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Evaluation of efficacy of L-PRF with and without hyaluronic acid on pain, soft tissue healing and swelling post surgical transalveolar extraction of mandibular molars: A comparative study

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ABSTRACT

Tooth extraction, a common dental procedure addressing decay, fractures, periodontal disease, infections, and orthodontic needs, initiates a natural healing process in the post-extraction socket involving bone cell migration and selective bone resorption and apposition. However, this process often leads to dimensional loss in the alveolar ridge, complicating tooth replacement, especially in implant therapy. Preventive measures like socket preservation with grafts and immediate or early implant placements are employed to mitigate post-extraction bone loss. Socket preservation aims to minimize dimensional changes in the alveolar ridge, while immediate implant placements, though advantageous, can sometimes cause buccal bone defects, necessitating grafts with lower success rates. Leukocyte-Platelet Rich Fibrin (L-PRF), a significant advancement in regenerative medicine, is derived from the patient's blood through controlled centrifugation, creating a fibrin matrix enriched with platelets, leukocytes, and growth factors. L-PRF's autologous healing properties have broad applications in dentistry, orthopedics, dermatology, and beyond. In dentistry, it enhances bone grafting, implantology, and periodontal surgery by promoting tissue regeneration and infection control. As an autologous therapy, L-PRF reduces the risk of immune reactions or disease transmission, offering a safe and effective regenerative solution. Hyaluronic Acid (HA), a naturally occurring glycosaminoglycan in the human body, is essential for skin hydration, joint lubrication, and tissue integrity. HA's ability to attract and retain water molecules makes it a key component in skincare for reducing fine lines and promoting a youthful complexion. In the medical field, HA is used in joint injections to alleviate osteoarthritis symptoms due to its biocompatibility and non-immunogenic properties. This study aims to evaluate the effectiveness of autologous Platelet-Rich Fibrin (PRF) membranes in enhancing post-extraction socket healing. Derived from non-anticoagulated blood, PRF is proposed to accelerate wound healing, increase bone fill, and reduce bone resorption. The research explores the broader applications of L-PRF and HA, highlighting their roles in advancing regenerative medicine and aesthetics. The intersection of these innovative approaches addresses immediate dental concerns and paves the way for broader medical applications, underscoring continuous advancements in medical science.

Key words: Extraction, PRF, Regeneration, Hyaluronic Acid, Wound Healing.

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INTRODUCTION

Tooth extraction, a routine dental procedure addressing issues like decay, fractures, periodontal disease, infections and orthodontic needs, initiates a natural healing process in the post-extraction socket. This intricate sequence involves bone cell migration, leading to selective bone resorption and apposition. Unfortunately, this process often results in dimensional loss in the residual alveolar ridge, creating challenges for the replacement of lost teeth, especially in implant therapy. To counteract post-extraction bone loss, various preventive measures are employed, such as socket preservation with grafts and immediate or early implant placements. Socket preservation, utilizing grafts or biomaterials, aims to minimize dimensional changes in the alveolar ridge following tooth extraction. Immediate implant placements, despite their advantages, can sometimes lead to buccal bone defects, necessitating grafts with lower success rates [1]. This complexity highlights the need for effective strategies to enhance socket healing and preserve bone volume. Leukocyte-Platelet Rich Fibrin (L-PRF) stands at the forefront of regenerative medicine, revolutionizing various medical disciplines with its autologous healing properties. Derived from the patient's own blood, L-PRF is obtained through a controlled centrifugation process that separates blood components based on their density. This results in a unique fibrin matrix enriched with platelets, leukocytes, and growth factors. L-PRF's versatility is evident in its widespread applications, notably in dentistry, where it has proven beneficial in procedures like bone grafting, implantology, and periodontal surgery. The concentrated platelets foster tissue regeneration, while the presence of leukocytes contributes to the body's natural defense mechanisms, aiding in infection control. This three-dimensional fibrin matrix acts as a scaffold, promoting a gradual release of growth factors, accelerating healing and minimizing inflammation.

