

## Effect of platelet-rich fibrin on extraction socket healing in diabetic patients – A split-mouth crossover study: A prospective clinical trial

### ABSTRACT

**Aims:** The aim of this study is to evaluate the effectiveness of platelet-rich fibrin (PRF) in postextraction socket healing in diabetic patients.

**Subjects and Methods:** The investigators implemented a randomized, split-mouth study in 100 Type 2 diabetic patients undergoing dental extraction of two or more teeth. Following extraction, the experimental socket was packed with PRF and sutured, while the control socket was sutured without packing. The primary outcome measures were soft-tissue healing (assessed by color, bleeding on palpation, granulation tissue, and incidence of suppuration and dry socket), hard-tissue healing (measured by visual interpretation, area of bone coverage, and grayscale analysis), and visual pain scores.

**Statistical Analysis:** Statistical analysis was done using the independent and paired *t*-tests, analysis of variance, and Chi-square test

**Results:** Both soft-tissue healing and hard-tissue healing were significantly better in the experimental socket as compared to the control socket. Pain levels, as measured by the visual analog score, were similar in both the extraction sockets.

**Conclusions:** The use of PRF has beneficial effects in extraction socket healing in diabetic patients.

**Keywords:** Diabetes, extraction, platelet-rich fibrin, wound healing

### INTRODUCTION

Diabetes mellitus is the most frequently encountered endocrine disorder in the world. The International Diabetes Federation has estimated that 415 million people in the world currently suffer from diabetes; this figure of patients is expected to reach 642 million by 2040, and one person of 11 is diabetic.<sup>[1]</sup> It is a well-known fact that diabetics are prone to impaired wound healing. It has been stated that wound healing is impaired due to several reasons. First, collagen structure is weakened due to the accumulation of glycemic end products. Second, blood circulation that is necessary for healing is impaired due to microangiopathy. Third, impaired neutrophil function increases the risk of postoperative wound infection.<sup>[2]</sup> This states the necessity to employ techniques that can expedite and foster the healing process.

One technique, currently gaining importance both in medicine and dentistry, involves the use of platelet

concentrates. In particular, the placement of platelet-rich fibrin (PRF) in the healing site delivers platelet-derived growth factors, which has been shown to reduce bleeding,<sup>[3]</sup> and stimulate soft tissue and bone regeneration in extraction sockets.<sup>[4]</sup> However, its effect on wound healing in diabetic patients has not been studied adequately.

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Therefore, this study aimed at evaluating the effectiveness of PRF in improving postextraction socket healing in diabetic patients. The objectives of the study were to assess the influence of PRF in facilitating soft tissue and hard tissue healing in diabetic patients following dental extraction.

## SUBJECTS AND METHODS

This study was performed as a single-blinded, crossover trial. The source of the study was patients who reported to the department of oral and maxillofacial surgery for extraction of teeth. Patients between 20 and 70 years of age, diagnosed with diabetes mellitus, who required extraction of two or more teeth, were included in the study. Patients who were smokers, those with poor oral hygiene, patients with hypertension, bleeding disorders, or other conditions affecting immunity such as AIDS; and patients with steroid therapy were excluded from the study. The indications for extraction included dental caries, periodontitis, root caries, vertical or horizontal root fracture, and endodontic lesions.

### Procedure

This study involved human participants and the guidelines laid down by the Helsinki Declaration were followed. This study was approved by the Institutional Review Board, SRM University No - SRMU/M&HS/SRMDC/2013/M.D.S-PG Student/408, dated 29-1-2015 Signed informed consent was obtained from all patients. The patient's demographic details such as age, gender, relevant medical history, and teeth indicated for extraction were recorded. The blood glucose level for each patient was checked immediately before the procedure.

After administration of local anesthesia (2% lignocaine with adrenaline), extraction was done by a closed method. Extraction for both the experimental and control teeth was carried out at the same time. The control socket was compressed and sutured without packing.

