12%) detected by the SEPHAR Study¹. This can be explained by the fact that OBPM and HBPM have some limits in detecting all types of hypertension. HBPM is best reliable when performed by patients who have been instructed and who use validated devices. The study confirms that patients can accurately measure and record their BP at home with the support of the GPs and that HBPM, compared with ABPM, has the great advantages of low equipment and staff costs.

OBPM is good for BP screening, but is limited in the amount of information that it can provide for rapid and adequate confirmation of hypertension, especially when BP values are around the thresholds. It is difficult to determine the true BP level only on the basis of 1 or 2 measurements at the time of a single office visit^{11, 12}.

HBPM is a simple and inexpensive way to obtain a large number of readings, that are representative of the BP profile over a longer period of time and that are not influenced by the "white-coat" effect, which may be present in the GPs office. That is why primary care practice must use out-of-office measurements, to obtain additional information for diagnosing hypertension¹³. The ESH Working Group on Blood Pressure Monitoring has proposed following indications for HBPM and ABPM: suspicion of WCHT, "white-coat effect", masked, nocturnal and resistant HT, great variability of BP during the same visit or different ones, HT in pregnancy and diagnosis of hypotension. It is considered that HBPM may be more suitable in primary care and ABPM in specialist care².

Our study demonstrates that HBPM can be especially useful in speeding up hypertension diagnosis in patients who, after two office visits, have high BP in the range of 140-179/and or 90-109mmHg. Relying only on OBPM, up to 3 to 4 office visits are needed before a diagnosis of hypertension can be made in these subjects. The best alternative too many clinic visits is to use HBPM.

The prevalence of 17% of WCHT in our sample is consistent with a number of published studies, which reported WCHT in 15% to 30% of subjects with newly diagnosed HT. WCHT is more common in women, newly diagnosed HT, with increasing age and in nonsmokers⁵.

Stergiou et al.⁸ found in untreated patients with office hypertension a specificity of 100%, a sensitivity of 61%, a positive predictive value of 100% and a negative predictive value of 77% for WCHT.

The diagnosis algorithm used in the study recommends HBPM after 2 repeated measurements with high OBPM, not waiting any longer for repeating other office measurements. HBPM appears to be useful, because it can speed the diagnosis and make the difference between WCHT and sustained HT. ABPM must be recommended if HBPM is close to the hypertension cut-off values.

Limitations

HBPM can't be recommended as the best diagnostic test for WCHT and sustained HT, as an approach using OBPM and HBPM followed by ABPM might be better, though more difficult for GP's practice. OBPM and HBPM can't detect masked and nocturnal HT, but ABPM does.

CONCLUSIONS

In our study OBPM values were higher than HBPM. The average difference between OBPM and HBPM in the total study group was for SBP 19.32 mmHg and 7.44 mmHg for DBP.

HBPM is a valuable, inexpensive tool, that gained in the recent years more and more acceptance by Romanian GPs and patients, demonstrating to be particularly useful for improving BP diagnosis, especially when BP values are around the thresholds. HBPM includes team based care, patient education and self-management skills. Because of cost, convenience, and advocacy from major consensus groups, HBPM has the greatest potential for being incorporated into the routine care of hypertensive patients. HBPM, compared with OBPM, has demonstrated to be a more accurate method for hypertension diagnostic. It permits a more rapid diagnosis of sustained HT as with repeated OBPM, overcomes many of the limitations of OBPM and can easily identify WCHT. Considering the working conditions of the Romanian GPs, HBPM needs to be larger used in hypertension diagnosis.

Conflict of Interest

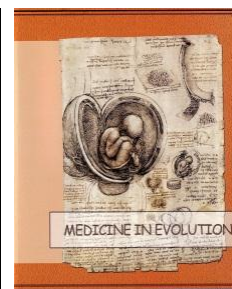
The authors have no potential conflict of interest to report.

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Glucocorticoid-induced osteoporosis after three decades of self-medication for asthma



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Abstract

Introduction: Bronchial asthma is a complex disorder with wide addressability, mainly involving general practitioners and pneumologists, but often requiring a multidisciplinary approach due to associated autoimmune diseases or treatment side effects, particularly in case of corticotherapy.

Case presentation: We report the case of a 60-year-old male smoker, diagnosed with asthma 36 years prior to admission. One year after initial diagnosis he became non-compliant with periodic monitoring and began self-medicating with betamethasone every 21 days, due to experiencing symptoms such as asthenia, muscle pain and nausea at the end of the 3 weeks following injection. On admission, the patient's phenotype was highly suggestive of hypercortisolism, with central obesity, kyphosis and high blood pressure (140/80 mmHg). Apart from vertebral compression fractures, osteoporosis was confirmed by Dual-Energy X-Ray Absorptiometry, which showed lumbar L2-4 Bone Mineral Density of 0.752 g/sqcm, T-score of -4.2SD, Z-score of -3.3SD. Betamethasone treatment was discontinued and the patient was prescribed inhaled corticosteroids (beclomethasone). The switch in corticotherapy was difficultly tolerated. Glucocorticoid-induced osteoporosis was treated with intravenous ibandronate 3 mg every 3 months and oral supplements of vitamin D 1000 IU/day and calcium 1000 mg/day.

Conclusion: The particularity of this case consists in the long history of self-medication with corticosteroids, which led to systemic consequences. Corticotherapy for asthma control may cause adverse effects such as Cushing's syndrome-related secondary osteoporosis. The lack of compliance to periodic monitoring as well as long-term self-medication can aggravate these issues.

Keywords: asthma; osteoporosis; glucocorticoids

INTRODUCTION

Bronchial asthma is a complex disorder with wide addressability, mainly involving general practitioners and pneumologists, but often requiring a multidisciplinary team due to associated autoimmune diseases or treatment side effects, especially in case of prolonged corticotherapy. **(1)** The latter can cause iatrogenic Cushing's syndrome, characterized by arterial hypertension, impaired glucose tolerance, dyslipidemia, obesity and also bone loss, in both female and male patients. **(2)** During corticotherapy there is inhibition of the hypothalamic-pituitary-adrenal axis, regardless of route of administration; sudden cessation of treatment can lead to adrenal insufficiency, so that gradual tapering is required. **(3)** We present a case of prolonged corticotherapy due to self-medication for three decades in a patient with asthma.

CASE PRESENTATION

A 60-year-old male patient with a history of smoking 1 pack/day for over four decades was diagnosed with asthma 36 years prior to admission. He initially underwent various treatment regimens, but one year after diagnosis he became non-compliant with regular pneumological follow-up and began self-medicating with betamethasone every 21 days, due to experiencing asthenia, muscle pain, anorexia and nausea, without exacerbation of asthma, at the end of the 3 weeks following injection. The patient also had a history of facial basal cell carcinoma, excised a few years prior. Currently, the patient presented for pneumological evaluation and was referred to the endocrinologist.

On admission, the patient's phenotype was highly suggestive of hypercortisolism, with central obesity, affecting mainly the face, neck and trunk, facial plethora, gracile arms and legs, kyphosis and high blood pressure (140/80 mmHg); the patient also complained of epigastric pain. Paraclinical investigations found vertebral compression fractures and osteoporosis was confirmed by Dual-Energy X-Ray Absorptiometry (DXA), which showed lumbar L2-4 Bone Mineral Density (BMD) of 0.752 g/sqcm (square centimeters), T-score of -4.2 SD (standard deviations), Z-score of -3.3 SD; BMD at femoral neck was 0.768 g/sqcm, T-score of -2.3 SD, Z-score of -1.1 SD; BMD at total hip was 0.849 g/sqcm, T-score of -1.8 SD, Z-score of -1 SD. **(4) (Figure 1)** The endocrine profile confirmed the diagnosis of iatrogenic Cushing's syndrome, showing suppressed basal ACTH (Adrenocorticotrophic hormone) levels of 1.5 pg/ml (normal range 7.2- 63.6 pg/ml). Betamethasone treatment was discontinued and the patient was prescribed inhaled corticosteroids (beclomethasone). The switch in corticotherapy was poorly tolerated, but the patient remained hypertensive, which was unusual for glucocorticoid-induced adrenal insufficiency; this was interpreted in the context of hypercortisolism. No acute asthma attacks occurred. The patient was prescribed omeprazole 20 mg/day for gastric protection and intravenous Ibandronate 3 mg every 3 months for glucocorticoid-induced osteoporosis, together with oral vitamin D 1000 IU/day and calcium 1000 mg/day. DXA scan was recommended after 1 year in order to evaluate treatment efficacy.

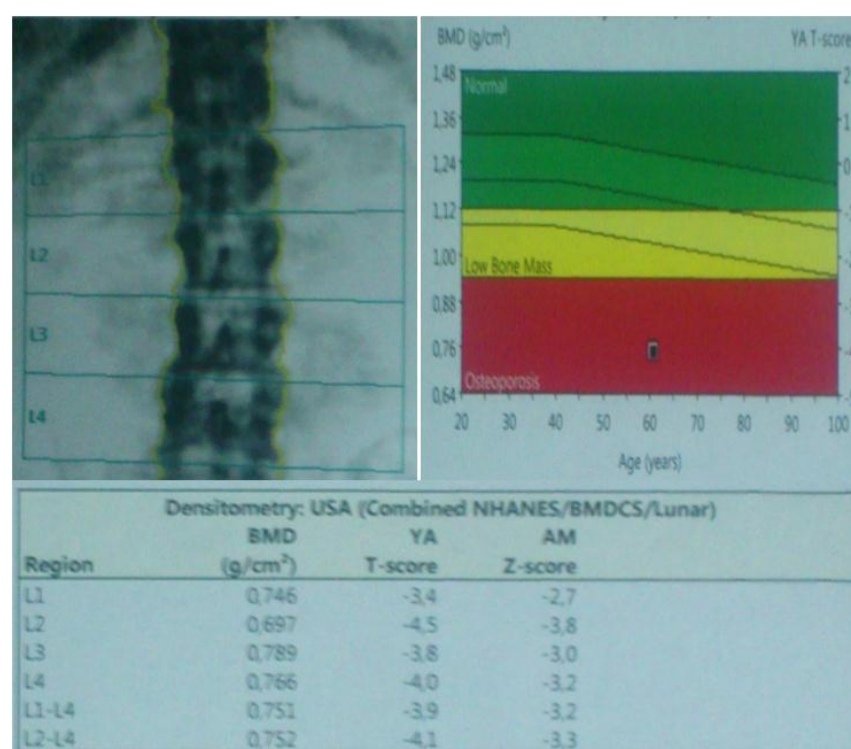


Figure 1. DXA scan

DISCUSSIONS

This case started with a classic respiratory disease (asthma), later complicated with a serious adverse effect of treatment (corticotherapy) due to prolonged and uncontrolled self-medication: Cushing's syndrome and glucocorticoid-induced osteoporosis; bone loss was also accelerated by smoking. Osteoporosis is rare in male patients and it usually occurs due to corticotherapy or hypogonadism. (5) Glucocorticoid-induced osteoporosis is the most frequent secondary form, regardless of gender. It has been shown that 10 mg prednisone/day for 3 months leads to a 7-fold increase in hip fracture risk and a 17-fold increase in vertebral fracture risk, so that almost half of patients undergoing corticotherapy suffer pathological fractures. (6) Our patient showed vertebral compression fractures. Glucocorticoids act directly on bone cells and influence skeletal resistance, microarchitecture and bone remodeling; their effects are particularly evident on long bones and cortical bone. At molecular level, it has been shown that glucocorticoids inhibit proliferation and differentiation of osteoblasts, interfere with the RANKL-osteoprotegerin system, reduce intestinal calcium absorption and parathyroid hormone secretion. (7,8) Specific treatment options for osteoporosis usually include bisphosphonates (administered orally such as alendronate, risedronate, ibandronate or intravenously such as zoledronic acid or ibandronate), as well as teriparatide or denosumab. The most important aspect is the individualized approach to case management, integratig cessation of corticotherapy, asthma control, supplementation with vitamin D and calcium and lifestyle changes (including smoking cessation). (9,10) In this case, given the patient's gastrointestinal complaints, we opted for injectable biphosphonate treatment. The particularity of this case consists in the three decade-long history of uncontrolled self-medication with corticosteroids, which led to systemic consequences.

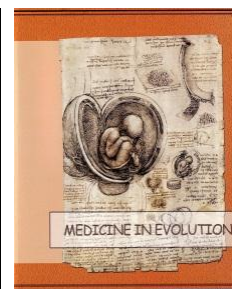
CONCLUSIONS

Corticotherapy for asthma can lead to serious adverse effects such as Cushing's syndrome-related osteoporosis and prolonged administration without regular monitoring exacerbates these issues.

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Morphological, immunohistochemical and prognostic analysis of gastrointestinal stromal tumors with gastric and small intestine origin



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Abstract

Gastrointestinal stromal tumors are mesenchymal neoplasms that originate in the interstitial cell of Cajal or in other precursor cells along the gastrointestinal tract. The prognosis of these tumors is based on the location, the tumor diameter as well as the number of mitotic figures. For a proper diagnosis and an accurate histopathological report immunohistochemical tests are mandatory. In this study we analyzed the clinico-pathological, immunohistochemical and prognostic features of 115 patients with gastric and small intestine GISTs.

Keywords: GIST, stomach, small intestine, survival, immunohistochemistry

INTRODUCTION

Gastrointestinal stromal tumors (GIST) are mesenchymal neoplasms that originate in the interstitial cell of Cajal or in other precursor cells along the gastrointestinal tract [1,2].

The key event in the pathogenesis lies so far in the development of gene mutations that encode tyrosine kinase receptors like KIT (80-90%) and PDGFRA (5-10%)[3-6].

Gastric location of GISTs is more frequent (55-60%) and is followed by small intestine (35%), rectum, esophagus and colon (5%) [7, 8, 9].

For a proper diagnosis we need to make an accurate histopathological report which needs to be completed by immunohistochemical tests. The markers useful for the diagnosis of GIST is CD117 (which highlights overexpression of KIT protein), CD34, and especially DOG1 which has a higher sensibility and specificity, being necessary especially in CD117 negative cases [10, 11, 12].

The prognosis of these tumors however is based on the location, the tumor diameter as well as the number of mitotic figures, parameter that can be easily established on hematoxylin-eosin stain [13-17].

There are just a few studies in Romania that described the clinical, pathological and the prognostic features of GISTs [28-30]. We present here a retrospective study which aims to highlights these clinico-pathological features of primary gastric and small intestine GIST as well as the outcome.

MATERIAL AND METHODS

From the archives of Pathology Department from Fundeni Clinical Institute we've selected all cases with gastric and small intestine GIST, diagnosed and treated between 2004-2015. All other locations of GISTs have been excluded. Clinical and histopathological data have been taken from the hospital charts and electronical data base.

In the study group we have included 115 patients with clinical data regarding age, sex and major symptomatology. Histopathologic data comprise tumor primary site, macroscopically features, tumor diameter, number of mitotic figures/50HPF, risk stratification according to Miettinen&Lasota (2006) (Tabel 1). Histological parameters studied were as follows: cellularity in terms of quantity (a subjective analysis was made based on cellular density: low, medium, high), cellular type (fusiform, epithelioid, mixt), nuclear pleomorphism (low, medium, high) and necrosis (yes or no).

Tissue samples were formalin fixed (10%), paraffin embedded, sectioned and hematoxylin-eosin stained for histopathological diagnosis. Paraffin sections of 2-4 µm were stored at 37 °C for 7-10 hours. All cases have been immunohistochemically stained with biotin-streptavidin method [27]. We assessed if the following antibodies were positive or negative: DOG1, CD117, PDGFRA, CD34, SMA, Desmine (Table2).

Table 1. Risk of aggressive behavior in GISTs by assessing: mitotic index, tumoral diameter and tumoral site (adapted from Miettinen si Lasota, *Seminars in Diagnostic Pathology* 2006; 23(2) 70-83)

Tumor parameters			The proportion of patients with progressive disease and risk characterization of metastases		
Group	Tumor diameter (cm)	Mitotic rate /50 HPF	Stomach	Jejunum and Ileum	Duodenum
1	≤2cm	≤5/50-HPF	0% absent	0% absent	0% absent
2	>2 cm ≤5 cm	≤5/50-HPFs	1.9% very low	4.3% low	8.3% low
3a	>5 cm ≤10cm	≤5/50-HPFs	3.6% low	24% moderate	34% high

Tumor parameters			The proportion of patients with progressive disease and risk characterization of metastases		
3b	>10 cm	≤5/50-HPFs	12% moderate	52% high	
4	≤2 cm	>5 / 50 HPFs	0% *	50%*	***
5	>2 cm ≤5 cm	>5 / 50 HPFs	16% moderate	73% high	50% high
6a	>5 cm ≤10cm	>5 / 50 HPFs	55% high	85% high	86% high
6b	>10cm	>5 / 50 HPFs	86% high	90% high	
* categories with very few cases					
** 3a and 3b and 6a and 6b groups are combined in duodenal GIST due to the small number of cases.					
*** tumors were not included in this category					
Note that GIST of the small intestine presents a significantly unfavorable prognosis in several types of tumor size and mitotic rate compared with gastric GIST. GIST: gastrointestinal stromal tumor; HPF: high power microscopic field.					

Table 2. Primary antibodies used for immunohistochemical tests (Antibody, Clone, Dilution)

Antigen	Clone	REACTIV	Dilution	Pretreatment	Source
CD117	T595	NCL-L-CD117	1:40 1:40	CITRAT EDTA	Novocastra, Labvision/ThermoFisher Scientific
PDGFRA	polyclonal	-	1:100	CITRAT	Labvision/ThermoFisher Scientific
CD34	QBEnd/10	NCL-L-END	1:50 1:50	TRYPSIN -	Novocastra Labvision/ThermoFisher Scientific
SMA	αsm-1 1A4	NCL-SMA	1:50	FARA	Novocastra, Labvision/ThermoFisher Scientific
DESMINA	DE-R-11 D33	NCL-L-DES-DERII	1:100	TRYPSIN	Novocastra, Labvision/ThermoFisher Scientific
DOG1 (Anoctamin1)	K9	NCL-L-DOG1	1:100	CITRAT	Novocastra

For the statistical analysis we used Microsoft Excel (2010) and SPSS (Statistical Package for the Social Sciences). The statistical tests used were t test, chi-squared test, simple linear regressions and a Kaplan-Meier estimate.

We performed descriptive statistics of the survival data. The survival was calculated in days, beginning with the data of the immunohistochemically conformed diagnosis. The cut off was represented by the last day in which the data base was updated for this study (January 15 th 2016). We followed two types of survival:

-overall survival = the number of days between the immunohistochemical diagnosis and the end point of the updated database or the date of death

-disease free survival = the number of days between the complete removal of the tumor and the relapse or the cutoff date.

RESULTS

The study group included 115 patients (62 females and 53 males) from which 62(54%) had GISTs located in the stomach (Photo1) and 53(46%) in the small intestine (Photo2). The medium age of the diagnosis was 57.47 years old (minimum 25, maximum 83)-Figure 1. The main symptomatology of the studied patients was bleeding (n=45, 39.1%), followed by

abdominal pain (n=41, 35.6%), nonspecific symptoms (weight loss, anorexia, fatigue) (n=17, 14.8%), bowel obstruction (n=3, 2.6%) and asymptomatic or incidental findings during investigation for other medical conditions (n=9, 7.8%).

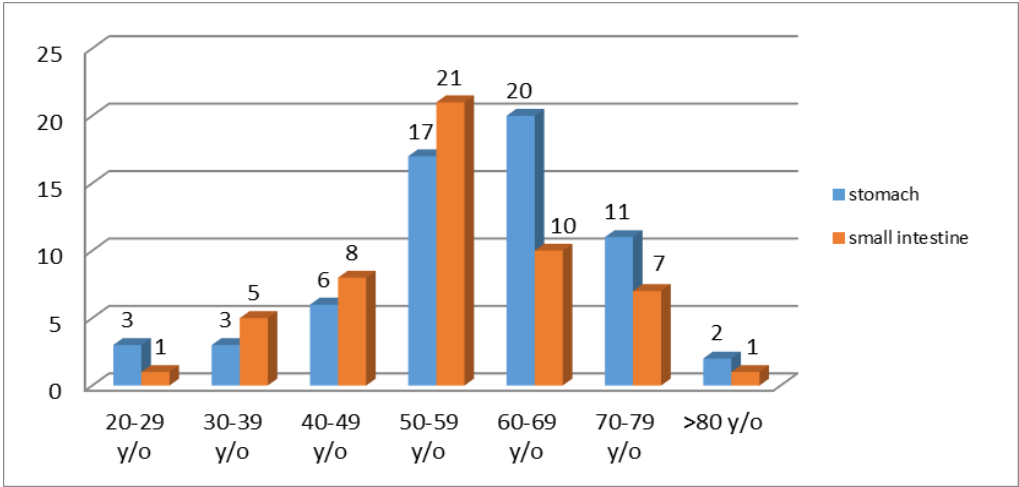


Figure 1. GISTs distribution according to age and tumor primary site

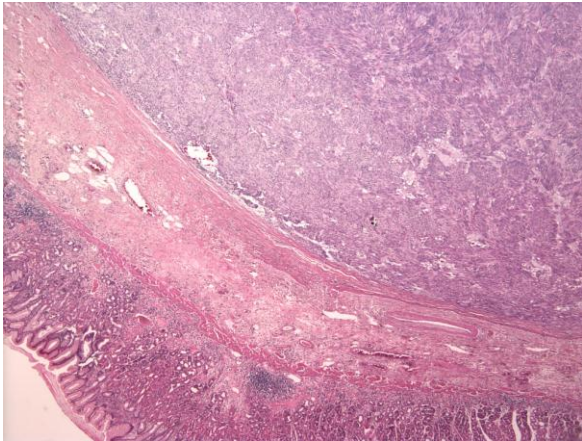


Photo 1. Gastric GIST, fusiform pattern HE x 40

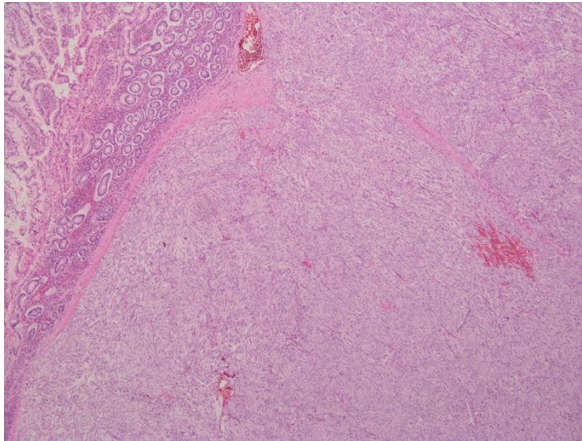


Photo 2. Small intestine GIST , HE x 40

From the 62(54%) patients with gastric GISTs (13 in the antrum and 49 in the body- Figure 3) 24 were males and 38 were females (Figure 2) with age between 26 years old and 83years old (median age 59.1years old). Tumor diameter was between 1 and 30 cm (average of 7.2cm). Most of the tumors (n=24, 20.8%) fit into type 2 prognostic group with very low risk of progressive disease (Figure 5)

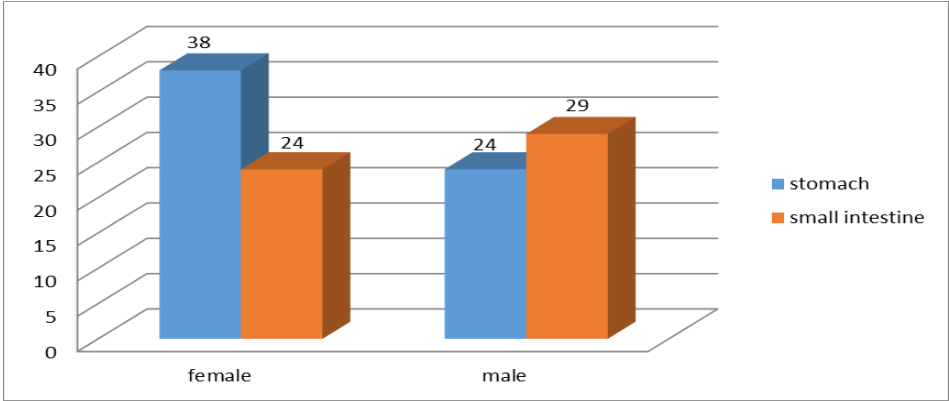


Figure 2. GISTs distribution according to sex and tumor primary site

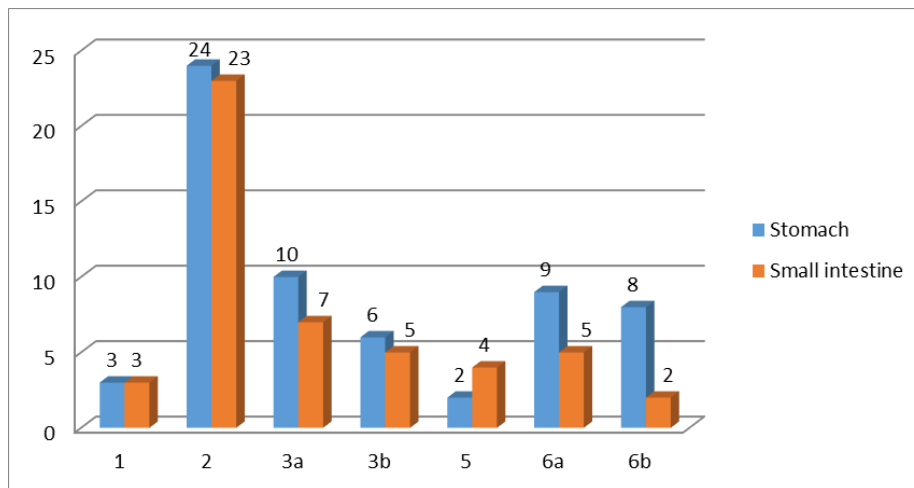


Figure 5. GIST distribution based on prognostic group and primary location

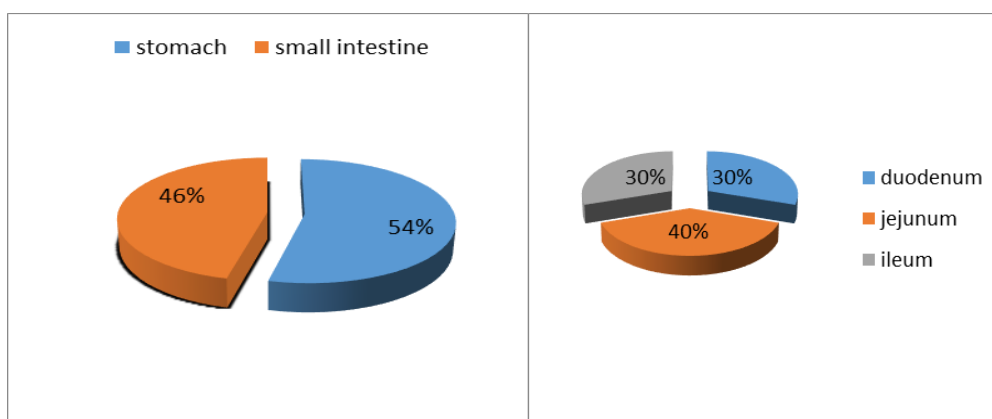


Figure 3. distribution based on the primary site tumor

Figure 4. The distribution of small intestine GISTs

From the 53(46%) patients with small intestine GISTs (16 of the duodenum, 21 of the jejunum and 16 of the ileum – Figure 4) 24 were females and 29 males (Figure 2) with age between 25 and 82 years old (average of 56.17 years old). Tumor diameter varied was between 0.6 and 20 cm (average of 6.2 cm) and the predominant prognostic group was 2 as well with a low risk of progression (n=23, 20%) (Figure 5).

Histological characteristics like cellularity, necrosis, cellular pleomorphism as well as the prognostic group risk according to Miettinen and Lasota 2006 are shown in Table 3. The major cell type encountered was spindle cell (n=83, 72.2%) followed by mixed cell type (n=21, 18.2%) and only 11 (9.6%) epithelioid. Mixed and epithelioid cell types were frequently encountered in the gastric GISTs while spindle cell type was equally distributed on the two locations (gastric and small intestine)

Table 3. Histopathological features of gastric and small intestinal GISTs

Histological parameters		Stomach	Small intestine
CELLULARITY	Low	4	6
	Medium	22	23
	High	36	24
NECROSIS	Yes	18	37
	No	44	16
CELLULAR PLEOMORPHISM	Low	26	21
	Moderate	29	25
	High	7	7
PROGNOSTIC GROUP	1	3	3
	2	24	23
	3a	10	7

Histological parameters		Stomach	Small intestine
	3b	6	5
	5	2	4
	6a	9	5
	6b	8	2

Immunohistochemical stains used for the diagnosis included the following antibodies: CD117, DOG1, CD34, SMA, Desmine, PDGFRA. The main results are present in Table 4. DOG1 (Foto 4) was performed in 18 cases, all of them being positive.

