Efficiency of platelets rich fibrin (PRF) in the treatment of alveolar osteitis and the subsequent bone formation (a randomized controlled clinical study)

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Abstract

Alveolar osteitis is the most common post-operative complication after dental extraction, with severe pain as the main complaint of patients. This study aimed to evaluate the effectiveness of platelet-rich fibrin in treating alveolar osteitis. The study scope included pain reduction, clinically assessed tissue healing, and radiographically evaluated socket bone formation. A total of 20 patients presenting with alveolar osteitis were included in the study. Ten of them were treated using Alveogyl as a control group, and 10 were patients treated using platelet-rich fibrin as a study group. The evaluation of pain reduction using the Visual Analogue Scale (VAS), gingival healing using the Landry Healing Index, and bone formation in the socket using standardized periapical x-rays at baseline, 3 months, and 6 months follow-up. Results showed significant relief of pain, resolution of inflammation, and bone formation in both groups. PRF was more effective in promoting healing compared to Alveogyl. The Alveogyl group experienced a better outcome, with complete elimination of pain. Bone formation was equal between the two groups, with a slightly higher density in the PRF group. Both treatment modalities demonstrated exemplary performance in treating alveolar osteitis, as evidenced by pain reduction, resolution of inflammation, and bone formation. Although PRF showed better tissue healing and significantly more bone formation, alveogyl remains faster in pain reduction, which is the primary concern of patients presenting with alveolar osteitis.
Keywords: Alveolar osteitis, Dry socket, Platelet-rich fibrin, Alveogyl, pain reduction, bone formation, gingival healing.

Introduction

Dental extraction is a painless procedure that results in even healing and no post-operative complications (1). However, one of the most common post-operative complications, like alveolar osteitis, or "dry socket," can be severe between 2 and 4 days after extraction and is more common in females aged 30 or older. With an incidence

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Table 1: The materials used

Alveogyl dental paste	**Articaine hydrochloride 4% with epinephrine 1/100 000**
Centrifuge machine	Diclofenac potassium 50 mg – Cataflam tablets
Silk sutures	Rim XCP and bite registration for standardization of periapical x-ray
Tube holder	Image J software
PRF box	Statistical package for social science (SPSS) version 24
Blood tubes without anticoagulant	Papillon

of range 0.5% to 5%, this condition is sensitive to tactile stimulation and can extend to the ear and neck, making it resistant to analgesics and anti-inflammatory medications (2).

Dry socket is caused by increased fibrinolytic activity, leading to premature blood clot dissolution after extraction, which is triggered by physiological or non-physiological factors that activate the plasminogen pathway (3).

Wound healing has been a topic of interest for years, with bioactive surgical additives developed to regulate inflammation and enhance healing. Platelets, containing growth factors, promote cell movement and multiplication. Autologous platelet concentrates utilize platelets from the patient's blood to form fibrin clots, facilitating faster healing.

Platelet-rich fibrin (PRF) is a second-generation biomaterial derived from blood harvest without anticoagulants, containing cytokines, platelets, and growth factors trapped and released after a brief period. It can serve as a resorbable membrane, aiding in wound healing by directing the movement of epithelial cells (4).

Leukocyte-rich platelet-rich fibrin (L-PRF) is a commonly used method in oral and maxillofacial surgery due to its ability to enhance healing, trap cytokines and growth factors, and contain leukocytes (4).

Platelet-rich fibrin (PRF) is a biologically active material made of cytokines, chemokines, and structural glycoproteins within a slowly forming fibrin network. It contains growth factors like PDGF, VEGF, TGF-β1, and BMP-1, as well as coagulation and adhesion molecules, which collectively support cell activation, wound healing, and bone regeneration. These components enhance angiogenesis and fibrin remodeling, leading to stronger connective tissue and improved soft tissue healing. Activated platelets, leukocytes, and macrophages in PRF also release signals that stimulate bone cells, aiding in the regeneration of mineralized tissue (2)

PRF is utilized in periodontal surgery as a barrier to impede healing, preventing damage to gingival tissues during bone grafting and expediting soft tissue recovery. It can also serve as a filler material and membrane in guided tissue regeneration (GTR). In implantology, it is used to preserve alveolar ridge proportions adjacent to dental implants and promote healing in socket grafting procedures. PRF can be combined with bone grafts or used to close perforated Schneiderian membranes in sinus lifting procedures (5).

