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Evaluation of the effects of A-PRF and oral dexamethasone use on postoperative complications in third molar extraction: a split-mouth randomized-controlled trial

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Abstract

Background The aim of this study was to compare the effects of advanced platelet-rich-fibrin (A-PRF) and oral dexamethasone on postoperative complications in patients undergoing impacted mandibular third molar extraction.

Methods This split-mouth, prospective, randomized-controlled study involved bilateral extraction of impacted mandibular third molars. A-PRF was applied to the extraction socket on one side, while postoperative oral dexamethasone was prescribed for the other side. Data were collected on pain, edema, trismus, and analgesic consumption. Intra-group and inter-group comparisons were performed. The Visual Analog Scale (VAS) was used for pain assessment. The patients were given a form to record their postoperative analgesic use. Pain assessments were conducted at postoperative 3, 6, 9, 12, 24 h, and on Days 2, 3, 4, 5, 6, 7, 14, and 30. Maximum interincisal distance was measured for trismus evaluation, while facial measurements between specific points were taken for edema assessment. Trismus and edema measurements were conducted on postoperative Days 2, 7, 14, and 30.

Results This study included 30 patients with bilateral impacted mandibular third molars (total of 60 extractions). The VAS scores were significantly lower on the side treated with oral dexamethasone compared to the A-PRF side at all measurement times ($p < 0.01$). Considering edema evaluation, measurements were similar between both sides at all time points except on Day 2, when the A-PRF side showed significantly higher values ($p = 0.001$ and $p < 0.01$). For trismus evaluation, maximum interincisal distance was significantly greater on the oral dexamethasone side on Days 2 and 7 compared to the A-PRF side ($p = 0.001$ and $p < 0.01$). Analgesic consumption was significantly higher in the A-PRF group than in the oral dexamethasone group at all measured time points between 12 h and Day 7 ($p < 0.01$).

Conclusion Oral dexamethasone appeared to be more effective than A-PRF in reducing postoperative complications. However, no significant difference was observed between the two groups in edema on Days 7, 14, and 30. Although not as effective as oral dexamethasone, A-PRF, being an autologous product with no side effects, can still be considered for reducing complications following impacted tooth extraction.

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Trial Registration The study was retrospectively registered at ClinicalTrials.gov with the number of NCT06823934, Registration date 02 June 2025.

Keywords A-PRF, Dexamethasone, Oral dexamethasone, Oral surgery, Postoperative Complications, Third Molar, Impacted wisdom teeth, Tooth extraction

Introduction

Extraction of impacted mandibular third molars is one of the most common procedures performed in the practice of oral surgery. However, the removal of impacted third molar teeth leads to significant inflammatory changes, resulting in edema, trismus, and pain. Complications encountered after the extraction of impacted mandibular third molars can adversely affect the daily lives of patient [1].

Corticosteroids are the type of drugs commonly used to prevent complications which may occur after tooth extraction. These agents are used to prevent pain, edema, and trismus and also play a key role in preventing flap opening and secondary infection formation due to their anti-inflammatory effects [2, 3]. Among corticosteroid drugs used in dentistry, dexamethasone is the most commonly preferred. It can provide an effective and long-lasting result even at low doses [4, 5]. Previous studies evaluating local dexamethasone administration have reported favorable outcomes in reducing postoperative pain, swelling, and trismus after impacted third molar surgery [6]. However, studies evaluating the effectiveness of oral dexamethasone in comparison with alternative postoperative management approaches remain limited.

Platelet-rich fibrin (PRF), which has become increasingly used in both medicine and dentistry, is a regenerative concentrate obtained by centrifugation of the patient's own blood. As a second-generation product, PRF is a platelet concentration network which includes platelets, leukocytes, fibrin, and stem cells surrounded by a cytokine matrix. Its production does not require anticoagulants, thrombin, or any gelling agents, and it is easy to obtain and autologous. Advanced-PRF(A-PRF) is an improved modification of PRF which is obtained via centrifugation at a lower speed [7, 8].

In the present study, we hypothesized that A-PRF could serve as a natural alternative treatment option. We, therefore, aimed to evaluate the effectiveness of A-PRF applied to the extraction socket on postoperative complications such as pain, edema, and trismus following impacted third molar extraction and to compare it with oral dexamethasone.

Methods

This single-center, split-mouth, prospective, randomized-controlled study was conducted at Department of Oral and Maxillofacial Surgery, Faculty of Dentistry of a tertiary care center. Prior to the study, all patients were

informed about the nature of the study and a written informed consent was obtained.