Table 4. Immunohistochemical results for CD117, CD34 and SMA antibodies

	positive		negative	
	stomach	small intestine	stomach	small intestine
CD117	37%	51%	10%	2%
CD34	44%	26%	7%	23%
SMA	28%	30%	26%	16%

We've made correlation between the immunohistochemical antibodies and morphological features based on the tumor location and the results with statistical significance were as follows:

-the association between CD34 and cellular pleomorphism (Photo 3) was statistically significant in gastric GISTs, χ^2 (2, N =41) = 6,86, $p < .05$. The positivity of CD34 was more frequent in the groups with low and moderate pleomorphism while CD34 negative was encountered more frequent in the moderate and high pleomorphic groups (Figure6).

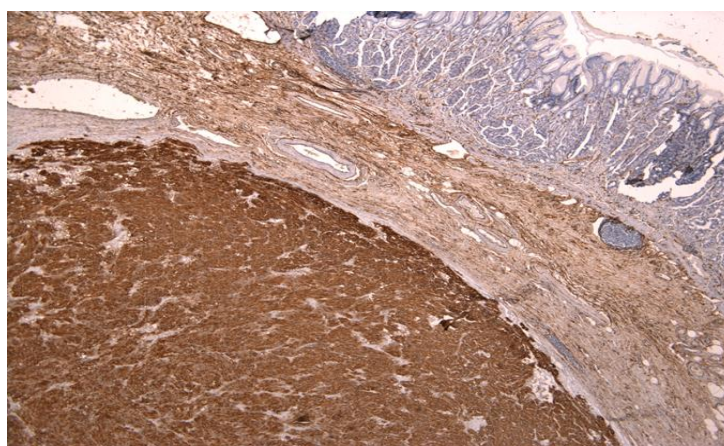


Photo 3. Gastric GIST immunohistochemical stain- CD34 ob.x 200

-the association between CD34 and mitotic count was also statistically significant in gastric GISTs (χ^2 (12, N =41) = 24.99, $p < .05$). As Figure 7 shows, positive CD34 tends to be more frequent among tumors with less mitotic figures.

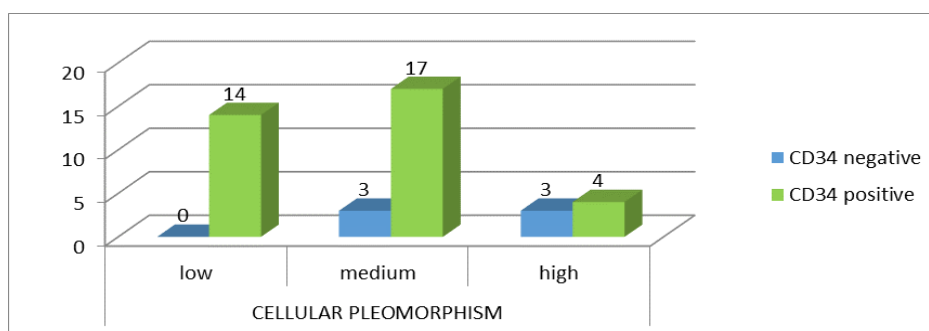


Figure 6. CD34 distribution according to cellular pleomorphism, in studied cases

We also have examined the differences between gastric and small intestine GISTs regarding the mitotic count, primary tumor diameter and the survival, using t-test. The results indicated that there are no statistically significant differences between gastric and small intestine GISTs.

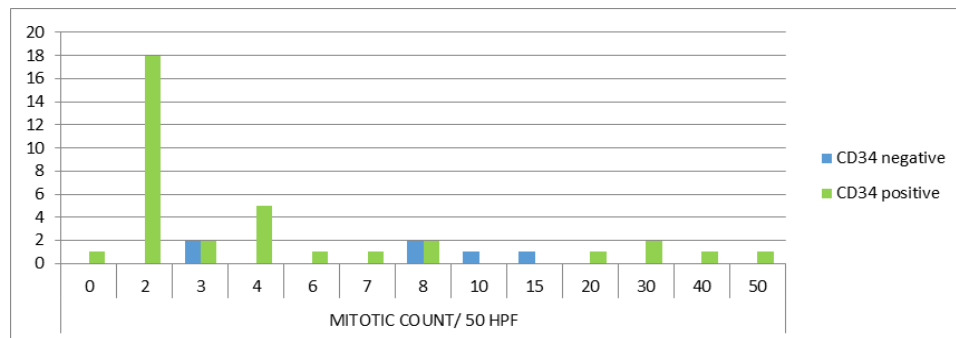


Figure 7. CD34 distribution according to mitotic count/50HPF

To analyse the differences between primary site (gastric, small intestine) regarding the survival rate (overall survival and disease free survival) we used Kaplan Meier curves.

On the overall survival we have found that the average number of survival days for each site was: 3693 days for gastric site and 3248 days for small intestine site. The differences had no statistically significance, based on the Kaplan Meier method, using Mantel-Cox, Breslow, and Tarone-Ware tests which had chi square values as follow: 1.90; 0.74 and 1.18 respectively. (Figure 8)

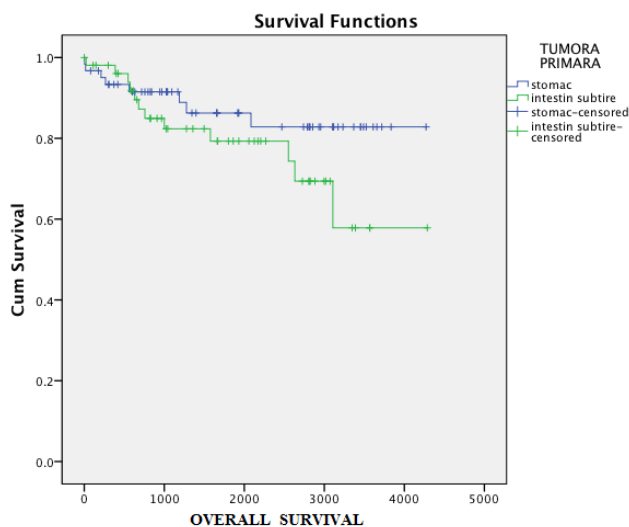


Figure 8. Kaplan Meier overall survival curves for gastric and small intestinal GISTs

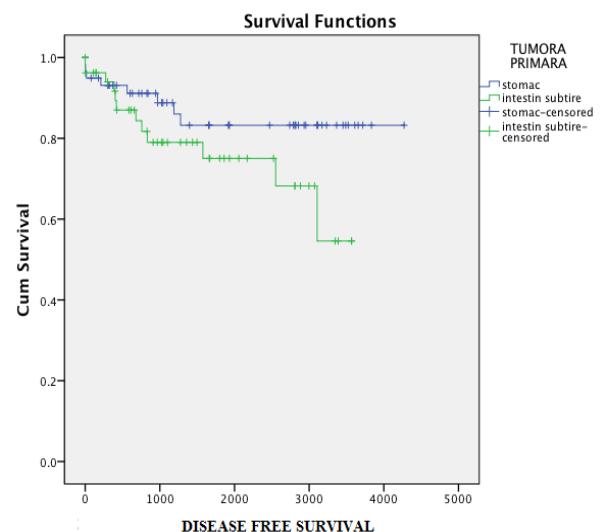


Figure 9. Kaplan Meier disease free survival curves for gastric and small intestinal GISTs

Disease free survival showed an average number of survival days of 3653 for the gastric GISTs and 2626 for small intestine GISTs. There was no statistically significant difference between the two groups based on the Kaplan Meier method using Mantel-Cox, Breslow, and Tarone-Ware tests which had chi square values of 2.46, 1.30 and 1.73 respectively (Figure 9).

Tumor primary site (gastric of small intestine) was inserted in the linear regression equation; the age and the risk (the risk was based on the risk stratification scheme described by Miettinen&Lasota in 2006) were also inserted in the equation to control the possible consequences of these factors. We assessed the overall survival and disease free survival as dependent variables. Regarding the overall survival, tumor primary site was not a significant

predictor, $R^2 = 0,104$, β standardized coefficient was $- 0.19$, $p=0,305$ (although age and risk were significant predictors). However, for the disease free survival, tumor primary site was a significant predictor, $R^2 = 0,113$, β standardized coefficient was $- 0,18$, $p < 0,05$. The risk was also a predictor but not the age.

DISCUSSIONS

GISTs are rare tumors that represent approximately 2% of all gastrointestinal neoplasms, stomach and small intestine being by far the most frequent location encountered. [16, 17].

The present study is a retrospective study and assesses the clinic-pathological, immunohistochemical and survival rates of the patients in order to reveal the influence exerted by gastric and small intestine primary site and age on the outcome of patients with GISTs.

The frequency of gastric and small intestine GISTs is almost similar in male (46%) and females (54%) [18].

These tumors have the tendency to appear over the age of 50 with an average around 60 years old [14]. The percentage of patients younger than 40 years old varies between 5 and 40% [8,15] in the present study we have found 10.43%. The average age may rise with almost 10 years in the studies that included patients diagnosed at necropsy [6,7].

GISTs have variable clinical manifestation, most of the time non-specific, abdominal pain and gastrointestinal bleeding being among the most frequent symptoms reported and of course influenced by the tumor location. In the literature though we can still find over 20-30% of cases as being asymptomatic and discovered incidentally during other medical or surgical procedures [16,17,26].

The size of the tumor varies from micro GIST with diameters less than 1cm to tumors over 30 cm . The present study included 6 tumors with a diameter less than 2 cm and an average tumor diameter of 7.2 cm, slightly elevated compared with the average dimensions reported by Tryggvason (4,5cm) or Miettinen (6 cm). [6, 15]

The cellularity assessment is available in several studies in the literature, being higher in the GISTs of the small intestine [19,20,21] .In the present study we have found the ratio reversed 36(58%) of gastric GISTs show high cellularity compared to 24(45%) of small intestine.

The spindle cell type was the most frequently encountered (72%), this being reported also in all the major international studies [22, 23, 24]. Necrosis was more often encountered in small intestine GISTs (70%) compared to gastric GISTs (29%) although many studies report a lower frequency or approximately equal on both locations [16,17].

Overexpression of KIT protein detected by CD117 immunohistochemical antibody represents a necessary step in the diagnosis of GIST. In this study the CD117 positivity (Photo 5) was recorded in 88% of cases, similar to those reported in other studies (85%-94%). But CD117 does not have a total specificity for GIST nowadays being accepted the fact that GISTs are not 100% CD117 positive and that CD117 negative usually are associated with PDGFRA [25].

DOG1 (Photo 4) is an immunohistochemical marker with a higher specificity than CD117. It is a protein, highly expressed in GIST whose function is not completely understood but with diagnostic value especially in CD117 negative cases [11].

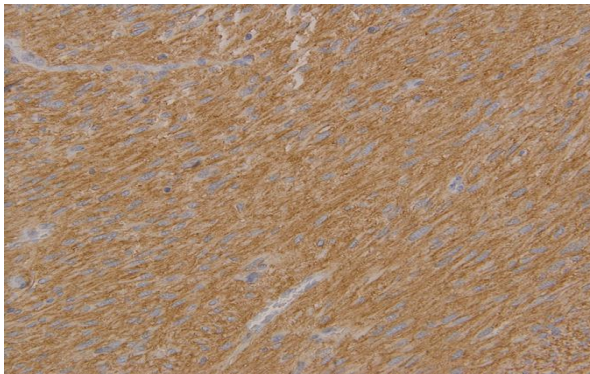


Photo 4. Small intestine GIST-immunohistochemical stain - DOG1 ob.X100

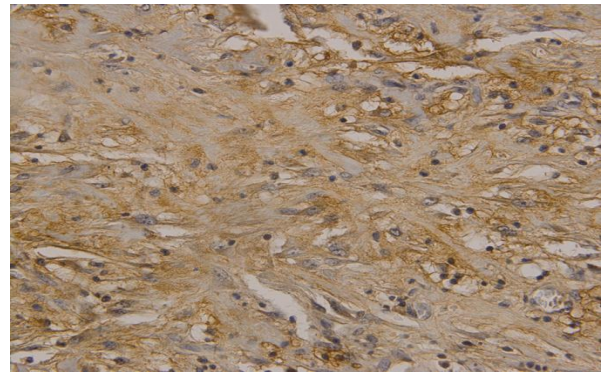


Photo 5. Gastric GIST- immunohistochemical stain CD117 ob.X400

70% of all studied cases were CD34 positive, 44% being gastric GISTs. CD34 was associated with a low or medium nuclear pleomorphism and with a low mitotic rate. In large cohort studies conducted by Miettinen & co, gastric GISTs had also presented a higher immunopositivity compared to small intestine [16,17] and the SMA immunopositivity expressed an opposite relationship compared to the expression of CD34, being higher in the small intestine [14].

Age and risk were significant predictors for the overall survival; thereby the higher the age, the lower the survival was in the studied patients and the higher the risk the lower the survival.

The risk and the tumor site were significant predictors for the disease free survival which was lower in the small intestine GISTs compared to gastric GISTs and also decreasing with the increasing risk.

CONCLUSIONS

In conclusion we have analyzed the clinico-pathological, immunohistochemical and prognostic features of 115 patients with gastric and small intestine GISTs. The clinic-pathological parameters assessed in the present study are mostly consistent with the literature data.

The histopathological report must be completed by immunohistochemical stains for a proper diagnosis which is essential in the patient management.

The disease free survival was lower among patients with small intestine GISTs than gastric ones, while overall survival was not influenced by the tumor primary site, which suggests that may be influenced by the treatment.

Conflict of interests

None declared.

Financial support

None declared.

Acknowledgement

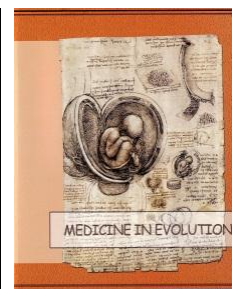
We undersigned, certificate that the procedures and the experiments we have done respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2000 (5), as well as the national law.

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A cross-sectional study on clinical and personality features associated with chronic medical comorbidity in recurrent depressive disorder inpatients



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Abstract

Background and aims: mood disorders represent the most prevalent psychiatric conditions in general population that are highly comorbid with chronic medical diseases. Our research aimed to identify those clinical and non-clinical features that are particularly associated with chronic medical comorbidities in unipolar depressed in comparison with bipolar affective disordered inpatients.

Material and Methods: a cross-sectional case-control study was carried out in 70 subjects with major depressive disorders that were admitted in Timișoara Psychiatric Clinic between January – May 2015. Additionally, a control sample which consisted of 30 bipolar affective patients was also done.

Results: cumulated cardiovascular diseases ($p = 0.044$) and endocrine – metabolic diseases ($p = 0.009$) were more represented in recurrent depressed subjects while respiratory diseases ($p = 0.037$) were more frequent in bipolar patients. In subjects with recurrent depression, the anxiety and aggression traits of personality were significantly more correlated with different types of medical comorbidities ($p < 0.05$).

Conclusions: recurrent depressed subjects could present a different pattern of chronic medical comorbidities in comparison with bipolar subjects. This result should be taken into consideration by the clinicians who treat patients with mood disorders. Moreover, besides the specific mental healthcare these kind of patients should be interdisciplinary addressed.

Keywords: medical comorbidity, personality, depression

INTRODUCTION

Based on the ICD-10 and DSM-IV-TR diagnostic manuals both recurrent depressive disorder and bipolar affective disorder belong to a broader psychiatric diagnostic category that are generic entitled mood or affective disorders [1,2]. According to an anthological epidemiological research, performed in the US, the mood disorders ranked on the third place among psychiatric diagnostic categories regarding lifetime prevalence in general population (20.8%) being exceeded only by anxiety disorders (28.8%) and impulse-control disorders (24.8%) [3]. Besides their high prevalence in general population, mood disorders should be considered as a national public health issue due to their increased rates of recurrence and chronicity along with the global costs related to disease [4,5,6]. Therefore, a WHO study has estimated that in 2020 unipolar depression will be ranked on the second place among the most disabling diseases if there are taking into account the global burden assigned to a general list that comprising 100 chronic diseases [7]. Among the factors that increase the financial burden of depression, chronic medical co-morbidity is significant one. Medical co-morbidity increase both, direct and indirect costs of depression. The indirect costs represent the majority of costs related to clinical depression due to the loss of productivity and professional disability [8].

Generally, following the same tendency such as that existing in general population, the most comorbid chronic medical conditions in mood disordered patients are represented by the cardiovascular diseases. Hence, a meta-analysis performed by Van der Kooy et al. found that while subclinical depression has moderately increased the risk for the occurrence of coronary heart disease, myocardial infarction and cerebrovascular diseases, depression that reached the clinical intensity represented a risk factor for developing the cardiovascular diseases at least as important as smoking and diabetes mellitus [9]. Moreover, individuals who present depressive symptoms have a twice risk to develop heart failure in comparison with their counterparts without depressive symptoms [10]. The presence of depressive symptoms increased three times the mortality in those with acute coronary syndrome and was a consistent prediction factor for the occurrence of hypertension in young adults [11,12]. Likewise, Osborn et al. has revealed that people with sever psychiatric disorders (including bipolar affective disorder) presented a higher relative risk rates of death in comparison with general population, the leading causes of death being due to coronary heart disease, stroke and lung cancer [13]. A ten-year population follow-up research has revealed that the presence of depressive symptoms had a predictive value on type 2 diabetes mellitus occurrence [14].

A relative recent meta-analysis on the irritable bowel syndrome has shown that this still debated condition has a high psychiatric comorbidity with major depressive disorder, anxiety disorders and somatoform disorders that were present in 98% of cases [15].

Despite the decreasing rate of death caused by the coronary heart disease in general population of Australia between 1980-1998, this rate remained relatively constant in male psychiatric patients and even increased with 2.2% per year among women with mental illness. However, the number of people with mental disorders who benefited from a revascularization procedure, especially in those with a psychotic disorder, was significantly lower in comparison with those without any psychiatric condition [16].

Also, in bipolar subjects it was found that obesity and cardiovascular diseases were among the most frequent medical comorbidities [17]. Perhaps, at least in part, these metabolic and chronic medical conditions are caused by antipsychotics that are used for a long-term treatment in bipolar patients very often being a life-time treatment [18]. An alternative explanation for the higher cardiovascular comorbidity in bipolar patient is based on pulse pressure which is a measure of large artery stiffness and which has been shown to be an important predictor of cardiovascular morbidity and mortality [19]. Moreover, at some extent, the pulse pressure bears a hereditary component.

Lastly, there are a plethora of researches that have found a closely relation between bipolar disorder and other chronic medical conditions such as diabetes mellitus, obesity, asthma, cancers, migraine and even other neurological diseases [20-25].

In addition to the effects of psychotropic drugs it is obvious that unhealthy behaviors, lifestyle and personality factors might be negatively involved in the occurrence of medical comorbidities of bipolar patients [26,27].

Given the current data regarding the increased medical comorbidity in subjects who suffer from both recurrent depressive and bipolar affective disorder, our research mainly aimed to analyze the frequency and patterns of chronic medical comorbidities in our bipolar inpatients in comparison with the recurrent depressive inpatients. As secondary objectives we researched those clinical and personality features that are highly correlated with the presence of medical comorbidity in inpatients with recurrent depression.

MATERIAL AND METHODS

Patients and study design

Clinical population of individuals with mood disorders was targeted in our research, represented by those who were hospitalized in Timișoara Psychiatric clinic between January and May 2015. All studied subjects were recruited by systematic random sampling technique. Of 114 initially approached patients, 10 (8.8%) declined to participate and 4 (3.5%) did not complete all the requested scales. Finally, there were 70 subjects with recurrent depressive disorders who composed the studied sample and 30 subjects with bipolar affective disorder irrespective of the type of current episode (depressive, hypomanic, manic or mixed episode) who represented the control sample.

Patients who agreed to participate provided written informed consent, and consecutively an in-person interview was undertaken. The study was carried out in concordance with the Code of Ethics of the Declaration of Helsinki and was approved by our institutional review board.

The inclusion criteria consisted of having a mood disorder related episode (either recurrent depression or bipolar affective disorder), no other significant psychiatric disorder comorbid with mood disorders (e.g. dementia, mental retardation, psychoactive substance related disorders including alcohol abuse or dependency and smoking) that could be interpreted as a confounding factor, age between 18 and 65 years old (because we considered that after 65 years old the medical morbidity increases in a natural manner). All socio-demographic data belonging to both samples were gathered in a standardized manner.

Design of the study consisted of a cross-sectional case-control research in recruited subjects after they written consented to participate in the study.

Measures

The chronic medical comorbidity was standardized collected and recorded by CIRS scale. CIRS scale consists of the following 14 domains of medical comorbidities: Cardiac, Hypertension, Vascular, Respiratory (lungs, bronchi, trachea below the larynx), EENT (eye, ear, nose, throat, larynx), Upper GI (esophagus, stomach, duodenum, biliary and pancreatic trees; do not include diabetes), Lower GI (intestines, hernias), Hepatic (liver only), Renal (kidneys only), Other GU (ureters, bladder, urethra, prostate, genitals), Musculo-skeletal-integumentary (muscles, bone, skin), Neurological (brain, spinal cord, nerves; do not include dementia), Endocrine-Metabolic (includes diabetes, diffuse infections, infections, toxicity), Psychiatric/Behavioral (includes depression, anxiety, agitation, psychosis, not dementia). Besides the categorical recording of the presence of any medical disease there is the possibility to quantify the severity of medical comorbidity by rating from 1 (it means none) to 5 (it means

extremely severe). The last item referred to psychiatric comorbidities was excluded due to the design of our research which not included other major psychiatric comorbid disorder.

The different facets of personality were dimensionally assessed using the Karolinska Scale of Personality (KSP) the Romanian translated and validated version [28,29]. The Karolinska Scale of Personality consists of a self-report inventory conceived for research purposes, which comprises a 135-item questionnaire with answers on a four-point [Likert scale](#). The items are grouped into 15 scales reflecting different facets of personality such as impulsiveness, monotony avoidance (sensation seeking), detachment, socialization, and social desirability, somatic anxiety, muscular tension, psychic anxiety, psychasthenia, inhibition of aggression, suspicion, guilt, indirect aggression, verbal aggression, and irritability [30].

The presence of suicide risk was gradually recorded starting with 0 (meaning none suicide risk and passing through 1 (presence of suicide ideation), 2 (presence of suicide plans) and finally 3 (that means the positive history of suicide attempts).

The severity of mood disorders was also quantified by the presence or absence of psychotic associated features during the history of mood episodes.

Data analyses

All data were statistically analyzed with SPSS version 17 for Windows. The descriptive statistic was used to describe and compare socio-demographic data of the two analyzed samples. The frequencies of categorical variables were compared using the Chi-squared test. A two-tailed parametric t-test was used for continuous data analyses and a non-parametric rank test (Mann-Whitney U-Test) was performed to analyze categorical variables originating from two independent subsamples. Spearman correlation coefficient (r_s) was used to test the non-parametric correlations between the CIRS score and the score of each of the 15 personality scales of KSP.

RESULTS

The socio-demographic data of the analyzed samples

As it is shown in table 1 there was a statistical significant difference in the mean age of the two samples, bipolar affective subjects had a younger average age in comparison to recurrent depressive subjects (52.8 *vs* 44.1; $p = 0.003$). Despite the younger average age, the bipolar subjects had a longer but not statistical significant total duration of their psychiatric disorder in comparison with their recurrent depressive counterparts (11.63 *vs* 8.04; $p = 0.076$). This result should be taken into consideration when we compare the chronic medical comorbidity of the two samples.

The educational level was significant higher in those who suffered from bipolar affective disorder than in patients diagnosed with recurrent depression (90% *vs* 74.3%; $p = 0.009$) most of them graduating at least high school studies.

With respect to marital status, subjects with bipolar affective disorders presented a worse marital status in comparison to individuals with recurrent depression who were almost two times more married (36.7% *vs* 62.9%; $p = 0.002$) than bipolar patients.

There were no statistical significant differences in the two compared samples regarding the gender distribution (females were more representative than males in both samples), residency (urban area was more representative than rural area) and professional status ($p < 0.05$). Hence, with respect to these socio-demographic parameters we could consider that the two researched groups were relatively homogenous and comparable.

Interestingly, although there was no difference in the self-reported alcohol use between the two samples, subjects with bipolar affective disorder have reported more cigarettes use than those with recurrent depression (60.0% *vs* 32.9%; $p = 0.011$).

Table 1. *The socio-demographic characteristics of the compared samples*

n (%)	Recurrent depressive subjects (n = 70)	Bipolar affective subjects (n = 30)	Significance of differences
Mean age in years (SD)	52.8 (10.2)	44.1 (13.5)	**p = 0.003
The total duration of the disorder in years (SD)	8.04 (6.551)	11.63 (9.898)	p = 0.076
Gender distribution, females	43 (61.4%)	21 (70.0%)	p = 0.413
Educational level, University and High School %	52 (74.3%)	27 (90.0%)	**p = 0.009
Residency, Urban area	48 (68.6%)	22 (73.3%)	p = 0.634
Professional status, Employed and Student	10 (14.3%)	9 (30.0%)	p = 0.170
Marital status, Married	44 (62.9%)	11 (36.7%)	**p = 0.002
Alcohol use	12 (17.1%)	7 (23.3%)	p = 0.470
Cigarette use	23 (32.9%)	18 (60.0%)	*p = 0.011

Note. The listed percentages are reported to either sample considered separately.

Chronic medical comorbidities existing in subjects belonging to the two analyzed samples

The magnitude of the chronic medical comorbidities quantified by using of the CIRS scale in the analyzed samples are listed in table II.

Although the cardiac, hypertension and vascular diseases taken into account separately were no statistical different in the two samples, reanalyzing the cumulative effect of these three types of medical conditions as cumulated cardiovascular diseases the subjects with recurrent depression presented significant higher scores than bipolar patients ($p = 0.044$). Also, subjects with recurrent depression had very significant higher scores of endocrine and metabolic comorbidities than bipolar patients ($p = 0.009$).

In comparison with the recurrent depressed patients, the subjects with bipolar affective disorder presented a significant higher score only in regard to respiratory diseases ($p = 0.037$).

For the rest of chronic medical comorbidities there were no significant difference between the two analyzed samples.

Table 2. *The chronic medical comorbidities in the analyzed samples*

Chronic medical comorbidities according to CIRS scale (mean rank)	Recurrent depressive subjects (n = 70)	Bipolar affective subjects (n = 30)	Significance of differences (Mann - Whitney Test)
a. Cardiac	50.44	50.63	p = 0.971
b. Hypertension	51.72	47.65	p = 0.451
c. Vascular	50.62	50.22	p = 0.851
Cumulated cardiovascular (a+b+c)	54.01	42.30	*p = 0.044
d. Respiratory	48.64	54.85	*p = 0.037
e. EENT	51.05	49.22	p = 0.734
f. Upper GI	49.36	53.51	p = 0.335
g. Lower GI	49.91	51.87	p = 0.364
h. Hepatic	50.35	50.85	p = 0.875
i. Renal	51.03	49.27	p = 0.575
j. Other GU	48.81	54.45	p = 0.114
k. Musculo-skeletal-integumentary	49.44	52.97	p = 0.525
l. Neurological	49.71	52.35	p = 0.310
m. Endocrine - metabolic	53.50	43.50	**p = 0.009

Note. The listed mean ranks are reported to either sample considered separately.

The personality traits significant correlated with chronic medical comorbidities in recurrent depressed subjects

In the recurrent depressive disorder subjects, we analyzed the correlation between the scores of different dimensions of personality and the magnitude of chronic medical comorbidities (listed in table 3)

The results were quite interesting. Thus we found an inversely significant correlation between the scores of *socialization* and that of upper gastrointestinal comorbidities ($r_s = -0.235$; $p = 0.050$). The *somatic anxiety* scores were direct correlated with the scores of ear, eye, nose, throat and larynx (EENT) ($r_s = 0.351$; $p = 0.003$) and with the scores of lower gastrointestinal score ($r_s = 0.239$; $p = 0.047$). *Muscular tension* score was direct correlated with score of EENT ($r_s = 0.255$; $p = 0.033$). Scores of *psychic anxiety* were direct correlated with EENT score ($r_s = 0.290$; $p = 0.015$). *Psychastenia* score was inversely correlated with the score of respiratory comorbidities ($r_s = -0.273$; $p = 0.022$). The score of *suspicion* was direct correlated with scores of upper gastrointestinal comorbidities ($r_s = 0.251$; $p = 0.036$) and that of other genitourinary comorbidities ($r_s = 0.344$; $p = 0.004$). *Guilty* has been positive correlated with the EENT score ($r_s = 0.246$; $p = 0.040$). Interestingly, other result has revealed that *verbal aggression* was inversely and significant correlated with the scores of cardiac comorbidities ($r_s = -0.294$; $p = 0.014$) and cumulated cardiovascular comorbidities ($r_s = -0.328$; $p = 0.006$). Finally, there were significant and inversely correlations between *irritability* and cardiac diseases ($r_s = -0.340$; $p = 0.004$) and respiratory diseases ($r_s = -0.249$; $p = 0.038$) scores. Conversely, there were a positive and significant correlations between *irritability* and EENT scores ($r_s = 0.255$; $p = 0.033$) and lower gastrointestinal diseases scores ($r_s = 0.269$; $p = 0.025$).