Beyond dentistry, L-PRF has found utility in orthopedics, dermatology, and other medical fields. Its effectiveness in promoting soft and hard tissue regeneration, reducing postoperative complications, and enhancing overall treatment outcomes has garnered significant attention. As an autologous therapy, L-PRF minimizes the risk of immune reactions or disease transmission, making it a safe and viable option for patients seeking advanced regenerative solutions [2]. The continuous exploration and refinement of L-PRF applications underscore its potential to reshape the landscape of regenerative medicine, offering personalized and effective treatments across diverse medical domains. Hyaluronic Acid (HA) is a naturally occurring substance in the human body that plays a crucial role in maintaining skin hydration, joint lubrication, and overall tissue integrity. This glycosaminoglycan, found in connective tissues and fluids, has become a key component in skincare and medical applications. In the realm of skincare, HA is renowned for its ability to attract and retain water molecules, providing essential hydration to the skin, reducing the appearance of fine lines and wrinkles, and contributing to a plump and youthful complexion. In the medical field, hyaluronic acid is frequently used in joint injections to alleviate symptoms of osteoarthritis, acting as a lubricant and shock absorber [3]. Its biocompatibility and non-immunogenic properties make it a safe option for various medical and cosmetic interventions. As a versatile compound with applications ranging from skincare to orthopedics, hyaluronic acid continues to be a prominent player in enhancing both aesthetic and therapeutic outcomes.

This study focuses on the application of autologous Platelet-Rich Fibrin (PRF) membrane, a second-generation platelet concentrate with leukocytes in a dense fibrin matrix. Derived from non-anticoagulated blood, PRF has been proposed to enhance healing, bone organization, and volume percentage. The study's primary aim is to conduct a comprehensive clinical and radiographic evaluation of extraction socket healing using the PRF membrane. The hypothesis suggests that PRF will accelerate wound healing, increase bone fill, and reduce bone resorption, contributing to improved outcomes in post-extraction socket preservation. Moving beyond dental applications, the discussion extends to Leukocyte-Platelet Rich Fibrin (L-PRF), a revolutionary player in regenerative medicine. Derived from a patient's blood through a controlled centrifugation process, L-PRF is a unique fibrin matrix enriched with platelets, leukocytes, and growth factors. Its versatility spans various medical disciplines, finding utility in dentistry, orthopedics, dermatology, and more [4]. The autologous nature of L-PRF minimizes the risk of immune reactions or disease transmission, establishing it as a safe and effective option for patients seeking regenerative solutions. Additionally, Hyaluronic Acid (HA), a naturally occurring substance in the human body, assumes significance in maintaining tissue integrity, joint lubrication, and skincare. Renowned for its ability to attract and retain water molecules, HA contributes to skin hydration, reducing the appearance of fine lines and wrinkles, and promoting a youthful complexion. In the medical field, HA is frequently used in joint injections to alleviate symptoms of osteoarthritis, owing to its biocompatibility and non-immunogenic properties. In conclusion, the intersection of dental procedures, regenerative medicine through L-PRF, and the multifaceted applications of hyaluronic acid underscore the continuous advancements in medical science. These innovative approaches not only address immediate concerns in dental care but also pave the way for broader applications in regenerative medicine and aesthetics [5-8].

OBJECTIVES OF THE STUDY

To evaluate the wound healing, pain and swelling of extraction sockets post-surgical transalveolar extractions in mandibular molars with using only L-PRF . To evaluate the wound healing, pain and swelling of extraction sockets post-surgical transalveolar extractions in mandibular molars with using L-PRF and hyaluronic acid. To compare the pain, soft tissue healing and swelling of the extraction sockets in the above two groups.

MATERIAL AND METHODS

A prospective in-vivo was carried out in the Department of Oral and Maxillofacial Surgery, Dr. D.Y. Patil Dental College and Hospital, Pimpri, Pune. A total of 32 patients were included in the study.