Ethics

The study was approved by the Van Yuzuncu Yil University Clinical Research Ethics Committee (YYU/13/20.09.2021) and conducted in accordance with the principles of the Declaration of Helsinki.

Controlled trial registration

The study was designed to followed the reporting standards provided by the CONSORT statement and was retrospectively registered at ClinicalTrials.gov with the number of NCT06823934.

Selection of patients

A preliminary evaluation was performed on a total of 40 untreated patients over the age of 18 who presented to our clinic with complaints related to impacted mandibular third molars. Of these patients, four were excluded due to not meeting the inclusion criteria (one resided in a different city, and three had chronic systemic conditions), and six patients declined to participate in the study. Inclusion criteria were as follows: age over 18 years, absence of any systemic disease, presence of bilaterally impacted mandibular third molars with mesioangular orientation and similar positioning according to the Pell and Gregory classification (Class II or III and Position A or B), exhibiting bony impaction, and no known allergies to the medications used in the study. Exclusion criteria were as follows: presence of impacted mandibular third molars with different positions between the two sides, presence of infection at the extraction site, pregnancy or breastfeeding, use of any medication within two weeks prior to tooth extraction, irregular use of the prescribed medications, and failure to attend scheduled follow-up appointments regularly. Finally, a total of 30 patients who met the inclusion criteria were recruited for the study. Figure 1 illustrates the CONSORT flow diagram.

Sample size calculation

In order to determine the sample size, a power analysis was performed using the G*Power software (version 3.1.9.2). The power of the study is expressed as $1-\beta$ (β =probability of a type II error), and it is generally accepted that studies should have at least 80% power. According to Cohen's effect size coefficients, assuming a moderate effect size ($d=0.55$) for the evaluations to be

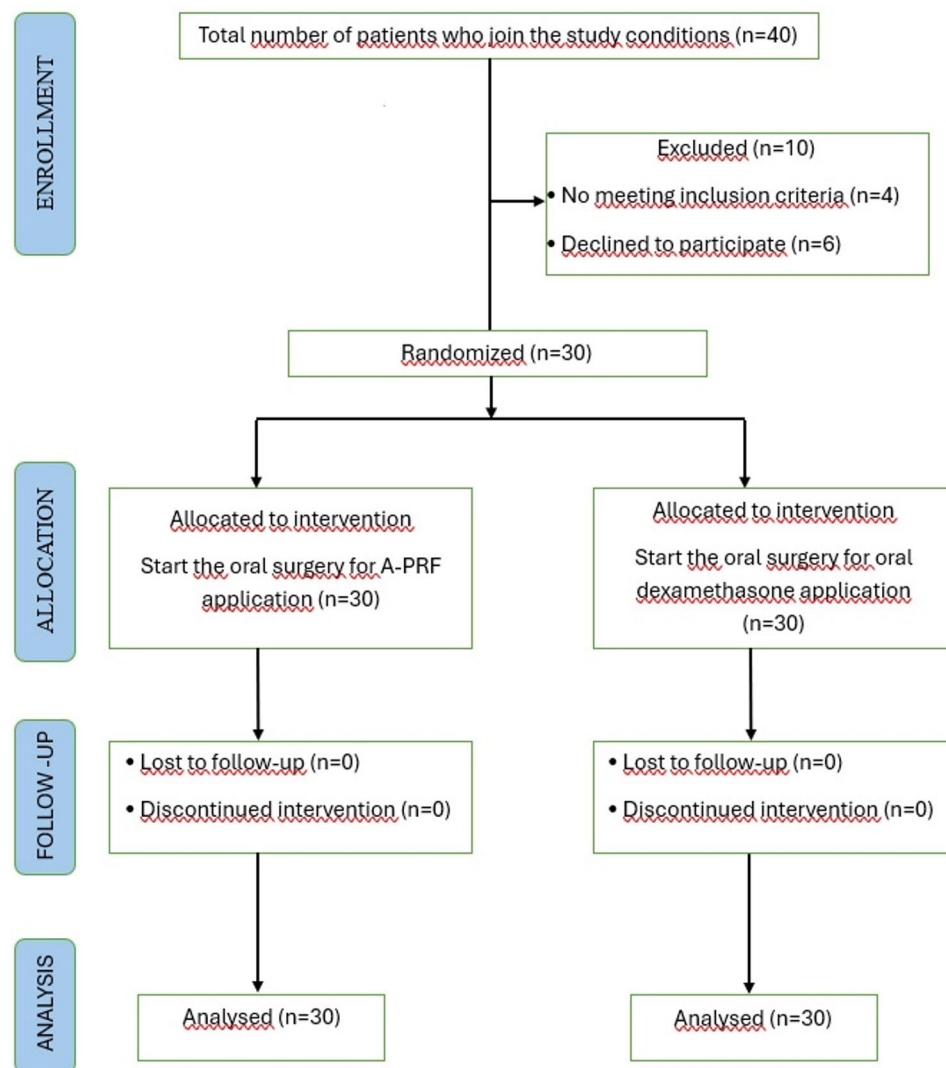


Fig. 1 CONSORT flow diagram

conducted between dependent groups, the calculation indicated that at least 28 participants would be required to achieve 80% power at a significance level of $\alpha = 0.05$.