### Preparation of platelet-rich fibrin

PRF was prepared by Choukroun's method.<sup>[5]</sup> Following extraction, 6 ml of blood was withdrawn from the patient's antecubital vein and collected in a sterile test tube. The test tube was centrifuged at 3000 rpm for 12 min. After centrifugation, the blood separated into three distinct layers – a bottom layer comprising red blood cells, middle layer containing PRF, and a top layer containing platelet-poor plasma. Both red blood cells and platelet-poor plasma were discarded. PRF was then collected and isolated.

For each patient, one extraction socket (experimental side) was packed with PRF and sealed with a figure of 8 sutures. The socket in the control side was sutured and left to heal.

### Follow-up

A postoperative review was done at 1, 3, and 6 weeks. The operator who performed the review was blinded to the experimental and control sides. The following parameters were assessed for each patient:

#### Soft-tissue parameters

Soft-tissue healing was assessed using a modified version of Landry's index.<sup>[6]</sup> This index measured tissue color (measured as a percentage of red vs. pink tissue), bleeding on palpation, presence or absence of granulation tissue, suture margin dehiscence, and presence or absence of suppuration. Alveolar osteitis, which was not included in the original index, was also assessed.

#### Hard-tissue parameters

Hard-tissue healing was assessed from an intraoral X-ray based on visual interpretation (completely radiolucent, less radiolucent than normal bone, or same as normal bone) and area of bone coverage (no socket fill, one-third of socket filled, and socket completely filled with bone). Grayscale analysis was also carried out using CorelDraw® X7 (V17, Corel Corporation, Ontario, Canada) software.

#### Pain assessment

This was measured using the visual analog scale for pain, on a scale from 0 (no pain) to 10 (worst possible pain).

All parameters were recorded in the data extraction form and analyzed. Statistical analysis was done using the SPSS software (V26, IBM Corporation, Armonk, USA). The tests that were carried out included independent *t*-test, paired *t*-test, repeated analysis of variance, and Chi-square test.

## RESULTS

A total of 104 patients were included in this study. Of these, four were lost to follow-up and were therefore excluded from

**Table 1: Patients baseline characteristics**

Variables	Descriptives
Age (years)	32-70
Sex	
Male	54
Female	46
Type I diabetes	3
Type II diabetes	97
Random blood sugar level (mean value)	182.67

**Table 2: Reasons for dental extraction**

Reason for extraction	Number of patients
Dental caries	47
Periodontitis	33
Root caries	4
Vertical/horizontal fractures	9
Endodontic lesions	7

the study. The demographic data collected from the patients are projected in Table 1. These patients had varied levels of glycemic control, ranging from 140 to 324 mg/dl (mean 182.67 mg/dl). The most common cause for extraction of teeth was unrestorable dental caries, followed by chronic periodontitis. The reasons for extraction are summarized in Table 2.

#### Soft tissue analysis

Initial healing was reasonably good in all patients. None of the patients developed serious complications such as alveolar osteitis. Complete socket closure was achieved at the 6-week check-up for approximately 50% of patients.

The outcome for each of the individual parameters is as follows:

#### Tissue color

At the end of the 1<sup>st</sup> week, 35% of the study sockets had achieved a reddish-pink color as compared to only 22% of the control sockets. At 3 weeks, 98% of the study sockets and 96% of the control sockets had achieved a reddish-pink color, while 2% of the study sockets had already moved on to pink. At 6 weeks, 92% of the study sockets and 86% of the control sockets were completely pink. Statistical analysis showed that these results were significant ( $P < 0.05$ ).

#### Response to palpation

At the end of 1<sup>st</sup> week, bleeding was absent in 35% of the study sockets and 18% of the control sockets. At 3 weeks, bleeding was absent in 98% of the study sockets and 93% of the control sockets. At 6 weeks, there was a complete absence of bleeding in both the study and control sockets. These results were statistically significant ( $P < 0.05$ ).

