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CLINICAL AND RADIOGRAPHIC EVALUATION OF ADVANCED PLATELET RICH FIBRIN IN THE PRESERVATION OF ALVEOLAR RIDGE FOLLOWING ATRAUMATIC TOOTH EXTRACTION: A RANDOMIZED CLINICAL TRIAL

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ABSTRACT

Aim: The study was aimed at determining the evaluation of hard and soft tissues at the extraction site when using advanced platelet rich fibrin compared to natural healing.

Methodology: The present study was conducted on 30 subjects. The patients were allocated to receive either advanced platelet rich fibrin (APRF) (test group) or left for natural healing (control group). Alveolar ridge width and mesial and distal marginal bone resorption were measured base line, at 2 months and 4 months follow up and then they were subjected to a statistical analysis.

Results: The buccolingual width result in the test group was decreased to 6.37±1.16mm while for the control groups, the values decreased to 5.95±0.53mm after 4 months with no statistical significance between the 2 groups. Both treatment protocols could not prevent bone resorption after 4 months. The mean mesial marginal bone level after 4 months in the test and control groups was 3.08 ± 1.43mm and 3.67 ± 1.37mm respectively with no statistical significance between the two groups. The mean distal marginal bone level after 4 months.

Conclusion: Despite the fact that ARP using APRF in our study did not totally avert bone loss, the values observed after 4 months were much lower than unassisted extraction.

KEYWORDS: Advanced platelet rich fibrin, socket preservation, hopeless tooth

INTRODUCTION

The use of dental implants has become a standard form of treatment for the rehabilitation of dentition segments **(Esposito et al., 2012)**. Dental implantology has continued to evolve to satisfy patients' practical and esthetic demands since its first launch **(Esposito et al., 2012; Arunyanak**

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et al., 2017). In areas with insufficient alveolar bone volume to support implant placement after dental extraction, one clinical problem is many surgical techniques and materials have been established to maintain or rebuild tissues in order to provide an optimum place to place an implant of appropriate size in the optimal position to address this obstacle **(Iasella et al., 2003; Avila-Ortiz, Chambrone and Vignoletti, 2019)**.

The aim of the protection of alveolar ridge is to minimize the reduction of the alveolus measurements after tooth extraction by immediately inserting a biomaterial inside the extraction socket **(Beck and Mealey, 2010)**. Materials available for this purpose typically consist of materials and/or biological agents for matrix scaffolding. Usually, matrix scaffolding materials are osteoconductive and can provide cell scaffolding and dimensional wound stabilization via space maintenance **(Susin and Wikesjö, 2013)**. These materials may be produced from sources that are allogeneic, xenogeneic, synthetic or autogenic **(Avila-Ortiz, Chambrone and Vignoletti, 2019)**. Biologic agents are molecular mediators that facilitate de novo bone formation with typical osteoinductive properties**. (Suárez-López del Amo et al., 2015)**. To achieve the desired surgical result, matrix scaffolding materials and biologic agents may be used separately or together **(Padial-Molina and Rios, 2014); (Suárez-López del Amo *et al.*, 2015)**.

Platelet-rich fibrin (PRF) has become increasingly popular among the biomaterials available since its first introduction in 2001 **(Choukroun et al., 2001)**. PRF is a platelet concentrate made of a dense fibrin matrix autologous bioscaffold with naturally incorporated growth factors that are released over a prolonged period from the scaffold to facilitate healing of hard and soft tissues **(Dohan et al., 2006a; Dohan et al., 2006b; Dohan et al., 2006c)**.

More recent improvements to the PRF preparation process have resulted in the production of advanced platelet rich fibrin (A-PRF), which uses lower G forces to achieve greater release of the growth factor compared to PRF **(Ghanaati et al., 2014; Fujioka-Kobayashi et al., 2017)**. There are many possible PRF clinical applications, but there is a lack of evidence to determine the efficacy of A-PRF **(Lei et al., 2020)**. Therefore, the aim of the present study was to compare the differences between A-PRF and natural healing at the site of extraction socket.