Surgical technique and data collection

Prior to the surgical procedure, panoramic radiographs (orthopantomograms) were obtained and clinical examinations were conducted for all patients included in the study. The impacted third molars were extracted under local anesthesia following randomization of the extraction sequence and group assignment. For each patient, one side was designated as Group 1 and the contralateral side as Group 2. If the patient had symptoms, the extraction began on the symptomatic side; if asymptomatic, the side for initial extraction was determined based on patient preference. The second surgery was scheduled five weeks after the first procedure.

Before the study begins, group assignment for each extraction was determined by coin toss by a blinded assistant: heads indicated the A-PRF group (Group 1, $n = 30$), and tails indicated the oral dexamethasone group (Group 2, $n = 30$). However, due to the nature of the interventions, operator blinding was not feasible. To ensure standardization and reduce inter-operator variability, all surgical procedures were performed by the same oral and maxillofacial surgery resident with three years of clinical surgical experience. Patients and outcome assessors remained blinded to the group allocations.

Local anesthesia was achieved using mandibular, lingual, and buccal infiltrations with Ultracain D-S Forte® (Sanofi Aventis, Istanbul, Türkiye), containing 1:100,000 epinephrine. A sulcular incision was made, and a muco-periosteal flap was elevated. When necessary, the tooth was sectioned or divided and extracted according to its position. The dental follicle or granulation tissue was

cleaned, the irregular bone tip was trimmed and the alveolar fossa was rinsed with normal saline.

Prior to the operation, for the surgical site where A-PRF would be applied, 10 cc of venous blood was drawn by auxiliary staff into a single tube (Ayset tube, Ayset Tıbbi Ürünler San. A.Ş., Adana, Türkiye). Blood collection was performed through the peripheral antecubital vein using an appropriate intravenous cannula selected according to the patient's vascular structure. Care was taken to ensure that the patient remained in a comfortable position during the procedure. The collected blood was centrifuged at 1,500 rpm for 14 min using a centrifuge device (Intra-Lock Intra-Spin L-PRF Device, Intra-Lock International, Inc., FL, USA). The resulting A-PRF clot was placed into the extraction socket of the impacted third molar, and the site was closed primarily.

For both groups, the duration of the procedures, from initiation to completion, was recorded. In Group 1, A-PRF was placed into the extraction socket, and the flap was closed primarily using 3/0 silk sutures. In Group 2, the socket was closed primarily with 3/0 silk sutures without placement of any biomaterial. Postoperatively, oral dexamethasone (Dekort 4 mg tablet, DEVA Pharmaceuticals, t.i.d. for a total of three days) was prescribed to the patients.

Postoperatively, all patients were prescribed amoxicillin 1,000 mg (Largopen 1000 mg, t.i.d.), ibuprofen 600 mg (Brufen 600 mg, t.i.d.), and a mouthwash containing benzylamine hydrochloride and chlorhexidine gluconate (Kloroben 200 mL, t.i.d.). Patients were instructed to use the antibiotic and mouthwash as prescribed and to take the analgesic only when needed. Sutures were removed one week after surgery.

Pain assessments were conducted using the Visual Analog Scale (VAS). The patients were instructed on how and when to complete the scale. They were asked to rate their pain on a scale from 0 (no pain) to 10 (unbearable pain) at postoperative 3, 6, 9, 12, and 24 h, as well as on Days 2, 3, 4, 5, 6, 7, 14, and 30 [9]. To evaluate analgesic consumption, patients were provided with forms to record their analgesic use during the postoperative period.

For edema evaluation, facial measurements were taken between the following anatomical landmarks: angulus-tragus, angulus-lateral canthus, angulus-ala nasi, angulus-labial commissure, and angulus-pogonion [10]. These measurements were recorded preoperatively, and on postoperative Days 2, 7, 14, and 30 (Fig. 2).

For the evaluation of trismus, maximum mouth opening was measured preoperatively and on postoperative Days 2, 7, 14, and 30. The measurement was taken as the distance between the incisal edges of the upper and lower central incisors when the patient opened their mouth to the maximum extent without assistance.