Table 3. The Spearman correlations between scores of chronic medical comorbidities and scores of dimensions of KSP scale in subjects with recurrent depression

Dimensions of KSP scale	Chronic medical comorbidities assessed by CIRS scale													
	a	b	c	a+b+c	d	e	f	g	h	i	j	k	l	m
Impulsiveness	$r_s = -0.130$; $p = 0.284$	$r_s = -0.105$; $p = 0.385$	$r_s = 0.005$; $p = 0.968$	$r_s = -0.132$; $p = 0.275$	$r_s = -0.104$; $p = 0.389$	$r_s = -0.079$; $p = 0.513$	$r_s = -0.051$; $p = 0.678$	$r_s = -0.006$; $p = 0.958$	$r_s = 0.028$; $p = 0.817$	$r_s = 0.214$; $p = 0.076$	$r_s = -0.224$; $p = 0.063$	$r_s = 0.060$; $p = 0.621$	$r_s = -0.061$; $p = 0.614$	$r_s = -0.028$; $p = 0.817$
Monotony avoidance	$r_s = 0.110$; $p = 0.366$	$r_s = 0.021$; $p = 0.864$	$r_s = -0.136$; $p = 0.263$	$r_s = 0.052$; $p = 0.670$	$r_s = -0.100$; $p = 0.411$	$r_s = -0.185$; $p = 0.124$	$r_s = 0.014$; $p = 0.910$	$r_s = 0.054$; $p = 0.656$	$r_s = -0.191$; $p = 0.114$	$r_s = 0.075$; $p = 0.535$	$r_s = -0.130$; $p = 0.283$	$r_s = -0.016$; $p = 0.898$	$r_s = -0.186$; $p = 0.124$	$r_s = -0.077$; $p = 0.527$
Detachment	$r_s = -0.058$; $p = 0.634$	$r_s = -0.020$; $p = 0.868$	$r_s = -0.095$; $p = 0.433$	$r_s = -0.032$; $p = 0.790$	$r_s = -0.082$; $p = 0.498$	$r_s = 0.030$; $p = 0.804$	$r_s = 0.041$; $p = 0.738$	$r_s = 0.165$; $p = 0.173$	$r_s = 0.078$; $p = 0.522$	$r_s = -0.021$; $p = 0.860$	$r_s = 0.077$; $p = 0.525$	$r_s = -0.102$; $p = 0.403$	$r_s = 0.025$; $p = 0.840$	$r_s = -0.032$; $p = 0.792$
Socialization	$r_s = 0.123$; $p = 0.309$	$r_s = -0.111$; $p = 0.361$	$r_s = -0.067$; $p = 0.581$	$r_s = 0.010$; $p = 0.933$	$r_s = 0.104$; $p = 0.392$	$r_s = -0.221$; $p = 0.067$	$r_s = -0.235$; $p = 0.050$	$r_s = -0.086$; $p = 0.478$	$r_s = -0.028$; $p = 0.818$	$r_s = 0.013$; $p = 0.917$	$r_s = 0.115$; $p = 0.345$	$r_s = -0.098$; $p = 0.422$	$r_s = -0.061$; $p = 0.615$	$r_s = 0.009$; $p = 0.939$
Social desirability	$r_s = 0.176$; $p = 0.144$	$r_s = 0.005$; $p = 0.970$	$r_s = 0.146$; $p = 0.228$	$r_s = 0.110$; $p = 0.364$	$r_s = 0.112$; $p = 0.357$	$r_s = 0.131$; $p = 0.282$	$r_s = 0.108$; $p = 0.375$	$r_s = 0.165$; $p = 0.172$	$r_s = 0.025$; $p = 0.837$	$r_s = 0.092$; $p = 0.449$	$r_s = 0.075$; $p = 0.538$	$r_s = 0.015$; $p = 0.899$	$r_s = 0.074$; $p = 0.544$	$r_s = 0.074$; $p = 0.540$
Somatic anxiety	$r_s = 0.000$; $p = 1.000$	$r_s = -0.026$; $p = 0.829$	$r_s = 0.227$; $p = 0.059$	$r_s = 0.012$; $p = 0.923$	$r_s = -0.203$; $p = 0.092$	$r_s = 0.351$; $p = 0.003$	$r_s = 0.130$; $p = 0.285$	$r_s = 0.239$; $p = 0.047$	$r_s = 0.109$; $p = 0.367$	$r_s = 0.022$; $p = 0.855$	$r_s = 0.073$; $p = 0.550$	$r_s = 0.011$; $p = 0.926$	$r_s = 0.114$; $p = 0.348$	$r_s = -0.074$; $p = 0.543$
Muscular tension	$r_s = 0.030$; $p = 0.803$	$r_s = 0.122$; $p = 0.312$	$r_s = 0.223$; $p = 0.064$	$r_s = 0.124$; $p = 0.306$	$r_s = -0.065$; $p = 0.592$	$r_s = 0.255$; $p = 0.033$	$r_s = 0.194$; $p = 0.107$	$r_s = 0.138$; $p = 0.255$	$r_s = 0.143$; $p = 0.237$	$r_s = 0.096$; $p = 0.429$	$r_s = -0.066$; $p = 0.585$	$r_s = 0.052$; $p = 0.671$	$r_s = 0.184$; $p = 0.127$	$r_s = -0.197$; $p = 0.103$
Psychic anxiety	$r_s = -0.062$; $p = 0.612$	$r_s = 0.037$; $p = 0.764$	$r_s = 0.165$; $p = 0.173$	$r_s = 0.050$; $p = 0.680$	$r_s = -0.146$; $p = 0.227$	$r_s = 0.290$; $p = 0.015$	$r_s = 0.153$; $p = 0.207$	$r_s = 0.195$; $p = 0.106$	$r_s = 0.121$; $p = 0.318$	$r_s = 0.036$; $p = 0.766$	$r_s = -0.134$; $p = 0.267$	$r_s = -0.027$; $p = 0.824$	$r_s = 0.019$; $p = 0.874$	$r_s = -0.228$; $p = 0.058$
Psychasthenia	$r_s = -0.028$; $p = 0.819$	$r_s = 0.110$; $p = 0.366$	$r_s = 0.017$; $p = 0.889$	$r_s = 0.052$; $p = 0.670$	$r_s = -0.273$; $p = 0.022$	$r_s = 0.120$; $p = 0.322$	$r_s = 0.064$; $p = 0.601$	$r_s = 0.148$; $p = 0.223$	$r_s = 0.110$; $p = 0.367$	$r_s = -0.059$; $p = 0.630$	$r_s = -0.026$; $p = 0.830$	$r_s = 0.014$; $p = 0.909$	$r_s = 0.086$; $p = 0.479$	$r_s = -0.054$; $p = 0.658$
Inhibition of aggression	$r_s = 0.156$; $p = 0.196$	$r_s = 0.125$; $p = 0.304$	$r_s = -0.093$; $p = 0.445$	$r_s = 0.151$; $p = 0.211$	$r_s = -0.075$; $p = 0.536$	$r_s = 0.057$; $p = 0.642$	$r_s = 0.199$; $p = 0.099$	$r_s = 0.102$; $p = 0.401$	$r_s = 0.108$; $p = 0.375$	$r_s = 0.094$; $p = 0.439$	$r_s = 0.153$; $p = 0.206$	$r_s = 0.053$; $p = 0.662$	$r_s = 0.058$; $p = 0.634$	$r_s = -0.095$; $p = 0.435$
Suspicion	$r_s = -0.047$; $p = 0.701$	$r_s = -0.180$; $p = 0.136$	$r_s = -0.004$; $p = 0.972$	$r_s = -0.084$; $p = 0.490$	$r_s = 0.025$; $p = 0.838$	$r_s = 0.116$; $p = 0.338$	$r_s = 0.251$; $p = 0.036$	$r_s = 0.229$; $p = 0.057$	$r_s = -0.130$; $p = 0.283$	$r_s = -0.067$; $p = 0.584$	$r_s = 0.344$; $p = 0.004$	$r_s = -0.165$; $p = 0.172$	$r_s = 0.072$; $p = 0.551$	$r_s = -0.184$; $p = 0.127$
Guilt	$r_s = 0.062$; $p = 0.609$	$r_s = 0.027$; $p = 0.827$	$r_s = 0.128$; $p = 0.292$	$r_s = 0.077$; $p = 0.526$	$r_s = 0.036$; $p = 0.769$	$r_s = 0.246$; $p = 0.040$	$r_s = 0.055$; $p = 0.654$	$r_s = 0.051$; $p = 0.676$	$r_s = -0.154$; $p = 0.203$	$r_s = 0.131$; $p = 0.280$	$r_s = 0.046$; $p = 0.706$	$r_s = 0.062$; $p = 0.609$	$r_s = -0.007$; $p = 0.953$	$r_s = 0.107$; $p = 0.378$
Indirect aggression	$r_s = 0.021$; $p = 0.861$	$r_s = -0.052$; $p = 0.669$	$r_s = -0.121$; $p = 0.320$	$r_s = -0.039$; $p = 0.751$	$r_s = -0.234$; $p = 0.051$	$r_s = -0.032$; $p = 0.791$	$r_s = 0.226$; $p = 0.060$	$r_s = 0.017$; $p = 0.887$	$r_s = 0.038$; $p = 0.754$	$r_s = -0.166$; $p = 0.170$	$r_s = 0.230$; $p = 0.055$	$r_s = 0.121$; $p = 0.318$	$r_s = 0.128$; $p = 0.293$	$r_s = -0.087$; $p = 0.475$
Verbal aggression	$r_s = -0.294$; $p = 0.014$	$r_s = -0.226$; $p = 0.060$	$r_s = -0.138$; $p = 0.255$	$r_s = -0.328$; $p = 0.006$	$r_s = 0.040$; $p = 0.741$	$r_s = -0.166$; $p = 0.170$	$r_s = 0.196$; $p = 0.104$	$r_s = 0.085$; $p = 0.482$	$r_s = 0.068$; $p = 0.577$	$r_s = -0.158$; $p = 0.190$	$r_s = -0.038$; $p = 0.753$	$r_s = 0.044$; $p = 0.720$	$r_s = -0.161$; $p = 0.182$	$r_s = -0.064$; $p = 0.600$
Irritability	$r_s = -0.340$; $p = 0.004$	$r_s = -0.038$; $p = 0.754$	$r_s = -0.085$; $p = 0.485$	$r_s = -0.226$; $p = 0.060$	$r_s = -0.249$; $p = 0.038$	$r_s = 0.255$; $p = 0.033$	$r_s = 0.140$; $p = 0.249$	$r_s = 0.269$; $p = 0.025$	$r_s = 0.013$; $p = 0.917$	$r_s = 0.044$; $p = 0.716$	$r_s = -0.093$; $p = 0.442$	$r_s = -0.003$; $p = 0.981$	$r_s = -0.106$; $p = 0.383$	$r_s = -0.081$; $p = 0.507$

Legend

a = cardiac, b = hypertension, c = vascular, a+b+c = cumulated cardiovascular, d = respiratory, e = eye, ear, nose, throat, larynx, f = upper gastrointestinal, g = lower gastrointestinal, h = hepatic, i = renal, j = other genitourinary, k = musculo-skeletal-integumentary, l = neurological and m = endocrine and metabolic comorbidities.

The correlations between suicide risk and chronic medical comorbidities in subjects with recurrent depression

Concerning the correlations between suicide risk and the degree of association with chronic medical comorbidities (see Table 4) the results were somehow debatable. Cardiac diseases were the only chronic medical diseases that were inversely correlated with the quantified risk of suicide. For the rest of the chronic medical diseases the correlations did not reach the statistical significance ($p > 0.05$).

Table 4. *The correlations between suicide risk and chronic medical comorbidities scores in subjects with recurrent depression*

Chronic medical comorbidities according to CIRS scale (mean rank)	Suicide risk in recurrent depressive subjects (n = 70)	Significance of differences (Spearman's correlation test)
a. Cardiac	$r_s = -0.240$	$p = 0.046$
b. Hypertension	$r_s = -0.148$	$p = 0.222$
c. Vascular	$r_s = -0.114$	$p = 0.349$
Cumulated cardiovascular (a+b+c)	$r_s = -0.223$	$p = 0.064$
d. Respiratory	$r_s = -0.115$	$p = 0.343$
e. EENT	$r_s = -0.090$	$p = 0.460$
f. Upper GI	$r_s = -0.002$	$p = 0.985$
g. Lower GI	$r_s = -0.168$	$p = 0.164$
h. Hepatic	$r_s = 0.165$	$p = 0.171$
i. Renal	$r_s = 0.152$	$p = 0.209$
j. Other GU	$r_s = -0.097$	$p = 0.424$
k. Musculo-skeletal-integumentary	$r_s = 0.023$	$p = 0.847$
l. Neurological	$r_s = 0.026$	$p = 0.830$
m. Endocrine - metabolic	$r_s = 0.007$	$p = 0.954$

Note. The listed correlations are reported only to the sample with recurrent depression

The differences between the subjects with and without associated psychotic features in respect to mean ranks for the chronic medical comorbidities

Unexpectedly, there were no statistical significant differences caused by the presence or absence of psychotic associated features in recurrent depressed patients with and without chronic medical comorbidities (see table 5). There were higher mean ranks for the most of chronic medical comorbidities in recurrent depressive subjects without psychotic features but these differences did not reach the statistical significance ($p > 0.05$). However, we have to note that while the cardiac diseases, hypertension and musculo-skeletal-integumentary diseases were more frequent in subjects with recurrent depression without psychotic features the endocrine and metabolic diseases were more frequent in patients with recurrent depression and psychotic features (36.5 *vs* 30.50, 36.62 *vs* 31.04, 36.48 *vs* 31.57 and 34.72 *vs* 38.61 respectively).

Table 5. *The correlations between the presence or absence of psychotic features during the course of recurrent depression and chronic medical comorbidities scores*

Chronic medical comorbidities according to CIRS scale (mean rank)	Subjects with recurrent depression without psychotic features (n = 56)	Subjects with recurrent depression with psychotic features (n = 14)	Significance of differences (Mann-Whitney test)
a. Cardiac	36.75	30.50	$p = 0.209$
b. Hypertension	36.62	31.04	$p = 0.294$
c. Vascular	35.26	36.46	$p = 0.572$
Cumulated cardiovascular (a+b+c)	36.73	30.57	$p = 0.278$
d. Respiratory	35.88	34.00	$p = 0.380$

Chronic medical comorbidities according to CIRS scale (mean rank)	Subjects with recurrent depression without psychotic features (n = 56)	Subjects with recurrent depression with psychotic features (n = 14)	Significance of differences (Mann-Whitney test)
e. EENT	35.77	34.43	p = 0.796
f. Upper GI	35.43	35.79	p = 0.919
g. Lower GI	35.75	34.50	p = 0.476
h. Hepatic	35.65	34.89	p = 0.797
i. Renal	35.10	37.11	p = 0.525
j. Other GU	35.60	35.11	p = 0.868
k. Musculo-skeletal-integumentary	36.48	31.57	p = 0.348
l. Neurological	35.88	34.00	p = 0.379
m. Endocrine - metabolic	34.72	38.61	p = 0.360

Note. The listed correlations are reported to either recurrent depressed subjects with and without psychotic features considered separately

DISCUSSIONS

In spite of the fact that bipolar subjects had a longer total duration of their psychiatric disorder, the average age of their sample was significant younger than that of subjects with recurrent depression. The similar demographic and clinical characteristics of bipolar patients in comparison with those who developed recurrent depression were revealed by a prestigious epidemiological study that was performed in U.S.A. (31). According to that study, bipolar subjects tend to have a younger age at the onset of their psychiatric condition than those with recurrent depression. There is the possibility that these demographic features of bipolar patients might be reflected at the clinical level. Moreover, the design of our study which used the sampling method by convenience also contributed to these differences. Certainly, the current age should to be viewed as a definitely contributing factor to the burden of chronic medical comorbidities in psychiatric patients. Nevertheless, in our study there were no statistical significant differences between the two compared samples regarding the magnitude of chronic medical comorbidities. Furthermore, in bipolar patients the mean ranks were slightly higher for the majority of the chronic medical diseases categories in comparison with recurrent depressive subjects. There is other research confirming that certain chronic medical comorbidities are more prevalent in bipolar patients than in unipolar subjects (32). Besides the underlying biological mechanisms that are assumed to be responsible for the higher chronic medical comorbidities, it should be taken into account the iatrogenic perspective, in sense that antipsychotics are more and longer prescribed in bipolar than in major depressed patients (33,34).

Regarding the education level, bipolar subjects were significantly more instructed than patients with recurrent depression. The better premorbid educational level of bipolar patient in comparison with unipolar patient was also revealed by a Danish population-based research (35). Differently from educational level, bipolar affective patients were less married than recurrent depressive patients. This result is supported by a research which found that the social functioning in bipolar patients is poor and comparable with that of schizophrenic patients (36).

In respect to smoking and alcohol use there are a plethora of studies that have definitely confirmed the higher patterns of using these addictive substances in bipolar patients in comparison with healthy subjects (37,38). From another point of view, the hedonic behaviors based on the reward neurobiological mechanisms might explain the more addictive habits of bipolar patients rather than those suffering from recurrent depression (39). The statistical differences that was found only in regard to cigarettes use but not to alcohol use might be related to the self-reported way of collecting data in our research corroborated with the more cultural acceptance for cigarettes use rather than for alcohol use.

The patterns of chronic medical comorbidities differed very interestingly between the analyzed samples. Hence, the cumulated cardiovascular comorbidities are more prevalent in recurrent depressed subjects than in bipolar patients. At least in part, this result might be related to the statistical difference in average ages of the two samples. In another train of thoughts, we found a comprehensible parallelism of higher cumulated cardiovascular diseases along with statistical significant higher levels of endocrine – metabolic diseases across the same sample of recurrent depressed subjects. There was other research that have linked the cardiometabolic diseases with cardiovascular conditions in subjects having depressive symptoms (40). However, our research was not able to make the distinction regarding the temporal sequence between the occurrences of cardiovascular and endocrine – metabolic diseases respectively. The close relation existing between the metabolic dysfunctions and depressive symptoms was also revealed by other several studies (41,42,43).

The higher frequency of respiratory diseases in bipolar than that in major depressive patients could be explained based on several possible hypotheses. On the one hand, the bipolar patients are more used to smoking than recurrent depressive patients as our study has already shown. One study has revealed that smoking has a serious impact by decreasing dramatically the life expectancy of people suffering from bipolar affective disorders (44). On the other hand, the excessive desire to smoke of bipolar patients may be a direct consequence of the underlying neurotransmitters dysfunction that accompanying this psychiatric disorder (45).

Regarding the personality traits that were significantly correlated with medical comorbidities the results were more or less surprisingly. Firstly, the most frequent medical comorbidities that were found as being correlated with personality traits in recurrent depressive patients belonged to eye, ear, nose, throat and larynx pathologies (EENT). In the same way, there were several researches that have found a significant link between ENT diseases and psychiatric disorders, especially between inner ear diseases and anxiety and depression syndromes (46,47). Moreover, in our research the EENT diseases were mainly positive correlated with somatic and psychic traits of personality. Furthermore, these traits of personality may mediate as an interface the coexistence of the ENT diseases and anxiety disorders.

Interestingly, the various facets of aggression traits of personality were inversely correlated with the presence of cumulated cardiovascular comorbidities and respiratory diseases. This results come to support one of the basic principles of psychosomatic according to which the persistent inhibited or repressed anger will result in an increased risk for physical disease especially for cardiovascular diseases (48). Conversely, EENT and lower gastrointestinal diseases scores seem to be positive correlated with the level of aggression traits of personality. Thus, we can draw the conclusion that aggression traits of personality would exert different effects depending on the distinct apparatuses which are involved in psychosomatic pathology.

The higher levels of suspicion and guilty traits of personality in depressive patients, which are more prone to experience more persistent and repetitive negative emotions, were directly correlated with upper gastrointestinal comorbidities, other genitourinary and EENT levels of comorbidity. The role of negative emotions on the increased rate of chronic medical comorbidity in depressive patients was already proven by the other research (49).

Finally, psychasthenia which is mainly characterized by the lack of energy was inversely correlated with the level of respiratory comorbidities. We want to mention that to our knowledge this result has not been revealed by other research. Moreover, this result may have emerged by the chance if we take into account that the sample size is quite small. Therefore, we have to interpret this finding with caution.

Last but not least, our research has found that generally there is not a linear relation between the severity of depression, quantified by the presence of suicide risk and the

necessity of antipsychotic treatment, and the occurrence of chronic medical comorbidities. Except cardiac comorbidities that were found as being in an inversely correlation with the suicide risk of recurrent depressive patients. Moreover, a further statistical analysis has shown that there was a very strong inverse correlation between the level of suicide risk and the current age of studied patients. So, we can conclude that less cardiac comorbidities in patients with higher risk of suicide was in fact caused by the younger age of this subcategory of recurrent depressive patients. However, these findings support the idea according to which despite the long-lasting treatment neither antidepressant nor antipsychotic medications is not entirely responsible for the higher occurrence of medical comorbidities in recurrent depressive patients.

The main limitation of our study consists of its own design in sense that is size-limited clinic population-based study and is a cross-sectional research. Certainly, an epidemiological study with larger cohorts of population along with a follow-up design of research should be considered more proper in order to find out the more accurate relations between mood disorders and chronic medical comorbidities.

CONCLUSIONS

The clinical profile of the medical comorbidities is quite different if we consider recurrent depressive patients in comparison with bipolar affective patients. The clinicians should be aware of these possible patterns of medical comorbidities in their mood disordered patients both during the evaluation process and prescribing of medications. Undoubtedly, the idea of multidisciplinary therapeutic team should be more implemented in our clinical practice. Moreover, some of medical comorbidities may be prevented by approaching of unhealthy habits of these patients at risk (e.g. smoking).

Some of personality's traits are more representative for both the increased risk or protective role for medical comorbidities in recurrent depressive patients. Furthermore, the same traits of personality may exert different effect depending on the organs or apparatuses that are involved in medical comorbidities. These results should make the clinicians more aware of the necessity for multidisciplinary approach in treating medical comorbidities in recurrent depressive patients.

The reductionist perspective according to which medical comorbidities represent the simple effect of psychotropic medications used to treat depressive symptoms should be replaced by a more complex and reliable explanatory model in supporting this higher rate of medical comorbidity in recurrent depressive patients.

Conflict of interests

The authors declare no conflict of interest of any kind.

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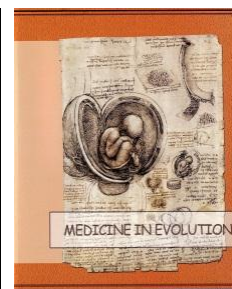
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Comparative histomorphometric study regarding the in vivo bone healing efficacy of anorganic bovine bone, β -tricalcium phosphate and bioactive glasses on rabbit tibia model



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Abstract

The aim of the present study was to evaluate the osteoconductive properties of three types of substitution materials substitutes in an experimental animal model and compare the degree of newly formed bone to the autologous graft. The study was performed on the standardized monocortical defects created in the proximal tibia of 20 New Zealand rabbits. The Defects were augmented with the three types of bone substituents. All three materials were compared between them and with the autologous bone graft. After a period of 6 months, bone fragments from the area of defects were harvested for histopathologic examination. The new bone formation was evaluated threw descriptive analysis based on the data obtained. The amount of bone formed around the particles of BioOss®, Beta Tricalcium Phosphate (Cerasorb®) and Bioactive glass (Bioglas®) do not show significant differences between them, with the autologous bone remaining the golden standard in bone augmentation.

Keywords: bone integration, histomorphometry, anorganic bovine bone, β -tricalcium phosphate, Bioactive glasses

INTRODUCTION

Bone defect reconstruction continues to be a research topic of great interest, both for Maxillo-facial surgery specialists and other specialities. The ideal substitution bone graft biomaterial used in bone defect augmentation must meet several features, including biocompatibility, sufficient mechanical characteristics to make it easy to use, biomechanically stable, be able to degrade within an appropriate time frame, exhibit osteoconductive, osteogenic and osteoinductive properties and provide a favourable environment for invading blood vessels and bone forming cell [1]

Although autologous bone is considered to be the golden standard in bone augmentation of the maxillary and mandibular bone, most of the times the availability of autogenous tissue material is limited [2]. Due to this fact, there was a need to develop bone substitute materials that had the closest properties with bone but without the drawbacks of autografts or allografts [3]

The aim of the present study was to evaluate the in vivo osteoconductive efficacy of three types of bone substitutes [Bovine bone (BioOss®)[4;5;6]; Beta Tricalcium Phosphate (Cerasorb®)][3;7]; Bioactive glasses (Perioglas®)[8], using a rabbit animal model. At the same time, we tried to compare the formation of appositional new bone to the bone defects compared between the three types of biomaterials and autologous tissue

MATERIAL AND METHODS

The study was conducted at the National Institute of Research and Development for Microbiology and Immunology "Cantacuzino" Bucharest on 20 mature New Zealand rabbits (10 males and 10 females) with an average weight of about 2.5 kg. The study protocol and the experimental design were approved by the by the INCDMI "Cantacuzino" Ethics Committee for work with laboratory animals. The animals were housed in special enclosures which were provided with a constant temperatures between 18 ° C - 24 ° C and 55% humidity and were fed a standard diet. The experimental animals were randomly divided based on the material of bone augmentation into three groups (Group A, Group B and Group C). The surgical procedures were performed under general anaesthesia with a 3 mL mixture of 2.3 ml and 0.7 ml ketamine Xylazine solution, which was divided into 2 equal doses of 1.5 ml intramuscular injections, administered at intervals of 3 minutes. The control group consisted of two experimental animals.

The surgical procedure consisted in making a circular defect in the cortical bone of the proximal section of the tibiae using rotating round burs under continuous saline irrigation. Tibial cortical exposure was realized with 5 cm incisions followed by fascial dissection. The periosteum was reflected and conserved using a periosteal elevator to obtain a good vascular supply for the augmentation material. The medial side of the tibia was exposed on a 6-cm length. A round intracortical defect was realised in each tibia using a round bur of 4mm internal diameter and 2 mm in outer diameter. A total of six defects were augmented with bovine hydroxyapatite (BioOss®); 6 other defects were augmented β tricalcium phosphate (TCP) and another 6 with bio glass (Perioglas®). In the two remaining defects, augmentation was performed by grinding the bone obtained from the intracortical defect bone drilling.



Figure 1. Circular bone defect in proximal tibia after drilling

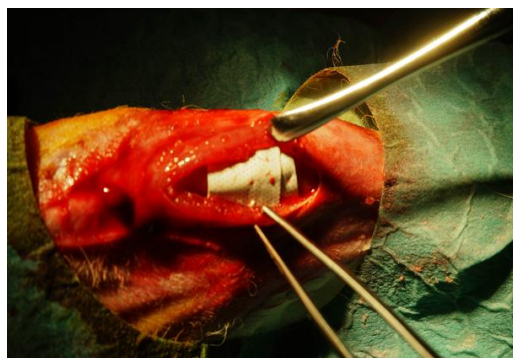


Figure 2. Non resorbable membrane applied over de augmented defect, ready for suturing

Non resorbable high-density PTFE membranes (Cytoplast®) were applied over the augmented biomaterials to exclude connective cells from the region in which bone regeneration was intended to occur. [9] After the application of the membranes the wound was sutured in three planes (periosteum, muscle tissue and skin). Postoperatively, the animals were administered ketoprofen for three days.

The euthanasia of the animals was accomplished at 180 days postoperatively by intravenous injection of phenobarbital 200mg/ml. Fragments were harvested from the areas of interest for histopathological examination

The bone fragments were decalcified in a solution of formic acid which was renewed regularly for 20 days and sections at the interested sites were realized prior to being histologically prepared after the standard protocols. After haematoxylin eosin colouring and microscopic examination, histomorphometric measuring of the new bone formation was evaluated threw descriptive analysis based on the data obtained. The examination was performed by an experienced pathologist. Histomorphometry was performed using Olympus CX 30 microscope (Olympus, Japan) connected to the image processing program (Dimension CellSens Olympus, Olympus, Japan) using Olympus DP21 Digital Camera (Olympus, Japan)

RESULTS

Histopathological examination of the bone sections revealed for all materials the presence of endogenous bone neoformation in both the cortical and medulla adjacent to the bone defect. Histomorphometric analysis showed that when using bovine bone (BioOss®), there is a noticeable amount of bone neoformation compared to the other two biomaterials used as bone graft. The thickness of newly formed lamellar bone around the augmentation material was discovered to have an average of 92.4385 μm , with a minimum of 10.20 μm , and a maximum of 363.80 μm in thickness.

Betatricalcic phosphate (TCP) had a mean thickness of new bone formation of 73.67 μm with a minimum of 20.3 μm , and a maximum of 230.30 μm .

As for the material Perioglas® the mean amount of bone around the particles was significantly reduced by an average of 31.88 μm with a minimum of 9.10 μm , and a maximum of 120.6 μm

In the control group, the newly formed bone had an average thickness of 249.68 μm , with a minimum of 115.3 μm and a maximum of 363.8 μm .