MATERIALS AND METHODS

The present study was conducted on 30 subjects. Dental patients were recruited in a consecutive manner from the outpatient Diagnostic center, Faculty of Dentistry, Cairo University. Participants who fulfilled the inclusion criteria and provided informed consent were randomly assigned to either test or control group by means of simple randomization with a 1:1 allocation ratio. Consequently, the patients were allocated to receive either advanced platelet rich fibrin (APRF) (test group) or left for natural healing (control group). Alveolar ridge width was measured at 2 months and 4 months follow up, then it was subjected to a statistical analysis.

Inclusion criteria included: Participants having at least one single or double rooted tooth indicated for extraction, participants older than 18 years, nonsmokers, systemically healthy patients, intact extraction socket with no dehiscence or fenestration, motivated participants willing to complete the follow-up period.

Exclusion criteria included: Patients reporting systemic conditions that may compromise healing or bone metabolism (i.e. uncontrolled diabetes, hyperthyroidism). Patients undergoing or having a history of radiotherapy, chemotherapy or bisphosphonate therapy. Local infection at the site of extraction.

Surgical procedure

After obtaining a preoperative radiograph, extraction process was started with flapless atraumatic extraction started by supracrestal periotomes. Following extraction, an inspection of socket integrity was carried out to ensure no remnants nor granulation tissues and for evaluation of alveolar bone morphology with a periodontal probe. After extraction and revealing the allocation sequence as an intervention group case, venous blood was collected. The blood sample was immediately centrifuged without anticoagulant at 1300 rpm (200 x g) for 8 minutes by an A-PRF centrifugation system.

A 5-0 monofilament polypropylene suture material was used to secure the orifice by an internal crisscross knot. Bucco-lingual dimension of alveolar ridge was measured by bone caliper base line, 2 months and 4 months follow up. The same was done for control group without APRF preparation. Subsequently, geometrically standardized pre-apical digital radiographs were taken using the paralleling technique, every patient with his own rubber index or bite blocks that was made immediately after extraction, alongside with film holder both help to assure elimination of geometric image distortion and magnification, all radiographs were exposed using the same machine and same exposure parameters at the OMFRadiology Department, Faculty of Dentistry, Cairo University. Radiographs were exposed using (Imaging plate, VistaScan-Durr Dental SE, Germany) the scanner (VistaScan Mini Easy, Durr Dental SE, Germany) and the machine (FONA SRL, Italy) at base line, T2 (8 weeks) and T3 (16 weeks) following tooth extraction. Measurements were performed as follows, a reference line was drawn to connect the cement-enamel junction of the adjacent teeth. The vertical lines perpendicular to the reference line were drawn and measured from the most coronal prominent points mesially (M) and distally (D) marginal crests.

RESULTS

Bucco-lingual bone width (mm)

Comparison between the groups

At base line, after two as well as four months; there was no statistically significant difference between mean bucco-lingual bone widths in the two groups.

Changes within each group

In both groups; there was a statistically significant change in mean bucco-lingual bone width by time (P-value <0.001, Effect size = 0.815) and (P-value <0.001, Effect size = 0.921), respectively. Pair-wise comparisons between time periods revealed that there was a statistically significant decrease in mean bucco-lingual bone width after two months as well as from two to four months.

Mesial marginal bone level (mm)

Comparison between the groups

At base line, after two as well as four months; there was no statistically significant difference between median mesial marginal bone levels in the two groups.

Changes within each group

In both groups; there was a statistically significant change in median mesial marginal bone level by time (P-value <0.001, Effect size = 1) for each group respectively. Pair-wise comparisons between time periods revealed that there was a statistically significant increase in median mesial marginal bone level after two months as well as from two to four months.

Distal marginal bone level (mm)

Comparison between the groups

At base line, after two as well as four months; there was no statistically significant difference between median distal marginal bone levels in the two groups.

