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Mini Review

Platelet Concentrates for Regeneration and Treatment of the Hard and Soft Tissues

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Abstract

As a result of a high density and consequences of periodontal recessions, this study aims to compare the effect of different types of platelet concentrates used to treat hard and soft oral tissue defects. For the purpose of methodology, clinical trials which treat the peri-implant and periodontal defects with platelet concentrates, compared with conventional treatments were searched in PubMed/Medline, EMBASE, Cochrane Oral Health Group, and Lilacs. No statistical differences were found in the main outcomes for the analyzed variables: probing depth, clinical attachment level, root coverage, coronal advance flap, keratinized gingival width. There were only found significant differences in the access flap variable, solely and related with platelet concentrates. To sum up, seems to be beneficial for the treatment of periodontal and peri-implant defects the utilization of platelet rich pplasma (PRP), platelet rich fibrin (PRF) and leucocyte platelet rich fibrin (L-PRF). Nevertheless, in order to analyze the biological behavior of this blood products it is imperative to perform further investigations of this subject.

Introduction

The exposure of dental roots as consequence of migration of the apical end of the gum is what we know as gum recession [1]. This event of complex ethology [2-6] causes our patients aesthetic and functional problems.

Nowadays gum recessions are one of the most common problems we can find on our daily practise being more pronounced on aged patients and can affect more than 50% of population [7]. That´s why is been studied numerous times and we can find many procedures to treat it, different examples are, connective tissue graft (CTG), Coronally advance flap (CAF) and guided tissue regeneration (GTR). To increase the success rate these procedures can be combined between them or with the use of enamel matrix derivates (EMG). Currently and because of the bio medics science constant evolution, the soft tissue regeneration was proposed as treatment of gum recession, there were studies suggesting the use of autologous blood derivatives which effect had already been investigated on the promotion of the improvement on scarring of the soft tissues. It was Whitman et al8 who introduced the usage of platelets pool on dentistry.

The usage of growing factors PDFG-AB, TGFb-1 and VEGF which is found on platelets, pretends to assist with the angiogenesis, the cell generation and bone shaping. At present there is a wide variety of autologous blood derivatives, in this revision we are going to focus on platelet rich plasma (PRP) which we will explain further later on the article and that can be use don combination with biomaterials or on its own [9,10].

i. **PRP:** after the spinning needs to agglutinate with thrombin and calcium chloride to achieve this high platelet concentration gel. As per protocol of extraction, we do venepuncture and this venous simple is mixed with the anticoagulant. Using the "soft spin" technique the blood is separated in 3 layers. We aspirate the plasma poor on platelets´(PPP) and by defect some red cells. This time we use "hard spin" on what we have obtained earlier and get another 3 layers with the platelets at the bottom of the tube. We collect the (PRP) and with soft pendulous movements of the simple get the concentrated rich platelets plasma (cPRP). When we are going to administer it we mix the cPRP with bovine thrombin and calcium chloride, getting a fibrin matrix gel [11].

ii. **PRF:** Unlike on the previous technique, we don´t need to use anticoagulant and gives the sample a higher number of white cells and a more natural fibrin structure. It doesn´t require the usage of bovin thrombin [12]. The extraction protocol is easier and once the venepuncture is done and the blood obtained, we spin the simple at 3000rpm for 10 minutes. As in this case we don´t use anticoagulants, the clotting cascade begins and the platelets on contact with the tube walls activate. On that moment the fibrinogen turns into fibrin and a clot form in the centre of the tube, separating the plasma with no cells on the bottom and the red cells on the top. The success of this technique lies on how fast we get the blood sample and spin it. It is possible to find an inflammatory reaction during the initial matrix remodulation because of the cytokines trapped on the fibrin mesh.

iii. **L-PRF:** This fibrin mesh containing leucocytes, cytokines [13], growing factors and proteins doesn´t require anticoagulants and as the previous one, does not need bovine thrombin [14,15]. We obtain a slow but vital release of growing factors, this is key on the first steps of coagulation [13,15-18], that helped out by the fibrin and it´s properties, can help promoting tissue regeneration [19]. As per protocol, we need to do the venepuncture and immediately spin at 2700 rpm for 12 minutes [20,15,18,21-25]. As a consequence of the action of fibrinogen and thrombin, there will be a clot formed in the middle of the tube separating the acellular plasma on the top and red cells on the bottom. (Table 1).