Figure 3. HE;10X;[Bovine bone]: Cross section of the tibiae with medullar space partially occupied by granules of bovine bone encircled by fibrous tissue

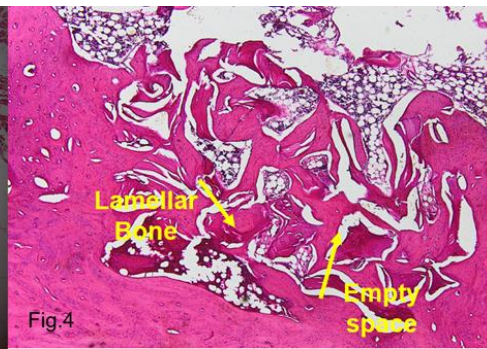


Figure 4. HE;40x Detail of the internal side of the cortical bone showing a matrix of lamellar bone and fibrous tissue around the particles and empty spaces inside the cortical bone



Figure 5. HE;10X[TCP]: Cross section of the tibiae with the medullar space occupied by lamellar bone and exogenous eosinophil material



Figure 6. HE;40x: Detail of the medullar space with lamellar bone, fibrous tissue and exogenous material



Figure 7. HE; Medullar space occupied by fine blades of new bone and fibrous tissue with empty spaces and fine granular material



Figure 8. HE;40x: Cortical bone with spaces from the resorption of the material and the non-resorbable membrane



Figure 9. HE;10X; [Autologous] Cross section of the tibiae with continuity of the cortical bone, and complete integration of the graft

DISCUSSIONS

The aim of the present study was to evaluate the osteoconductive properties of three types of substitution materials in an experimental animal model and compare the degree of newly formed bone to the autologous graft.

The animal of choice as an experimental animal was the rabbit. This is one of the species most commonly used in medical research, being used in approximately 35% of all animal musculoskeletal research studies [10]. One of the reason of its popularity is because the rabbits bone turn-over is 6 weeks compared with 17 weeks in the human species. This allows extrapolation of the results by a ratio of 1: 3 [11]. The rabbit is also a convenient choice because they reach skeletal maturity shortly after sexual maturity at about 6 months of age. [12]

A disadvantage of using a rabbit model as an experimental model in the current study is that given the limited size of the tibia there is an impossibility of using the same tibia for several bone graft materials. Also, the defects size is limited. A defect in the tibia greater than 6 mm in diameter threatens the bone strength [13]. This diameter is half of that recommended for other larger species. Despite this, the rabbit remains a very popular choice of species for the testing of implant materials in bone.[13]

Osteoconductivity is a three-dimensional process in which the augmentation biomaterial acts as a matrix for capillary proliferation, and migration of pro-osteoblasts from the adjacent tissue [14]. Osteoconductive biomaterials promote bone regeneration without directly stimulating a differentiation of the pro-osteoblasts [15]. Osteoconductive materials can't be used in the reconstruction of large bone defects because bone formation is limited by the distance on which the replacement material is applied [15]. To repair large defects, it is preferred to use osteoinductive materials [16].

Despite its osteoinductive property, the use of autologous bone is limited by the possibility of complications in the acceptor site. The local morbidity and the need to use local and spongy structure, responsible for generating bone regeneration phenomenon [17;18].

The new bone formation pattern that can be seen mostly in the cortical bone, confirms the direction of bone formation from the periphery toward the centre of the defect, a phenomenon typical for osteoconduction[19]. In comparison, when using autologous bone augmentation material, new bone formation takes place from the centre to the periphery of the tissue defect [20;21].

In terms of the degree of material resorption, the results of our observations are almost similar with the conclusions supported by the studies in the literature. Thus, if hydroxyapatite resorption begins at 14 weeks [22] the resorption rate at 2 years was 56.8% [23]. TCP resorption begins at 6 months [24], complete disappearance of the material being 15-18 months [25]. In the case of Bio glass, the proportion of the remaining material falls from 37% at 6 weeks to 23% at 12 weeks [26].

Regarding the limitations of the study, it lies in the use of a single species of experience animal and the short 180-day term used for osteointegration. This time used for new bone formation assessment may have had a different outcome at least 1 year after insertion, during which it is possible that an advanced resorption of the substitution material may have occurred.

CONCLUSIONS

All three materials exhibit characteristics consistent with their osteoconductive role, favouring apposition of endogenous bone in the spaces resulted from the resorption of the exogenous implanted material.

The amount of bone formed around the particles of bovine bone (BioOss®), Beta Tricalcium Phosphate (Cerasorb®) and Bioactive glass (Bioglas®) do not show significant

differences between them, but the three materials show a noticeable lower bone apposition to that achieved by autologous bone inserted in the created defects. Further clinical studies are necessary to evaluate the long-term efficacy of the materials and the behaviour of the materials in relation with their physical and chemical properties.

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Finite element analysis of an implant-artificial cortical tissue structure



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Abstract

The long-term clinical follow-up studies have demonstrated outstanding performance of artificial bone implant-supported. Biomechanics is the study of the implant by means of the methods of “mechanics” which is the branch of physics involving analysis of the actions of forces. A 3D modeling software was used to prepare a model and evaluate the results in the form of stresses by applying the calculated loads in the finite element analysis software ANSYS. The aim is to study and evaluate the loads and stresses acting on an implant- artificial cortical tissue.

Keywords: finite element analysis, implant, artificial bone

INTRODUCTION

Inadequate stresses cause disuse atrophy of the bone, while excessive local stresses around an implant result in marginal bone loss with potential implant failure¹. Rational stress distribution obtained in bone surrounding implants is critical to maintain the bone-implant interface and determine the success of dental implants².

Finite element analysis has been used extensively to predict the biomechanical performance of implants. By understanding the application and limitations of this method, clinician will be better equipped to interpret the results of FEA implant studies and extrapolate these results to real situations³.

The aim of this study was to use a finite element model of the implant- artificial cortical tissue structure to examine stresses behaviors in peri-implant area. The calculated stress distribution is discussed with respect to stress shielding and bone remodeling issues in artificial cortical tissue implant-supported cases.

MATERIAL AND METHODS

Three analysis cases will be presented according to the surgical procedure that was used: case I: cortical tissue – implant – trabecular tissue structure; case II: cortical tissue – trabecular tissue – implant structure; case III: implant – artificial cortical tissue addition – trabecular tissue – cortical tissue.

For each case, analyses was performed, considering the replacement of missing cortical tissue with artificial cortical tissue according to each patient.

Regarding the multitude of elements used in medical technics, we have chosen a certain type of screw, 13 mm length, which is frequently used in dental implantology for which we designed the geometrical model.

Only one geometrical model of the implant was designed and then, using copying operations, the other three were generated.

The geometrical model exported from SolidWorks software was imported in ANSYS, a software that will help preparing the numeric model for analysis using finite element method.

For all three cases, the tetrahedral method was used as mesh method, a couple of restrictions regarding the dimension of the finite element were imposed – considering the small dimensions of the bone tissue – implant assembly, the generated finite elements were as small as possible. This option brings the advantage of creating a fine mesh for the analyzed structure, and the disadvantage of longer time for the calculation according to the configuration of the work station. In the following figure, finite element models are presented after meshing for the three cases.

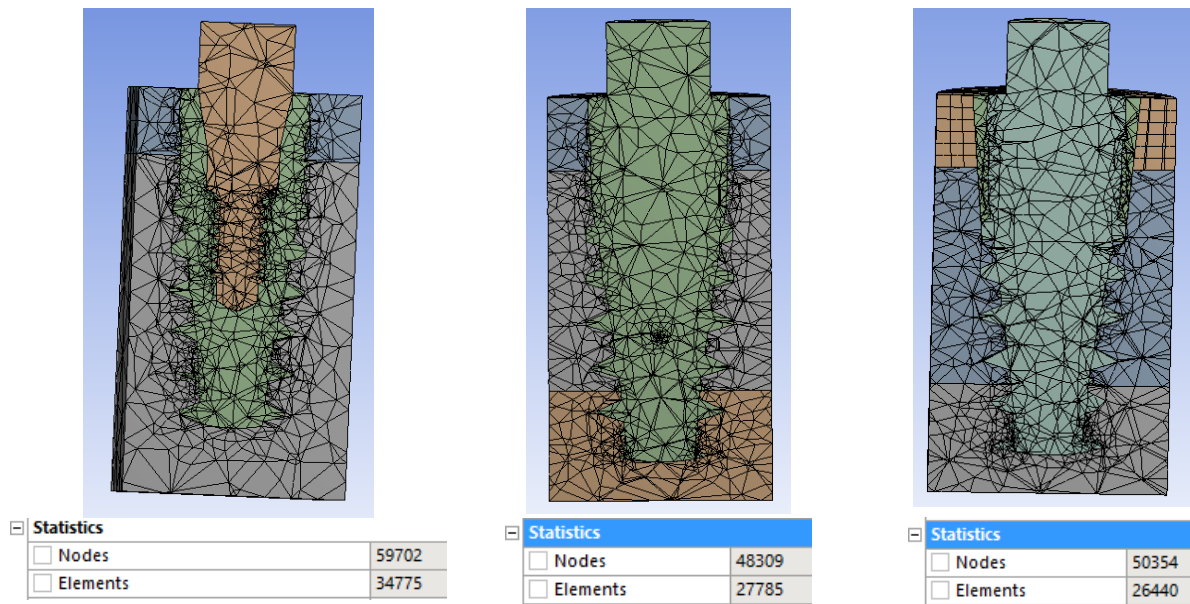


Figure 1. Finite element mesh models

In all three cases, the same boundary conditions were applied, the implant-bone tissue structure was fixed on the external contour because the analyzed model represents only a certain area from maxillofacial system.

RESULTS

The finite element analysis has been carried out in ANSYS software and find out von-Misses stresses for various conditions explain above are shown:

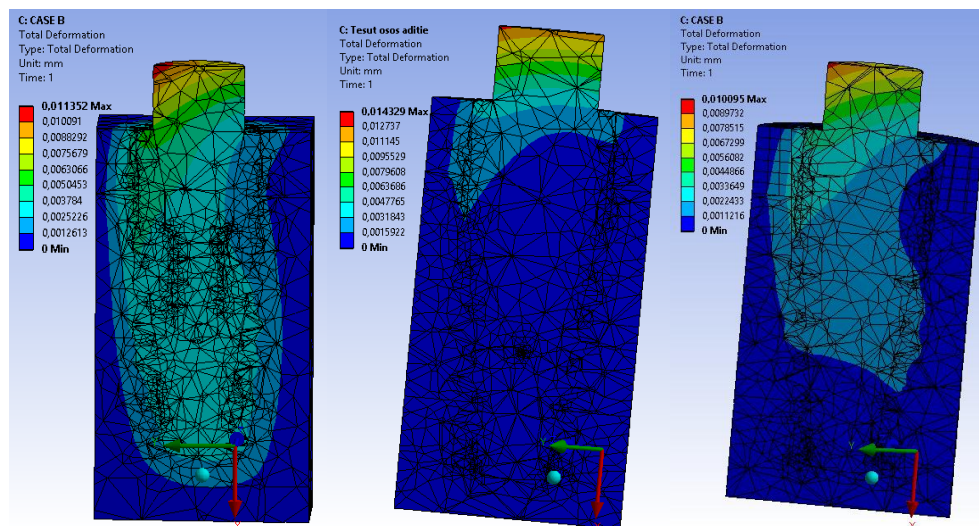


Figure 2. Total displacements of the implant-bone structure

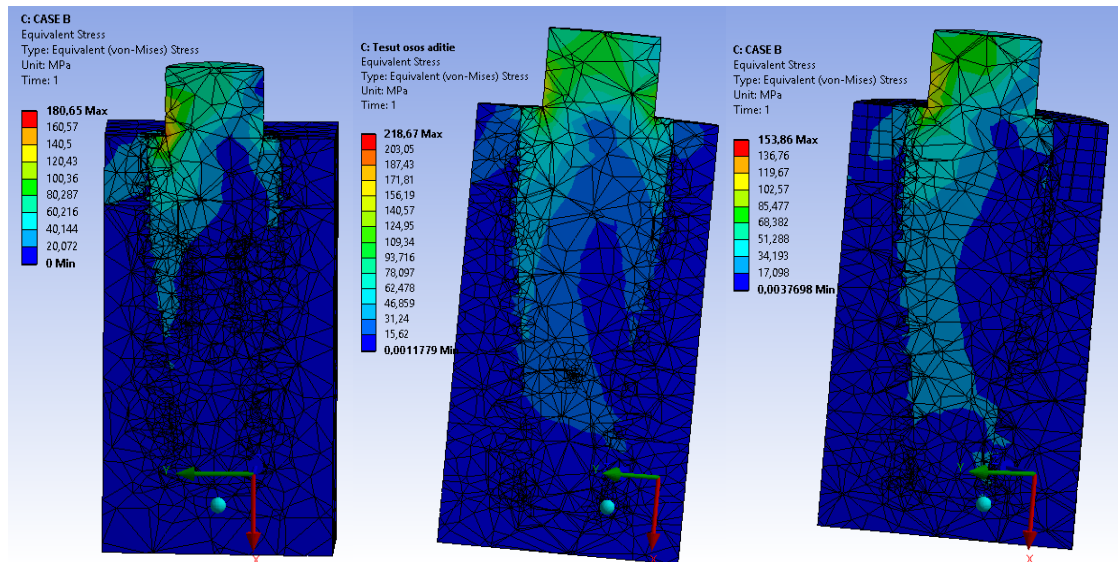


Figure 3. Contour plots of von Mises stress distribution

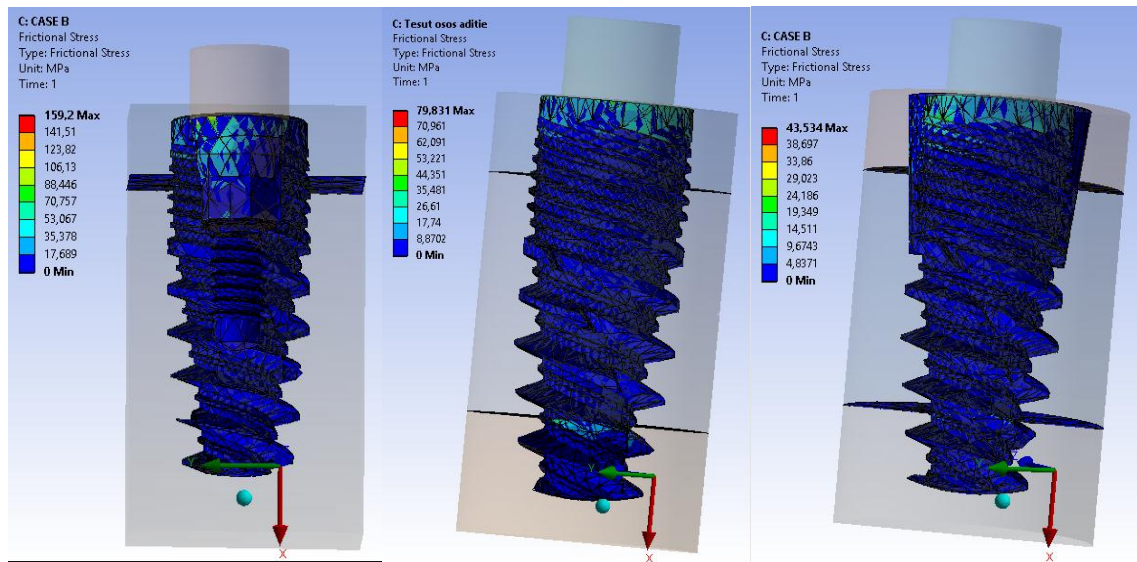


Figure 4. Contact pressure

DISCUSSIONS

We can observe that total displacements values in the analyzed models have risen if the native cortical tissue in the upper part of the structure is replaced with artificial bone tissue.

From the three analyzed situations, we can conclude that the third case offers best biomechanical behavior regarding the tension state that develops in the model under the action of external loads.

Comparing the state of tangential tensions for each three investigated cases, we can conclude that model III represents the model with the best biomechanical behavior, the artificial tissue offering a better resistance for the functioning assembly.

Also, contact pressure in third case is lower than case I and II.

From the analysis, several conclusions are made which are listed below:

1. replacing native cortical tissue with the artificial one leads to greater deformation properties of the assembly;

2. the equivalent tensions, determined using von Mises criteria, are larger, but overall, the values of the equivalent tension are lower;
3. the values of contact pressure which develop in contact area between implant and artificial bone for the models used in this case are lower.

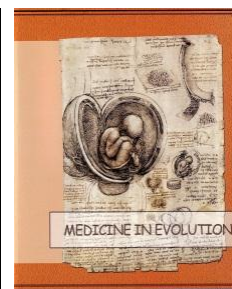
CONCLUSIONS

The biomechanical behavior of an osseointegrated dental implant plays an important role in its functional longevity inside the bone. Proper stress and strain distribution along implant- artificial cortical tissue structure will enhance the function. The artificial cortical tissue plays a big role in order to reduce stress shielding problems. The artificial cortical tissue is a promise to enhance stability and to reduce implant loosening.

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The use of iliac crest blocks in atrophic maxilla



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Abstract

The atrophic maxilla represents a major challenge in oral rehabilitation. There are many procedures and materials available for the maxillofacial surgeons but the autologous bone represents the gold standard for hard tissue management. In severe defects only extraoral sites provide sufficient bone volume. The iliac crest is the most accessible site and supplies a good amount a bone to be transplanted in the oral cavity. A group of 10 patients that required iliac bone grafts was followed for a period of 18 months. The results were promising with a low bone loss rate.

Keywords: atrophic maxilla, iliac crest, bone blocks, oral rehabilitation

INTRODUCTION

Reconstructing the atrophic maxilla can be a painful task for the surgeons. A team of multiple specialists are needed: surgeon, prosthodontist, and orthodontist and lab technician. A thorough treatment plan is needed, that includes the exact number of implants and their position in order to properly evaluate the bone bed. With the use of cone beam computer tomography (CBCT) an exact map of the underlying bone can be traced. After the imagistic stage, the team is now able to see the exact volume of bone to be replaced. After a careful general examination of the patients including blood tests and a general examination, the surgeon must select the proper procedure. Graft success requires a few general rules:

- The graft should remain stable throughout the healing phase;
- The graft should ensure a proper situ for future dental implants;
- The graft should be able to ensure bone remodeling in order to be transformed in native bone at the end of the healing stage;
- The graft should cause the patients the least amount of morbidity [1].

There are many materials available for oral grafting (xenograft, allograft) but autologous bone is the only one able to accommodate the above requirements. It can be harvested from the oral cavity or for large defects from extraoral sites (calvaria, iliac crest, and fibula). The surgical team selects the appropriate procedure taking into consideration the defect size, the defect position, the dental prosthesis needed, patients consent and not last patient needs.

The iliac crest is the most used site for large bone reconstruction in the oral cavity. It can be harvested vascularized or non vascularized (cortical, cancellous, cortico-cancellous, cortico-cancellous-cortical, marrow or block). The surgeon can harvest from the anterior or posterior aspect of the crest. The posterior crest implies repositioning the patient after harvest and is not as accessible as the anterior. The anterior crest is the most used site. The amount of bone to be harvested is up to 50 cc. Bone blocks can consist of cortex and cancellous or bicortical [2], large bone blocks can be transplanted (3X5cm). The outer cortex is a great source of cortical bone.

The procedure is straight forward as the site can be palpated manually. The incision is usually 5-6cm long lateral to the ileum. The deep circumflex artery provides the vast majority of blood supply and is the main pedicle of the region. There are a few cutaneous sensory nerve branches found in the area. After dissection of the subcutaneous tissue the muscle plan is encountered (external oblique and tensor fascia lata). The bone is easily accessed. Often there is no need of drainage. Closure is generally done in 3 layers [3].

MATERIAL AND METHODS

10 patients were monitored in the maxillofacial department of Euroclinic Hospital Bucharest. The group of patients had iliac bone blocks transplanted to the maxilla. 6 were women and 4 males. The mean age was 43, 6 years. 6 patients were diagnosed with bone atrophy class 5/6 Cawood and required bone reconstruction for implant placement in oral rehabilitation. 2 patients had serious bone defects following tumor resection (ameloblastoma) and 2 patients required a bone graft for cleft surgery. The mean follow up period was 12.4 months [Table 1].

Age	Sex	Pathology	Type of graft	No of dental implants	Complications	Follow up period
41	F	ameloblastoma	Bicortical	3	Seroma	18
29	M	ameloblastoma	Bicortical	2	No	18
56	M	Bone atrophy	Cortico-cancellous	2	No	6

Age	Sex	Pathology	Type of graft	No of dental implants	Complications	Follow up period
46	F	Bone atrophy	Cortico-cancelous	4	Seroma	10
58	F	Bone atrophy	Cortico-cancelous	4	Hematoma	18
47	M	Bone atrophy	Cortico-cancelous	3	No	12
62	F	Bone atrophy	Cortico-cancelous	2	No	10
19	F	Cleft	Bicortical	2	Hematoma	18
22	F	Cleft	Bicortical	2	No	6
56	M	Bone atrophy	Cortico-cancelous	3	Failed implant	18

The surgical procedure for bone harvest was performed under general anesthesia following the protocol described by Cricchio and Lundgren [4]. A skin incision was performed medial to the iliac crest following the skin lines. After subcutaneous tissue dissection the muscle aponevrosis was identified. The fascia lata was kept intact. For block harvest a piezosurgery device was used and the bone block was splitted from the crest with chisels. The wound was closed in 3 layers. There was no need to place drainage. A pressure dressing was applied at the end. Patients received cephaloporines for 5 days. Mobilization was done early and the patients were discharged from the hospital 48 hours after surgery.

The recipient site was visualized after mucoperiosteal flap reflection. A trapezoidal flap was preferred with 2 vertical releasing incisions one tooth away mesial and distal from the defect. The bone blocks were fixed with osteosynthesis screws (2 for each block). The flap was replaced after periosteal releasing incisions and sutured with 4/0 horizontal mattress Polytetrafluoroethylene (PTFE) suture. Sutures were removed 10 days for both sites.

After 12 weeks the grafts were uncovered and dental implants were fixed under local anesthesia. Following another 12 weeks dental prosthesis were delivered.

RESULTS

The surgical sites healed uneventfully. Postoperative pain in the hip was recorded in 9 patients in the first 2 weeks and in 3 patients after 6 months. 90% of the patients were happy with the final rehabilitation. Seroma of the donor site was observed in 2 patients and 2 patients had small hematoma that required no treatment. Infection was not encountered. After the healing phase all the patients could receive dental implants. In the first 6 months after implant placement there was a 15% bone loss around dental implants that remained stable at the 12 month check-up. From the total of 10 patients only 6 were followed for 18 months and the bone loss was approximately 20%.

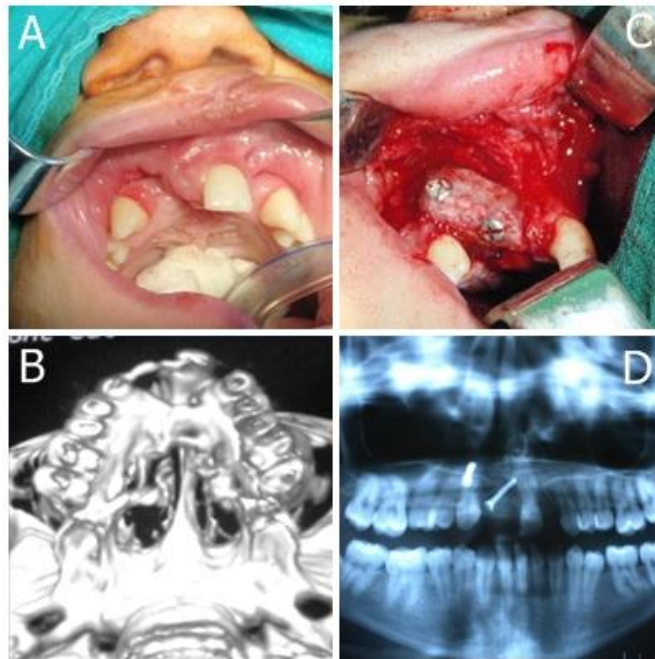


Figure 1. 18 years old male patient with large bone defect due to cleft malformation. A. Intraoral view, B. 3D reconstruction from CBCT, C bone block fixed in place, D Panoramic X-ray after 3 months showing good osteointegration of the graft

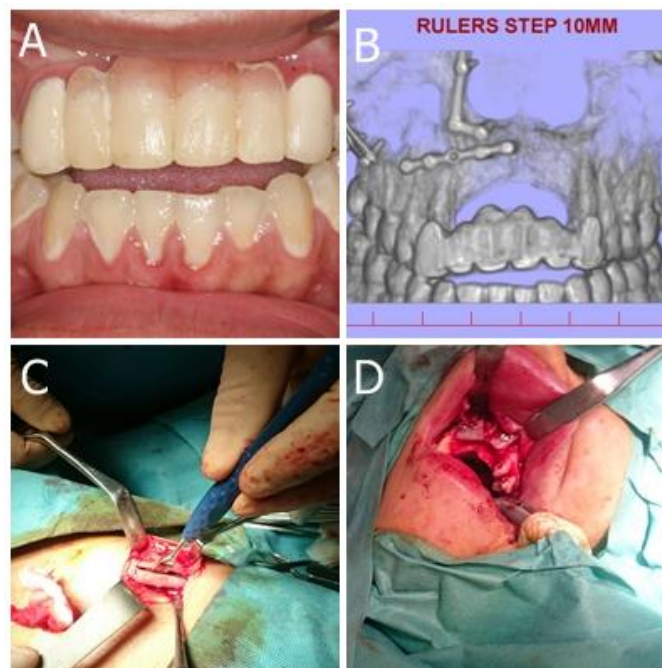


Figure 2. 25 years old female with total loss of superior incisive alveolar process due to car accident A. Intraoral view; B. 3D CBCT reconstruction showing the loss of upper frontal alveolar process; C Iliac bone harvest; D. Iliac bone block fixed to site

DISCUSSIONS

The reconstruction of the atrophied maxilla with the use of vascularized or non vascularized ileum bone blocks is becoming a widespread and effective procedure. Dental implants insertion in these sites has a similar osteointegration rate to those placed into non grafted sites (95%) [5].

Long term results of dental implants placed into autologous grafted sites show very good results (over 95%) at 10 years follow ups [6].

Although partial graft resorption can occur, all the patients that returned for the 18 month checkup had maintained a good bone level. The most severe bone loss around dental implants (up 1 mm) takes place in the first year, many reports suggest that after that the result is stable.

Complications associated with the harvesting of the graft are: postoperative pain up to a couple of months, sensory disturbances, ileum fracture, altered gait, hematoma, seroma, altered bone contour [7].

The postoperative pain lasting up to 6 month or more is related to muscle and periosteum stripping. To reduce it some authors recommend the use of bupivacaine [8]. Also modification of the incision has been suggested with unsatisfactory results.

Sensory disturbances are caused by trauma of the lateral cutaneous nerves [9]. Gait disturbances are not uncommon but usually related to hematoma. The hematoma can be caused by ineffective intraoperative bleeding or tearing of the periosteum. Respecting the surgical steps should decrease to a minimum the presence of hematoma. Hematoma can resolve by itself or it can be surgically drained. Seroma is a rare complications and it resolves easily by drainage. Ilium fracture usually involves the superior spine and occurs when bone is harvested too close to the spine or the patient does not comply with the indications regarding the post operative physical effort.

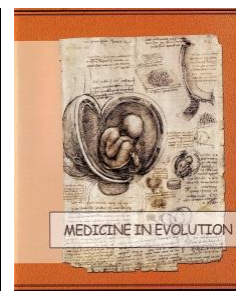
CONCLUSIONS

Large bone defects in the oral cavity can be routinely treated with ileum crest graft. Dental implants placed into these sites show optimal osteointegration and maintain a good bone volume in time. Complications associated with bone harvest are minimal and patient acceptance is high.

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Aesthetic improvement of Emax crowns with nanoceramic posts



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Abstract

Introduction: Dental ceramics present excellent ability to reproduce the natural teeth regarding esthetic and biomechanics. It is essential to know the specificity of each ceramic system available in order to apply it properly to various clinical situations.

Case report: A 28 year old patient sought dental consultation regarding the pronounced discolouration of a lateral incisor (2.2). Besides the conspicuous orthodontic anomaly, clinical examination revealed large secondary caries pertaining to an old, overflowing restoration and the presence of a palatal dentatus post.

Conclusions: Rehabilitation has provided functional and aesthetic restorations, harmony of the stomatognathic system and improvement of life quality.

Hierarchical distinctions between aesthetics, functionality and biocompatibility must be avoided at all costs otherwise harm caused by the initial iatrogenic fault may very well end up reiterating itself, despite the best efforts to mend it.

Keywords: discolouration, nanoceramic post, aesthetic area

INTRODUCTION

It is widely acknowledged that most materials used in endodontic treatment are responsible for various degrees of teeth discolouration.

This case presentation aims at augmenting the aesthetic value of dental restorations while also adding emphasis to the risks associated with inadequate choosing of restorative materials.