Changes within each group

In Group I; there was a statistically significant change in median distal marginal bone level by time (*P*-value <0.001, Effect size = 0.984). Pair-wise comparisons between time periods revealed that there was a statistically significant increase in median distal marginal bone level after two months as well as from two to four months. In Group II; there was a statistically significant change in median distal marginal bone level by time (*P*-value <0.001, Effect size = 0.984). Pair-wise comparisons between time periods revealed that there was no statistically significant change in median distal marginal bone level after two months followed by a statistically significant increase from two to four months.

TABLE (1) Descriptive statistics and results of repeated measures ANOVA test for comparison between bucco-lingual bone width (mm) in the two groups

Time	Group I (n = 15)		Group II (n = 15)		95% CI for the mean difference		*P*-value	*Effect size (Partial Eta Squared)*
	Mean	SD	Mean	SD	Lower limit	Upper limit		
Base line	7.61	0.89	7.99	0.58	-0.94	0.19	0.184	0.062
2 months	6.95	1.08	6.74	0.6	-0.44	0.87	0.510	0.016
4 months	6.37	1.16	5.95	0.53	-0.25	1.1	0.205	0.057

TABLE (2) Descriptive statistics and results of repeated measures ANOVA test for comparison between bucco-lingual bone widths (mm) at different times within each group

Time	Group I (n = 15)		Group II (n = 15)	
	Mean	SD	Mean	SD
Base line	7.61 ^{A}	0.89	7.99 ^{A}	0.58
2 months	6.95 ^{B}	1.08	6.74 ^{B}	0.6
4 months	6.37 ^{C}	1.16	5.95 ^{C}	0.53
P-value	<0.001*		<0.001*	
Effect size (*Partial Eta Squared*)	0.815		0.921	

: Significant at P ≤ 0.05, Different superscripts in the same column indicate statistically significant changes by time

TABLE (3) Descriptive statistics and results of Mann-Whitney U test for comparison between mesial marginal bone levels (mm) in the two groups

Time	Group I (n = 15)		Group II (n = 15)		95% CI for the mean difference		*P*-value	*Effect size (d)*
	Median (Range)	Mean (SD)	Median (Range)	Mean (SD)	Lower limit	Upper limit		
Base line	1.7 (0.3 – 3.1)	1.61 (0.91)	1.6 (0.2 – 3.4)	1.58 (1.06)	-0.71	0.76	0.917	0.038
2 months	2.7 (0.7 – 4.5)	2.52 (1.29)	2.3 (0.5 – 5)	2.57 (1.4)	-1.05	0.96	1	0
4 months	3.4 (0.9 – 5)	3.08 (1.43)	3.4 (0.8 – 5.8)	3.67 (1.37)	-1.64	0.46	0.361	0.338

: Significant at P ≤ 0.05

TABLE (4) Descriptive statistics and results of Friedman's test for comparison between mesial marginal bone levels (mm) at different times within each group

Time	Group I (n = 15)		Group II (n = 15)	
	Median (Range)	Mean (SD)	Median (Range)	Mean (SD)
Base line	1.7 (0.3 – 3.1) C	1.61 (0.91)	1.6 (0.2 – 3.4) C	1.58 (1.06)
2 months	2.7 (0.7 – 4.5) B	2.52 (1.29)	2.3 (0.5 – 5) B	2.57 (1.4)
4 months	3.4 (0.9 – 5) A	3.08 (1.43)	3.4 (0.8 – 5.8) A	3.67 (1.37)
P-value	<0.001*		<0.001*	
Effect size (*w*)	1		1	

: Significant at P ≤ 0.05, Different superscripts in the same column indicate statistically significant changes by time

TABLE (5) Descriptive statistics and results of Mann-Whitney U test for comparison between distal marginal bone levels (mm) in the two groups

Time	Group I (n = 15)		Group II (n = 15)		95% CI for the mean difference		*P*-value	*Effect size (d)*
	Median (Range)	Mean (SD)	Median (Range)	Mean (SD)	Lower limit	Upper limit		
Base line	1.9 (0.2 – 4.1)	1.87 (1.11)	2 (1 – 3.4)	1.85 (0.94)	-0.75	0.79	0.967	0.015
2 months	2.5 (0.5 – 5.2)	2.39 (1.25)	2.2 (1 – 3.7)	2.31 (0.92)	-0.75	0.89	0.967	0.015
4 months	3.1 (0.8 – 5.9)	2.81 (1.35)	3.4 (1.5 – 4.8)	3.3 (0.94)	-1.36	0.39	0.198	0.483

