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THE EFFECT OF THE USE OF AUTOLOGOUS PLATELET-ENRICHED PLASMA ON THE SECONDARY STABILITY OF DENTAL IMPLANTS PLACED IN THE LOWER JAW

ВЛИЈАНИЕТО ОД УПОТРЕБАТА НА АВТОЛОГНА ПЛАЗМА ЗБОГАТЕНА СО ТРОМБОЦИТИ ВРЗ СЕКУНДАРНА СТАБИЛНОСТ КАЈ ДЕНТАЛНИ ИМПЛАНТИ ВО ДОЛНА ВИЛИЦА

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Abstract

Applicative use of growth factors in regenerative dentistry has a key role in the multifactorial osteointegrative process, affecting its acceleration and the success of the final therapy. **Objective:** The objective of this study is to determine the relationship between the level of early osseointegration and secondary stability of dental implants with and without the use of autologous platelet concentrate in all 3 phases, at the very placement of the dental implant, after 4 and after 8 weeks of placement. **Material and method:** In 32 patients of both sexes aged 31-77, dental implants were placed on the right side of the mandible with pre-prepared and locally applied autologous "protein-enriched plasma with appropriate concentration-PRP" on the implant bed (experimental group). The control group consisted of the same patients in whom only the standard protocol for implant bed preparation was applied on the contralateral side (left). After the completion of the oral surgical procedure, the stability of the placed dental implants was measured using a Penguin RF device, on the day of the intervention, after 4 and after 8 weeks after the placement of the implant. **Results:** In the experimental group, higher average values were observed regarding the stability of the dental implants, namely: postoperative -79.59; after 4 weeks - 80.46 and after 8 weeks - 84. The results showed statistical significance regarding the differences for all three periods: postoperative (p≤0.02), after 4 weeks (p≤;0.03) and 8 weeks (p≤; 0.04 compared to the control group). **Conclusion:** Dental implants that were placed with PRP showed a statistically significant difference in stability, in all three time periods, which is the reason to recommend this method for achieving satisfactory stability and for temporary loading of the dental implant. **Key words:** PRP, dental implants, osseointegration.

Апстракт

Апликативнатаупотребанафакторитенарастворегенеративнатастоматологијаимаатклучнаулогавомултифакторијалниотостеоинтегративенпроцес, влијаејќи-нанеговотозабрзувањеиуспехотнакрајнататерапија. **Цел:** Целта на оваа студија е да се утврди врската помеѓу нивото на рана остеоинтеграција и секундарната стабилност на имплантите со и без употреба на автологен тромбоцитен концентрат во сите 3 фази, при самото поставување на имплантот, по 4 и по 8 недели од поставувањето. **Материјал и метод:** Кај 32 пациенти од двата пола на возраст од 31-77 години, денталните импланти беа поставени на десната страна на мандибулата со претходно подготвена и локално аплицирана автологна „плазма збогатена со протеини со соодветна концентрација-PRP“ на имплантантниот кревет (експериментална група). Контролната група се состоеше од истите пациенти кај кои беше применет само стандардниот протокол за подготовка на имплантниот кревет на контралатералната страна (лево). По завршувањето на оралнохируршката процедура, стабилноста на поставените импланти беше мерена со помош на апарат PenguinRF, на денот на интервенцијата, по 4 и по 8 недели по поставувањето на имплантот. **Резултати:** Во експерименталната група забележани се повисоки просечни вредности во однос на стабилноста на денталните импланти и тоа: постоперативна -79,59; по 4 недели - 80,46 и по 8 недели - 84. Резултатитепостигнаастатистичказначајност на разликите за сите три периоди: постоперативно (p≤0,02), по 4 недели (p≤;0,03) и 8 недели (p≤; 0,04 споредено на контролнатагрупа). **Заклучок:** Денталните импланти кои беа поставени со PRP покажаа статистички значајна разлика во стабилноста, во сите три временски периоди, што е причина да се препорача овој метод за постигнување на задоволителна стабилност и за привремено оптеретување на денталниот имплант. **Клучни зборови:** PRP, дентални импланти, остеоинтеграција.

ntroduction

Modern methods and treatments for using bioactive materials to achieve osseointegration of dental implants can affect osteoblastic adhesion on the surface of the implant. Although it can be said that the technique of placing dental implants has not changed significantly, a number of studies are investigating the possibility of using and applying platelet concentrate (PRP- Platelet - RichPlasma) derived from plasma that can influence the improvement of the stability and osseointegrative process in placed dental implants.