#### Granulation tissue

Granulation tissue was present in 58% of the study sockets and 67% of the control sockets at the end of 1<sup>st</sup> week. At 3 weeks, granulation tissue was present only in 1% of the control group and was completely absent in both the study and control sockets in the 6<sup>th</sup> week. Statistical analysis showed that these results were significant ( $P < 0.05$ ).

#### Suture margin dehiscence

At the end of 1<sup>st</sup> week, 5% of the control sockets showed

suture margin dehiscence, whereas it was completely absent in the study sockets. Suture margin dehiscence was absent in the 3<sup>rd</sup> and 6<sup>th</sup> weeks in both the study and control sockets. The results were statistically significant ( $P < 0.05$ ).

#### Suppuration

Suppuration was present only in 1% of the study socket at the end of the 1<sup>st</sup> week. It was completely absent in the 3<sup>rd</sup> and 6<sup>th</sup> weeks in both the study and control sockets. The results were statistically significant ( $P < 0.05$ ).

#### Hard-tissue analysis

##### Visual interpretation

At the end of 1<sup>st</sup> week, 65% of the study sockets were found to be less radiolucent than the normal bone and 38% of the control sockets were found to be less radiolucent than the normal bone. After 3 weeks, 98% of the study sockets were found to be less radiolucent than normal bone and 88% of the control sockets were found to be less radiolucent than the normal bone. In the 6<sup>th</sup> week, 18% of the study sockets were found to be the same as normal bone and 4% of the control sockets were found to be the same as normal bone. The results were statistically significant ( $P < 0.05$ ).

#### Area of bone coverage

In the 1<sup>st</sup> week, the socket was filled with one-third bone level in 63% in the study group and only 37% in the control group. In the 3<sup>rd</sup> week, 98% of the sockets in the study group were covered with one-third bone level and 87% of the sockets in the control group were covered with one-third bone level. In the 6<sup>th</sup> week, 85% of the sockets in the control side were filled with one-third bone level and 95% of the sockets in the control side were covered with one-third bone level. Eighteen percent of the study side sockets were completely covered with bone, whereas in the control group, only 4% was covered with bone.

#### Grayscale analysis

The mean value at the end of 1<sup>st</sup> week in the study side was 70.03 and in the control side was 60.79. In the 3<sup>rd</sup> week, the mean value was 96.36 in the study side and 90.52 in the control side. In the 6<sup>th</sup> week, the mean scale value was 111.30 in the study side and 97.36 in the control side.

#### Pain assessment

The mean visual analog scale value at the end of 1<sup>st</sup> week was found to be 1.45 in the study group and 1.40 in the control group. The value was nearly equal for the two sides, decreasing to zero after the 3<sup>rd</sup> week. These results were not significant.

The healing differences between a typical study and control socket are shown in Figures 1 and 2.



Figure 1: Soft tissue healing with and without platelet-rich fibrin

## DISCUSSION

This study was a prospective randomized control trial comparing the wound healing of extraction sockets in diabetic patients with and without the use of PRF. It was hypothesized that the use of PRF would improve wound healing in this particular population.

There are few studies that evaluate extraction socket healing in diabetics. In a study conducted on diabetic rabbits, Younis *et al.*<sup>[6]</sup> stated that untreated rabbits had longer healing times than rabbits treated with insulin, due to delay in the onset of cell proliferation and osteoblast differentiation. The same results, however, have not been reproduced in humans. Huang *et al.*<sup>[7]</sup> prospectively analyzed extraction socket healing in 224 diabetics and 232 nondiabetics, and stated that there was no difference in the healing rates between the two groups. Aronovich *et al.*<sup>[2]</sup> prospectively observed 115 diabetic patients who required dental extractions, and attempted to detect an association between the rate of postextraction epithelialization and glycemic control status. They stated that there was no statistically significant association between postextraction epithelialization and preoperative blood glucose levels. However, more well-designed studies would be required to validate this viewpoint.

Despite the view of the above studies, any additional help in wound healing would be beneficial for the diabetic patient.