Statistical analysis

Statistical analysis was performed using the NCSS version 2020 Statistical Software (NCSS LLC, Kaysville, UT, USA). Continuous data were expressed in mean $\pm$ standard deviation (SD) or median (min-max), while categorical data were expressed in number and frequency. The Shapiro-Wilk test and box plot graphs were used to assess the normality of data distribution. For intra-group comparisons of parameters not showing normal distribution, the Wilcoxon signed-rank test was used, while the Dunn test was applied to identify the group responsible for the significant differences. A p value of <0.05 was considered statistically significant with 95% confidence interval (CI).

Results

This study included a total of 30 patients who underwent impacted mandibular third molar surgery. No complications occurred in any patient. Among the participants, 76.7% ($n=23$) were females and 23.3% ($n=7$) were males with a mean age of 21.70 ± 1.98 years. The duration of surgeries in which oral dexamethasone was administered ranged from 10 to 45 min with a mean of 23.33 ± 6.73 min. In the A-PRF group, surgical durations ranged from 15 to 35 min with a mean of 25.00 ± 6.15 min. No statistically significant difference was observed between the two groups in terms of surgical duration.

On postoperative Days 2 and 7, the mean mouth opening measurements in the oral dexamethasone group were significantly greater than those in the A-PRF group ($p=0.001$ and $p<0.01$), indicating a statistically significant difference between the two groups. In the A-PRF group, comparison of mouth opening measurements between the preoperative period and postoperative Days 2 and 7 revealed statistically significant reductions ($p=0.001$ and $p<0.01$). In the oral dexamethasone group, the mean decrease in mouth opening on postoperative Day 2 compared to baseline was 9.86 ± 5.73 mm, which was also statistically significant ($p=0.001$ and $p<0.01$). However, no significant differences were found in mouth opening measurements between the preoperative period and postoperative Days 7, 14, and 30 in either group ($p>0.05$) (Fig. 3).

On postoperative Day 2, the angulus-tragus distance in patients who received oral dexamethasone was found to be significantly shorter than in those who received A-PRF ($p=0.001$ and $p<0.01$). No significant differences were observed in angulus-tragus distance changes on postoperative Days 7, 14, and 30 compared to baseline in either group ($p>0.05$).

Furthermore, on postoperative Day 2, the angulus-lateral canthus distance was significantly greater on the side where A-PRF was applied compared to the side where oral dexamethasone was administered ($p=0.001$ and