In conclusion, platelet-rich fibrin is a promising alternative to traditional blood clots and has shown promising results in wound healing.

In light of the above-mentioned versatility of PRF, the present trial aimed to assess the efficacy of PRF in managing pain, delayed wound healing, and bone formation associated with established AO, following the extraction of mandibular molars.

Materials and Methods

This Study is an experimental, randomized controlled clinical trial. Patients were selected from the outpatient Clinics of the Oral Surgical Sciences Department, Faculty of Dentistry, Beirut Arab University, Beirut, Lebanon. A sample size calculation is conducted using the epitools.ausvet.com.au website, similar to a study by Keshini et al (2020) (6). This yielded a total number of 18 participants (divided into control and study groups). To avoid dropout from the sample throughout the entire study period, two additional participants were included, bringing the total sample size to 20 participants.

The patients were selected conveniently to fulfill the following inclusion and exclusion criteria.

- Inclusion criteria:
  - Age ranges from 18 to 60 years
  - Both genders
  - Recent non-surgical extraction of mandibular molars, 2 – 3 days with alveolar osteitis
  - Free from any systemic diseases
  - Without any sign of active infection in the extracted socket
- Exclusion criteria:
  - Recent radiation therapy at the site of extraction
  - Pregnant and lactating women
  - Women on oral contraceptives
  - Previous history of antibiotic therapy for the treatment of dry socket
  - Underlying systemic disease or compromised immunity
  - Tumor or large cyst at the site.

sample was randomly divided into two groups, each consisting of 10 cases, by tossing a coin. The face was the study side, and the back was the control side:

i. Group A (control group): Socket treated with alveogyl (n=10)
ii. Group B (study group): Socket treated using PRF (n=10)

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After obtaining University Institutional Review Board (**IRB**) approval (IRB number: 2024-H-0141-D-M-0589), patients were informed about the nature of the study and signed an informed consent form before undergoing surgery.

Methods

Pre-operative Phase

Patients presenting significant symptoms like continuous throbbing pain radiating to the ear, temple, and neck. Pain starts 2-3 days after extraction, and is not relieved even after medication. Patients present with a foul taste and signs devoid of blood clots.

The severity of the AO is evaluated according to the signs and symptoms listed in Table 2.

Operative Phase

Group A Control Group)

This group was treated using Alveogyl. It consists of a brown, fibrous paste, available in jars of 12g. It contains the following ingredients per 100 g (Septodont).

Active ingredients:

- Penghawar djambi - A styptic is a specific type of antihemorrhagic agent that works by contracting tissue to seal injured blood vessels.
- Eugenol
- Sodium lauryl sulphate (SLS) – a microbicide against pathogens
- Calcium carbonate
- Mint flavor
- Excipients (Vehicle)

The socket was gently irrigated with warm normal saline. 0.2 grams of Alveogyl (according to its instructions for use) were placed in the socket.

Group B (Study Group)

- According to the protocol of Choukroun et al. in 2001, the PRF was prepared as follows: 10 ml of intravenous blood was withdrawn from the vein in the antecubital fossa (Figure 1) (8). Samples were retrieved from the patient without the addition of any anticoagulant. 10 ml of blood was collected with glass-coated plastic tubes and subjected to centrifugation at 3000 rpm for 10 minutes (Figure 2). A fibrin clot formed in the middle part, while acellular plasma was present in the upper part of the tube, and red corpuscles were located at the bottom part. The fibrin clot was abstracted comfortably from the basal part of the tube (Figure 3).
- Using the appropriate PRF set, the segregated PRF (Figure 4) was placed into the socket after gentle irrigation of the socket with warm normal saline and stabilized with the help of figure-of-eight sutures or X sutures (Fig. 5,6,7,8,9) (7).