SOURCE OF DATA COLLECTION

Patients indicated for transalveolar surgical extraction of mandibular molars under local anaesthesia.

Sampling technique used was convenience sampling with random allocation. A total of 32 patients were included in the study. There were split into 2 groups of 16 patients each.

Group A: 16 patients (L-PRF)

Group B: 16 patients (L-PRF and Hyaluronic Acid)

Inclusion Criteria

Patients indicated for transalveolar surgical extraction of mandibular molars. Patients in the age group of 18 years to 45 years. Patients willing to participate in the study.

Exclusion Criteria

Patients having history of systemic disorders like uncontrolled diabetes mellitus, hypertension, asthma, thyroid disorders or bleeding disorders. Patients not willing for follow up.

METHODOLOGY

This prospective study was carried out in Dr DY Patil Dental College and hospital, Pimpri, Pune, for patients who fit the inclusion criteria. A thorough case history was taken. The standards for reporting clinical trials in this investigation were the Consolidated Standards of Reporting Trials and the Declaration of Helsinki on medical ethics and protocol. All patients gave their informed permission after the hospital ethics committee gave their approval. The researchers created and carried out an open-label, monocentric, parallel-group, randomized clinical trial to address the goal of the study [9]. The trial cohort was prospectively allocated for extraction of mandibular molars throughout a 12-month period. Participants were randomly assigned to either of the groups. The primary endpoint of the study was to show the superiority of the combination of L-PRF and hyaluronic acid in the extraction sockets over the use of only L-PRF on the extraction sockets in extent of pain, wound healing and swelling after surgery. Lines A through E were measured, and their sum was calculated at various times to estimate the swelling. Secondary endpoints were to show between study arm differences in 1) extent of swelling on postoperative days 1 (T1), 3 (T3), and 7 (T7); 2) extent of maximal swelling; 3) measurement of subjective pain using a Visual Analog Scale (VAS) and 4) measurement of subjective outcomes (measured by patient questionnaire). Demographics and baseline characteristics also were obtained for assurance of group comparability (Figure 1).

SURGICAL PROCEDURE

All surgical procedures were performed by two oral and maxillofacial residents under local anesthesia. Surgery was carried out under sterile circumstances in accordance with a set surgical protocol. 20ml blood is withdrawn for L-PRF preparation. For Group B patients, Inj Hyaluronic Acid is kept ready [10-13]. Local anaesthesia 2% lignocaine with adrenaline 1:2,00,000 given as inferior alveolar, lingual and long buccal nerve block. Crevicular incision made and mucoperiosteal flap raised. Bone guttering was done using Burs 702 and HP 8. The transalveolar extraction of the mandibular molar(s) was carried out. Post extraction, either L-PRF was placed for Group A patients and L-PRF along with ABGel soaked with Hyaluronic Acid for Group B patients. Resorbable sutures were used for mucosal wound closure (Vicryl; Ethicon).

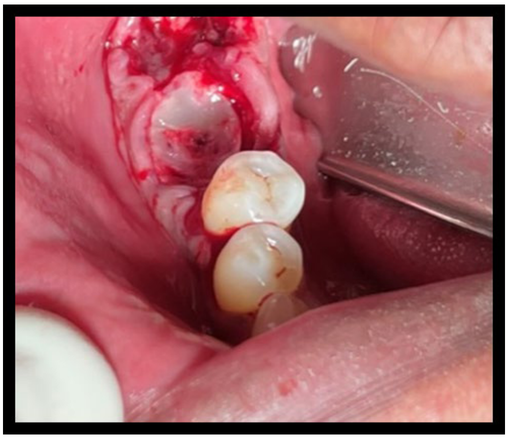


Figure 1: Placement of L-PRF in extraction socket.

Oral antibiotics were given post-operatively (Amoxicillin and potassium clavulanate). Post-operative instructions were given to the patients. Patient was recalled for follow up on the first, third and seventh day respectively and wound healing, pain and swelling was assessed (Figures 2 and 3).