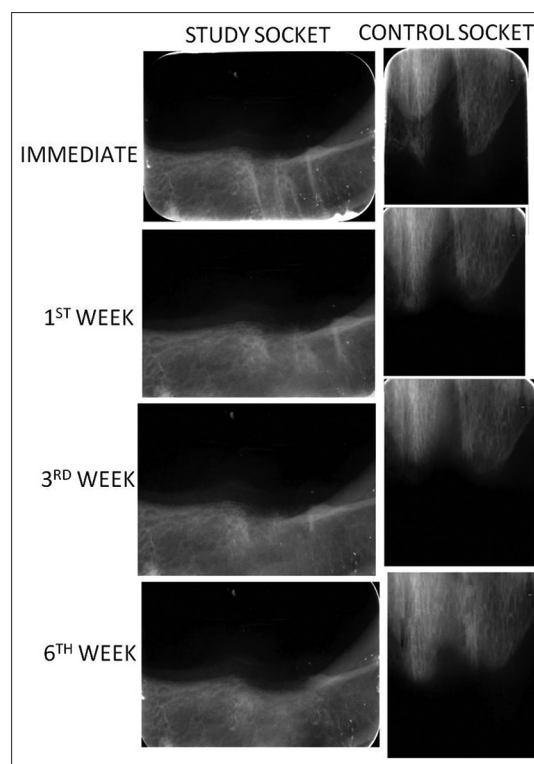


Figure 2: Hard-tissue healing with and without platelet-rich fibrin

Platelet concentrate has been used in surgery for innumerable years. The objective of using autologous preparations was to concentrate platelets along with growth factors to deliver it to a surgical site for promotion of local healing. Platelet concentrate has been reported to have favorable effects on hard- and soft-tissue healing, as well as on postoperative pain discomfort. PRF, the new generation of platelet concentrate, was developed by Choukroun *et al.* in 2001.<sup>[5]</sup> PRF has several advantages over PRP, including ease of preparation as well as application, minimal expenditure, and the absence of biochemical modification because bovine thrombin or anticoagulant is not required for preparation. PRF contains a strong fibrin matrix that ensures continuous, slow release of growth factors to the wound site.<sup>[8]</sup> We therefore decided to use PRF in this study.

The use of PRF in patients whose wound healing is compromised has not been adequately evaluated. Mozzati *et al.*<sup>[9]</sup> evaluated the effectiveness of plasma-rich growth factors in enhancing socket healing following tooth extraction in 34 Type I diabetic patients. This was also a split-mouth study in which each patient also served as the control. These authors stated that the side treated with PRGF had better and faster healing, while pain levels were nearly equal on both sides. The authors also administered a questionnaire which showed that patients were satisfied and were 100% in favor of treatment with PRGF. Hard-tissue healing, however, was not evaluated in this study. Moreover,

the follow-up period was short (21 days). The present study attempted to improve the design of the study by Mozzati *et al.*<sup>[9]</sup> by increasing the sample size as well as the follow-up period. Hard-tissue healing was also evaluated in the current study.

In general, the results of the present study support the results given by Mozzati *et al.*<sup>[9]</sup> Wound healing, both hard and soft tissue, was significantly better in extraction sockets filled with PRF than in the control sockets, while pain levels were comparable.

Although this study shows that the use of PRF accelerates extraction socket healing in diabetic patients, the drawbacks of this technique must be considered. PRF preparation necessarily involves a venipuncture for drawing of blood from the patient. This additional invasive procedure is not accepted by all patients, particularly those who have “needle-phobia.”

This study did not attempt to assess healing based on the glycemic status of the patient, as each patient served as their own control. This might have led to some confounding. Future studies should consider using randomized, separate patients for experimental and control sockets to eliminate this bias.

## CONCLUSIONS

Both hard-tissue healing and soft-tissue healing were found to be better in the sockets containing PRF, while pain levels were comparable. We therefore believe that the use of PRF has beneficial effects in extraction socket healing in diabetic patients, and, given the simplicity of the methodology involved, must be considered for routine use in all diabetic patients.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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