Figure 1. Blood withdrawal from the antecubital area

Table 2. Evaluation criteria (7)

	Pain	Degree of Inflammation	Exposed Bone
Method	Visual analogue scale	Landry Healing Index	Number of socket walls exposed
Score	1 – 10	1. Very poor 2. Poor 3. Good 4. Very good	1. One wall 2. Two walls 3. Three walls 4. Four walls
	Taste	**Radiographically**	
Method	Subjective questions	Rim XCP film; Image J software	
Score	1. Sour 2. Bitter 3. Metallic 4. Salty		

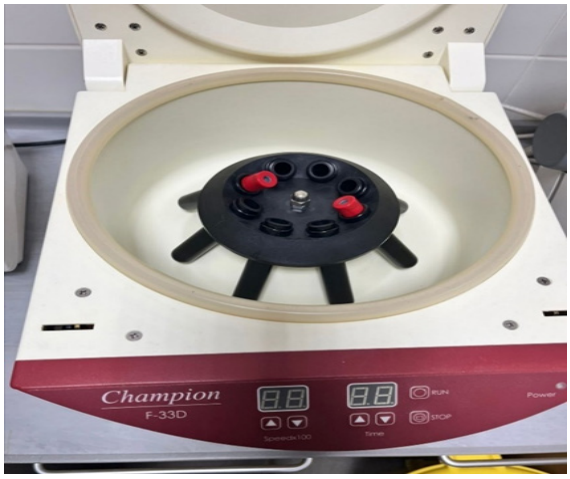

Figure 2. Champion F-33D centrifuge machine

Figure 3. PRF tube after centrifugation showing 3 layers.

Post-operative Evaluation Criteria

- Pain was evaluated before dry socket treatment and at the 7th and 14th day. Pain and discomfort were examined using a visual analogue scale.
- The soft tissue healing was measured using the Landry et al. healing index score at the baseline, 7th, and 14th day post-treatment (9). Inflammation was assessed clinically by gently probing the extraction socket to determine the presence or absence of bleeding.
- Granulation tissue formation at the treated site was assessed clinically on the Baseline, 7th, and 14th day post-treatment. This is evident clinically by the coverage of the exposed bony walls of the extraction site associated with AO by soft granulation tissue which can be graded as: 0 - no bony walls exposed, 1 - only one bony wall exposed, 2 - two bony walls exposed, 3 - three bony walls exposed, and 4 - four bony walls exposed.
- Subjective questions are asked of the patient to identify whether the taste is Sour, Bitter, Metallic, or Salty.
- The radiographic examination of the socket was evaluated at baseline, 3 months, and 6 months post-operatively. Standardized digital periapical x-rays were used to measure bone density using an XCP film (sensor) holder and ImageJ software. A standardized-sized square (33 x 33 pixels) was inserted and determined by identification the intersected point between 2 straight lines: a horizontal line extending from the distal wall of the socket of the mesial root to the mesial wall of the socket, and a vertical line extending from the alveolar bone crest to the apex of the socket. The bone density within this square was measured by selecting a Region of Interest (ROI) from the tools, and then the given data were analyzed in terms of pixels. The same square was drawn for all patients, and bone density was measured; the results were then subjected to statistical analysis (10).