Table 1: Platelet concentrates.

	Platelet concentrates
PRP	No leucocyte and low fibrin leves after their activation
PRF	No leucocyte and high fibrin net
L-PRF	Leucocyte and low fibrin leves after their activation

Based on the studies of Rose et al [26] about the platelet regenerative potential, today we know the value of fibrin and leucocytes on periodontal tissue regeneration, although there are no many studies found about the use of these on peri implant and gum recessions.

Material and Methods

The search was done on the data bases of PubMed/Medline, EMBASE, Registry of Essay of the Cochrane Oral Health Group, Lilacs. Key words used, gingival recession, platelet-rich plasma, platelet-rich fibrin, soft tissue regeneration, furcation defects, periodontal healing period. In this clinical revision they were excluded studies with repeated headings and nonconcrete data. They were included those with random clinical studies with a minimum follow up of three months on patients with no other pathologies and with dental or peri implant recessions.

Results

The amalgamation of search terms, such as quality evaluation CAPS and PRISMA, yielded an extensive array of studies. Ultimately, seventeen studies met the specified criteria. This paper encompasses a total of clinical trials that scrutinize the comparison between PRP, PRF, and L-PRF utilization across various tissue regeneration methods and conventional techniques. The follow up period varies from 3 to 12 months (Table 2). The authors of the studies didn't exhibit particular emphasis on the tools utilized in traditional interventions. However, Jankovick et al [27] showcased the use of enamel matrix derivative (EMD) (Emdogain®, Straumann®). Similarly, only three centrifuges were noted: EBA 20 by Hettich GMbH & Co KG in Tuttlingen, Germany; RC-4 by REMi in Mumbai, India; and Nüve Laboratory Equipments' NF200 in Ankara, Turkey. The primary outcomes assessed post-interventions were probing depth (PD) and clinical attachment level (CAL). In periodontics, probing depth refers to the measured distance from the free end of the gingival margin to the bottom of the periodontal pocket. Thorat et al [28], Rosamma et al [29], Ajwani et al [30], Sharma et al [31], Dhiman et al [32], Hamzacebi et al [33], and Najeeb et al [34] presented favourable results in the test group undergoing open flap debridement (OFD) + PRF in comparison to the control group (OFD). Only one study demonstrated significant improvement with PRF + ALENDRONATE. Agarwal et al [35] showcased statistically significant outcomes in the test group (PRF/decalcified freeze-dried bone allograft (DFDBA)) (Refer to Table 3).

Table 2: Studies selected characteristics.

Authors	Year	Participants	Time	Age (media)	Tipe of study
Aroca et al	2009	20	6 months	38	RTC (non blinded)
Jankovick et al	2010	20	12 months	…..	RCT (non blinded)
Sharma et al	2011	18	9 months	34,2	RCT (non blinded)
Thorat et al	2011	40	9 months	31 +/- 2	RCT (simple blinded)
Rosamma et al	2012	15	12 months	29+/- 7	RCT (non blinded)
Padma et al	2013	15	6 months	…..	RCT (non blinded)
Agarwal et al	2015	32	12 months	52+/- 7	RCT (doubled blinded)
Ajwani et al	2015	20	9 months	30,5	RCT (simple blinded)
Dhiman et al	2015	30	12 months	…..	RCT (oubled blinded)
Tunaliota et al	2015	10	12 months	43,2	RCT (simple blinded)
Boora et al	2015	20	3 months	24,6	RCT (non blinded)
Thamaraiselvan et al	2015	20	6 months	…..	RCT (simple blinded)
Oncü et al	2015	20	6 months	44,2 +/- 12,5	RCT (non blinded)
Kanoriya et al	2016	78	9 months	38	RCT (non blinded)
Hamzacebi et al	2015	19	6 months	60,98 +/- 11,9	RCT (simple blinded)
Tabrizi et al	2017	20	6 weeks	39,6+/- 6,74	RCT (non blinded)
Najeeb et al	2017	477	12 months	…..	Systematic Review

Table 3: Probing depth results.