PRP is, in fact, an "extract" from the blood that contains various growth factors, from which a final product for clinical application is obtained by centrifugation. Thrombin is a substitute for serine protease, which in humans is encoded by the "F2" gene and converts the soluble fibrinogen in insoluble fibrin[1].

Today, implant therapy is considered a predictive treatment with excellent and long-term results. The osteointegrative process is multifactorial, so the use of autologous materials can help and at the same time speed up the success of the therapy. PRP, as a method, has been a proven tool for a successful therapy in dentistry.

The stability of the placed dental implant is defined as the ability or condition to absorb adequate force coming from multiple directions, from an axial aspect, lateral or rotational movements.

Wound healing and bone regeneration are replete with a series of orchestrated sequences of biological factors that can be of crucial importance for the long-term durability of dental implants, for their primary and secondary stability. Perhaps one of the most "candidates" to provide the above is plasma enriched with platelets. This can be clarified by the fact that:

1) it is of autologous origin; without risk of disease transmission, and
2) contains natural growth factors that can influence bone regeneration[2,3,4.]

The aim of this stady

The objective of this paper is to evaluate the effect of platelet-rich plasma and its seven fundamental protein growth factors in improving the stability of the dental implant in relation to the topographic features of the implant surface.

Material and methods

Within the framework of this study, for the realization of the set goals, a total of 32 patients, of both sexes, with an indication for the implantation of dental implants in the lower jaw, depending on the loss and the remodeled bone surface, were observed in the Dentoria Dental Practice in Ohrid.

Inclusion criteria in this study were:

- patients aged 31-77;
- patients with bone resorption not < 6 mm in the lower jaw;
- patients with a lack of one or more teeth in the posterior/distal region;
- patients with adequate inter-occlusal distance and mesio-distal space sufficient for dental implantation;
- absence of acute or chronic symptomatology of an inflammatory nature that may affect the success of osseointegration of the dental implant;
- indication for the extraction of cariously destroyed teeth for the purpose of replacing dental implants;
- indication for performing multiple extractions for the purpose of planning and placing dental implants;
- partial or total toothlessness of the lower jaw;
- patients who have signed a written document for the surgical intervention, as well as consent for placement of dental implants.

Patients aged 31–77 years who met the inclusion criteria were selected in this double-blind, randomized clinical trial. A survey questionnaire was administered to all respondents along with consent for voluntary participation in our study, following WHO recommendations. This research was approved by the Ethics Committee of the Faculty of Dentistry-Skopje, UKIM. With the indication for the implantation of dental implants in the lower jaw, depending on the loss and the remodeled bone surface, the patients were then divided into two groups, experimental and control.

In the first group (experimental) dental implants were placed in the lower jaw-right side, with pre-prepared and locally applied autologous "protein-enriched plasma with appropriate concentration-PRP" on the implant bed, while in the second group (control), in the same patient on the left side of the mandible, only a standard protocol was used for the preparation of the implant bed without the application of concentrated autologous plasma.

Method of preparation of PRP

Venous blood was collected from each patient with venipuncture. The blood was stored in a plasmolifting tube with citrate as an anticoagulant, which has a patented separation gel, which, through the degranulation of blood clots, releases appropriate growth factors and other cytokines that stimulate the growth of bone and soft tissues. For producing the final product, all aseptic prerequisites for obtaining 8 ml of liquid blood from an

antecubital vein were met. After obtaining the blood, it was transferred to a sterile vacutainer containing 0.5 ml of 3.2% sodium citrate whose action is based on the principle of anticoagulant.