The clinician can choose from a variety of user-friendly post-and-core systems for different endodontic restorative, and aesthetic requirements. No single system provides the perfect restorative solution for every clinical circumstance, and each situation requires an individual evaluation. The reconstruction of endodontically treated teeth can present restorative and aesthetic challenges for the technician and clinician.^[1]

Patients' needs and desires and developments in adhesive dentistry have made the use of all-ceramic restorations increasingly frequent, particularly silica-based ones such as crowns, inlay-onlays, and laminate veneers.^[2] Lava Ultimate RNC (3M ESPE, St. Paul, MN, USA) is a new composite/nanoceramic material for CAD/CAM manufacturing. This material allows the possibility to use composite materials to characterize and adjust the restoration after milling. Unlike conventional ceramic restorations, customization and glaze firing is neither necessary nor possible with RNC restorations. This opens up the opportunity for intraoral individualization and adaptation of the restorations.^[3]

CASE PRESENTATION

A 28 year old patient sought dental consultation regarding the pronounced discolouration of a lateral incisor (2.2) and inflammation of the marginal gingiva (Figure 1). Besides the conspicuous orthodontic anomaly (Figure 2), clinical examination revealed large secondary caries pertaining to an old, overflowing restoration in the frontal area and the presence of a palatal dentatus post (Figure 3). The patient refused orthodontic treatment and settled for a prosthetic restoration of the afflicted tooth. Both, the old restoration and the dentatus post were removed (Figure 4). We proceeded with cleaning the dental abutments of secondary caries (Figure 5). Following tooth preparation and polishing the dental abutment, a provisional crown was set in place. Inflammatory symptoms mitigated considerably shortly after removal of the overflowing restoration. Endodontic retreatment concluded with designing a post and core layout which was later used for the nanoceramic recast (Figure 6). Ultimately, the lithium disilicate Emax cape loaded with Emax ceramic was cemented (Figure 7). Eight month after cementing the final prosthetic restoration, a follow-up confirmed the effectiveness of treatment by bringing forth evidence of complete healing.



Figure 1. _____



Figure 2. _____



Figure 3. _____



Figure 4. _____



Figure 5. _____



Figure 6. _____



Figure 7. _____

DISCUSSIONS

As the clinician continues the search for optimal functional and aesthetic success of a post-retained crown system, the current selection of restorative materials and techniques may prove overwhelming. While no single system provides the ideal restorative solution for every clinical circumstance, understanding both general design criteria and the components for the various post-and-core systems available allow the clinician to appropriately select the method and materials compatible with the existing tooth structure and desired result.(1)

Endodontic therapy should not focus solely on biological and functional aspects, but take aesthetic considerations into account as well. To reduce the risk of material-induced tooth discoloration, all materials should be applied carefully in areas of aesthetic concern. [4]

An understanding of the various materials which have a potential to cause unaesthetic tooth discolouration is useful in selection of alternative materials and methods for use in the root canals. [5]

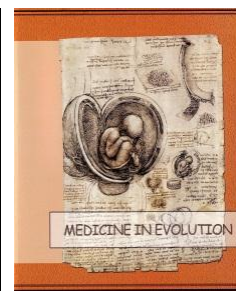
CONCLUSIONS

It is important to understand that simply placing an all-ceramic restoration instead of a metal-ceramic restoration will not guarantee outstanding aesthetics. The clinician must accomplish a number of details meticulously to ensure success.

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Orthodontic treatment in canine impaction - A case report



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Abstract

The maxillary canine is the second most common tooth to become impacted because of the order of eruption on the upper jaw. There are several approaches for a case with impacted teeth, but considering the importance of the upper canine in the inter-occlusal guidance or further prosthodontics, the extraction is rarely recommended.

The presented case report is a treatment alternative for a patient with an impacted upper canine and teeth misalignment: achievement of space and alignment within the dental arch. The patient complaints were mostly aesthetic, but after clinical examination, an obvious lack of canine guidance and the absence of a balanced occlusion were observed. After the orthodontic alignment of the upper jaw, the impacted canine was exposed, to after be guide into its correct position and braces were also applied on the lower jaw, to achieve proper inter-occlusal relations.

This particular case report represents an example of what is considered the best solution for a patient with an impacted canine. A good collaboration between different departments can lead to optimal result and a stabile occlusion.

Keywords: impacted canine, misalignment, orthodontics, non-extraction

INTRODUCTION

Tooth impaction can occur to any dental groups and it can be caused by different factors. Being the last of the front teeth to erupt into place, the maxillary canines are the second most common, after the third molars, to become impacted. [1,2]

More than 60% of the impacted canines can be found on the palatal side of the dental arch, when we can observe the absence of the labial bulge and the presence of palatal bulge. In the rest of the cases the canine it is situated in the middle or on the labial side of the supporting bone. The absence of the tooth on the dental is followed by a diminished space where the canine should be, caused by the distal tipping and migration of the lateral incisor and first premolar. [3,4,5]

After a careful evaluation of the case, the clinician can consider various treatment options:

1. No treatment, with periodical evaluation,
2. Auto-transplant of the canine,
3. Extraction of the canine with the movement of the first bicuspid in its place,
4. Extraction of the canine and prosthetic replacement,

Surgical exposure of the canine and orthodontic treatment to bring the tooth in a correct position within the dental arch, this being the optimal solution for proper inter-occlusal relations and guidance. [6,7,8,9]

CASE REPORT

An 18-year-old female presents for comprehensive orthodontic treatment. After the anamnesis the patient revealed the lack of eruption of the upper left canine after the loss of the temporary canine, without any extractions in the past.

At the clinical examination we find a Class 1 molar on the left side and Class 3 molar on the right side. The necessary space for proper eruption of the upper left canine is not available after the tilting and migration of the lateral incisor and first bicuspid. A bulge is present in the palatal side of the arch. On the right side we can observe a unilateral crossbite in the canine area. (Figure 1)

Panoramic radiograph reveal unilateral maxillary canine impaction, with positioning favorable to extrusion and placement within the dental arch. (Figure 2).



Figure 1. Initial situation, frontal view



Figure 2. Initial Panoramic X-Ray

Braces were applied on the upper arch to open a space which will provide room for the impacted canine. After the space was created and the upper arch aligned, the patient was referred to a surgeon for exposure and placement of retention on the impacted canine, to pull it directly down from its current position. A few days after the surgery, the patient returned to the orthodontist for an elastomeric chain to be placed on the impacted tooth. This way, the light eruptive force would help guide the tooth into place. Meanwhile, braces were also placed on the lower arch. (Figure 3, Figure 4).



Figure 3. Intermediate clinical situation after the surgical exposure of the canine and the application of lower fixed appliance



Figure 4. Orthodontic alignment of the canine with NiTi archwires

At the end of the orthodontic treatment, after all the teeth were correctly aligned, with correct occlusal relations, the braces were removed and fixed long term retainers were placed on both upper and lower arches. (Figure 5, Figure 6, Figure 7, Figure 8, Figure 9, Figure 10). The wisdom molars were indicated for monitoring and possible extractions. The periodontal tissue around the upper left canine was evaluated to make sure the gum is correctly attached to the tooth with the absence of gingival sockets.



Figure 5. Final panoramic X-Ray



Figure 6. Final result - frontal view



Figure 7. Final result - right view



Figure 8. Final result - left view



Figure 9. Upper fixed retention



Figure 10. Lower fixed retention

DISCUSSIONS

The absence of a tooth within the dental arch leads the patient towards a specialist for a consult. After a correct diagnosis, a clinical and para-clinical examination is indispensable to determine the position of the impacted tooth and the possibility of correct alignment.

The first step in the treatment of impacted canines is a thorough analysis of every case in particular. From the various treatment possibilities, the clinician has to choose the most beneficial one for each patient in particular. In this case, the best solution was a collaboration between surgery and orthodontics. The first step is a thorough analysis of the case. The next phase is represented by the start of orthodontics treatment. This way we achieved the space necessary for the width of the upper canine. The surgical phase was meant to reveal the impacted tooth, and then for the orthodontist to pull the canine in a correct position, for the second phase of the orthodontic treatment.

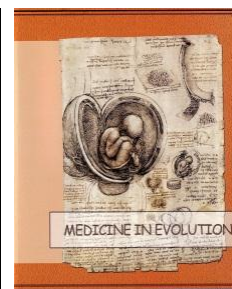
A periodontal evaluation was required to make sure the gums are appropriately attached to the surface of the tooth. From a radiographic point of view, the bone level was satisfactory for a proper usage of the canine. Inter-occlusal relations reveal optimal guidance in jaw movement.

Through a good collaboration between different specialties, and between the patient and the clinician, this case was completely rehabilitated, with also aesthetics and functionality established, and the results maintained through a correct retainer system.

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Internal and marginal adaptation of anatomic and uniform thickness metal frameworks fabricated with two CAD/CAM technologies: milling and Selective Laser Melting- in vitro study



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Abstract

Even though patients esthetic demandings are higher and higher, and integral-ceramic restoration gain popularity among both patients and dental practitioners, their cost and fracture susceptibility make metal-ceramic crowns still the most-used restorations. They had proved their qualities: long-term stability, aesthetics, biocompatibility. Now, new technologies are emerging, to replace conventional slip-casting, to overcome its shortcomings. CAD/CAM technologies are becoming more interesting and used, providing rapid, standardised, precise restorations. Crown adaptability is one of the most important factors who determine clinical success and outcome. The aim of this study was to evaluate two relatively new manufacturing techniques: CAD/CAD milling, and selective laser melting (SLM) and how tooth preparation affects adaptability of frameworks produced this way. Two upper first molars were prepared with two different finishing lines. Two different copings designs were made for each one. Mean marginal discrepancies for all preparations with both anatomical-reduced and uniform-thickness copings were found in range of clinical acceptability.

Keywords: CAD/CAM system, innovative technologies, metal-ceramic crowns, selective laser melting

INTRODUCTION

With new ceramic materials development the clinicians have to decide which type of infrastructure, ceramic, fabrication method, design and luting agent is more appropriate for their patient. Esthetic demands are increasing, and with that the number of integral-ceramic fixed dental prostheses, but these are more prone to fracture and marginal leakage [1].

Although integral-ceramic crowns become more popular, conventional metal ceramic dental restorations obtained by lost wax and casting techniques using different metal alloys are still the most widely used in common practice, especially in molar area, due to their long-term clinical results, equipment costs, and the fact that failure is more likely to happen due to biology than mechanical failure [2].

Eventhough casting technologies are in continuous evolution for more than a century in dental field, they still have limitations. Obtaining frameworks for dental restorations with these metod imply many time-consuming technological steps, with different materials with different mechanical properties, wax pattern deformation risk, human factor, irregularities in the cast metal, all of these potential leading to errors [2,3]. Besides that, the castability of Co-Cr alloy is lower than that of nobel alloys, more technique sensitive [4]. This is why CAD/CAM technologies arouse more and more interest among practitioners. Their evolution is a consequence of data acquisition development and computing technologies.

Advantages derived from utilization of CAD/CAM technologies consists in improving material quality, by using prefabricated, controlled materials, time saving production, data can be saved and stored and human errors can be virtually eliminated. [4,5,6,7].

Early CAD/CAM dental systems where subtractive sistems, milling machines, able to process chairside ceramic materials for small sizes dental restorations. Subsequent labside units (NobelProcera, Nobel Biocare) allowed to process larger ceramic and metalic prosthesis. For this, tooth preparation is scanned and digitized, a virtual restoration is designed by the soft-ware, then the actual restoration is milled from a solid Co-Cr block. This method, although precise, implyes a waste of material. Later on, CAD/CAM aditive technologies where imported in dental field, enabled us to produce metal copings from metal powder, for metal-ceramic restorations, by selective laser-melting technology (Bego medical, Phenix System)[4]. In this technique, the final step- CAM, uses a high-temperature laser-beam to selectively melt and consolydate the metal powder, layer-by-layer, based on CAD data for fabricating 3D parts. Unused powder can be then reused. However, the accuracy of this procedure must be further-more investigated, due to internal-tensions which appears while the finite-piece is cooling [8].

One of the most important factors affecting the long term success of fixed dental restorations are internal and marginal fit, relevant for retention, marginal seal and cement gap [9,10].

Increased marginal gap expose the luting agent to oral environment, which results in its dissolution with marginal percolation, bacterial infiltration, decay, pulp inflammation. Also, can lead to gingival inflammation, bleeding, retraction, marginal discoloration, functional and aesthetic failure. Marginal adaptation can be clinically evaluated, and be considered acceptable if it cannot be detected visually, or using a dental probe[11]. Marginal and internal gap can be evaluated by several methods, destructive, and nondestructive. It is defined as perpendicular distance between prepared tooth and coping [12].

There is no consensus regarding the thickness of cement film, but most follow-up studies indicates as clinically acceptable 120 μm maximum gap [13].

Problem formulation

Alternative CAD/CAM technologies are developed for replacing conventional lost-wax technique used in dental technology. However, there are not precise guidelines for dental preparations or most indicated design for metal-ceramic restorations infrastructures obtained by these new methods.

Purpose

The purpose of this in vitro study was to evaluate the effect of framework design and tooth preparation on metal copings accuracy fabricated by milling and selective laser melting.

MATERIAL AND METHODS

Two resin maxillary right first molars (Frasaco GmbH) were prepared for metal-ceramic crowns. one of them was prepared leaving a chamfer finishing line, anatomical occlusal reduction, 6° occlusal convergence angle and the palatal surface of the functional cusp was reduced in two planes. The other one was prepared with right angle shoulder, anatomical occlusal reduction and also 6° taper angle. The preparations were duplicated with silicone (Variotime, Heraeus Kulzer, Hanau). Then twenty stone-casts of each preparation were poured using Type 4 Dental Stone GC Fujirock Gc, Leuven, Belgium). These abutments were scanned with Dental Wings 7Series Scanner (Dental Wings INC., Montreal (Quebec) Canada). Two framework designs were made using DWOS software ((Dental Wings INC., Montreal (Quebec) Canada), one with uniform thickness of 0.4 mm, and one anatomic for each tooth preparation. Ten anatomic and ten non anatomic metal coping using Cobalt-Chromium bonding alloy for the manufacturing of removable and fixed restorations by Selective Laser Melting (SLM) using Starbond CoS Powder 30, free of beryllium and nickel (Fig.1). Ten anatomic and ten non anatomic metal coping from Cobalt-Chromium metal disc (White Peaks Dental Systems GmbH & Co. KG, Essen, Germany) were milled (Fig. 2).



Figure 1. All designs for SLM copings



Figure 2. All designs for milled copings

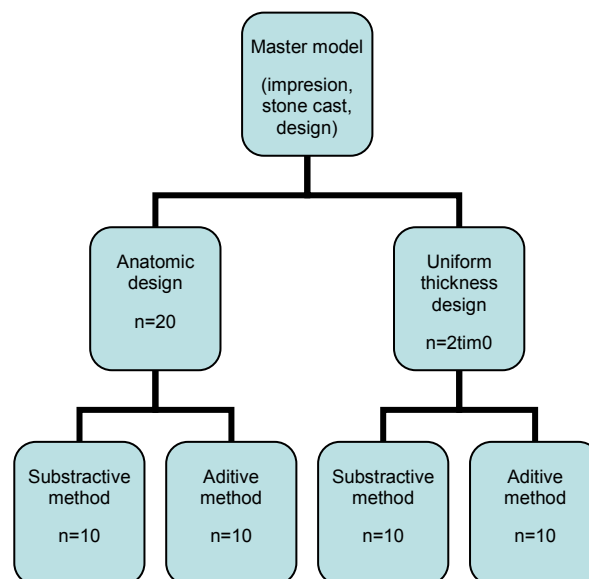


Figure 3. Study work-flow

Marginal and internal evaluation was made using the replica technique, using a low viscosity silicone to simulate the luting agent: Zetaflow light (, Zhermack, Badia Polesine, Italy). This was embedded in hard silicone: Zetalabor, and covered with another contrasting color silicone Oranwash L. (Zetaplus, Zhermack, Badia Polesine, Italy) [14]. To avoid discrepancies caused by hydrostatic pressure, holes of 1 mm diameter were milled in areas we did not follow to perform measurements, to allow silicone to flow.



Figure 4. Sample prepared for microscope

Two random sections for each sample were made and were analyzed with Leica DM500 microscope (Leica, Wetzlar, Germania) at 4x magnifications with a hundred microns scale (Fig. 4).

Nine mesiodistal and vestibulolingual positions were measured, and each of these were divided into the following categories: marginal gap (MG), cervical gap (CG), axial wall at internal gap (AG), axio-occlusal angle (AOG) and oclusal wall at internal gap (OG), using this silicone key for measuring the gap between coping and abutment (Fig. 5).

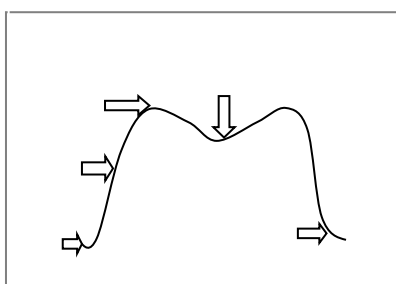


Figure 5. Measurements positions

Measurements were made with ImageJ software (ImageJ Launcher, National Institute for Health, Bethesda, USA) (Fig. 6).

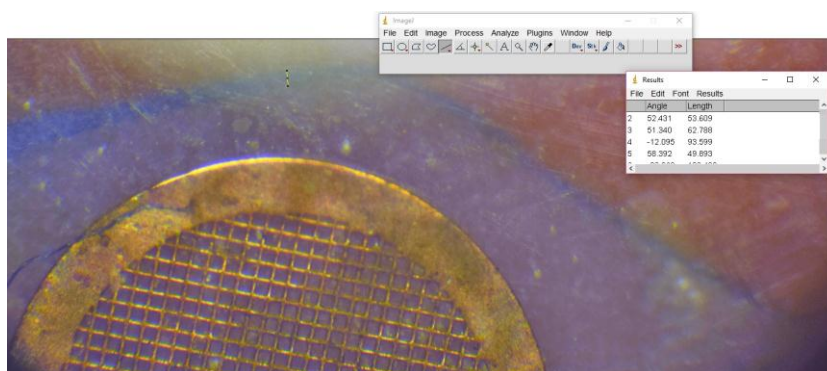


Figure 6. Measurements made with ImageJ software

RESULTS AND DISCUSSIONS

Mean values for marginal adaptation where minimal for first and last groups: milled uniform thickness coping on shoulder preparation and SLS anamic framework on chamfer preparation. The highest numbers for marginal discrepancy were found in second and fifth groups: milled anatomic on shoulder preparation and SLM equal thickness on shoulder. Mean occlusal gap was smaller for all SLM copings compared to milled oanes, independent of the type of the preparations.

Best internal and marginal adaptation was obtained in case of milled anatomic restorations, regardless preparation finishing line. Besides better adaptation, this type of design offers better support for ceramic,, improving once more restorations durability, decreasing the risk of ceramic fracture. (Table I).

Table I. The mean gap values measured (in μm) for all groups. Group 1: shoulder preparation, milled uniform thickness framework; Group 2: shoulder preparation, milled anatomic coping; Group 3: chamfer preparation, milled uniform thickness framework; Group 4: chamfer preparation, milled anatomic coping. Group 5: shoulder preparation, SLM uniform thickness framework; Group 6: shoulder preparation, SLM anatomic coping; Group 7: chamfer preparation, SLM uniform thickness framework; Group 8: chamfer preparation, SLM anatomic coping

Group	MG	CG	AG	AOG	OG
1	43.10	49.16	47.89	53.94	76.79
2	83.98	95.86	73.42	90	103.3
3	56.52	50.72	66.41	89.61	93.92
4	50.41	45.85	55.94	72.44	91.09
5	77.30	95.29	89.22	85.11	86.91
6	48.65	58.37	67.22	71.07	64.13
7	66.24	72.51	77.61	79.51	87.63
8	46.72	84.6	92.33	61.08	65.56

The mean outcome numbers for all metal structures, obtained with two different innovative, both additive and subtractive CAD/CAM technologies are in the range of clinical acceptability, between 24.09 and 120 μm . However, marginal gap was less than 100 μm for all preparation finishing lines and framework. The highest gap was found occlusally, and axial gap exceeds marginal discrepancy for all specimens. Virtual spacer used in designing step and applied 1mm shorter than finishing line can be an explanation for that. Previous limitations regarding CAD/CAM restorations on teeth prepared with right-angle shoulder seems to be overcome by development of these sistemns regarding scanning performances and improved milling instruments.

The most accurate technique for adaptation evaluation is direct measurements, under microscope, of the sectioned tooth-restoration complex, embedded in resin. This is a destructive technique. We choosed o similar, but non-destructive technique for this evaluation, which could be also used in-vivo studies. The force applied to crown while light-silicone is setting it cannot be standardized. All probes were made by one investigator to minimize the influences which can occur on silicone layer thickness.

CONCLUSIONS

Both kind of metal infrastructures, milled and SLM, exhibits similar, clinically acceptable internal and marginal gaps.

Differences in adaptability between restorations obtained by these methods are not clinically significant.

The highest gap was found in occlusal regionfor all grops.

Types of preparation does not significantly influence adaptability, minimally invasive attitude being recommended.

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Microbial colonization in orthodontic mini-implants



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Abstract

Introduction: The aim of this study is to compare in-vivo values of adhesion and growth of *Mutans Streptococcus*, *Lactobacillus casei* and *Porphyromonas gingivalis* on temporary anchorage devices (mini screws) made of standard metal, consoles and orthodontic ceramic composites.

Materials and Methods: In order to obtain valid data, twelve subjects - patients in the Department of Orthodontics of the Faculty of Dentistry at the University of Medicine and Pharmacy “Carol Davila” Bucharest were included in this study and samples were collected on three specific time periods and on specific areas of the orthodontic devices. Special agar test were used for each type of bacteria. Means, standard deviations, and relative frequencies were tabulated for each variable being assessed. ANOVA and the Tukey-Kramer test were used to analyze data with p value ≤ 0.05 utilized as statistical significance.

Results: The present study found no significant differences among bacterial type, location or time and there were no significant differences on the interaction of these variables. The greatest increase in bacterial accumulation occurred shortly after the appliances were placed for both the bracket and the mini screw.

Conclusions: After analyzing all the data there were no significant differences between appliance type and bacterial adherence in-vivo and no significant differences regarding the time period and bacterial accumulation. The titanium mini screw is another addition to the armamentarium that has been introduced for use in orthodontics.

Keywords: orthodontic anchorage procedures, mini screws, microbiological colonization

INTRODUCTION

Mutans Streptococcus, *Lactobacillus casei* and *Porphyromonas gingivalis* are the three main bacteria present in the oral cavity and each one has different effects on the local microbiological status. *Mutans Streptococci* can adhere to the tooth structure, produce lactic acid from sugar and can tolerate acid environment. They have a specific sugar transport mechanism and can produce intra and extracellular polysaccharides. *Lactobacilli* are the main responsible for the progression of carries and can produce alterations of tooth structure. They form colonies in retentive cavities, produce acid and can tolerate acid environment similar to *Mutans Streptococci*. Using these self-protective mechanisms, these bacteria can seriously damage the tooth structure on patients receiving orthodontic treatment. Previous studies have focused on studying the accumulation and the adhesion of bacteria on orthodontic devices^{1,2}, but none of them contains specific information about mini screws. In the present study, bacterial accumulation was examined, counted and recorded on temporary anchorage devices – mini screws.

MATERIALS AND METHODS

For this in-vivo study twelve patients who fulfilled the following criteria were admitted: males treated by extraction of upper and lower 1st premolars, no history of any systemic diseases, no history of antibiotic treatment for the past two weeks, no gingivitis or carious lesions. Each patient received information about the study and signed the informed consent before the beginning of the study. All patients were given oral hygiene instructions which consisted of proper brushing and flossing techniques from the Department of Orthodontics at the beginning of the orthodontic treatment. Patients were instructed on how to properly brush and floss with the appliances in place and were reminded at the initial appointment not to perform any oral hygiene measures twelve hours prior to their next appointment. The orthodontic appliance was done following the treatment plan. On first appointment composite brackets were applied on the six upper and lower anterior teeth, ceramic bracket on the upper and lower 2nd premolars. On the second appointment, after one month from placement of orthodontic brackets, three plaque samples were taken prior to any other treatment being initiated and the s.s bands were applied on the upper and lower 1st molar and titanium mini screws on the right side. The same areas were sampled at each visit and a total of nine samples were taken from each patient throughout the course of the data collection process. The three specific areas were: the gingival base of the bracket of a maxillary right central incisor, the gingival base of the bracket of a mandibular right central incisor and the head of the temporary anchorage devices – mini screws. Plaque samples were collected from areas isolated using a cotton pad and then used seven periodontal probes (one for each brackets and mini screw); the method of obtaining the sample was by scraping the probe across the gingival base of the bracket. The specimen was inoculated in specific agar plates: Mitis Salivarius Agar with Tellurite (MSTAT) plate was used to specifically culture *streptococcus mutans*, Trypticase Soy blood agar plate (TSBA) was used to identify *Lactobacillus casei* and TSBA and HK agar plate was used to identify *Porphyromonas gingivalis*. A total of three plates per vial were used for the data collection. Once spread out, all of the plates were placed into a 5% CO₂ incubator at 37°C for a period of seven days to allow for bacterial growth. The plates were placed upside down in order to prevent condensation falling onto the culture surface. The plates were read and analyzed after seven days in the incubator inside of the anaerobic chamber. *Mutans S.* were identified using MAST plates, specific for these bacteria. *Lactobacillus casei* on TSBA plates were counted using the gram stain technique and microscopy and *Porphyromonas gingivalis* was identified under long-wave UV light using a trypsin reagent. After all data was collected, ANOVA and Tukey-Kramer test were used to

analyze each set with p value ≤ 0.05 considered of statistical significance and means, standard deviations and relative frequencies were registered.

RESULTS

After applying the statistical analysis, the following results were obtained.

In Table 1 mean amounts and S.E of *Mutans Streptococcus* in the three sites are presented, with a $p=0.0994$.

Table 1. Mean and S.E. of *Mutans S.* in the three different sites (CFUs)

	Site	Mean	Std Error
1	Mx Ce	805.33	241.26
2	Md Ce	792.00	241.26
3	Mini screw	874.00	241.26

*Mx Ce - maxillary central incisor bracket; Md Ce - mandibular centra incisor bracket; Mini screw - mini screw head

Table 2 show the mean and S.E. of *S. mutans* for the three time periods. ANOVA showed no significant differences among the three time periods ($p=0.851$).

Table 2. Mean and S.E. of *S. mutans* at three different time periods (CFU's)

	Time pd	Mean	Std Error
1	month	740.66	241.26
2	month	930.66	241.26
3	month	800.00	241.26

Table 3 show the mean and S.E. of *S. mutans* with regard to a site and time interaction. ANOVA showed no significant differences with a site vs. time interaction ($P=0.9895$).

Table 3. Mean and S.E. interactions of sites and time periods on the levels of *S. mutans* (CFU's)

	Site, time pd	Mean	Std Error
1,1		634.00	417.88
1,2		1058.00	417.88
1,3		724.00	417.88
2,1		752.00	417.88
2,2		856.00	417.88
2,3		768.00	417.88
3,1		836.00	417.88
3,2		878.00	417.88
3,3		908.00	417.88

A second bacterial type that sampled was *Lactobacillus casei*. Table 4 show the mean and S.E. of *Lactobacillus casei* for the three sites. ANOVA showed no significant differences among the three sites ($p=0.998$).

Table 4. Mean and S.E. of *Lactobacillus casei* at three different sites (CFU's)

	Site	Mean	Std Error
1	Mx Ce	456.60	160.83
2	Md Ce	463.26	160.83
3	Miniscrew	452.00	160.83

Table 5 shows the mean and S.E. of *Lactobacillus casei* for the three time periods. ANOVA showed no significant differences among the three time periods ($p=0.7074$).

Table 5. Mean and S.E. of *Lactobacillus casei* at three different time periods (CFU's)

(CFU's)		
Site	Mean	Std Error
1 month	377.86	160.83
2 month	562.66	160.83
3 month	431.33	160.83

Table 6 show the mean and S.E. of *Lactobacillus casei* with regard to a site and time interaction. ANOVA showed no significant differences with a site vs. time interaction ($p=0.723$).

Table 6. Mean and S.E. interactions of sites and time periods on the levels of *Lactobacillus casei* (CFU's)

(CFU's)		
Site, time pd	Mean	Std Error
1,1	167.80	278.58
1,2	668.00	278.58
1,3	534.00	278.58
2,1	387.80	278.58
2,2	490.00	278.58
2,3	512.00	278.58
3,1	578.00	278.58
3,2	530.00	278.58
3,3	248.00	278.58

The third type of bacteria cultured in the study was *P. gingivalis*. Table 7 show the mean and S.E. of *P. gingivalis* for the three different sites. ANOVA showed no significant differences among the three sites ($p=0.447$).

Table 7. Mean and S.E. of *P. gingivalis* at three different sites (CFU's)

(CFU's)		
Site	Mean	Std Error
1 Mx Ce	6.00	12.17
2 Md Ce	28.00	12.17
3 miniscrew	18.66	12.17

Table 8 show the mean and S.E. of *P. gingivalis* for the three time periods. ANOVA showed no significant differences among the three time periods ($p=0.267$).