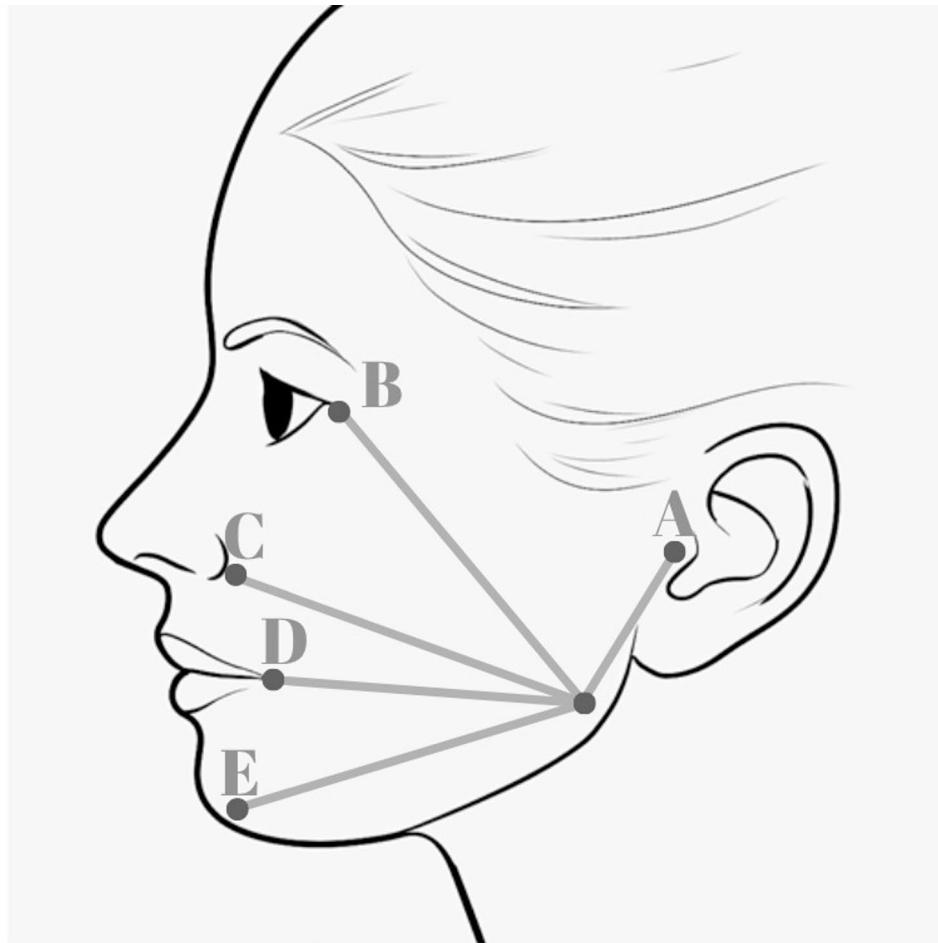


Fig. 2 Facial measurement points for edema **A** Angulus-Tragus, **B** Angulus- Lateral Cantus, **C** Angulus- Ala Nasi, **D** Angulus-Labial Comissura, **E** Angulus-Pogonion

$p < 0.01$). However, no significant differences were found in the angulus-lateral canthus measurements between the two groups on the preoperative day 0, and on postoperative Days 7, 14, and 30 ($p > 0.05$). Similarly, compared to preoperative values, no statistically significant changes in angulus-lateral canthus distances were observed on postoperative Days 7, 14, and 30 ($p > 0.05$) (Fig. 4).

The changes in the distance between the angulus and lateral canthus on the second day after surgery in cases included in the study, where A-PRF was applied, were found to be higher compared to the side where oral dexamethasone was administered ($p = 0.001$ and $p < 0.01$). There were no significant differences in the changes of the distance between the angulus and lateral canthus on postoperative Days 7, 14, and 30 compared to the preoperative measurements ($p > 0.05$).

The mean increase of 4.70 ± 2.78 in the distance between the angulus and the nasal wing on the second day after surgery on the side where oral dexamethasone was administered was significant ($p = 0.001$ and $p < 0.01$). The mean increase of 8.26 ± 2.81 in the distance between

the angulus and the nasal wing on the second day after surgery on the side where A-PRF was applied was also significant ($p = 0.001$ and $p < 0.01$). On Day 2, the mean distance between the angulus and the nasal wing on the dexamethasone side with A-PRF was higher than that of the side with oral dexamethasone ($p = 0.001$ and $p < 0.01$). There was no significant difference in the distances between the angulus and the nasal wing on the sides where oral dexamethasone and A-PRF dexamethasone were applied before surgery on postoperative Days 7, 14, and 30 ($p > 0.05$) (Fig. 5).

The mean increase of 6.06 ± 3.86 in the distance between the angle and the labial commissure on the second day, compared to preoperative measurements, was significant for the sides treated with oral dexamethasone ($p = 0.001$ and $p < 0.01$). The mean increase of 10.46 ± 4.63 in the distance between the angle and the labial commissure on the second day, compared to preoperative measurements, was also significant for the sides treated with A-PRF ($p = 0.001$ and $p < 0.01$). The change in the distance between the angle and the labial commissure on the