The test tubes were centrifuged at 4000 rpm for 6 minutes, after which the required plasma was obtained in the upper-superior part of the test tube. In the lower part, the erythrocytes, leukocytes and the separation gel are denatured. The obtained plasma was injected before the placement of the implants in the formed place for the implant itself, on the surface of the dental implant, as well as after the placement of the implant. After the completion of the oral surgery procedure, the stability of the placed dental implants was measured using the device for resonant frequency analysis (Penguin RFA) on the day of the intervention - immediately after its completion, on the 4th week from placement and on the 8th week from implant placement

The obtained results were statistically processed, where the student's "t" test was used to determine the significance of the differences between the examined and the control group, where $p \leq 0.05$ values were considered statistically significant.

Results

In the research, 32 implants from the experimental and 28 implants from the control group (Table 1) were analyzed, although, everything was for the same patients, we had to take a look of the characteristics of the groups, which could affect the outcome of the therapy.

Table 1. Structural distribution

		f	%
Group	implants WITH plasma *	32	53.3
	implants without plasma **	28	46.7
	Total	60	100.0

χ^2=0.267, df =1, p=0.606, f = frequency , %= percentage ;
*PRP group , ** Control group

Table 2. Type on dental implant

		f	%
Length (mm)	8 mm	6	10.0
	10 mm	54	90.0
	Total	60	100.0
Form	Cylinder	60	100.0
Diameter (mm)	3.5 mm	26	43.3
	4.0 mm	34	56.7
	Total	60	100.0

f = frequency, %= percentage;

It is evident from table 2 that 6 implants were built with length of 8 mm (10%) and 54 implants with length of 10 mm(90%), and with cylindrical shape. A total of 26 implants (43.3%) have a diameter of 3.5 mm (43.3%), and the rest 34 have a diameter of 4 mm (56.7%).

The average age of the patients ranges from Min=31 to Max=77 years (Table 3). The average age of the total number of patients (sample) is M=54.91 ± 10.45 years. The age of the PRP group is M=54.50 ± 10.45 years, and the control group has a mean value of M=55.39 ± 10.63. These samples of respondents are leveled according to the average value of years (F =0.107, p =0.745).

Table number 4 shows the structural distribution of patients by gender, in which the female patients are represented by 34.3% (N =11). A total of 65.7% (N =21) are male respondents. If we consider only the observation of dental implants as a statistical unit, then the groups are equivalently equalized in terms of gender (χ^2=0.033, df =1, p =0.855). The group of respondents with PRP is represented by 56.6% of males and 34.4% of females, and in the control group, males dominate with 67.9% compared to females 32.1%.

Table 3. Average old age on the respondents

	Min	Max	M	SD	F	p
PRP group	31.00	77.00	54.50	10.45	0.107	0.745
Control group	31.00	77.00	55.39	10.63		
In total respondents	31.00	77.00	54.91	10.45		

Min=maximum value on the sample, Max=minimum value on sample, M=arithmetic mean, SD=standard deviation,
F – ANOVA test, p=statisticsignificance

Table 4. Structural distribution of patients by gender

			Group		all respondents
			PRP group	Control group	
Gender	**male**	f	21	19	40
		%	56,6%	67,9%	66,7%
	female	f	11	9	20
		%	34,4%	32,1%	33,3%
Total		f	32	28	60
		%	100.0%	100.0%	100.0%

Table 5. Stability of dental implant – difference between PRP and control group

		Group	N	M	SD	t	df	p
Dental stability postoperatively	implant	PRP group	32	79.59	2.72	3,166	58	**0.002**
		Control group	28	77.50	2.34			
Dental implant stability after 4 weeks	implant	PRP group	32	80.46	2.44	3,063	58	**0.003**
		Control group	28	78.53	2.42			
Dental stability after 8 weeks	implant	PRP group	32	84.00	2.09	2,970	58	**0.004**
		Control group	28	82.50	1.77			

N = number of respondents, M = arithmetic mean, SD = standard deviation, t – t test , df- degree of freedom, p = statistical significance;