: Significant at P ≤ 0.05

TABLE (6) Descriptive statistics and results of Friedman's test for comparison between distal marginal bone levels (mm) at different times within each group

Time	Group I (n = 15)		Group II (n = 15)	
	Median (Range)	Mean (SD)	Median (Range)	Mean (SD)
Base line	1.9 (0.2 – 4.1) C	1.87 (1.11)	2 (1 – 3.4) B	1.85 (0.94)
2 months	2.5 (0.5 – 5.2) B	2.39 (1.25)	2.2 (1 – 3.7) B	2.31 (0.92)
4 months	3.1 (0.8 – 5.9) A	2.81 (1.35)	3.4 (1.5 – 4.8) A	3.3 (0.94)
P-value	<0.001*		<0.001*	
Effect size (*w*)	0.984		0.984	

: Significant at P ≤ 0.05, Different superscripts in the same column indicate statistically significant changes by time

DISCUSSION

When compared to negative controls, alveolar ridge preservation has shown to have a high degree of success in reducing bone loss that occurs naturally after tooth extraction. As a result, the procedure will improve ridge measurements for implant placement and reduce the need for subsequent bone grafting or augmentation

(Weng, Stock and Schliephake, 2011; Willenbacher et al., 2016). There is a wealth of literature available that supports the use of allografts, xenografts, or alloplasts in the oral cavity, each with its own set of benefits and drawbacks**(Kumar, Vinitha and Fathima, 2013).**

While some drawbacks, such as the additional site of surgery, the prolonged period of operation, volatile resorption, the chance of donor site complications, and restricted autologous bone availability from bone graft harvesting techniques **(Clavero and Lundgren, 2003)**, motivate the search for alternatives in bone regeneration, autogenous bone as a bone graft material is still considered the “gold standard” for bone regeneration**(Stumbras et al., 2019)**.

Platelet concentrates are one of the most effective surrogates for alveolar ridge preservation. Advanced platelet rich fibrin (APRF) is one of the most recent strong generations that demonstrated a desired feature of a biomaterial for ridge preservation by providing space maintenance**(Clark et al., 2018)**. Similarly, it has all of the biological features to promote optimal healing **(Cabaro et al., 2018).** Success is dependent on platelet concentration, the number/type of leukocytes entrapped in the fibrin membrane, and the release of bioactive molecules at the sites of injury that will initiate the regenerative process and release of growth factors **(Anitua et al., 2009; Caruana et al., 2019).**

In a randomized controlled clinical trial, researchers compared A-PRF to a natural blood clot to see how successful it is as a biomaterial for ridge protection. Changes in ridge dimensions, pain, and soft tissue thickness were assessed in both classes, allowing for a clinically valid assessment of the materials’ usefulness for ridge preservation.

Bone remodeling is also considered to be affected by metabolic disorders like diabetes and hyperthyroidism, as well as systemic drugs like chemotherapy and bisphosphonates**(Albandar, Susin and Hughes, 2018).**

As a result, patients who reported having all of these conditions were removed from the study. Despite the fact that ARP is considered a safe procedure for teenagers, only patients over the age of 18 were included in the study so that informed consent could be given to avoid the effect of bone growth and passive eruption of teeth on the quantitative measurements.

In addition to the general exclusion criteria listed above, local site-specific criteria have been developed. Since the bone quality, as well as the size and configuration of molar sockets, differ from single and double rooted teeth, molars were excluded. As a result, healing time and processes were assumed to be different **(Avila-Ortiz, Chambrone and Vignoletti, 2019; Lee *et al.*, 2018)**

Damaged extraction sockets are commonly thought to be unsuitable for supporting graft material and necessitate wall replacement by block graft **(Elnayef et al., 2018)**, so they were left out of the study. Finally, local infection at the extraction site is known to delay healing, the high acidity is due to inflammation, and bacterial byproducts may trigger graft particle dissolution through cell-mediated or solution -mediated process **(Tanaka et al., 2017)** and hence no infected site was included.