Authors	Year	Groups		Results	
		Control	Test	Initial probing depth	Final probing depth
Thorat et al	2011	OFD (n=16)	OFD+ PRF (n=16)	C: 6.75 +- 1.69 T: 7.88 +- 2.19	C: 3.19 +- 1.52 T: 3.19 +- 1.05
Sharma et al	2011	OFD (n=18)	PRF (n=18)	C: 6.33 - 1.029 T: 6.39 - 1.145	C: 2.889 +- 0.6762 T: 4.056 +- 0.416
Rossama et al	2012	OFD (n=15)	OFD+PRF (n=15)	C: 7.07-1.03 T: 7.53-1.06	C: 4.67+-0.82 T: 2.87+-0.99
Ajwani et al	2012	OFD (n=20)	OFD+ PRF (n=20)	C: 6.20±0.632; T: 5.90±0.994	C: 4.60±0.699; T: 4.00±0.816
Dhiman et al	2015	OFD (n=15)	OFD+PRF (n=15)	C: 8.67 +-0.98; T: 9.07+-0.80	C: 1.4 +-0.63; T: 1.07+-0.26
Hamzacebi et al	2015	OFD (n=9)	PRF (n=19)	C: 5.78 ± 0.71mm; T: 6.13 ± 1.05mm	C: 3.71 ± 0.42mm; T: 3.30 ± 0.49mm
Agarwal et al	2015	DFDBA (n= 32)	DFDBA + PRF (n= 32)	C: 7.12 ± 0.78; T: 7.13 ± 0.88	C: 3.52 ± 0.79; T: 2.98 ± 0.46

Expanding on the primary findings, the clinical attachment level (CAL) is could be defined as the distance between the cement-enamel junction and the gingival sulcus. Notably, several papers do not mention specific data regarding CAL. Aroca et al [36], Padma et al [37], Rosamma et al [29], Ajwani et al [30], Sharma et al [31], Dhiman et al [32], and Hamzacebi et al [33] reported statistically significant increases in results within the test groups (Table 4). As a secondary outcome, we observed the keratinized gingival width (KGW), measured from the mucogingival junction to the buccal marginal free gingiva. Nine papers investigated this factor, with most studies demonstrating a statistically significant increase in KGW from baseline. Padma et al [37] was the sole paper that showcased a statistically significant increase in the test group.

Table 4: Clinical attachment level results.

Authors	Year	Groups		Results	
		Control	Test	Initial CAL	Final CAL
Aroca et al	2009	CAF (n=21)	CAF+PRF (n= 21)	C: 3.93 - 1.43; T: 4.23 - 1.56	C: 1.37 - 0.62 T: 1.76 - 0.97
Sharma	2011	OFD (n=18)	OFD+PRF (n= 18)	C: 7.33 - 1.029 T: 7.39 - 1.145	C: 1.278 - 0.461 T: 2.333 - 0.485
Rosamma et al	2012	OFD (n=15)	OFD+PRF (n= 15)	C: 7.53-1.30 T: 8.20-1.21	C: 6.13+-1.46; T: 3.47+-1.45
Padma et al	2013	CAF (n= 15)	CAF+PRF (n= 15)	C: 4.69±1.25 mm; T: 4.75±1.29mm	C: 2.00 ± 0.89 mm; T: 1.00 ± 0.00 mm
Ajwani et al	2015	OFD (n=20)	OFD+PRF (n= 20)	C: 9.20±1.932; T: 9.50±1.354	C: 7.90±1.729; T: 7.70±1.418
Dhiman et al	2015	OFD (n=15)	OFD+PRF (n= 15)	C: 8.80+- 1.52; T: 9.67+-0.90	C: 2.2+- 0.68; T: 2.67+-0.98
Hamzacebi et al	2015	OFD (n=19)	OFD+PRF (n= 19)	C: 6.59 ± 1.00mm; T: 6.74 ± 1.03 mm	C: 4.75 ± 1.07; T: 3.44 ± 0.57 SD

Finally, concerning root coverage (RC), Padma et al [37] noted statistically significant results in the test group employing coronal advance flap (CAF) + PRF. Thamaraiselvan et al [38] compared CAF + connective tissue graft (CTG) and CAF + PRF, finding no statistically significant differences. However, they did observe better stability over time in the test group.