Table 5 shows the obtained results for the stability of the implants for the studied periods as well as the differences between the studied and the control group, it is evident that the studied group mean value for the stability of the implant postoperatively after 4 weeks and after 8 weeks is 79.59, 80.46 and 84.0, while in the control group, the mean value of the measured stability for the time intervals postoperatively was 77.50, after 4 weeks 78.53, and after 8 weeks 82.50. Statistical significance of differences of $p \leq 0.05$ was obtained for all time intervals. Thus, the achieved difference postoperatively reached a significance of differences of $p \leq 0.02$ for the period of 4 weeks $p \leq 0.03$ and the least significant but still statistically visible for the period of 8 weeks $p \leq 0.04$

Discussion

The stability of dental implants is one of the most important parameters that influence and are an indicator of early loading of the implant, which also affects the success of the osseointegrative process with the bone structure and geographical surface of the implant itself. Most studies that have examined the stability of dental implants based on the so-called ISQ - stability quotient, indicate that the implant with a value of ISQ<49 obtained postoperatively, should not undergo the next step, which is prosthetic loading, which is actually inversely proportional to the values with ISQ >54.

The process of healing and enabling bony regeneration represents one species of an orchestra on biologically sequences regulated from multiple factors which affect the bone healing, which is crucial for providing appropriate stability on the implant bearing. For promoting and encouraging wound osseointegration with qualitative bony formation, most researchers, laboratories and centers for development of innovative dental materials[3,5,6,7] suggested more types of modifications on the dental implant which, on the other hand, will provide maximum bone-implant contact for the whole period, everything until the moment of prosthetic burden.

The dental implant provides its first contact in the recipient human organism (i.e. oral cavity) through blood. One of the novelties in oral implantology, used in recent history, is actually the application of autologous platelet concentrate (PRP) on the very surface of the dental implant, immediately before applying it to the implant bed.

In our paper, the difference postoperatively between the examined group versus the control group was statistically significant for p = 0.002, which indicates slight stability at the beginning of the placement of the implants. According to the first innovator Kingsley[1] of this autologous concentrate, α -granules release growth factors in the first 3-5 days of platelet activation and their stimulation is reflected in the proliferative phase after 10 days of application. In fact, those growth factors activate, i.e. accelerate the healing process only when their level is functional with the reached level of platelet concentrate, which in turn will influence the synthesis of collagen and α - granules through the initial formation of callus in bone tissue. Platelets persist for 7-10 days and collide with other platelets, forming a stable fibrin network with a stable thrombus. In 1998, Marx et al.[8] for the first time used PRP as a basis that supported the reconstructive graft on a bone base, therefore a series of studies followed to prove and apply the postulate. When analyzing the experimental studies related to the applied application of plasma concentrate, most authors highlight the positive effect in improving bone quality and stability, enabling significantly improved bone regeneration compared to isolated application of autologous bone graft[9].

The local application of platelet concentrate during placement of dental implants is a relatively simple and simplified method that can contribute to ensuring early implant-osseous contact. According to a group of authors[10,11,12,13,] whose purpose was perceived in the immediate loading of dental implants in the distal segments of the lower jaw, where the probability of the maximum masticatory effect is precisely in those anatomical regions, suggest that the bioactive potential of the platelet concentrate can be affected directly or indirectly through several selected factors, some of them are: careful selection of the implant bed, computerized analysis of bone quality and quantity in order to ensure adequate length of the implant, ensuring satisfactory primary stability of the placed implants and excluding high-risk patients with compromised health, which may affect primary and secondary stability.As a result, our obtained results in this study for loading after 8 weeks recorded a statistical significance of p =0.004 which is correlated with some of the conclusions obtained in the study of the above-mentioned authors.

The results obtained in our paper are in accordance with some of the conclusions obtained in the study of a group of authors[13,14,15,16] where dental implants placed with platelet concentrate showed a statistically significant difference in stability measured using Penguin-resonance frequency analysis in all three time periods.

Conclusion

This study confirms that dental implants, which were placed with platelet concentrate (PRP), showed statistically significant difference in stability measured with help of the device for resonant frequent analysis Penguin and that in all three temporary periods and refers on the possibility for timely burden on dental implants.

We confirm that the use of autologous materials accelerates the osteointegrative process and affects the therapeutic success in dental implantology.

The obtained results of our examination allow us to recommend the use of PRP during the placement of implants, which will enable faster stabilization and the possibility of loading the implant.

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