METHODS FOR COLLECTING DATA

All measurements acquired were performed by 2 of the investigators at 5 specific time points: preoperatively (T - 1) and at baseline (T0), T1, T3, and postoperative day 7 (T7) (Figure 4).

SWELLING MEASUREMENTS

Swelling was assessed by a 5-line measurement using a standard flexible tape.

Line AC - most posterior point of the tragus to most lateral point of the lip commissure. Line AD - most posterior point of the tragus to the pogonion.

Line AB - most posterior point of the tragus to the lateral canthus of the eye.

Line BE - lateral canthus of the eye to most inferior point of angle of the mandible.

Line EF - most inferior point of the angle of the mandible to the middle of the nasal bone. Endpoints for tape measurements were marked using fine waterproof felt-tip pen.

Pain Measurements (Figure 5) Pain was assessed using the VAS Numerical rating scale assessed on the first, third and seventh day.

WOUND HEALING MEASUREMENT

Assessed using Landry's wound healing scale (Figure 6)

STATISTICAL ANALYSIS

The data was entered and analyzed using the Statistical Package for Social Sciences (SPSS) for Windows, Version 28.0. (Armonk, NY: IBM Corp) Confidence intervals were set at 95%, and a p-value ≤ of 0.05 was considered statistically significant. Categorical variables are presented in the form of a frequency table. Continuous variables are presented as Mean ± Std Deviation form. Independent t-test was applied to compare both groups for post-operative swelling, wound healing and pain scores after transalveolar extraction of mandibular molars [14-17].

RESULTS

Unpaired T test

Comparison of mean pain VAS score at all time interval in both the groups showed statistically insignificant difference between both the groups at pre op and day 1. Statistically significant difference was seen at day 3 and 7 showing time intervals with mean difference between group at day 3 1.00 ($p=0.001$) & day 7 ($p<0.001$) (Table 1) and (Graph 1).

Unpaired T test

Comparison of mean wound healing score at all time interval in both the groups showed statistically insignificant difference between both the groups at post op day 1. Statistically significant difference was seen at day 2 &7 time intervals with mean difference between group at day 3 0.438 ($p=0.014$) & day 7 ($p=0.009$) (Table 2) (Graph 2).

Unpaired T test

Comparison of mean facial swelling score at all time interval in both the groups showed

Figure 2: Injection Hyaluronic Acid.

Figure 3: Saturation of Ab Gel sponge with HA.

Figure 4: Placement of HA soaked Ab Gel in the extraction socket.