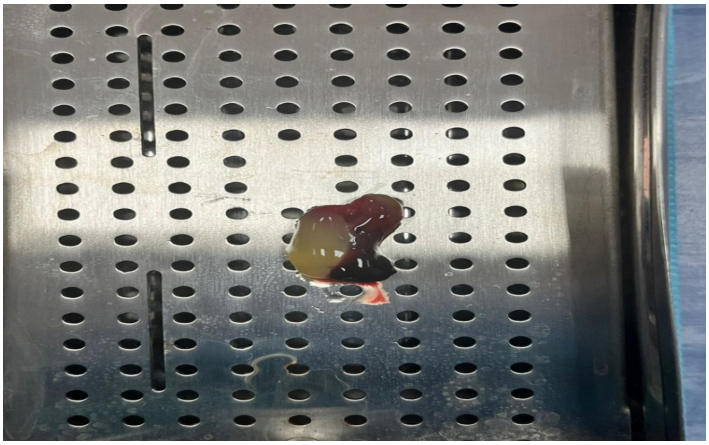

Figure 4. PRF membrane after centrifuge

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Control group: Alveogyl

Figure 5. Baseline clinical picture showing alveolar osteitis affecting lower second molar

Figure 6. Directly after the application of Alveogyl inside the socket

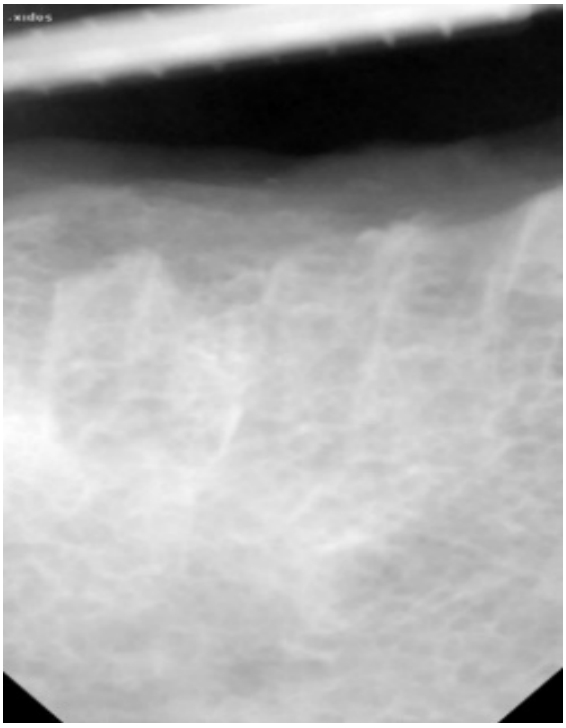

Figure 7. Radiographical examination after 6 months

Study group: PRF

Figure 8. Baseline clinical picture showing alveolar osteitis affecting the lower first molar

Figure 9. Clinical picture directly after the placement of PRF

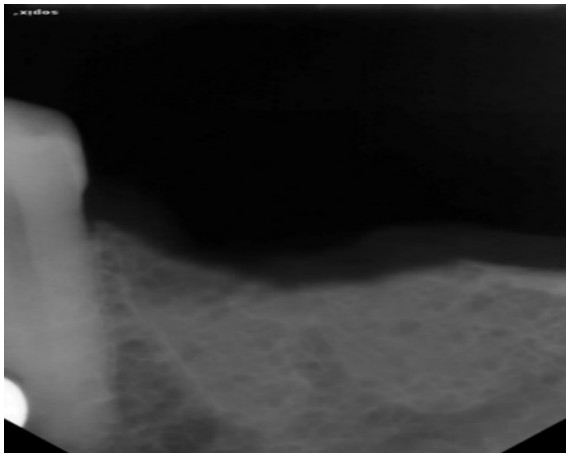

Figure 10. Radiographical examination after 6 months

Results

The entire study sample consisted of females, who represented the majority, with 13 cases (65%), while males accounted for 7 cases (35%). According to the affected tooth, we have a predominance of second and third molars, with 40% and 35% of the cases, respectively. According to the age of the subjects, the mean age of the entire study sample was 36.6.

The analysis indicates that both treatment groups exhibited improvements in the Landry Healing Index scores over time, with PRF showing a higher percentage of "Good" and "Very Good" scores, particularly on Day 14. This suggests that PRF is more effective in promoting healing compared to Alveogyl.