Argument

The goal of this study is to evaluate and compare the different platelet aggregates used on its own or in conjunction with soft tissue regeneration techniques or using enamel's matrix by-products. As previously explained, there is been a great production of different platelet aggregates [9,10] to be used on gum and peri implant recessions [4,39], given the well-known performance of leucocytes, fibrin and platelets on tissue regeneration, being the goal of periodontia. There is been a broad number of studies about the benign response of using platelets and growth factors on bone regeneration, its review on gum recession and peri implant tissue is scarce.

Sorting the obtained data on different periodontal plastic surgery fields we would get:

a. Coronary advanced flap (CAF) alone or associated to blood by-products, we can observe that there is no significant difference on the variables reviewed (PD, CAL, KGW o RC). Only Padma et al [37] reveals improvement on CAL, KGW and RC using PRF under the CAF.

b. About the CAF associated to CTG or platelet aggregates, there weren't found any significant differences, apart from the opposite results we found between the studies of Jankovic et al [26] who observed a larger KCG gain on the CAF+CTG as opposed from Thamaraiselvan et al [38] who found a larger gain on the group CAF + PRF. Tunaliota et al [40] the only author that uses L-PRF, didn't find any significant variation.

c. On the study of OFD alone ad OFD + PRF, every author 29-34 confirms improvement on bone defect, of FURCA, PD, CAL and KCG. Just Kanoriya et al [41] compares a third cathegory OFD+PRF+ ALENDRONATE being this one the one getting the best results on filling bone defect, PD and CAL.

d. In relation to the peri implant defect there were only find 4 authors being PRF the chosen platelet concentrates for the study.

e. On the study of Boora et al [42], the starting point is the placement of an implant on the anterior region of the superior maxillae, with immediate provisional, not functional. The use of PRF was random. There were not statistically significant differences on the depth of the probing or on bleeding. Concludes saying PRF might be beneficial for peri implant tissues.

f. Oncu et al [43] was looking for comparison, by calculating the frequency of resonance when the implant was placed, after a week and after the first month, the stability of those associated or not to PRF. He observed a higher stability on the period of early scarring on those who had placed PRF.

g. On the study of Hamzacebi et al [33] what is examined is the loss of periimplantaria bone comparing the use of PRF against surgery with access flap. The test group (PFR) showed a higher gain of CAL, less PD and after 6 months, less KGW.

h. Tabrizi et al [44] found a rise on the values of the Implant Stability Quotient (ISQ) increased on the posterior part of the maxillary after 2,4 and 6 weeks.

After the evaluation of these studies, we find some limitations to highlight, like the presence of some risk essays of moderate bias, apart from the assorted methods used and the limited studies in relation to the peri implant tissue.

Regardless of the limitations of the study, we can highlight the possible benefits of using platelets concentrates on clinical practice, as for the authors there are no significant differences between this treatment and more conventional techniques. We can point out the benefits of using these components as they reduce the morbidity and cost of treatment. Despite the fact that we still need more studies to prove the affordability and time stability.

Outcome

a. It is seemed to be beneficial the use of autologous blood by-products on gum and peri-implant recessions.

b. When performing an access flap, by using platelet rich plasma (PFP), fibrin rich plasma (PRF) and fibrin and leucocytes rich plasma (L-PRF), better results were obtained on probe depth, clinical level of insertion, width of keratinised gum, and radicular coverage.

c. About keratinised gum, there were better results using connective tissue grafting.

d. There is still need for more studies correlating autologous blood by-products.

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