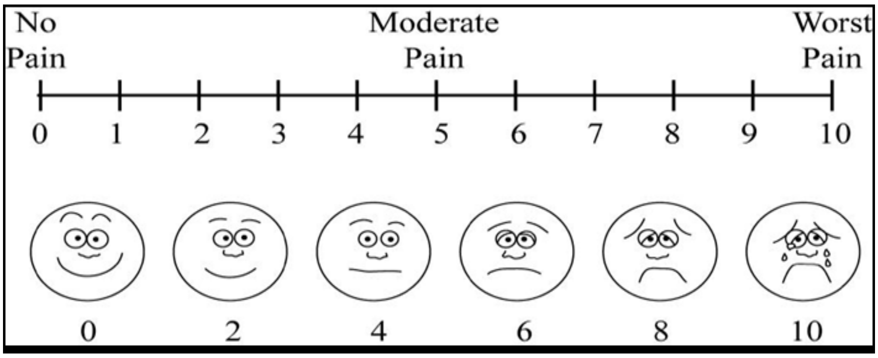


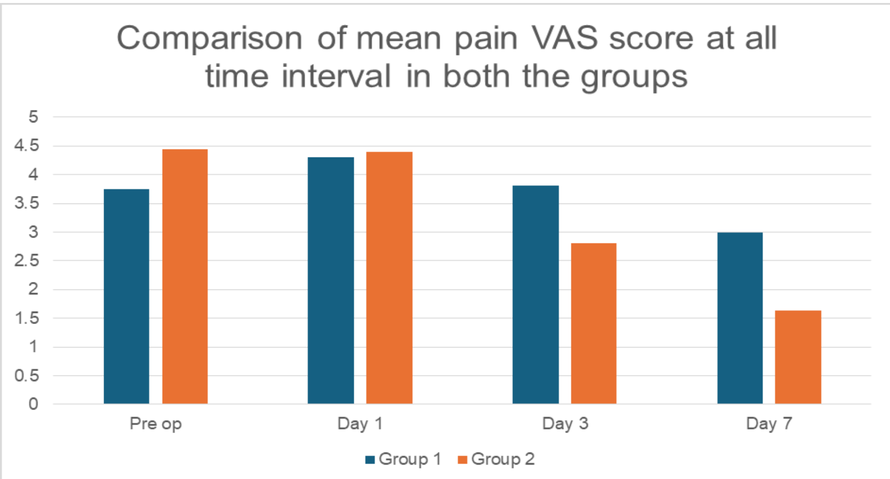
Figure 5: VAS Numerical Scale.

Score	*Clinical signs*
Healing index 1: very poor	Tissue color: ≥50% of gingiva red
	Response to palpation: bleeding
	Granulation tissue: present
	Incision margin: not epithelialized with loss of epithelium beyond incision margin
	Suppuration: present
Healing index 2: poor	Tissue color: ≥50% of gingiva red
	Response to palpation: bleeding
	Granulation tissue: present
	Incision margin: not epithelialized with connective tissue exposed
Healing index 3: good	Tissue colorr: ≥25% and <50% of gingiva red
	Response to palpation: no bleeding
	Granulation tissue: none
	Incision margin: no connective tissue exposed
Healing index 4: very good	Tissue color: <25% of gingiva red
	Response to palpation: no bleeding
	Granulation tissue: none
	Incision margin: no connective tissue exposed
Healing index 5: excellent	Tissue color: all tissues pink
	Response to palpation: no bleeding
	Granulation tissue: none
	Incision margin: no connective tissue exposed

Figure 6: Landry Index.

Table 1: Comparison of mean pain VAS score at all-time interval in both the groups.

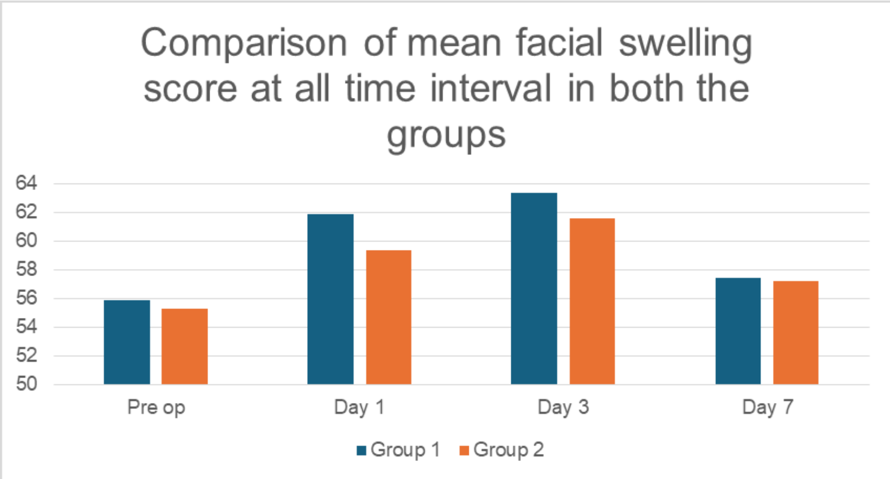
	GROUP	N	MEAN	STD. DEVIATION	MEAN DIFF	T	P VALUE
Pre op	1	16	3.75	0.856	-0.688	-1.98	0.057
	2	16	4.44	1.094			
Day1	1	16	4.31	1.014	-0.125	-0.357	0.723
	2	16	4.44	0.964			
Day3	1	16	3.81	0.834	1	3.771	0.001
	2	16	2.81	0.655			
Day7	1	16	3	0.816	1.375	5.056	<.001
	2	16	1.63	0.719			



Graph 1: Comparison of mean pain VAS score at all time interval in both the groups.