Pain scores were grouped in categories: 0=no pain, 1-3=mild pain, 4-6=moderate pain, 7-10= severe pain.

Table 3. Distribution of laundry healing index scores for PRF and Alveogyl groups at different time points

		Group			
	PRF		**Alveogyl**		
	Count	%	Count	%	
Landry Healing Index Baseline	Very Poor	4	44.4%	2	25.0%
	Poor	5	55.6%	6	75.0%
	Good	0	0.0%	0	0.0%
	Very good	0	0.0%	0	0.0%
Landry Healing Index Day 14	Very Poor	0	0.0%	0	0.0%
	Poor	0	0.0%	2	25.0%
	Good	4	40.0%	5	62.5%
	Very good	6	60.0%	1	12.5%

Table 4. Distribution of pain (VAS) scores for PRF and Alveogyl groups at different time points

		Group			
	PRF		**Alveogyl**		
	Count	Layer N %	Count	Layer N %	
Pain (VAS) Baseline	no pain	0	0.0%	0	0.0%
	mild pain	0	0.0%	0	0.0%
	moderate pain	1	5.0%	1	5.0%
	severe pain	9	45.0%	9	45.0%
Pain (VAS) Day 14	no pain	9	45.0%	10	50.0%
	mild pain	1	5.0%	0	0.0%
	moderate pain	0	0.0%	0	0.0%
	severe pain	0	0.0%	0	0.0%

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This progression illustrates a successful alleviation of pain in both groups over two weeks, with a slightly better outcome for the Alveogyl group, as it eliminated pain by Day 14.

Regarding taste preferences for the two different groups (PRF and Alveogyl) on two different days (Baseline and Day 7). On the Baseline, for the PRF group, 50% of participants reported “No taste,” 30% reported “Sour,” and 20% reported “Metallic.” Meanwhile, for the Alveogyl group on the same day, 40% reported “No taste,” 40% reported “Sour,” and 20% reported “Metallic”. On Day 7, the taste preferences in both groups converged, with 100% of participants in both PRF and Alveogyl groups reporting “No taste”. This suggests that both groups experienced a shift in taste preference over a week, moving towards a loss of taste sensation.

Radiographically Results

This analysis suggests that while both groups exhibited radiographic improvement over time, there was no significant difference between the two groups at any measured time point. Similarly, neither group displayed statistically substantial changes over the respective periods.

Discussion

Dry socket is a common complication after dental extractions, often causing pain that is resistant to analgesics and anti-inflammatory medications. Preventive measures include the use of hemostatic agents, gelatin sponges, growth factor plasma, and laser application. Treatment involves debris removal using 0.2% chlorhexidine or saline solution, sedatives such as eugenol, and antibiotics as a prophylactic measure. However, the effectiveness of antibiotics as a therapeutic tool remains a topic of debate (11)

The studies included in the analysis exhibited significant variations in the process of selecting participants. The mean age for the control group was 35.5, while the study group had a mean age of 37.6. The average age of the patients included in the study was 36.6. Several studies, including those by Rastogi et al. in 2018 and Chybicki and Janas-Naze in 2022, found that the average age of the participants was 18, with a maximum age of 60. Age can influence the level of surgical difficulty because of the differences in root and bone stiffness, which can result in more challenging and perhaps more traumatic surgeries (12)(13)

The majority of the remaining studies, such as the ones conducted by Rastogi et al. in 2018 and Reeshma and Dain in 2021, showed a predominance of women. This finding aligns with the results of this study, which reported that 65% of the participants were females. This is likely because women of reproductive age experience constant sinusoidal fluctuations in estrogen levels, which might alter the inflammatory response and consequently affect pain perception. Furthermore, the utilization of oral contraceptives may elevate plasma fibrinolysis and increase the risk of dry socket. However, females who are using oral contraceptives are typically not included in this type of study, as was the case in the present research (12)(14)