(Temmerman et al., 2016**; Alzahrani et al.,** 2017) PRF was used for ridge protection, and the researchers found that it reduced alveolar width resorption from 8 weeks to up to 6 months after surgery. Two RCTs investigated the clinical benefits of PRF in ridge protection, both with favorable adjunctive effects, according to a systematic analysis. At 1, 4, and 8 weeks after tooth extraction, PRF increased radiographic bone fill and decreased alveolar ridge resorption **(Alzahrani et al.,** 2017).

Temmerman et al. (2016) found that PRF helped to maintain horizontal and vertical ridge measurements three months after tooth extraction. One study found that when PRF was combined with DFDBA and a collagen membrane, alveolar ridge height was maintained to a greater degree **(Thakkar et al., 2016).**

In our study, for bucco-lingual bone width measurements, we found that, in both groups; there was a statistically significant change in mean bucco-lingual bone width by time (*P*-value <0.001, Effect size = 0.815) and (*P*-value <0.001, Effect size = 0.921), respectively. Pair-wise comparisons between time periods revealed that there was a statistically significant decrease in mean bucco-lingual bone width after two months as well as from two to four months. Despite the fact that ARP using APRF in our study did not totally avert bone loss, the values observed after 4 months were much lower than unassisted extraction. For comparison between both groups, the mean change in width in blood clot group at 4 month, was 5.95(SD± 0.53), and in the APRF group was 6.37(SD±1.16).Although, there was no statistically significant difference between mean bucco-lingual bone widths in the two groups

One of studies that showed similar results, was done by **Clark et al 2018**, he reported that the loss of ridge width in the blood clot group (2.9 ± 1.7 mm) compared to A-PRF (2.8 ± 1.2 mm). No statistical significant differences in ridge width reduction were noted between both groups.

For mesial marginal bone level changes, the mean changes in the APRF group was 2.52(SD±1.29) and the median (range) was 2.7 (0.7 – 4.5), and in the blood clot group, the mean was 2.57 (SD±1.4) and the median (range) was 2.3 (0.5 – 5).Despite there was no statistical significance between both groups, the statistical significance was noted in each group.

(Suttapreyasri and Leepong, 2013) reported same results in his study, he found that, the mean radiographic resorption of marginal bone levels at mesial to the extraction site in PRF 2.22 (±0.51) was comparable to the control 2.86 (± 0.65).No statistically significant differences were detected among the groups after 8 weeks follow up after extraction.

For distal marginal bone level changes, the mean changes in the APRF group was 2.39(SD±1.25) and the median (range) was 2.5 (0.5-5.2), and in the blood clot group, the mean was 2.31 (SD±0.92) and the median (range) was 2.2 (1-3.7).

As **(Suttapreyasri and Leepong, 2013)** assumed, the mean radiographic resorption of marginal bone levels at distal to the extraction site in PRF 2.08 (±0.09) was comparable to the control 2.10 (±0.50). No statistically significant differences were detected among the groups after 8 weeks follow up after extraction.

Intraoral radiography using parallel technique has long been preferred method for measuring marginal bone level, and intraoral radiographs have higher resolution **(Mupparapu and Singer, 2004).** In this study we aimed at assuring to be more standardized by every single radiograph.

CONCLUSIONS

- A-PRF has been shown to be a suitable biomaterial for ridge protection in this randomized controlled clinical trial.
- When compared to a blood clot alone, A-PRF maintained ridge measurements better.
- These results show A-regenerative PRF's capacity in a healing extraction site and indicate that it may be used for more than just ridge preservation.

RECOMMENDATIONS

- Future researches should extrapolate the osteogenic capacity of A-PRF in more comprehensive ridge augmentation procedures and explore more regenerative capacities in periodontal regeneration, with a longer follow-up period.

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