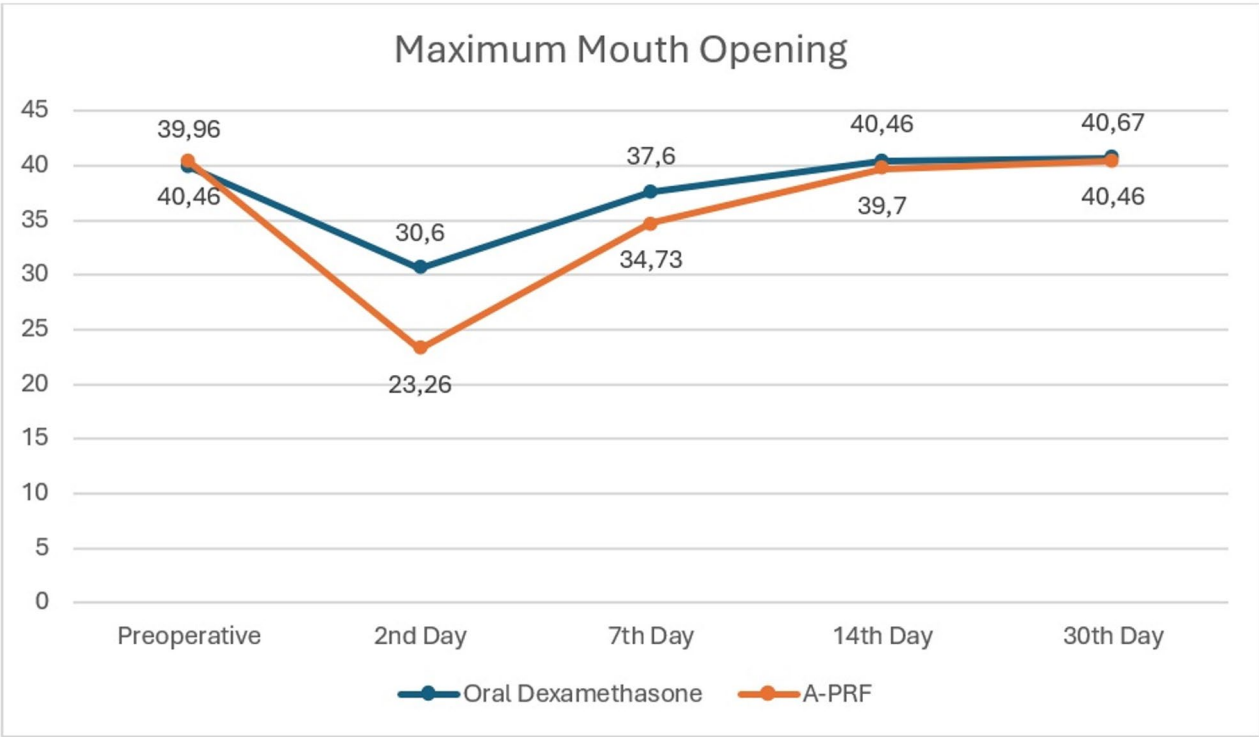


Fig. 3 Maximum mouth opening measurement follow-ups for groups

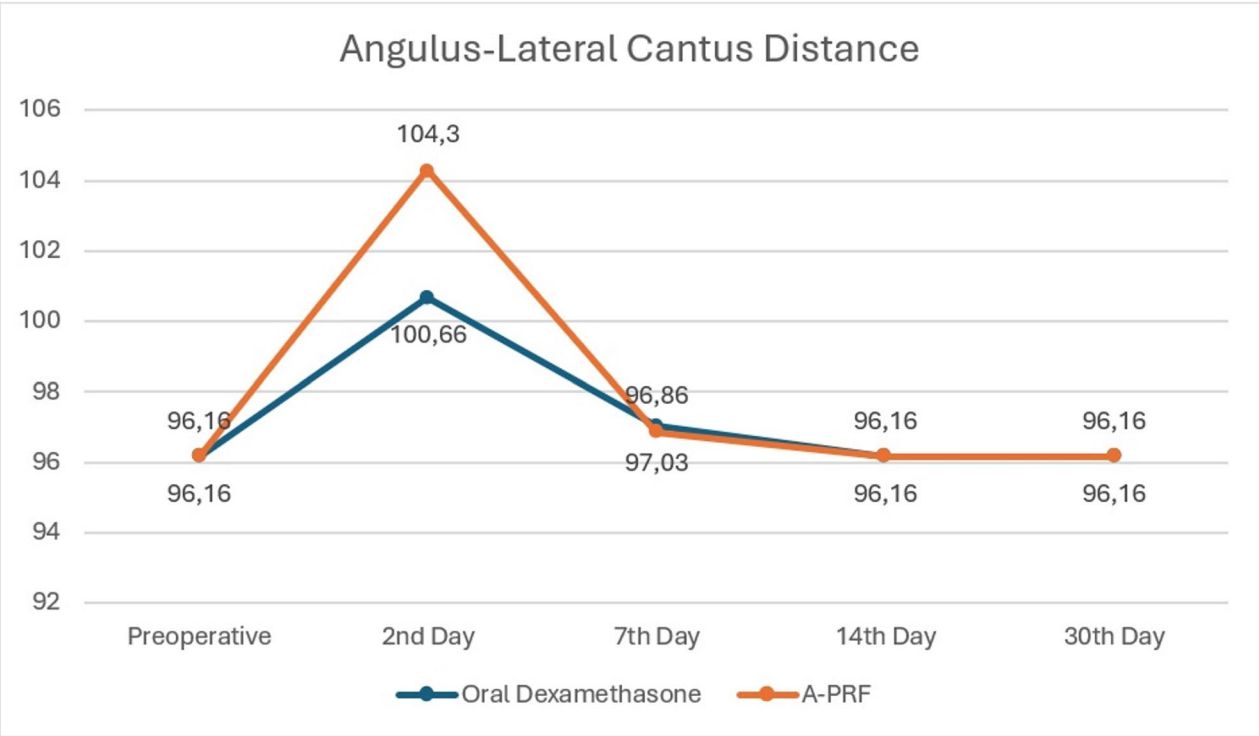


Fig. 4 Angulus-lateral cantus distance follow-ups for groups

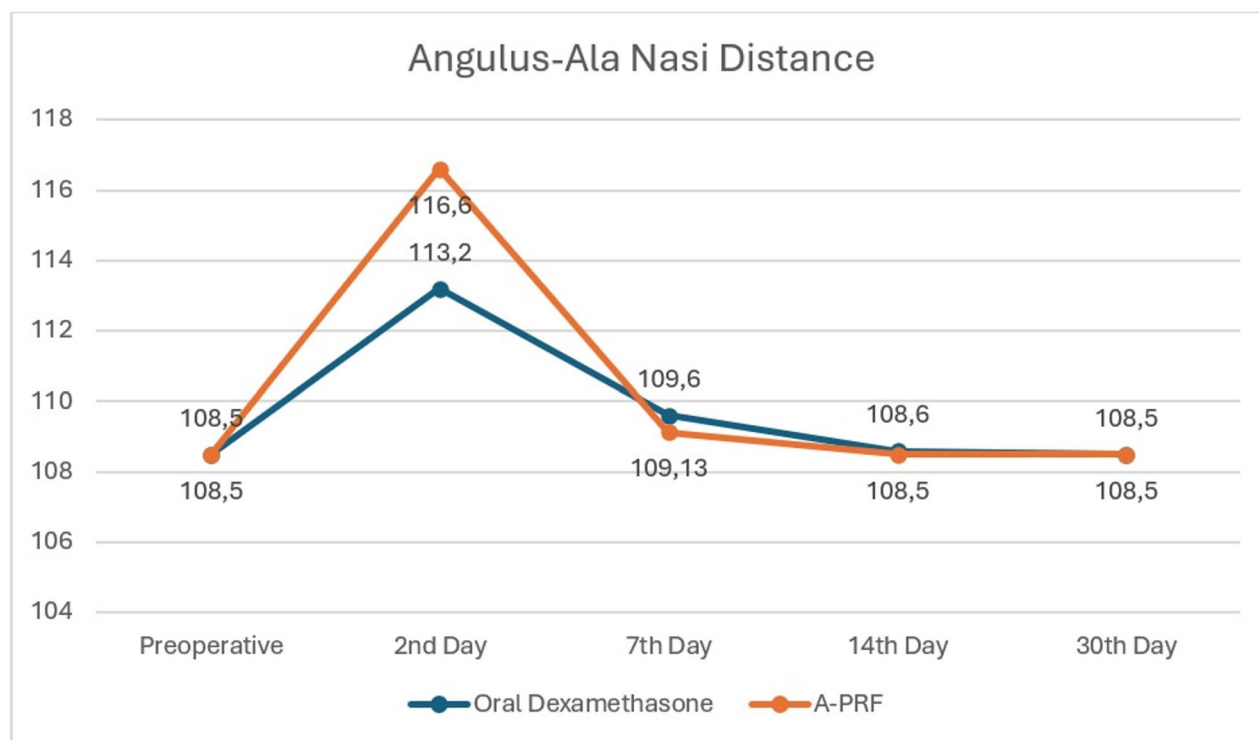


Fig. 5 Follow-up of Angulus-ala nasi distance measurements for groups

second day for the sides treated with A-PRF and dexamethasone was higher compared to the sides treated with oral dexamethasone ($p=0.001$ and $p<0.01$). Changes in the distance between the angle and the labial commissure on Days 7, 14, and 30 compared to preoperative measurements did not indicate significant differences ($p>0.05$) (Fig. 6).

The mean increase of 5.70 ± 3.96 in the measurements of the angulus-pogonion distance on the day after oral dexamethasone application compared to preoperative measurements was significant ($p=0.001$ and $p<0.01$). The mean increase of 9.46 ± 4.75 in the measurements of the angulus-pogonion distance on the second day after A-PRF application compared to preoperative measurements was also significant ($p=0.001$ and $p<0.01$). The change in the angulus-pogonion distance on the second day in the cases where A-PRF dexamethasone was applied was higher compared to the side where oral dexamethasone was applied ($p=0.001$ and $p<0.01$). The changes in the angulus-pogonion distance on Days 7, 14, and 30 compared to preoperative measurements did not indicate significant differences ($p>0.05$).