In this study, the mandibular second molar was the most affected tooth by AO, followed by the mandibular third molar. Multiple investigations corroborated this finding, including Chakravarthi’s research in 2017 (15). In 2020, Sharma et al. found that the third molar area was the most frequent location for alveolar osteitis.(2) However, Reeshma and Dain in 2021, and Chybicki and Janas-Naze in 2022 did not provide details about the specific extraction site they examined. It is worth noting that surgical extractions in the molar region may be required more regularly. A surgical approach led to a tenfold higher occurrence of AO compared to the non-surgical approach (14)(13)

Bacteria can ferment food particles in a dry socket, producing toxins or antigens that can irritate the exposed bone, cause a foul taste, and lead to jaw pain. Most patients experience a loss of taste, while some report tasting sour or metallic flavors. After surgery, all patients reported that the unpleasant tastes had disappeared. Mamoun suggests irrigating the socket with saline, chlorhexidine, or medication to help resolve the taste issue. Eliminating leftover food particles and covering the socket effectively eliminates all associated symptoms (1)

In 2020, Keshini et al. studied the effectiveness of PRF and alveogyl in treating alveolar osteitis. Alveogyl is a dressing material used to control alveolar osteitis, providing rapid pain relief and a relaxing effect during healing. PRF, distinguished by its gradual polymerization, forms a fibrin network that resembles natural fibrin, promoting cell movement and growth. PRF serves as a storage of platelets, leukocytes, cytokines, and growth factors, facilitating the release of essential factors for angiogenesis, tissue healing, and cicatrization (6)

Regarding pain reduction, the study found that both alveogyl and PRF were effective in reducing pain. However, the alveogyl group noted faster pain relief compared to the PRF group. This finding aligns with the research conducted by Keshini et al. in 2020, which also demonstrated a statistically significant difference in pain reduction between Alveogyl and PRF. Thus, both groups exhibited a comparable reduction in pain by the 10th day after surgery (6)

In 2019, Rashed, Elsharkawy, and Zaied reported further significant findings regarding the reduction of pain. The study found a substantial statistical difference in pain reduction and pain remission between the Alveogyl group and the PRF group. However, there was no statistically significant change between the groups on day 7. Our findings align with the results regarding pain reduction, demonstrating successful pain relief in both groups over two weeks. The Alveogyl group exhibited a slightly superior outcome, with complete pain elimination by Day 14 (17)

According to Chybibki and Janas-Naze in 2022, the observed benefits in pain control are likely due to the accelerated wound healing facilitated by PRF (13) This is because PRF increases chemotaxis, angiogenesis, and the proliferation and differentiation of human osteoblasts and fibroblasts in human bone mesenchymal stem cells. Furthermore, Sharma et al. in 2020 and La Rosa et al. in 2023 stated that PRF promotes the natural healing process of the dry socket

wound by protecting the exposed nerve endings, resulting in a soothing effect (2)(16) In addition, Chakravarthi stated in 2017 that the growth factors counteract the inflammatory kinins released from the dry socket, hence promoting pain alleviation. Therefore, PRF can be regarded as a suitable biomaterial for pain control and healing (15)

Rashed, Elsharkawy, and Zaied in 2019 found that soft tissue healing was more rapid and superior in the PRF group compared to the Alveogyl group. However, no statistically significant difference was observed between the groups on days 7 and 14, as they exhibited practically identical findings. The use of PRF for managing alveolar osteitis resulted in significantly better outcomes, including enhanced healing of the socket and decreased inflammation, as compared to the use of Alveogyl packing. Our investigation confirmed that PRF is potentially more efficacious than Alveogyl in accelerating soft tissue healing. This indicates that the PRF membrane exhibits a gradual and sustained release of growth factors for a minimum of 7 days and up to 28 days, demonstrating the prolonged activation of its underlying properties (17)

According to the exposed bone walls, Keshini et al. in 2020 observed a statistically significant decrease in the number of socket wall exposures in both the Alveogyl and PRF groups after treatment. Our findings align with the results we obtained, which indicate a more significant enhancement during the first week post-operative compared to the subsequent week. However, the results suggest that there are no significant statistical differences in the measurements of exposed bone between the two groups on the specified days. This indicates that both PRF and Alveogyl have an equivalent effect on the exposure of bone walls (6)