Table 8. Mean and S.E. of *P. gingivalis* at three different time periods (CFU's)

(CFU's)		
Time	Mean	Std Error
1 month	34.00	12.17
2 month	8.66	12.17
3 month	10.00	12.17

Table 9 show the mean and S.E. of *P. gingivalis* with regard to a site and time interaction. ANOVA showed no significant differences with a site vs. time interaction ($p=0.829$).

Table 9. Mean and S.E. interactions of sites and time periods on the levels of *Lactobacillus casei* (CFU's)

Site, time pd	Mean	Std Error
1,1	8.00	21.08
1,2	2.00	21.08
1,3	8.00	21.08
2,1	58.00	21.08
2,2	10.00	21.08
2,3	16.00	21.08
3,1	36.00	21.08
3,2	14.00	21.08
3,3	6.00	21.08

DISCUSSIONS

The adherence of specific bacteria, including *S. mutans*, *Lactobacillus casei*, and *P. gingivalis*, to standard metal brackets and titanium miniscrew implants was studied to determine if these specific bacteria adhered in greater amount to the miniscrew and to find which bacterial type was the most abundant on the appliances. Location of bacteria and time period and their respective interactions, were also variables that were studied. Several studies have investigated the accumulation of bacteria to orthodontic appliances

Most of these studies concentrated on adherence of bacteria to orthodontic brackets and adhesives with no information specifically on mini screws.

Even though all of the patients in the study were given the same oral hygiene instructions as every patient in the UNIVERSITY OF MEDICINE AND PHARMACY "Carol Davila" – Bucharest department of Dentistry, Department of Orthodontics, they may have varied influences to maintain oral hygiene.

The three marker organisms chosen in this study were *S. mutans*, *Lactobacillus casei*, and *P. gingivalis*. All of these organisms have been found to be elevated in orthodontic patients undergoing treatment. This study found a difference between the rank (order) of the bacteria. It was found that *S. mutans* was the most predominant bacteria on the appliances. It was found in greatest number on all sampled areas, as well as, at all time periods. Although these results were not found to be statistically significant, there was a trend of greatest adherence of *S. mutans*, followed by *Lactobacillus casei*, and finally, *P. gingivalis*. These findings were similar to a study that found an increase in supragingival plaque on orthodontic appliances and found an increase in subgingival plaque and elevations of subgingival bacteria after 3 months. Periodontal pathogens, including *P. gingivalis*, were found to be elevated in this study. This study suggests that orthodontic treatment may affect the number of bacteria present on appliances and might affect the overall presence of periodontal microorganisms³. This is also consistent with a study comparing the colony forming unit levels of *Lactobacillus casei* and *S. mutans* in orthodontic patients. This study confirmed that significantly higher levels of *Lactobacillus casei* were found from patients wearing orthodontic appliances after 2 months of orthodontic wear. No difference was found in *S. mutans*.⁴

This study found an initial increase in bacterial accumulation on both orthodontic brackets and miniscrews and then a drop in adherence over time. The miniscrew appliance was found to have similar amounts of bacterial accumulation when compared to the standard orthodontic brackets. However, these differences were not statistically significant *in-vivo*. The results of this study suggest that patients undergoing orthodontic therapy will have an increased plaque challenge and may have an increase in all bacterial types specifically, *S. mutans*, *Lactobacillus casei*, and *P. gingivalis*. These bacteria may cause decalcification around teeth and potential loss of the miniscrew appliance if strict oral hygiene measures are not followed. Although no loss of any miniscrew implants occurred during this study, loss of the

miniscrew appliance can be attributed to bacteria around the appliance. Duyck et. al found that microbial infections are known to be a possible cause of implant failure and usually occur after the initial insertion of the appliance ⁵. It is of the utmost importance for orthodontists to stress oral hygiene measures to their patients to make sure that the periodontium remains healthy throughout the course of treatment.

Based on the findings of this study, further clinical studies could be performed to determine other specific bacterial types that accumulate on orthodontic appliances. A study on the periodontal area surrounding the titanium implant could also be studied to determine what specific bacterial types, if any, contribute to loss of the mini screw implants and the importance of bacterial synergy. It is important to find out some of the causes of early loss of the anchorage devices. This study could be expanded even further to get a larger number of subjects involved in the study and to have an increase in the amount of data. Also, SEM could be utilized to gather a more in depth look at the bacteria as well as 3D studies. As more mini screws are being placed, various studies could be conducted to examine the effects on the external gingival tissue, as well as, the bone into which it is placed.

CONCLUSIONS

There were no significant differences between appliance type and bacterial adherence *in-vivo*. There were no significant differences with regard to time period and bacterial accumulation *in-vivo*. There was an initial increase in bacterial adherence to the appliances from one month to two months and a subsequent decrease in bacterial accumulation between two months and three months, these differences were not found to be significant *in-vivo*. The bacterial species found in greatest amount on both appliance types was *S. mutans*, followed by *Lactobacillus casei*, and finally, *P. gingivalis*, although these differences were not found to be significant *in-vivo*.

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Drug prescription in paediatric dentistry: a retrospective study



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Abstract

Aim and objectives: The objectives of the study were to assess the drug prescription patterns of the dentists working in Paediatric Dentistry Department.

Material and methods: The study was conducted on the clinical records of a sample of 340 patients aged between 1 year 2 months and 17 years and 11 months, with an average age of 8.31 ± 0.22 years.

Results: An average of 1.34 ± 0.034 medicines per patient was prescribed.

The prevalence of drugs prescription was higher in soft tissue diseases (100%) than in dental diseases (65.1%, $p=0.004$).

The most frequently prescribed drugs were analgesics 71.3%, followed by antibiotics 19.5% like penicillins (90.5%), especially amoxicillin (84.8%).

The most frequently medicated age group was <6 years (85.2%. $p=0.005$).

Conclusions: Drug prescription in children occupied an important place in our paedodontic practice especially for curative purposes, to treat both oral mucosa and teeth diseases.

Keywords: drug prescription, analgesics, antibiotics

INTRODUCTION

Drug prescription plays an important role in the management of paediatric dentistry patients, becoming today a routine practice [1].

The clinicians are dealing with an increasing number of medicines used by paedodontists [1, 2]. That is why the prescription of medications is more complicated today than in the past because paediatric clinicians are dealing with microbial resistance to prescribed antibiotics and drug interactions [3].

The aims of medicines prescribed by the paedodontist sometimes in collaboration with the paediatrician are to improve or suppress pain, reduce inflammation, fight against infection and reducing anxiety [4].

Many dental conditions such as irreversible pulpitis, periapical pathology, dento-alveolar or facial injuries a.s.o. may require a professional help by pharmacotherapy as an either adjunct to dental therapeutic procedure or as a monotherapy [1, 5].

The medicines prescription in children shows some special features because the child patient is a growing body reacting differently to the drugs. Thus, drugs prescription in the paediatric patient requires carefully dose adjustment and the choice of the proper route of administration, considering the pharmacokinetic and pharmacodynamic particularities of medicines in children [5, 6].

The administration of drugs to paediatric patients require to adjust the dosages of medications to accommodate their lower weight and body size [3].

Several rules exist to compute the dosage of a drug for a child: Clark's rule: child's dose = child's weight (kg) / 70 (kg) X adult dose, Gaubius - Cottureau rule: 1 to 3 years - 1/6 adult's dose, 3 to 7 years - 1/3 adult's dose, 7 to 13 years - 1/2 adult's dose, 13 to 20 years - 2/3 adult's dose, Fried rule (for children < 2 years): child's dose = adult's dose x age in months / 150 a.s.o. [3, 4, 5].

The choice of the route of administration of the drugs is also important. There are many routes of administration: oral, parenteral, mucosal (oral, rectal) and cutaneous of which oral and rectal administration are the most common for children [4].

The most frequently prescribed drugs are: anti-infective drugs (antimicrobial, antiviral, antifungal), analgesics, anti-inflammatory drugs, systemic fluorides for caries prevention [3].

Aim

The objectives of the study were to assess the medicine prescribing patterns of the dentists working at the emergency service of the Paediatric Dentistry Department.

MATERIAL AND METHODS

This retrospective study ran during the last six months of 2014 in the Paediatric Dentistry Department, Faculty of Dental Medicine "Carol Davila", Bucharest.

Our study was conducted on the clinical records of a *sample* of 340 *patients* aged between 1year 2 months and 17 years and 11 months, with an average age of 8.31 ± 0.22 years. The sample of affected teeth (470) included 289 primary teeth and 181 permanent teeth.

The inclusion criteria for the patients were: patients which were at the first presentation in our clinic, with no general condition that would have interfered with the dental medical prescription, accompanied by a parent / adult caregiver who agreed to participate in the study.

Each clinical record included the following sections: personal data of the child (age, gender), the diagnosis at the first visit: high risk of caries, uncomplicated caries, complicated caries (acute and chronic pulpitis, necrosis, pulpal infections, periapical infections with or

without cellulitis or abscess) dental trauma, periodontal diseases, oral mucosa diseases, eruption conditions a.s.o.), the pharmacological and non-pharmacological treatment applied at the first presentation at the Paediatric Dentistry Department.

Data were statistically analysed using PSPP program v.0.8.4 and the graphic illustration of the results was performed using Microsoft Excel 2010.

RESULTS

The gender distribution in the patients sample was as follows: girls 41.8% (n=142); boys 58.2 % (n=198).

The patients sample was divided into the following age groups, corresponding to primary, mixed and permanent dentition: group 1 (<6 years) 33.8% (n=115); group 2 (6-12 years) 45% (n=153); group 3 (12-18 years) 21.2% (n=72).

The frequency of subjects who received drug prescription was 74.4% (n=253) while those who did not received any prescribed medication were 25.6% (n=87).

The distribution of the patients which received drug prescriptions according to gender was: girls – 39.1% (n=99), boys – 60.9% (n=154).

Within each age group, the frequency of medicines prescription was the following: <6 years – 85.2% (n=98), 6-12 years – 68.6% (n=105) and 12-18 years – 69.4% (n=50). The differences between these values were statistically significant in what concerns the <6 years age group versus the older age groups ($p=0.006$).

Out of the 253 patients that received medication, 1.18% (n=3) of patients received drugs for prophylactic purposes only, 6.32% (n=16) for both prophylactic and curative purposes while 98.81% (n= 250) received drugs for curative purposes only.

The number of prescribed medicines was 339 for 253 patients, resulting in an average of 1.34 ± 0.034 prescribed medicines per patient. The number of the prescribed medicines per patients was: 1 drug was prescribed in 68.4% of patients (n=173), 2 drugs were prescribed in 28.5% of patients (72) and 3 drugs were prescribed in 3.2% of patients (n=8).

The overall distribution of prescribed medicines according to the age group was the following: <6 years 40.72% (n=138), 6-12 years 37.16% (n=126) and 12-18 years 22.12% (n=75).

Dental diseases have been treated pharmacologically in a proportion of 65.1% of the cases, while the soft tissue diseases in 100% of cases ($p=0.004$).

The distribution of prescribed drugs was: analgesics 71.3% (n=241, of which NSAIDs 43.8%, n=148 and non-opioid analgesics 27.5%, n=93), antibiotics 19.5% (n=66), antifungals 2.1% (n=7), antivirals 1.5% (n=5) and other drugs 5.6% (n=19).

The distribution of prescribed antibiotics by diagnosis was: periapical infections 5 (7.6%), cellulitis 32 (48.5%), dental trauma 18 (27.3%), pulpitis 2 (3%), soft tissues diseases 9 (13.6%).

Considering the proportion of patients receiving antibiotics for each type of disease (Table I), cellulitis (33.7%) benefited more of the antibiotics prescription than periapical infections (7.2%). The difference between the two diseases was statistically significant ($p<0.001$).

The distribution of prescribed NSAIDs by diagnosis was: periapical infections 41 (27.7%), cellulitis 56 (37.8%), dental trauma 29 (19.6%), pulpitis 18 (12.2%), soft tissues diseases 4 (2.7%).

Considering the proportion of patients receiving drugs for each type of disease (Table I), cellulitis (59.4%) benefited slightly more of the NSAIDs prescription than periapical infections (58.9%) however the difference between the two diseases was not statistically significant.

The distribution of prescribed analgesics by diagnosis was: periapical infections 28 (29.8%), cellulitis 39 (41.5%), dental trauma 11 (11.7%), pulpitis 15 (16%), soft tissues diseases

1 (1.1%). There were no statistically significant differences between the frequencies of painkillers' prescribing depending on the type of disease.

Table I. The proportion of patients who received medication according to diagnosis

Type of medication	Periapical infection	Cellulitis	Soft tissues disease	Dental trauma	Pulpitis
Antibiotics	7.2% (n=5)	33.7% (n=32)	64.3% (n=9)	45% (n=18)	6.1% (n=2)
NSAIDs	59.4% (n=41)	58.9% (n=56)	28.6% (n=4)	72.5% (n=29)	54.5% (n=18)
Non-opioid analgesics	40.6% (n=28)	41.1% (n=39)	7.1% (n=1)	27.5% (n=11)	45.5% (n=15)

The distribution of antibiotics by the active ingredient indicated that 90.5% (n=60) of the patients received penicillins of which amoxicillin was the most prevalent 84.8% (n=56).

The distribution of systemic medication within each age group is reported in Table II. Statistically significant differences were recorded for NSAIDs between the <6 years age group and the older age groups ($p<0.001$), for antibiotics between the 6-12 years age group and the 12-18 years age group ($p=0.026$) and for analgesics between the <6 years age group and the older age groups ($p<0.001$).

Table II. The distribution of the main systemic medication within each age group

Medication	<6 years	6-12 years	12-18 years
NSAIDs	25.2% (n=29)	53.6% (n=82)	51.4% (n=37)
Antibiotics	18.3% (n=21)	14.4% (n=22)	3.9% (n=23)
Non-opioid analgesics	52.2% (n=60)	14.4% (n=22)	16.7% (n=12)

The patients' distribution according to the medication's administration route was the following: oral administration 95.2% (n=241), rectal administration 2.4% (n=6) and topical administration 2.4% (n=6).

The patients' distribution according to the pharmaceutical form of the received medication was the following: pills 65.2% (n=165), suspension 30% (n=76), suppositories 2.4% (n=6) and colutory 2.4% (n=6).

The patients' distribution according to the pharmaceutical form of the received medication by age groups is presented in Table III.

Table III. The patients' distribution according to the pharmaceutical form of the received medication by age groups

Pharmaceutical form	Age group		
	< 6 years	6-12 years	12-18 years
Suspension	72.5% (n=71)	4.8% (n=5)	-
Pills	17.3% (n=17)	94.2% (n=99)	98.0% (n=49)
Suppositories	5.1% (n=5)	1.0% (n=1)	-
Colutory	5.1% (n=5)	-	2.0% (n=1)

The frequency of drugs prescribing in primary and permanent teeth was the following: primary teeth - 67.8% (n=289), permanent teeth 62.4% (n=181) ($p>0.05$). The frequency of the prescription of each type of medicine according to the type of tooth (primary or permanent) is illustrated in Table IV.

Table IV. The frequency of drugs prescription for each type of tooth

Type of medication	Tooth's type	
	Primary	Permanent
Non opioide analgesics	52.6% (n=103)	15% (n=17)
Antibiotics	17.9% (n=35)	42.5% (n=48)
NSAID's	43.9% (n=86)	85% (n=96)

The prescribed medication produced the desired results in 88.93% (n=225) of cases. In 11.06% (n=28) of cases, medication was only partially successful these situations being associated with the refusal of dental treatment and the failure to comply with instructions given by the doctor.

DISCUSSIONS

Almost three quarters of all patients received a drug prescription (74.4%) meaning that three out of four patients took drugs which represents a higher consumption of medicines than reported by Jayanthi and Naidu (2014) which showed that every fifth child was exposed to drugs [7].

Boys predominated 58.2 % (n=198) in the group of paediatric patients who visited the emergency room of the Paediatric Dentistry Department during six months, as well as in the patients' group who received medication. Although these results are in accordance with Paudel et al. (2010), there were no statistically significant differences concerning the frequency of medicine prescription according to gender [1].

An average of 1.34 ± 0.034 medicines were prescribed to each patient which is similar to the results of Paudel et al. (1.78). Comparing the results in the present study with the aforementioned authors, it was observed that a single drug was administered more frequently in our study (68.4% vs. 13.5%) while two or three drugs were administered less frequently in our patients (28.5% vs. 56.5% and 3.2% vs. 30%, respectively) [1].

The prevalence of drugs prescription was significantly higher in soft tissue diseases (100%) than in dental diseases (65.1%, $p=0.004$).

The most frequently prescribed drugs were analgesics (all types, 71.3%), followed by antibiotics (19.5%) and other drugs (9.2%). These results are in accordance with the studies published by Paudel et al. (2010), Sharma et al. (2014), Tanwir et al. (2015) [1, 2, 8]. Anderson et al. (2000) reported a higher frequency of antibiotic prescription – 38% [9].

Penicillins (90.5%), especially amoxicillin (84.8%), were the most frequently prescribed antibiotics (90.5%), which is in accordance with several other studies [1, 2, 7, 8, 9, 10, 11, 12, 13].

Patients with periapical infections accompanied by cellulitis benefited significantly ($p<0.001$) more of antibiotics prescription (33.7%) than the other types of periapical infections (7.2%). The proportion of patients with diffuse swelling receiving antibiotics was, however, smaller than the proportion reported by Harte et al. – 63% (2005) [14]. Patients with cellulitis benefited slightly more of the NSAIDs and analgesics prescription than periapical infections; however the difference between the two diseases was not statistically significant (Table 1).

In this study the age group of 6-12 years was the most prevalent (45%). These results are in accordance with those of Paudel et al. (2010) who found that the age group 6-10 years was the most frequent group but with a much higher proportion (70%) [1].

The most frequently medicated age group was <6 years (85.2%), followed by the 12-18 years age group (69.4%) and the 6-12 years age group (68.6%) ($p=0.005$).

Analgesics were prescribed with a higher frequency in patients in the <6 years group ($p<0.001$), NSAIDs were prescribed less frequently in patients in the <6 years old group compared to older age groups ($p<0.001$), while antibiotics were prescribed more often in patients in the 12-18 years group than in patients in the 6-12 years group ($p=0.026$).

Oral route was the most frequently used for drugs administration (95.2%), while the most common pharmaceutical forms of the prescribed medication was represented by pills (65.2%) followed by suspension (30%).

In what concerns the patients' distribution according to the pharmaceutical form of the received medication by age groups, suspensions were administered more frequently in children below the age of 6 years ($p<0.001$) while pills were administered mostly in children older than 6 years ($p<0.001$) (Table III).

CONCLUSIONS

The drug prescription pattern in our Paediatric Department enrolls in the general guidelines for prescribing medicines in children.

Therapeutic or prophylactic drug prescription has become an important aspect of dental practice. The necessity of the thorough knowledge of the medicines' indications and effects is underlined by the fact that, in our study, almost three quarters of all patients received a drug prescription and the highest frequency of medicines prescription was registered in children belonging to the below 6 years old age group.

The most frequently prescribed drugs were analgesics (about three quarters) followed by antibiotics (especially amoxicillin) which represented almost one fifth of all prescribed medicines.

Only about a third of the patients with cellulitis received antibiotic treatment, indicating a judicious choice of the cases in which this was necessary, which is important for limiting side effects and preventing the appearance of microbial resistance.

Authors' contribution

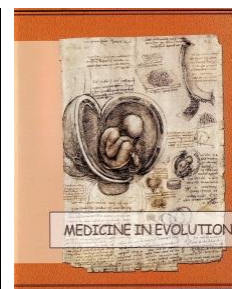
All authors contributed equally in the elaboration of the study.

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Extraoral vs. intraoral approach in surgical treatment of mandible subcondylar fracture - case reports and review of the literature



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Abstract

Treatment of facial fractures, tumors with various localization, management of paranasal sinus diseases, osteotomies or esthetic procedures require a specific approach to the facial skeleton. For each region, there are many approach possibilities. The treatment for mandibular ascending ramus fractures (and particularly condylar and subcondylar fractures) remains one of the most controversial themes in maxillofacial surgery. In this paper we report two cases of mandibular fractures involving the subcondylar area in which both the intraoral and the extraoral approach were used and we try to summarize the advantages and disadvantages of each approach based on our experience and also on the review of the literature.

Keywords: mandible, subcondylar fracture, extraoral approach, intraoral approach

INTRODUCTION

Because of its position and prominence, the mandible is a common fractured part of maxillofacial skeleton. After various authors, condylar and subcondylar fractures represent 26-40% of all mandible fractures. The treatment for condylar and subcondylar fractures remains one of the most controversial theme in maxillofacial surgery. Although a open reduction was first applied to a low subcondylar fracture in 1925, in the 20th century closed reduction has been the choice of treatment with many disadvantages: varying periods of maxillomandibular fixation (1 to 3 weeks), difficulties in maintaining nutrition and oral hygiene, long term complications (pain, limitation of mouth opening, inadequate repositioning of bone fractured fragments).[1] However, in recent years, due to the development of the osteosynthesis equipment and the sophistication of surgical techniques, the treatment indications for subcondylar fractures has changed from an nonsurgical approach towards a possible surgical treatment.[2]

Nowadays, the surgical procedure has absolute and relative indications. The absolute indications are represented by limitation of mandibular function due to a foreign body within the joint capsule or to an extracapsular dislocation of the condylar head or by severe and irreversible oclusal changes. The relative indications can be divided in medical restrictions like seizure disorders, psychiatric disorders, severe mental retardation, concomitant head or chest injury and local conditions like in cases of displaced fractures where dentures or splints are not feasible because of miss of teeth or severe mandibular atrophy.

For surgical treatment there are two types of approaches to take into consideration, the extraoral approach (cutaneous) or the intraoral approach (mucous), both with advantages and disadvantages.

The approaches to the condylar and subcondylar region described in the literature are pre-auricular, submandibular, retromandibular, and face-lift approach for the extraoral ones and the vestibular incisions with or without endoscopic assist for the intraoral. The choice of the surgical approach is usually based on the surgeon's technical conditions, training and experience. The most common incisions used in practice are the mandibular vestibular incision (for the mucosal approach) and the retromandibular incision (for the cutaneous approach).

CASE REPORTS

We report two cases of mandibular fractures involving the subcondylar area in which both the intraoral and the extraoral approach were used and we try to summarize the advantages and disadvantages of each approach based on our experience and also on the review of the literature.

Case 1

We present a case of a 43 years old female patient who was hospitalized in Timisoara's Maxillofacial Clinic presenting a right parasymphysis and left subcondylar fracture of the mandible. The diagnosis was supported by clinical aspects like pain and dental occlusion disorders and a panoramic x-ray. Fig 1A, D. The patient underwent surgical treatment consisting in an open reduction of both fractures with an intraoral approach and fixation with mini plates and screws. For the left subcondylar fracture intraoral vestibular incision approach was used. Fig 1B. Postoperative images show a good dental occlusion. Fig 1C. Also postoperative panoramic x-ray shows a good reduction of both fracture sites. Fig 1E.

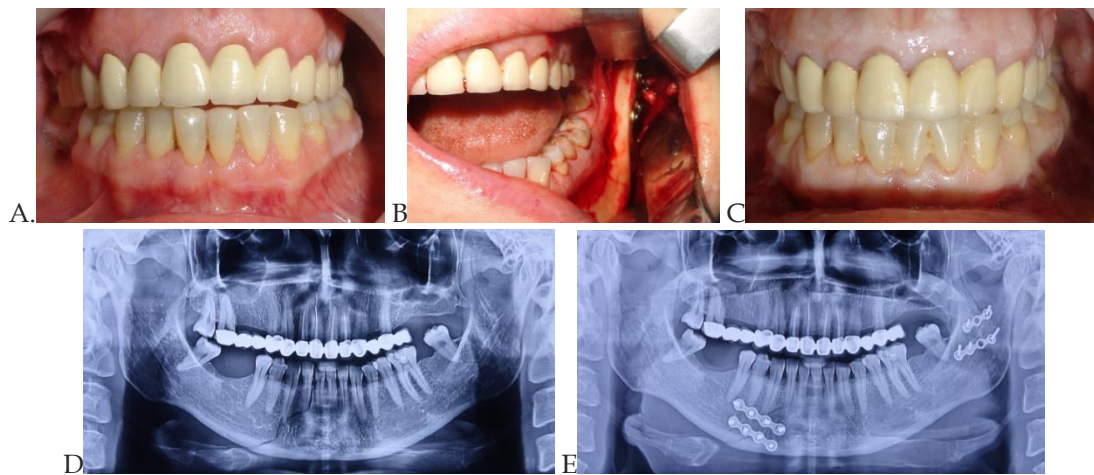


Figure 1. A. Initial clinical aspect with dental occlusion disorder. B. Intraoperative aspect. C. Postoperative clinical aspect. D. Initial preoperative panoramic x-ray E. Postoperative panoramic x-ray

Case 2

We present a case of a 22 years old female patient who was hospitalized in Timisoara's Maxillofacial Clinic presenting also a right parasymphysis and left subcondylar fracture of the mandible. The diagnosis was supported by clinical aspects, a panoramic x-ray and a CT scan with a 3D reconstruction. Fig 2A, B, C. The patient underwent surgical treatment consisting in an open reduction of both fractures and fixation with mini plates and screws. For the parasymphysis fracture an intraoral approach was used and for the left subcondylar fracture an extraoral retromandibular incision was performed. Fig 2D. Postoperative images show a good dental occlusion. Fig 2E. Also postoperative panoramic x-ray shows a good reduction of the subcondylar fracture site. Fig 2F.

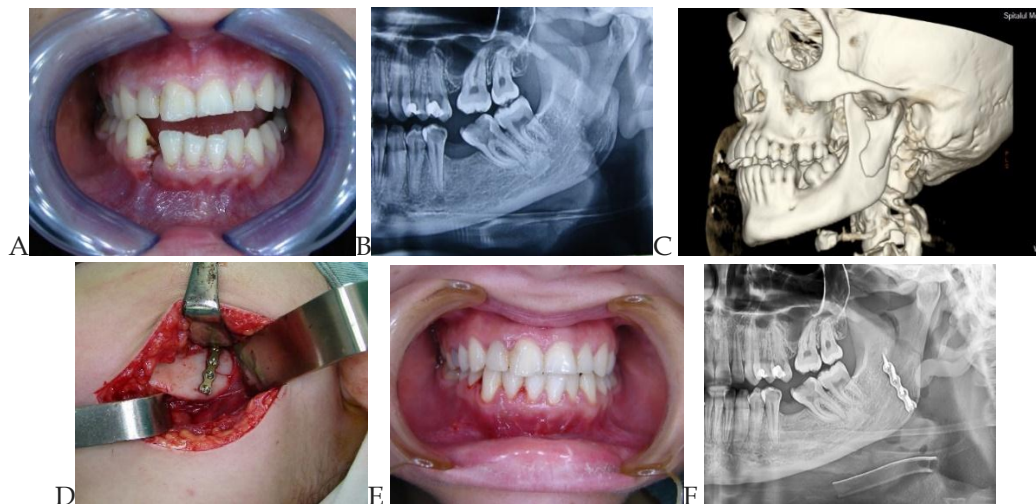


Figure 2. A. Initial clinical aspect with dental occlusion disorder. B. Initial preoperative panoramic x-ray. C. Initial CT scan with 3D reconstruction D. Intraoperative aspect. E. Postoperative clinical aspect. F. Postoperative panoramic x-ray

DISCUSSIONS

In head surgery the first and most important factor in incision placement is facial esthetics and not surgical comfort. Thus, all of the skin incisions must be placed in unseen areas (groove, folds), sometimes distant from the underlying osseous skeleton on which the surgery is performed. For instance, placement of incisions in the oral cavity allows an exposure of the facial skeleton in the vicinity of the fracture, with an intraoral hidden scar. A

second factor governing incision placement on the face is the presence of the facial nerve (cranial nerve VII) of facial expression. The facial nerve branches can be traumatized if incisions are placed in their zone. This can result in severe facial cosmetic deformity, and great functional problems. Thus, placement of incisions and tissue dissections that expose the facial skeleton must ensure that damage to the facial nerve is improbable. From this point of view, oral approach is preferred. A third factor in facial incision placement is the presence of many local important sensory nerves (the facial sensory nerves density is greater than anywhere else in the body). Loss of the local sensitivity can create discomfort to the patient. Thus, placement of incisions and tissue dissections that expose the facial skeleton must attempt to protect the sensory nerves from injury. Other important factors are the age of the patient (because of the possible presence of the wrinkles) and his expectations. Many patients are very concerned regarding local cutaneous approaches because of the resulting facial scars.

The mandibular vestibular approach allows a safe access to the entire mandibular skeleton, from the condyle to the symphysis and a control of the dental occlusion during surgery. It also has the advantage of a hidden intraoral scar. The disadvantages of this approach are the limited access in some regions, such as the lower border of the mandible in the angle area and parts of the ramus, risk of mental nerve damage and risk of lip malposition. [2]

The retromandibular approach exposes the entire ramus from behind the posterior border. The distance from the skin incision to the area of bone fracture is reduced in comparison to the submandibular approach. It avoids the lesions of facial nerve, which is contained within the parotid gland. It has the disadvantage that the incision is not placed in the proximity of the mandible [2, 3] and also the presence of a postoperative facial scar.