Table 2: Comparison of mean wound healing score at all time interval in both the groups.

	1	N	Mean	Std. Deviation	Mean diff	t	P value
Post Op 1	1	16	2.25	0.447	-0.313	-1.838	0.076
	2	16	2.56	0.512			
Post Op 2	1	16	2.63	0.5	-0.438	-2.621	0.014
	2	16	3.06	0.443			
Post Op 7	1	16	3.19	0.834	-0.813	-2.784	0.009
	2	16	4	0.816			



Graph 2: Comparison of mean facial swelling score at all time interval in both the groups.

Table 3: Comparison of mean facial swelling score at all time interval in both the groups.

	1	N	Mean	Std. Deviation	Mean diff	t	P value
Pre op	1	16	55.88	0.719	0.625	1.746	0.091
	2	16	55.25	1.238			
Day1	1	16	61.88	1.893	2.563	3.908	<.001
	2	16	59.31	1.815			
Day3	1	16	63.31	2.701	1.75	2.096	0.045
	2	16	61.56	1.965			
Day7	1	16	57.44	2.476	0.25	0.325	0.748
	2	16	57.19	1.834			

statistically insignificant difference between both the groups at pre op and day 7. Statistically significant difference was seen at day 1 & 3 time intervals with mean difference between group at day 1 2.563 (p<0.001) & day3 1.750 (p=0.045) (Table 3).