Osteoblasts emerge in the tooth socket following tooth extraction, and these cells stimulate the formation of bone that occupies the tooth socket. Two hypotheses have been proposed about the source of osteoblasts during socket healing. The first one is the differentiation of mesenchymal stem cells (MSCs) in the periodontal ligament (PDL) into osteoblasts. Another potential scenario is that mesenchymal stem cells (MSCs) are sourced from the bone marrow in conjunction with the development of newly formed blood vessels.

Several growth factors and cytokines, including bone morphogenetic protein (BMP), transforming growth factor (TGF)-β, and Wnt genes, are involved in the process of bone formation and regeneration.

Platelet-rich plasma (PRF) comprises a large number of platelets and leukocytes. Within this group of cells, macrophages can directly stimulate osteogenesis. The primary growth factors in PRF include transforming growth factor-β1 (TGF-β1), vascular endothelial growth factor (VEGF), bone morphogenetic protein-1 (BMP-1), platelet-derived growth factors (PDGFs), and insulin-like growth factor-1 (IGF-1).

In 2018, a study by Zhang, Ruan, and Shen found that the PRF group significantly reduced resorption in the height and width of the buccal and lingual alveolar crests compared to the control group. However, the study did not provide sufficient evidence to support the effectiveness of PRF in reducing alveolar bone resorption and encouraging bone growth in extraction sockets. The researchers found that PRF membrane enhanced gum healing and reduced discomfort post-surgery, but did not significantly reduce alveolar bone resorption. The study also found no significant difference in bone regeneration between the study and control groups (18)

In 2018, Srinivas et al. conducted a study on 30 patients who underwent a procedure with PRF at one extraction site. The bone density in the PRF group was evaluated using CBCT at 24 hours and 3 months after the procedure. The results showed a significant increase in bone regeneration compared to the control group. Despite post-operative follow-up, the PRF group exhibited superior outcomes, contradicting previous findings on radiographic bone growth (19)

In 2023, Guan et al. published a meta-analysis that assessed postoperative radiography, explicitly focusing on residual graft, graft volume, and bone volume density. The article conducted a comparison of the newly developed bone height between the two groups, six months following the procedure (20). The findings revealed that the PRF group exhibited a greater height than the control group (21)

The study found that the PRF group exhibited faster and more effective gingival healing compared to the Alveogyl group. PRF management of alveolar osteitis improved socket healing, reduced inflammation, and was more economical compared to Alveogyl packing. Exposed bony walls in dry sockets demonstrated better healing, characterized by early granulation tissue formation and complete coverage with healthy granulation tissue after 2 weeks. This is due to the slow, continuous release of growth factors by the PRF membrane.

The study found that PRF placement in alveolar osteitis cases improved bone formation inside the socket compared to alveogyl placement. Over the course of six months, there was no statistically significant difference between the control and study groups; however, a slightly higher rate of bone formation was observed in the PRF group. Further histopathological studies are needed to understand the newly formed bone between the socket filled with alveogyl and the one treated with PRF. The nature of the newly formed bone at 4 and 6 months also warrants further study.

Conclusion

PRF showed superior tissue healing over alveogyl treatment. As well as a slightly more bone formation than alveogyl. However, it was not statistically significant. In terms of pain relief, alveogyl showed a faster decrease in pain than the PRF group. According to the exposed bony walls as well as the taste, both groups showed equal improvement.

At the end of this study, we can conclude that Alveogyl and PRF demonstrated an ideal treatment of alveolar osteitis in terms of tissue healing, pain relief, and bone formation.

Since the healing of PRF cases was superior, it can be used as a good inflammatory moderator in cases of alveolar osteitis.

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Conflict of interests

The authors declare that there are no competing interests regarding the publication of this paper.

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