An alternate retromandibular approach was described by Hinds. The incision is more vertically, placed 1-2 cm posterior from the ramus, just below the earlobe. Dissection to the posterior border of the mandible is direct, traversing the parotid gland blind. The injury some branches of the facial nerve is also possible. [2]

In 1999, Alpert said: "In most cases open techniques prove no better than closed techniques for most types of condylar fractures. As such, there are few indications to risk the complications of open repair of the fractured condyle". Despite this statement, for a variety of situation, surgeons and patients together can choose surgical treatment. [4]

The final choice of treatment modality for each individual patient takes into account a number of factors, including location of the fracture, position of the condyle, age of the fracture, age of the patient, character of the patient, presence or absence of other associated injuries, presence of other systemic medical conditions, history of previous joint disease, cosmetic impact of the surgery, and desires of the patient. [5, 6]

Patients should be informed about the treatment possibilities and risks: asymmetry and malocclusion in closed procedures, scars and nervous disorders in surgical procedures.

When surgical reduction is indicated, the procedure must be performed precise, the most important landmark is patient's occlusal relations, and it must be followed by a physical therapy and periodical controls. [7]

Ellis and Throckmorton analyzed the occlusal relationships after surgical or closed treatment for fractures of the mandibular condylar process, in 137 patients with unilateral fractures of the mandibular subcondylar process (77 treated closed and 65 treated surgical). The study revealed that patients treated by closed techniques had a worse occlusion compared with patients treated by surgical reduction. [8]

In both extraoral and intraoral approach for subcondylar fractures, some complications may arise (pain, infection, edema, malocclusion, trismus, ankylosis, extrusion of the dentition). Others important complications include avascular necrosis of the condylar head (particularly when the condyle is removed and reinserted in a correct position), injury to the facial nerve, hemorrhage and nonunion. This type of complications can occur also in

closed treatment, especially if physical therapy is not considered. However, some complications are associated more with open treatment. [8, 9]

The main difficulties of the extraoral surgical approach are related to the identification and isolation of the facial nerve. The mucous approach often offers difficult surgical access, poor visibility and limited exposure to the mandible ascendant ramus (particularly in patients with posttraumatic trismus or patients with reduced mouth opening). Other encountered difficulties were the identification of the fractured condylar fragment and his repositioning in the correct anatomic position.

The intraoral approach often requires using a transbuccal system for inserting the screws. This technique involves a small scar in the genio-masseter area that will not be visible in time.

CONCLUSIONS

The absolute indications for surgical treatment in condylar fractures are cases of fractures with considerable dislocations (when orthopedic treatment does not restore occlusion) or the presence of foreign bodies or small bone chips in the condylar zone.

To treat subcondylar fractures, several surgical approaches have been reported and each approach has its own set of advantages and disadvantages.

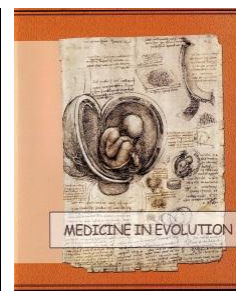
The choice of surgical approach depends on the need to create an optimal view of the whole fracture region, without injury to the facial or sensory nerves and without destroying the vascularization to the condylar head during surgery.

Despite the advances in the surgical treatment of the mandible fractures, we agree with the actual opinion of the majority of the maxillofacial surgeons which recommend a closed treatment for intracapsular fractures, condylar/subcondylar fractures in children, and most condylar/subcondylar fractures in adults.

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Preliminary photographic documentation in esthetic dentistry



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Abstract

The contemporary evolution of the digital photography has revolutionized the way that dental clinicians establish the esthetic diagnosis, perform the treatment and communicate with their patients, the dental technicians and the interdisciplinary collaborators.

Photographic documentation of cases helps not only to inform and motivate the patient, but also to evaluate the work done by the dentist during various stages of treatment. Of major importance is the role that digital photography plays in esthetic analysis of cases and the filling in of esthetic checklist. The material presented in this paper helps to obtain the documentation related to the initial clinical status of the patient.

Keywords: *photographic documentation, esthetic dentistry, esthetic diagnosis*

INTRODUCTION

The use of digital photography is becoming a standard of care for today's modern dental practice, through photographic documentation of clinical status prior to beginning of the treatment [1,2]. Digital intraoral photography has eased the documentation and storage of clinical images of specific clinical situations [3,4]. There are numerous applications for digital photography in dentistry, as following: diagnosis and treatment planning, legal documentation, forensic documentation, patient education and communication, laboratory communication, professional instruction, insurance verification, patient education and motivation [2,5,6].

Aim and objectives

The aim of this paper was to illustrate the preliminary photographic documentation in esthetic dentistry, through an example of a clinical case.

MATERIAL AND METHODS

The patient (female, 30 years old) came into dental office with the purpose to improve the appearance of the smile and to restore the mandibular edentulous spaces (given by the absence of first molars). After discussion (anamnesis) and exo- and intraoral examination, the dentist performed a set of photographs, which served to filling in the esthetic checklist and to formulate the esthetic diagnosis. Originally, the patient gave her written consent to filming / photography in the dental office, and to participate to the medical education.

The equipment used to take the pictures was (fig.1): digital DSLR camera Nikon D7100; Nikon 18-105mm lens, f/3.5-5.6G ED VR; Nikon 105mm macro lens, f/2.8G IF ED; Nikon flash system; retractors; Smile Line contrast device; intraoral photography mirrors. Image settings were: ISO 100; f22 (smile), f11 (macro), f32 (dental arches); exposure time S 125 ss.



Figure 1. a. Digital DSLR camera Nikon D7100 body; b. Nikon lens; c. Nikon Flash system; d. Smile Line contrast device; e. retractors; f. intraoral photography mirrors

The set of photographs included images without removing of lips (facial composition: frontal and lateral view- portrait and portrait with smile; full smile- dentolabial composition: frontal and half-lateral view); images with removing of lips (dentogingival composition:

frontal and half-lateral view; maximal intercuspation position: frontal and half-lateral view; maxillary anterior teeth: frontal and half-lateral view) and mirrors images (maxillary arch and mandibular arch: occlusal view).

RESULTS

A. Images without removing of lips (fig. 2,3,4,5)

1. Facial composition, portrait and portrait with smile. Frontal and lateral view, scale 1/10.

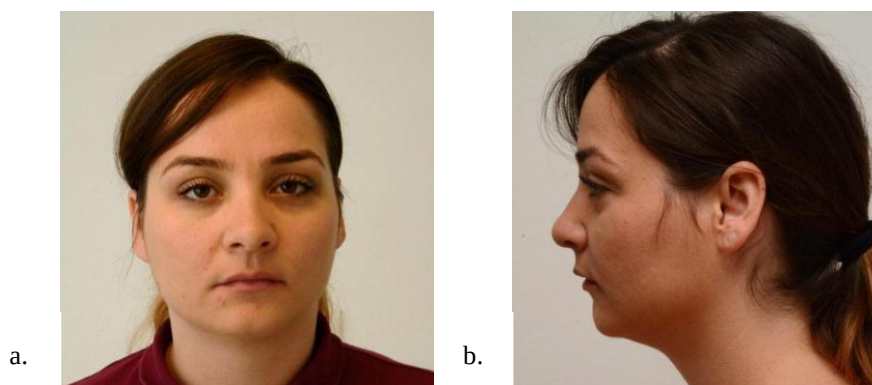


Figure 2. Facial composition- portrait: frontal view (a) and lateral view (b)



Figure 3. Facial composition- portrait with smile: frontal view (a) and lateral view (b)

2. Dentolabial composition- full smile, frontal view, scale 1/2.



Figure 4. Full smile: frontal view

3. Full smile, half-lateral view, scale 1/2

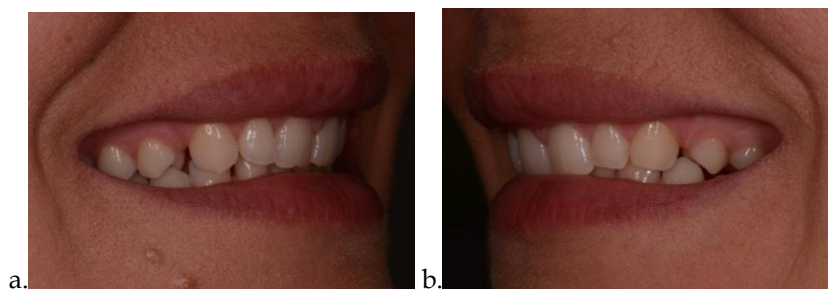


Figure 5. Full smile- right half-lateral view (a) and left half-lateral view (b)

B. Images with removing of lips (fig. 6,7,8,9,10,11)

1. Dentogingival composition, frontal view, scale 1/2



Figure 6. Dentogingival composition: retracted frontal view

2. Dentogingival composition, right and left half-lateral view, scale 1/2



Figure 7. Dentogingival composition: retracted right half-lateral view (a) and left half-lateral view (b)

3. Maximal intercuspation position, frontal view, scale 1/2



Figure 8. Maximal intercuspation position: retracted frontal view

4. Maximal intercuspation position, right and left half-lateral view, scale 1/2

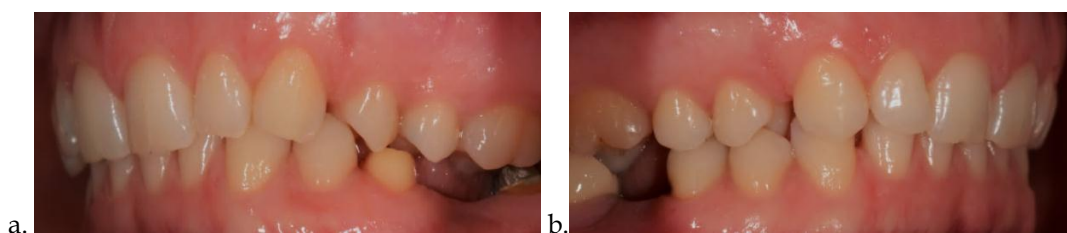


Figure 9. Maximal intercuspation position: retracted right half-lateral view (a) and left half-lateral view (b)

5. Maxillary anterior teeth, frontal view, scale 1/1



Figure 10. Maxillary anterior teeth, retracted frontal view

6. Maxillary anterior teeth, right and left half-lateral view, scale 1/1

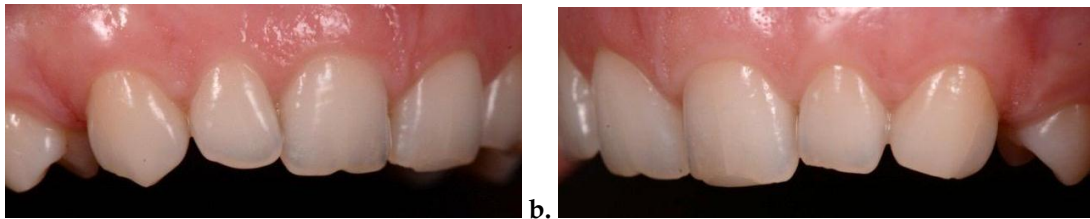


Figure 11. Maxillary anterior teeth: retracted right half-lateral view (a) and left half-lateral view (b)

C. Mirror images (fig.12)

Maxillary arch and mandibular arch: occlusal view, scale 1/1

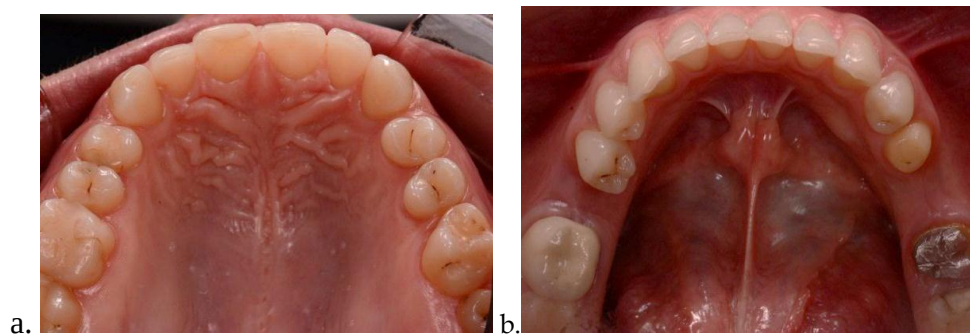


Figure 12. Maxillary arch (a) and mandibular arch (b): occlusal view

CONCLUSIONS

Photographic documentation in esthetic dentistry is a team work and requires trained personnel (physician, nurse), proper equipment and a cooperative patient. The material presented in this paper helps to obtain the documentation related to the initial clinical status of the patient and also to formulate the diagnosis.

The diagnosis accuracy is the point at which the specialist in esthetic dentistry must start any treatment, because it leads to development of an appropriate treatment plan.

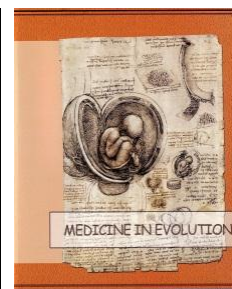
Photographic documentation of cases helps not only to inform and motivate the patient but also the objective evaluation of the work done by the dentist during various phases of treatment.

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Communication barriers in the doctor's office or medical organizations



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Abstract

The relationship between doctor and patient defines the content of medical activity; It is the matrix in which each medical care is maintained and serviced. There are a number of disturbing factors in the medical unit that can interfere negatively in communicating with the patient, no matter if we talk about a practice family medicine, a dental office, a room emergency room, a hospital ward or clinic care. Thus, there are several types of communication barriers found. Barriers in the communication process due to either errors in communication, either hinder or block can occur at any stage of communication, sometimes even before its dowry mental, physical or socio-cultural that interlocutors are presented in the communication process, determinantly influencing them.

Keywords: Communication, doctor-patient relationship, disturbance, communication barriers

INTRODUCTION

The relationship that can be established between doctor and patient depends on several factors, such as [1]:

- institutional framework,
- doctor's type of filed,
- social barriers between doctor and patient, etc.
- honest communication from the patient
- patient's ignorance,
- the circumstances in which he requires medical aid

If the patient isn't well informed, he will be often unsatisfied, confused and uncooperative[2]. The visit, the treatment, any medical act, in this context generally becomes a stressful act[3].

Whenever we use language in its spoken and written form, we follow the same four main goals (whatever the pursued objective is, to explain, to influence, educate or persuade). Those are:

- to be heard;
- to be understood;
- to be accepted;
- to provoke a reaction(a change in behavior or attitude).

The barriers in the communication process either cause errors in communication, either hinder or jam; barriers may occur at any stage of communication, sometimes even before its dowry mental, through physical or socio-cultural interlocutors that are presented in the communication process, influencing them in a decisive way. [4, 5]

The most frequent interpersonal communication barriers are:

- perceptions of reality;
- cliches and stereotypes;

Perceptions of reality

Perception - elementary psychological cognitive process through which unified and fully reflects the characteristics of objects and phenomena when they directly influence on the sense organs. [6]

Perception is psyche feature to reflect the objects' impressions, involving thought, memory, imagination, forming synthetic images of objects perceived, it is based on subjective experience, causing interests, skills, emotional states. Perception involves the presence of different sensations and feelings arising with.

Failure to achieve these objectives in the development of communication means that something is not working properly, that something interfered in sending messages. Anything interferes with the process of communication is called the **barrier** difficulty or noise. Communication barriers occur when the receiver receives the message communicated or not, and misconstrues the meaning of the desired transmitter. Effective communication aims to reduce the reasons for these phenomena.

CHARACTERIZATION OF THE MAIN COMMUNICATION BARRIERS

Communication barriers don't act separately from each other. Thus in the communication process, communication barriers follow, intertwine, influence each other, typically are added together, and in certain combinations can cause serious distortion of information or to impair, or even block communication. The term "noise" used by some authors to name all communication barriers, is the expression of this combined effect, which is seen as a general factor of diminishing communication skills. Analyzing the communication

barriers on types and components, we can find optimal solutions to mitigate their harmful effects, to ensure a stable and optimal communication environment.

As stated by Samuel C. Certo, "communication macrolimitations are factors that impede communication success in a general process of communication." With a broader characterization, communication macrolimitations are the factors acting on the outside of the communication process. The particularities of these factors are that they do not intervene directly in the structure of communication, being different by the material communication which is the actual information. Therefore these barriers can be called contextual barriers. [7, 8].

Technical-economic macrolimitations- Act within the environment in which communication occurs. Thus, the growing need for information, so their increasing volume, due to volume increasing and complexity of social and cultural life, comes at a time, in contradiction with the operating capacity of information networks, but also with the capacity to absorb them by actors of communication: the source and receiver. The solution to counter this barrier is selecting information according to their importance and their distribution only to receivers interested in them. Therewith, choosing optimal redundancy of information, even if using more signs than necessary for reception, it would seem an even more loading of communication channels. According to the growing complexity of information, this is all related to the social-cultural context. Computerization and mathematization of socio-economic processes, the more stressed incorporation of new scientific knowledge in social life inevitably involves an increase in the complexity of the material required to be communicated, which also may reduce the ability to retrieve this complexity by systems communication. Offsetting this macrolimitation solutions can be found in two converging directions:

- simplifying the communication process within and selecting receptor according to the comprehension
- proximity receptor complex through a permanent scientific training.

Economic development is a macrobarrier communication, particularly in external communication between different organizations, but also internationally. Different levels of economic development organizations, states or regions are factors hampering the development of effective communication. Each of the parties in the process has a different system of communication channels, another model of categories and codes, even an object of communication. Beyond the differences in language, which can be mitigated through good organization of the meanings of transfer, differences remain technological, operational, conceptual which make impossible the effective engagement of information systems. The currently difficulties experienced by the countries acceding to the EU and NATO largely, are due to communication barriers caused by different levels of economic development. This area is the most difficult to address in terms of countering solutions. The approach of economic level development is a very lengthy desideratum without spectacular achievements in the short term. However, certain measures are taken internationally, especially on rapprochement line models and communication systems. To this end, developed countries as well as international organizations invest considerable sums in both, the modernization of communication infrastructure and the introduction into the education systems of countries lagging behind, new concepts and communication patterns.

Cultural macrolimitations. Cultural context has a major significance for determining the effectiveness of communication. Jean-Claude Abric observed that "strictly speaking, the microculture of an organization, an institution, a given social group determines types of communication and a system of interaction that could be entirely specific. In a broad sense, each of us knows from experience that the attempt to communicate with interlocutors from a different background - in the absence of suitable means of encoding and decoding information transmitted - may be a step of extreme difficulty. " Major problems arise in terms

of religious differences. It is known that various religious doctrines favors certain symbols, meanings, behaviors, attitudes and practices that go beyond religious experience in practical experience, including the communication. Therefore, communication between individuals or groups of people with different religious affiliations is made sometimes in difficulty. To all this are added differences related to the customs, traditions, mentalities, incorporated into different systems and different ethical codes.

A cultural macrobarrier is the language barrier. Communication, especially in multi-ethnic organizations, is strongly affected by linguistic differences between members of these organizations. We already know that in attempting of a large number of Romanian citizens to find jobs in developed countries, the first barrier is not speaking the official language of that country. At the level of communication between organizations, the barrier is easily countered by special training of interpreters. At the domestic level organizations, neither the time nor the organization's resources don't permit the use of the interpreter.

Countermeasures of linguistic barrier communication:

- The development of certain actions of mutual culture knowledge in communication relationship;
- Identifying those habits, mentalities, communication partners' rules of conduct that have significance for communication;

Each partner's respect for religious beliefs without discrimination. They are counterproductive:

- negative discrimination (banning, blaming, oppressing, binding)
- positive discrimination (difference stimulation, proselytizing encouragement, granting bonuses based on religion etc.);
- Thorough preparation of interpretation channels when running certain communication acts between human groups or individuals who use different languages. The attempt to use the partner's dialogue language by psychologists din terms of approximate knowledge of it is counterproductive and may cause significant losses in mutual understanding.

Socio-political macrolimitations. Neglecting their influence on communication would however be a mistake, given that occur quite often communication difficulties caused by them. It is enough to highlight the difficulties of communication in a human group in which its members belong to or are sympathizers of political parties are in a state of opposition. When these members of the parties have also senior management functions, communication gap is even more evident with all recommendations of those who claim that political sympathies can be circumvented. Counteracting the social-political barriers is almost as hard as the techno-economical barriers and also dependent on them. It means continual updating of legislation, international openness, and international assistance to disadvantaged segments of society and the political class in the political maturation, changing political message from a destructive one into a constructive one, assimilation of domestic and international political game rules

COMMUNICATION MICROBARRIERS

Considered by Samuel C. Certo as "success factors hindering communication in a specific communication process" microbarriers can be called also process barriers, operating from the privacy process, its components and phases. The literature assigns the greatest importance to this type of communication barriers. Being relative to a process that can be isolated and analyzed on parties, these types of barriers seem easier to conceptualize and measure. Content analysis and significance of these barriers is considering the components of the communication process (source, channel receiver) and the relationships between them.[1,11-14].

A. Environmental barriers

The environment of unit's medication may cause communication barriers for the patient. Here are some examples:

- inadequate furniture in the medical center (example: improper seat size, existence of old furniture, antique scale, bed with holes, drilled dental chair, stained, etc.);
- small waiting room, heaped (the patient cannot enter the waiting room from congestion or noise), inadequate furniture in the waiting room, mismatched magazines, unsuitable TV programs, etc.;
- the phone ringing constantly and no one answers, the whole staff being busy with patients (phone at the same time can be stressful);
- presence of another person between doctor and patient (when another person comes between patient and doctor communication elements are altered);
- lack of space for intimate discussions between doctor and patient (space privacy encountered especially in hospital wards, in emergency rooms reception);
- ambient temperature of the medical office (too cold or too hot by lack of adequate heating or air conditioning);
- malodor (different situations: the smell of sweat, faulty drains, tightly enclosed space, disinfectants malodorous etc.);
- medical unit noises from the external environment (construction site nearby, rehabilitation of street, traffic, medical office located at an intersection where horns are heard frequently, etc).

B. Barriers related to patient

- patient's mistrust on medical currant (previous unpleasant experiences, the doctor is inexperienced or has held inadequate attitude etc.);
- patient anxiety due to illness (pain, fever, cough, stress, limitation of movement etc.);
- patient typology (shy, irritable, nervous, silent);
- the patient's age (infant, child, elderly person);
- disabilities (of speech, cognitive, etc.);
- prejudices of the patient (e.g., the patient considers that medical and if not ill, the doctor prescribes medications that seem important, etc);
- unpleasant experiences in the past;
- fatigue;
- personal problems;
- semantic barriers;
- the patient does not know how to listen or is not ready to listen;
- lack of communication skills;
- different cultural model;
- lack of mutual respect.

C. Barriers due to doctor:

- his shyness;
- fatigue;
- personal problems;
- semantic barriers;
- inexperience in patient's communication, lack of communication skills;
- choosing inappropriate messages (the message is ambiguous because of inappropriate words, using specialist language);
- lack of trust in interpersonal communication;
- fear of not cope to patients' questions;

- gaps in training;
- inattention to a patient (running multiple tasks simultaneously);
- prejudices, false perceptions;
- do not provide patient feedback;
- lack of mutual respect.

D. Other barriers to communication

Outside the barriers identified above may occur other barriers such as:

- multitude of activities in the medical room, medical unit;
- lack of effective communication time (crowded waiting room and the doctor hurries);
- activities understaffed medical unit;
- language barriers. [1,9,10,11,12]

So, effective communication involves expressing open and active listening, without the existence of communication barriers, while ineffective communication supposes the presence of communication barriers, parties refusal to share openly their feelings and refusing to listen to what the other one has to say [1, 13].

Effective communication steps are:

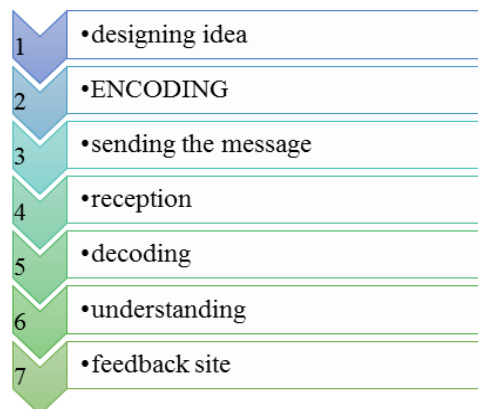


Figure 1. Steps in effective communication [14]

For effective communication must take into account that:

- All people can communicate in one way or another, it is important to encourage them
- Communicating requires self-knowledge and self-esteem
- Communicating involves awareness of each other's needs
- Communicating involves knowing how to listen
- Communicating involves giving a message that you understand each other's
- Communicating means understanding a relationship processuality
- Communicating suppose to know how to express your feelings
- Communicating involves accepting conflicts
- Communicating involves the assumption of conflict resolution
- Communicating means understanding messages

Ineffective communicate means to take into account when you send or receive information, only from their own needs or other's strict needs. This communication determines a passive or aggressive behavior towards each other.

We can talk about good communication, only if the balance inclined towards the first communication component or at least if you keep it in balance.

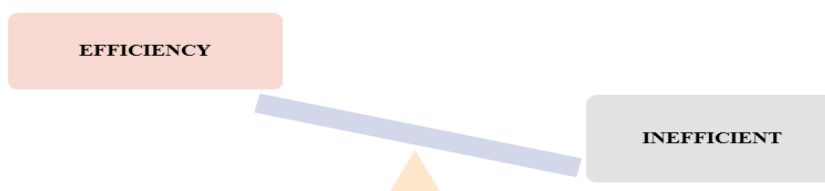


Figure 2. Communication balance [1]

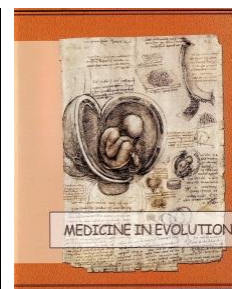
The relationship between doctor and patient defines the content of medical activity; It is the matrix in which each medical care is maintained and serviced. When the patient is for medical services, he expects primarily to be heard, understood, to recount all the sufferings, not necessarily those strictly related to the specialty which presents, to answer the question and his concerns to leave doctor with a greater peace of mind and then to be treated. Wellness consultation at the end of treatment depends not only on treatment received, but also trust that the doctor has earned the patient's face through communication. Obviously, all this requires energy from the doctor for active listening to show empathy to identify patient expectations and especially to answer them.

Modern doctor should know the typology of each patient, must know how this perceives it, is necessary that its relationship with the patient should not be limited to the development of services that the latter does not know very much. Doctor as a good psychologist will perform a close proximity with the patient. Emotional opening of the doctor on the patient is "the keystone in medical psychology", dispelling anxiety, uncertainty and humanization of care.

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Leadership in dental health services



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Abstract

Dental competitive practice imposes as a priority necessity the management practice. In most cases, the doctor is responsible for both the clinical performance of the cabinet and for its success, as well as business. Very few dentists have extensive knowledge of business management, leading sooner or later to a chaotic activity in the cabinet. The solution in this case is the creation and documentation of step-by-step management and marketing systems. In this way, the physician may delegate absolutely all non-medical activities. Clearly, even if it represents a challenge for physicians, forming a team is essential. Without an effective team-building, is difficult to take care of patients and to lead a team at the same time. Some doctors believe that a teambuilding will be easy for team members because they share the same job. The definition of team is "a group of people who share the same vision." Successful leaders can take a group of individuals to develop into a team through clear communication, training and meditation. As a leader, the doctor should determine the role of each member in achieving the cabinet vision.

Keywords: Medical business management, leadership, teamwork, communication, dental health services

DEFINING LEADERSHIP IN HEALTHCARE ORGANIZATIONS

Lately, due to widespread use of the concept of leadership, there were a lot of debates about the definition and content of his views ranging from extreme (counterbalance) to confusion (overlapping).

To define the leader we should remind some currents in which they are discussing the difference between leader and manager, clear distinction between the two concepts, confusion between the two concepts, leadership seen as part of management, the manager saw as part of leadership, partial coincidence relationship of the two notions of spheres.

Bennis one of the advocates of the concept shows that there is a *clear distinction between the two concepts* and believes that:

- manager owns and the leader develops;
- the manager focuses on systems and structure, the leader focuses on people;
- the manager administers, the leader innovates;
- the manager is based on contract, the leader inspires trust;
- the manager imitates, the leader conceives;
- the manager has a short-term perspective, the leader has a long-term perspective;
- the manager asks how and when, the leader asks what and why.

The manager is seen as an administrator who makes the organization to work, the leader is one who provides motivation for people to go a certain direction [1, 2, 3, 4, 5]

- the manager provides and plans, the leader creates an inspiring vision;
- the manager sets budgets, evaluates investments, spending, while the leader designs a long-term strategy by showing flexibility in budgetary reasoning, anticipating opportunities, weaknesses;
- the manager organizes, the leader guides, he is adapting, showing opportunism in action;
- the manager controls, the leader gives a motivation in quality and self-control;
- the manager measure and recovers deviations, the leader goes further, making vision to evolve, adapting the positioning of the organization and its products, with an ongoing effort to anticipate the market and keep under observation.