DISCUSSION

The provided data outlines the comparison of mean pain Visual Analog Scale (VAS) scores, wound healing scores, and facial swelling scores at various time intervals between two groups. Group A represents the use of L-PRF and Hyaluronic Acid (HA) in extraction sockets, while Group B likely represents a control group or a different treatment approach. The statistical analyses include t-tests, ANOVA, and post hoc tests to assess differences within and between groups [18-22]. The comparison of mean pain VAS scores reveals interesting insights. Initially, there's no significant difference between the groups at pre-operation and day 1. However, at day 3 and day 7, Group A shows significantly lower pain scores compared to Group B. This indicates that the use of L-PRF and HA may contribute to better pain management in the postoperative period, possibly due to enhanced tissue healing and reduced inflammation. Similarly, the wound healing scores exhibit significant differences between the groups. While there's no significant distinction at post-op day 1, Group A demonstrates superior wound healing at post-op day 2 and day 7 compared to Group B. This suggests that the application of L-PRF and HA accelerates the healing process, leading to better outcomes in terms of tissue regeneration and closure of the extraction socket. Facial swelling scores also portray noteworthy findings. Although there's no significant difference at pre-operation and day 7, Group A exhibits significantly lower swelling at day 1 and day 3 compared to Group B. This indicates that the use of L-PRF and HA may help in reducing postoperative edema, contributing to improved patient comfort and faster recovery. Analyzing within each group provides additional insights. In Group A, significant differences are observed in pain VAS scores between different time intervals, with postoperative days showing higher pain scores compared to pre-operation. However, these scores decrease significantly over time, indicating an improvement in pain levels as healing progresses. Similarly, wound healing scores significantly improve over time in Group A, suggesting effective tissue regeneration [23-26]. In Group B, while there's no significant difference in pain scores between pre-operation and day 1, there's a notable increase in pain scores at postoperative days 3 and 7, indicating a delayed recovery compared to Group A. Moreover, wound healing scores also show a significant improvement over time, albeit at a slower rate compared to Group A. The findings from this study have significant clinical implications. The use of L-PRF and HA in extraction sockets appears to offer several advantages, including better pain management, enhanced wound healing, and reduced facial swelling. These benefits can lead to improved patient satisfaction, faster recovery, and potentially lower risk of complications such as infection or dry socket. In conclusion, the data presented in this study suggest that the use of L-PRF and HA in extraction sockets contributes to improved pain management, wound healing, and reduction in facial swelling compared to conventional approaches. These findings highlight the potential of L-PRF and HA as valuable adjuncts in dental practice, offering enhanced outcomes and improved patient experiences [27-29]. The compiled data encompasses a plethora of studies investigating various interventions and their impacts on postoperative consequences subsequent to dental procedures, particularly tooth extraction. These studies delve into the efficacy of treatments such as Platelet-Rich Fibrin (PRF), Hyaluronic Acid (HA), and their amalgamations in mitigating pain, swelling, trismus, and fostering tissue healing. Numerous investigations, including those, Fabien exploring the utilization of PRF in bolstering wound healing and conserving alveolar ridge dimensions. These studies unveil that PRF application expedites soft tissue recovery, diminishes bone resorption, and alleviates postoperative pain compared to control cohorts. Moreover, PRF contributes to augmenting bone microarchitecture and intrinsic quality, signifying its potential in enhancing the recuperative process subsequent to tooth extraction and subsequent implantation. Studies conducted delve into the efficacy of HA in curtailing postoperative complications like swelling, pain, and trismus. These investigations posit that HA administration engenders noteworthy reductions in swelling and trismus, thereby ameliorating patient comfort during the postoperative convalescence. However, outcomes concerning pain alleviation exhibit variance across studies, with some demonstrating marked enhancements with HA application while others delineate mixed results. Furthermore, research endeavors delve into the cumulative effects of PRF and HA on postoperative outcomes. These inquiries propose that the synergy between PRF and HA precipitates diminished edema and analgesic consumption, implying a collaborative approach in managing postoperative complications. Studies elucidate the impact of HA in isolation on socket healing and osseous regeneration. Although initial findings showcase hastened bone formation with HA application, the enduring repercussions on alveolar dimensions remain ambiguous, underscoring the necessity for further elucidation of HA's role in tissue revitalization. Additionally, meta-analyses orchestrated furnish comprehensive assessments of the overarching efficacy of PRF and HA in abating postoperative symptoms. These analyses underscore that the application of PRF and HA precipitates significant reductions in pain, swelling, and trismus, bolstering their utility as efficacious interventions in fostering postoperative convalescence. Collectively, the amalgamated studies spotlight the promise of PRF and HA, independently or in tandem, in ameliorating postoperative outcomes ensuing dental procedures. However, further inquiry is imperative to unravel their mechanistic underpinnings and enduring ramifications on tissue healing and rejuvenation. Further research is warranted to validate these findings and explore additional applications of L-PRF and HA in various dental procedure [30-36].

CONCLUSION

In conclusion, the utilization of L-PRF (Leukocyte-Platelet Rich Fibrin) and Hyaluronic Acid (HA) in extraction sockets presents a promising approach in modern dentistry. Through their synergistic action, these biomaterials offer numerous advantages in promoting wound healing, reducing postoperative complications, and enhancing bone and soft tissue regeneration. The combination of L-PRF and HA has shown to accelerate the healing process by providing a scaffold for cell migration, proliferation, and differentiation. L-PRF facilitates the release of growth factors and cytokines, promoting angiogenesis and tissue regeneration, while HA contributes to tissue hydration and lubrication, facilitating cellular activities and maintaining a favourable microenvironment for healing. Moreover, the use of L-PRF and HA has demonstrated efficacy in preserving the alveolar bone, minimizing bone resorption, and preserving the ridge dimensions, which are crucial for successful implant placement and aesthetic outcomes. Additionally, their biocompatibility and safety profile make them ideal choices for socket preservation procedures. However, further research is warranted to explore the optimal protocols, concentrations, and combinations of L-PRF and HA for different clinical scenarios. Additionally, long-term clinical studies are necessary to assess their efficacy and sustainability over time. Thus, the incorporation of L-PRF and HA into extraction socket management represents a valuable adjunctive therapy to promote optimal healing outcomes, enhance tissue regeneration, and improve overall patient satisfaction in dental practice.

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