According to [6] leaders are distinguished from managers, according to four criteria (Table no.1)

Table 1. Differences between leaders and managers [7]

Criteria	Categories of leaders	
	leaders	managers
Purpose	Manifesting active personal attitudes	Manifested impersonal, passive attitudes
Concept about work	Stimulates work, provides and creates opportunities of choosing it	Coordinating and balancing work. Resorting to value compromises
Relations with others	They are empathetic, pay attention to the significance of actions and events	Less emotionally involved in relationships with others
Self-perception	Have a lower self-identity, facing change	Identifies the need to maintain the present order, they are more conservative

This trend assumes that the manager has increased with the industrial revolution and technological, in order to regulate control and order in the workplace, leading to obedience, lack of initiative and creation of the subjects, which led Alan Briskin [8] to confirm that *"It began as a method of control, allowing them to channel managers to motivate their subordinates productivity has become a sort of psychological contract expired"* to consider that management is an outdated concept.

The management is very good in a stable world, with stable markets, except that now the world has changed dramatically in recent times, and being in a constantly changing, so now is needed the *leadership*. Leadership is no longer seen as an improvement or a management transformation, but a completely new concept which removes the first. We quit the objectives, targets, rules and pass on to motivation, self-control, free enterprise, without control, only collaboration and exchange of ideas. This approach could lead to anarchy or even to system dissolution.

Supporters of the concept say that the two terms merge *"the leadership is also a manager and therefore they don't see content differences, and as such, it considers only a fashion"*. They also believe that an organization can not be conducted without hierarchy, structure and rules. Such an approach is not appropriate to the world we live in, which is in continuous evolution, it cannot lead to performance.

Kerr and Schriesheim [9] consider the leadership as a subset of managerial behavior, *leadership containing just one of the ways in which management ensures organizational effectiveness*. Jaques and Clement[10] show that the core managerial hierarchy are in managerial roles and a good manager includes a component of leadership. In Romania, the adepts of this theory are teachers Nicolescu and Verboncu.[11]

Hersey, Blanchard and Johnson think of the manager as part of leadership, the manager being one of the instruments through which the leadership is achieved. They find *"In essence, leadership is a broader concept than the manager. The manager is a special type of leadership where the aim is to achieve the basic purpose"*. [12]

Mielu Zlate believes that previous approaches are unsatisfactory, considering that this leadership and management has specific elements that ensure their individuality, autonomy, and common elements that facilitate interaction and mutual intensification. He believes that [13]:

- both leaders and managers meet approximately the same functions: foresight, organization, coordination, training, control. It is possible that the same person to be a leader and manager;
- it is possible that leaders and managers have about the same capabilities and skills, but in different proportions, with the possibility that if the leaders prevail human and conceptual skills, and managers, technical ones;
- mutual intensification of traits, skills, balance or their unbalance, compensation or conflict between them are only possible due to possession by the same person both leadership qualities, and those managerial

Leadership must be seen as a process in which members of the organization interact, is objectified and empowering, this process is reciprocal, transactional, transformational, oriented. Excellent leadership must ensure optimization between relational orientation, socio-emotional, emotional and tasks orientation, purpose, production, administration.

The structure of health organizations, especially at the hospital level is different from the industry. The difference is especially from each different problematic sections, some problems are encountered on polling surgery to those on gastroenterology, emergency. ATI, etc. This difference makes no matter how competent, professional should be the leader in health, these differences may not include all sections.

The health leader should take priority on following powers (Table 2):

Table 2. Skills of the leader in health [7]

Categories of competence	Interface
Self-control (EQ)	• <i>self-control</i> - Handling emotions and impulses that disrupts channeling it in a positive direction; cold blood and calm under stress or crisis; • <i>transparency</i> - Flexibility in thought and action; • <i>ambition</i> - High personal standards, pragmatism, challenging goals and risk taking; • <i>initiative</i> - Take advantage of opportunities, creates opportunities, consciously deviate from rules and patterns; • <i>optimism</i> - Obstacles become opportunities, not hardship, positive thinking: "glass half full".
The sense of the situation (social intelligence)	• <i>conscious</i> context and meanings that they create it; • <i>understand</i> feelings and intentions; • <i>know</i> unwritten rules, social paradigms and conventions; • <i>show interest</i> and respect for the people around you.
Presence (Social Intelligence)	• <i>Yes</i> feeling of trust, professionalism and kindness; • <i>It has science</i> listening, creating and giving a confidence and efficiency for establishing connections; • <i>is the express image</i> friendly or rather sullen, stubborn, provocative; • <i>He has charisma</i> - Grace, passion, social energy.
Clarity (Social Intelligence)	• <i>It has the ability to clearly express its</i> thoughts, opinions, ideas and intentions; • <i>He can think what he says and say what he thinks;</i> • <i>using the right language</i> for the right place; • <i>uses short and concise sentences;</i> • <i>says exactly what you need when is needed;</i> • <i>conscious psychological phenomena</i> beyond the language area
Empathy (Social Intelligence)	• <i>sensitive subordinates</i> et al; • <i>encourages the progress of others;</i> • <i>interprets, thinks, sees and hears the other's emotions.</i>

LEADERSHIP IN DENTAL HEALTH SERVICES

Dental Medicine is a health profession that has a dual purpose:

- *to provide health orodental services for the population;*
- *to profit as a small business.*

As a *care service* of oro-dental health, dentistry offers quality specialized care for each patient, so respecting the standards set current legislation in force and the profession itself.[14]

Dental competitive practice imposes as a priority necessity the management practice. Dental management is in no way comparable or similar to a type of a set of marketing techniques to sell more, earn more money, or manipulate the patients.

The relationship with the patient often seen as a "customer" or "consumer health" is actually an internal cabinet and not a facade. Unfortunately, some of us have lost along the way the essential: the notion of "trust" that cement the relationship between doctor and patient: this is not just a subjective concept of minimum morality, but also and above all, framed legally (Ethics code of the dentist).[15,16]

It is possible for a dentist to be able to imagine that success lies in the commercial and marketing techniques as they can be visibly materialized in money, and to make a dental practice in a business like any other.

Management is not a concept or an action charming or seductive: it is at least one additional workload when we are in the implementation phase of a management change or reorganization required an approach to quality. Management is a set of universal rules that every dentist should know, but the most important thing you need to learn is to adapt to the

specific medical and dental practice human. Just here should define the role of "Management Consulting" which teaches the practitioner to adapt the theories and practices of management infrastructure and human resources in a dental office.[14-17]

In most cases, the doctor is responsible for both the clinical performance of the cabinet and for its success, as well as business. Very few dentists have extensive knowledge of business management, leading sooner or later to a chaotic activity in the cabinet. The solution in this case is the creation and documentation of step-by-step management and marketing systems. In this way, the physician may delegate absolutely all non-medical activities.

Clearly, even if it represents a challenge for physicians, forming a team is essential. Without an effective team-building, is difficult to take care of patients and to lead a team at the same time.

Empowering still not makes part in many dental cabinets. Many doctors have a sense of personal responsibility for everything that happens in cabinet. This happens for several reasons: physicians tend to be perfectionists - if something goes wrong (administrative, financial, customer care), they often feel the need to intervene, team members have experience; opportunity to engage properly accredited and experienced persons is rare. Capabilities required for a particular job is developed through training; often, the doctor intervenes and solves the problem, instead of learning the person what to do and making it responsible for the activity.[18]

The team development team ultimately comes down to its professionalization. This means:

- Defining what is needed for each task
- Ensuring that each member understands what is responsible for
- Performance measuring against objectives

Intangible things such as staff attitude, are difficult to measure; but most daily activities that take place in a cabinet can be converted to numbers, making them easier to follow. [19]

Define the desired performance objectives for both the cabinet and for each person. Some sample objectives for the person at the reception [20]:

- 90% of active patients permanently scheduled
- 10% in missed appointment reduction
- confirming appointments for the next day

It is recommended to split the goals into daily or weekly tasks, for ensuring their achievement.

Empowerment plays an important role in team development. By creating specific and measurable objectives, assign responsibilities and track progress, the dentist creates a system that motivate their team to excel, which inevitably leads to the development of dental practice.

Some doctors believe that a teambuilding will be easy for the team members just because they share the same job. But, are they sharing the same vision and objectives? In many offices there is a high level of stress because the team members don't work in the same direction as the doctor for the same purpose.

The definition of team is "a group of people who share the same vision." Successful leaders can take a group of individuals to develop into a team through clear communication, training and meditation. [3,7,10,15,19,20]

As a leader, the doctor should determine the role of each member in achieving the cabinet vision. For a cabinet to be efficient, each team member must have a clear focus on what has to be done, to lead the cabinet on the right track [21].

It is important for the team to:

- use positive language that creates enthusiasm and motivation
- focus on the patient's benefits during treatment plan presentation
- continuously build value for the cabinet's services
- ask for the opinion and help of colleagues on various issues regarding the design of this attitude

Doctors should provide positive feedback to team members when they do a very good job. The team must be complimented when doing well in a tough situation, praised when their manner of speaking convince a patient to accept treatment and thankful for the effort you submit to the cabinet success.

The business manager, the dentist or specialized management is constantly the leader of a dental cabinet (CMD) in Romania. A good leader is a vital person for [1,5,7,20-24]:

- *maintaining and /or increasing turnover;*
- *business system implementation;*
- *business management,*
- *and, not least, in maintaining good communications between dentist and dental technician (rendering services for public dental prosthetic), human resources, patient and community.*

In this particular context, it supports the role of coordinator and entrepreneur and delegate responsibilities as follows:

- *divide the work between collaborators;*
- *delegates responsibilities with secondary health professionals;*
- *additional business management for the responsibility manager (assistant manager).*

The management and leadership, generally and specifically, is vital to professional success in the business of CMD.

In this context it is particularly important **the management style** and **managerial communication**.

There are three types of leaders in CMD leadership:

- *authoritarian;*
- *participatory;*
- *free.*

AUTHORITARIAN MANAGEMENT

Dentist with authoritarian management style alone will take the necessary decisions without consulting members of the team work, human resources employees are passive and waiting for indications for solving the problems of CMD. [25]

Features:

- It allows the dental technician to take all decisions as **central authority figure**.
- Human resources are involved only in the actual process of service delivery, but no access to the CMD management activities.
- working group members are simply people who perform the given orders.

- It has a low efficiency, although it has the obvious advantage of requiring less involvement than other managerial styles.
- is used in many government institutions, administrative or education, its use is limited in the health and dental private practice this style should be used with caution and only when circumstances require (eg solving emergencies).
- communication possibilities are reduced, the dentist will not listen and will not be able to properly receive ideas and information coming from members of his team working and will not consider.

FREE MANAGEMENT

This management style is characteristic of professionals performing routine dental practice. [22]

Features:

- not conferring to any person managerial responsibilities.
- The doctor will not provide information to members of the working group and each person will execute common tasks, entered into routine.
- Team members will do their work without trying new techniques because it is easier to "*practice*" their profession in a way already known.
- This management style is refractory to new and changing at that time, lowers the quality of works and services and hence loss of orders and ... *bankruptcy*.
- Application of management freely in Romania is especially visible in the public network and sometimes in private during the onset of a CMD.
- Resistance to new of the team members can be overcome only by developing collaboration among team members.

He is likely to continue only in the context:

- *periods of crisis* (due to a chronic shortage of financial and material resources when CMD aims only to survive);
- *of inappropriate tasks*;
- or when, after a long practice routine doctor resistance from team members if they try to introduce new practices.

PARTICIPATORY MANAGEMENT

Existing management styles of participatory management is considered as the best for CMD.

Features:

- recognizes the importance of each team member in achieving the goals set by practice and providing quality health services;
- it requires the involvement of all the team members in the decision-making process (in accordance with each preparation and the role and place of each team);
- each team member is considered a "human resource" whose knowledge and information should be managed through appropriate management;
- Team members need to be professionally competent person able to acquire new information and new techniques to be able to adapt to new ideas and change, and be willing to take responsibility and make decisions in everyday professional activity;
- the team is functioning together to give oral-dental health services of the highest quality, appropriate health needs, in a cost / benefit ratio favorable.[21-23]

Communication skills and communication management develops on the basis of characteristic features of each team member, such as:

- *openness to experience;*
- *enthusiasm*
- *integrity, honesty;*
- *acceptance of the value of other team members;*
- *confidence in his own powers;*
- *courtesy*
- *sense of humor;*
- *recognizing the needs of others;*
- *the ability to be a good listener.*

Confidence in own strength - it is the ability to believe that an activity can provide professional quality. This is a prerequisite for the continuous improvement of quality of services provided. You must have good mental health and accentuate your positive features to enhance confidence in his own powers. [25]

A manager who has the self-confidence to accept their responsibilities, adapt to change, is always interested in improving the activity of CMD and involved in the decision process. Such a manager will know and will highlight the marketing needs of the practice that will adapt to social requirements. He also runs the risk being able to impose change and overcome resistance to new team members work.

Openness to experience - *The medical profession is dynamic*, in order to give health care to underserved populations, the physician should be open to experience, be motivated to implement new techniques to adapt to buzz scientific, technical and technological field. Team members with a routine practice long are frightened by the idea of new and change, and hence resistance to implementing the new. Effective management communication between manager and team members is a factor that can reduce resistance to change.

Resistance to change opposable by the manager, when activity at the CMD is in accordance with certain standards considered acceptable level over the change would not, in his vision, neither acceptable nor necessary, supracalitatea is expensive and the investment is not justified by quality improvement services rendered.[22]

Accepting the value of others - Professional value of each member of the team is the sum of knowledge and experience to some moment. It is important for the manager to assess with maximum objectivity professional value of its employees and to motivate it to provide services of the highest quality to patients. It is imperative that the physician staff to accept what can (each of them) and not for what manager would like them to be. [17]

Effective listening - requires a thoughtful listening, manager understanding the sent message before giving an answer. This type of listening is creating ideal conditions for a better understanding of the situation. A manager must be a good listener, educated in listening effectively, in order to understand the message and to sense what can hide behind the message received. Effective listening can be restricted / blocked for various reasons (objective, subjective) as: tiredness, loss of hearing, dental distraction to the execution of maneuvers, misconceptions and false premises etc. In this context, the manager can not actually listen to the message sent.

Recognizing the needs of others - all team members need recognition and appreciation for their contribution to the effective exercise of professional and organizational success. Recognizing and rewarding employees work and thus their needs for professional development creates conditions for a good professional cooperation to achieve organizational objectives proposed.[12-16]

Character traits necessary in relational system development of the team:

- *honesty* - developing a correct behavior towards others, whether patients, employees or business partners;

- *integrity* - Developing responsibility for their actions, risk taking and its own mistakes without blaming others for any failures;
- *enthusiasm* - interest to their professional activity, sincere desire for professional development and involvement in professional activities of the team;
- *insistently* - taking the initiative and assuming the risk until professional tasks or solving a situation favorable;
- *sense of humor* - ability to pass with a smart and well-placed joke over stressful situations, to resolve conflicts and to diminish tensions at a time between different members of the team work;
- *label* - Behavior, or rather "manners" business; "good manners" can lead to the promotion of CMD, success in business and building a good relationship system, so doctors collaborators and business partners.

The most difficult for a manager dealing with a direct management and control of dental offices is to harmonize the following parameters: the technical specialty (if applicable), ethics, medical degrees and professional expertise in the management team, the skills profile of human resources (leverage technical, behavioral and motivational relational), its development objectives, and above all, articulating its decisions and proactive vision of his cabinet. If team members know clearly that they are powers have handy systems and know that they are responsible for their performance, their performance will improve [23-25]. Cabinet discusses performance in monthly meetings with employees. Responsible for each objective submit a performance report and if any problems occur, the whole team helps to improve the system, finding solutions in a constructive atmosphere.

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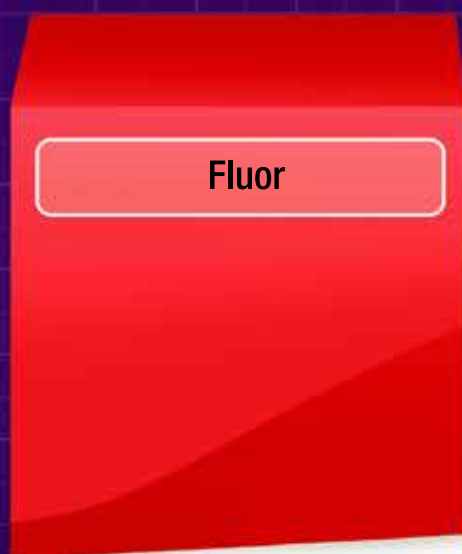
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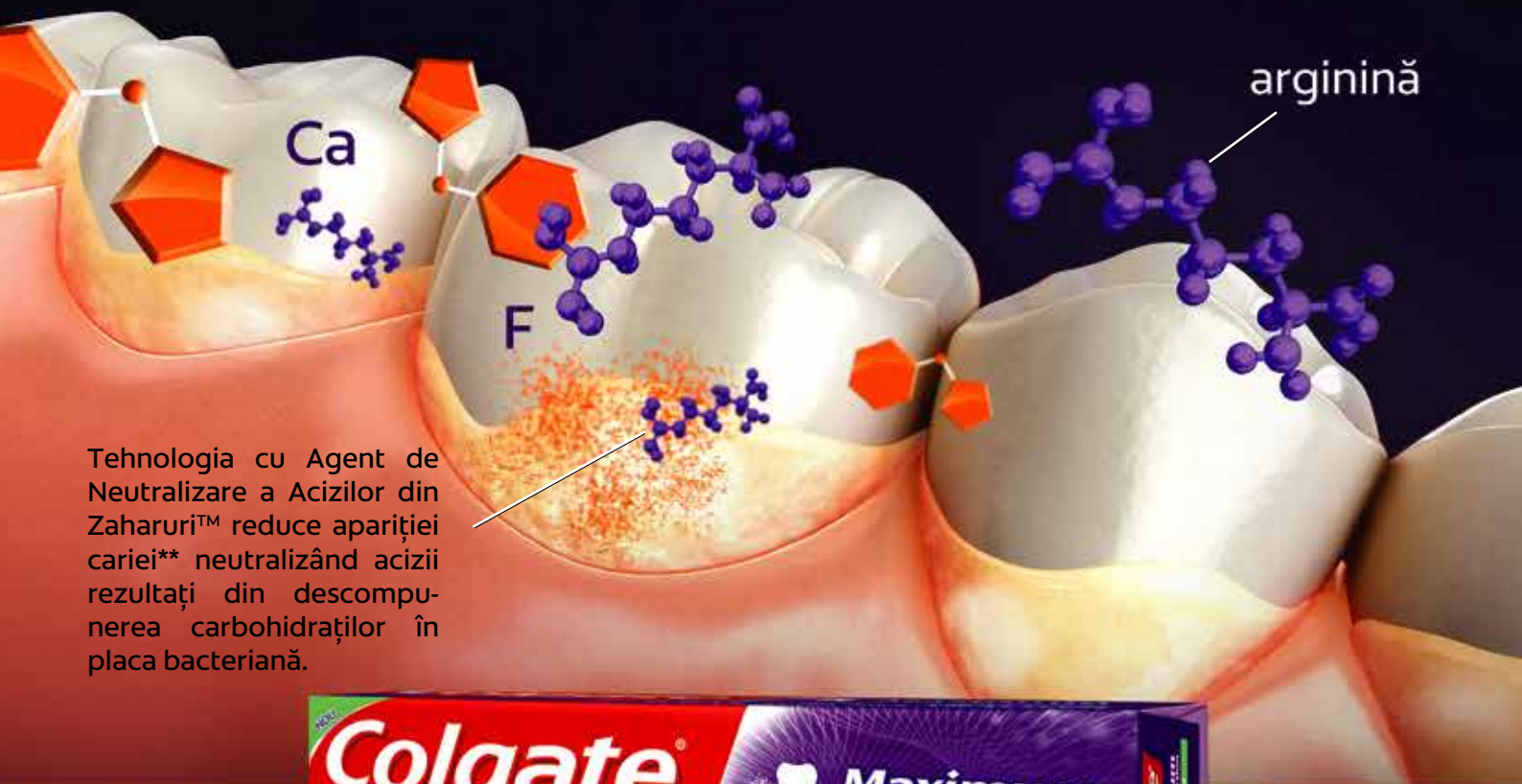
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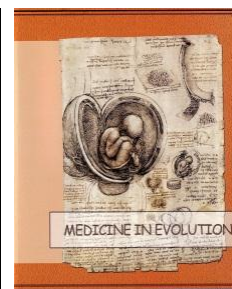
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ERRATA - Cardiovascular risk profile of remote process of coronary dezobstruction



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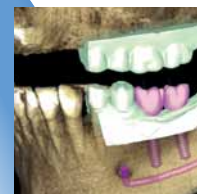
ERATTA

Table no. 3 Evaluation of cardiovascular events occurred after myocardial revascularization surgery

n= 341			Cardiovascular Events						
	Death cv	Death non-cv	Restenosis	AVC/ AIT	Pacemaker implant	New by-pass	New stent	Hearth failure hospitalization	New diabetes
n	0	4	3	1	3	5	3	5	3
%	0	1,17	0,87	0,29	0,87	1,46	0,87	1,46	0,87



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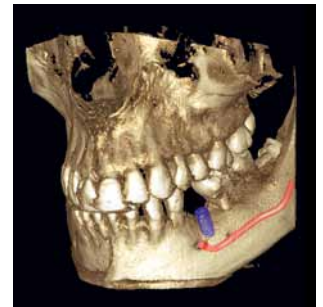
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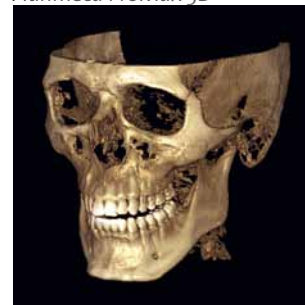


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- general reviews: 6-8 pages
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The paper will be edited according to international editing rules for manuscripts. The title will be written in capital characters and it will be followed by the name and surname of the author (authors), followed by their place of work (place where the paper has been elaborated). Studies and researches will be followed by a brief abstract, followed by 3-4 key-words.

The body of the paper will be structured on the following chapters: introduction, aim, objectives, material and method, results and discussions, conclusions. The references will be presented alphabetically and in conformity to the Vancouver Convention, including:

- for articles: name of the authors and surname initials, title of the article in the original language, title of the journal according to the international abbreviation system, year of issue, volume, number, pages;
- for books: name of the authors and surname initials, volume, publisher (editors), city of publishing, year of issue.

Citation of references inside the body of the paper will be put between brackets, Harvard style (author, year) or Vancouver style (number in square brackets or superscript). Cited reference titles will be selected, maximum 6 for studies and case presentations and 12 for general reviews. Acceptance, rejection or the need of alterations in sent materials, or in inconography, will be communicated to the authors in due time. For this, the authors will indicate the person and address for correspondence (phone number, e-mail address). Given the less pleasant experience of the editorial board with some articles being rejected because they did not meet publishing criteria, we decided to support those who intend to publish in this journal by detailing the way such a paper should be elaborated, as well as our requirements.

Except some particular aspects concerning this journal, the following details are general requirements asked or imposed by other journals as well. Conditions to be met in order to propose a paper for publishing. The main author has the responsibility to make sure the article has been approved by all the other authors. The journal will have copyright

for papers accepted for publishing. The editorial board reserves the right to change the style and dimensions of an article (major changes will be discussed with the main author) and to decide the date of issue.

2. FIRST PUBLICATION

The editorial board will not consider a paper already reported in a published general review or described in a paper proposed to or accepted by another journal. This does not exclude papers which have been rejected by other journals. Also, papers which have been presented at a scientific meeting will be accepted for discussion if they have not been entirely or partially published in a similar publication. „Multiple“ publishing of the same study is seldom justified. One of the possible justifications is publishing in a second language but only if the following conditions are met:

- Editors of both journals involved are fully informed;
- Priority of the initial publication will be respected by a minimum publishing interval of two weeks;
- For the second publication, a shortened version will suffice;
- The second version strictly reflects data and interpretations in the first;
- A footnote may state: „This article is based upon a study initially published in [title of the journal]“.

3. PATERNITY

Paternity must reflect the common decision of the coauthors. Each author must have participated enough to take public responsibility for the content. A paper with collective paternity must have a key person responsible for the article.

4. COPYRIGHT

In order to reproduce materials from other sources, written agreement from the copyright owner must be obtained:

- photographer – for unpublished photographs;
- hospital where the photographer (physician) is employed – for unpublished photographs performed during the employment period;
- initial publisher – for a table, picture or text which have previously been published elsewhere.

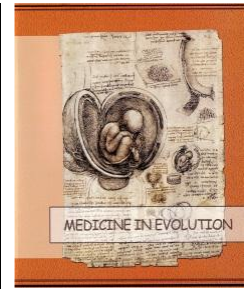
5. ETHICAL ASPECTS

Do not use name of patients, initials or hospital observation charts numbers. If a photograph of a body part which could allow direct or deductive recognition of the patient needs publishing, then the paper must be accompanied by the written consent of the patient and clinician, as well.

6. PRESENTING THE MANUSCRIPT

6.1. CONTENT OF THE PAPER - INDICATIONS FOR ORIGINAL ARTICLES

Paper title [Book Antiqua 20, bold, left alignment]



Surname N.¹, Surname N.² [Book Antiqua, 14, bold]

¹ *Author Affiliation (DEPARTMENT, FACULTY, UNIVERSITY, CITY/COMPANY) [10, italic]*

² *Author Affiliation (DEPARTMENT, FACULTY, UNIVERSITY, CITY/COMPANY) [10, italic]*

Correspondence to:

Surname Name: [10, italic]

Address: [10, italic]

Phone: +40 [10, italic]

E-mail address: [10, italic]

Abstract [Book Antiqua, 12, bold, justify alignment]

Recommendations for original studies

Original studies must include a structured abstract of maximum 150 words, containing the following titles and informations: Aim and objectives; Material and methods; Results; Conclusions; Key words: give 3-5 key words; The abstract will be translated into an international circulation language.

Keywords: Innovation, technology, research projects, etc. [Book Antiqua 9].

INTRODUCTION [Book Antiqua, 11, bold, left alignment]

Introduction presentation of general aspects, in the context of the approached theme.

Introduction include **Aim and objectives** – Define the aim of the article. Briefly expose the rationale of the presented study or observation. Make strictly pertinent referrals and do not exhaustively review the subject. Do not include data or conclusions from the paper.

There is a limitation of 4/6 pages. All pages size should be A4 (21 x 29,7cm). The top margins should be 2 cm, the bottom, right, margins should be 2cm and left margins should be 2,85 cm. All the text must be in one column and Book Antiqua font, including figures and tables, with single-spaced 10-point interline spacing.

***Aim and objectives* [Book Antiqua 11, bold italic, left alignment]**

The text included in the sections or subsections must begin one line after the section or subsection title. Do not use hard tabs and limit the use of hard returns to one return at the end of a paragraph. Please, do not number manually the sections and subsections; the template will do it automatically.

[Book Antiqua, 11 point, normal, justified alignment].

MATERIAL AND METHODS [Book Antiqua, 11, bold, left alignment]

Describe the selection of observations or subjects for the experiment (including controls). Identify methods, equipments (with the name and address of the manufacturer in brackets) and give sufficient details on procedures. Give references for the selected methods, including statistical methods; offer details and brief descriptions for previously published methods which are not well known; describe new or substantially modified methods, justify their use and assess their limitations. Precisely identify all used drugs and chemicals, including generic names, dosage and administration ways. Describe statistical methods with sufficient details for reported results to be verified. Whenever possible, quantify discovered aspects and present them with appropriate measurement indicators for the uncertainty or error of measurement (such as confidence intervals). [Book Antiqua, 11 point, normal, justified alignment].

RESULTS [Book Antiqua, 11, bold, left alignment]

Present results in a logical succession as text, tables and illustrations. Emphasize or briefly describe only important observations. [Book Antiqua, 11 point, normal, justified alignment].

DISCUSSIONS [Book Antiqua, 11, bold, left alignment]

Underline new, important aspects of the study. Do not repeat in detail data which have been presented in previous sections. Include implications of revealed aspects and their limitations, including implications for future studies. Connect your observations to other relevant studies. Relate the results to the aim proposed for the study. [Book Antiqua, 11 point, normal, justified alignment].

CONCLUSIONS [Book Antiqua, 11, bold, left alignment]

Organize conclusions which emerge from the study. In the end state: a) contributions to be acknowledged but which do not justify paternity right; b) thanks for technical support;

c) thanks for financial or material support. [Book Antiqua, 11 point, normal, justified alignment].

REFERENCES [Book Antiqua, 11, bold, left alignment]

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.

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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, ABBREVIATIONS

All measurements must be expressed in International System (IS) units. Abbreviations 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.

Papers submitted for publishing will be addressed to:

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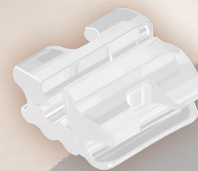
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