The VAS scores for the sides where A-PRF was applied at 3, 6, 9, 12, and 24 h and on Days 2, 3, 4, 5, 6, and 7 were higher compared to the sides where oral dexamethasone was applied ($p=0.001$; $p=0.001$; $p=0.007$; $p=0.001$; $p=0.0004$; $p=0.0001$; $p=0.001$; $p=0.002$; $p=0.001$; $p=0.001$; $p=0.001$; $p<0.01$, respectively) (Fig. 7). There

was no significant difference between the VAS scores on Days 14 and 30 in the cases included in the study ($p>0.05$).

Analgesic requirements were statistically higher on the A-PRF-applied side compared to oral dexamethasone at 12 and 24 h and on Days 2, 3, 4, 5, 6, and 7 ($p<0.05$ and $p<0.01$). The amount of analgesics used by patients at different times after the procedure is shown in Table 1.

Discussion

Although various studies have investigated the management of postoperative complications following impacted mandibular third molar surgery, there is no head-to-head study comparing A-PRF applied locally and orally administered dexamethasone in the literature. To the best of our knowledge, this study is the first to evaluate the effectiveness of A-PRF versus oral dexamethasone.

In the literature, the 24–30 age range is considered optimal for third molar extraction due to favorable bone flexibility, regenerative capacity, and adequate vascularization [11, 12]. In our study, the age of the participants ranged from 18 to 26 years, with a mean age of 21.70 ± 1.98 years [13, 14]. This suggests that many of the extractions were performed before the age considered optimal, which may have implications for surgical outcomes and healing [15]. Regarding the sex distribution, previous studies have consistently demonstrated a higher prevalence of female patients undergoing impacted third molar

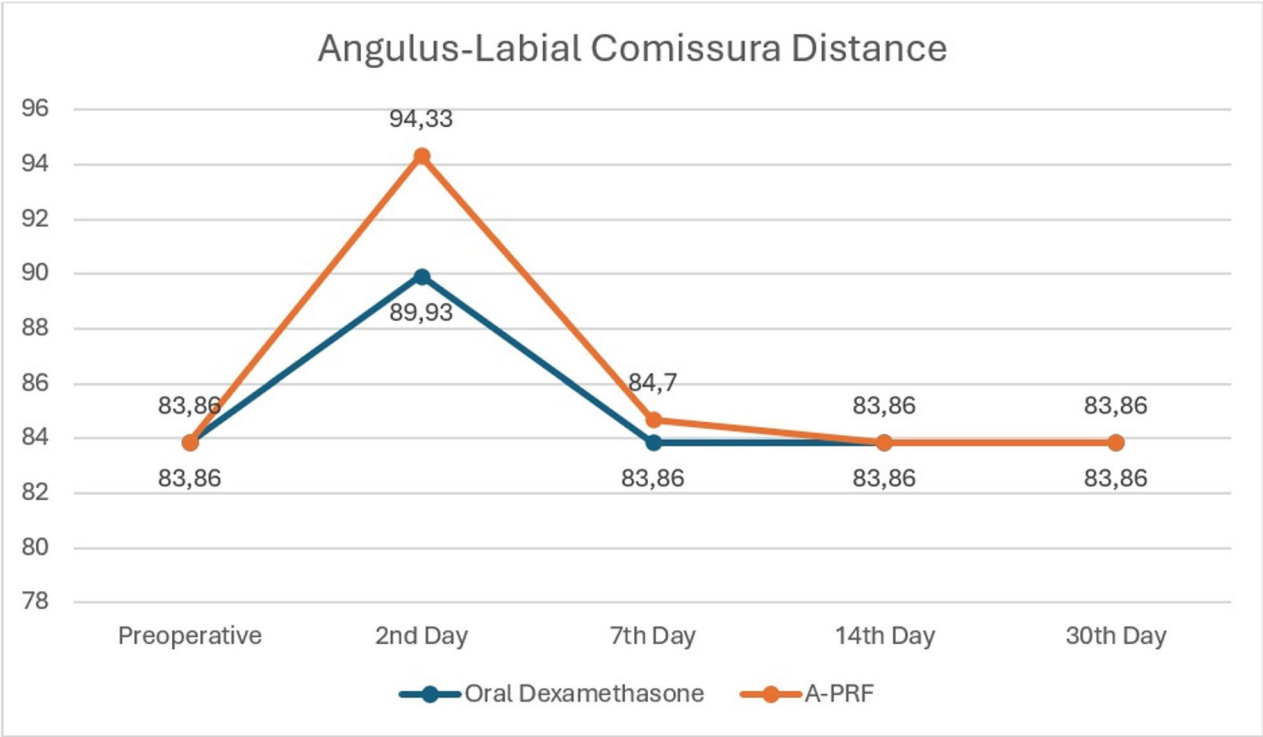


Fig. 6 Angulus-labial commissure distance follow-ups for groups

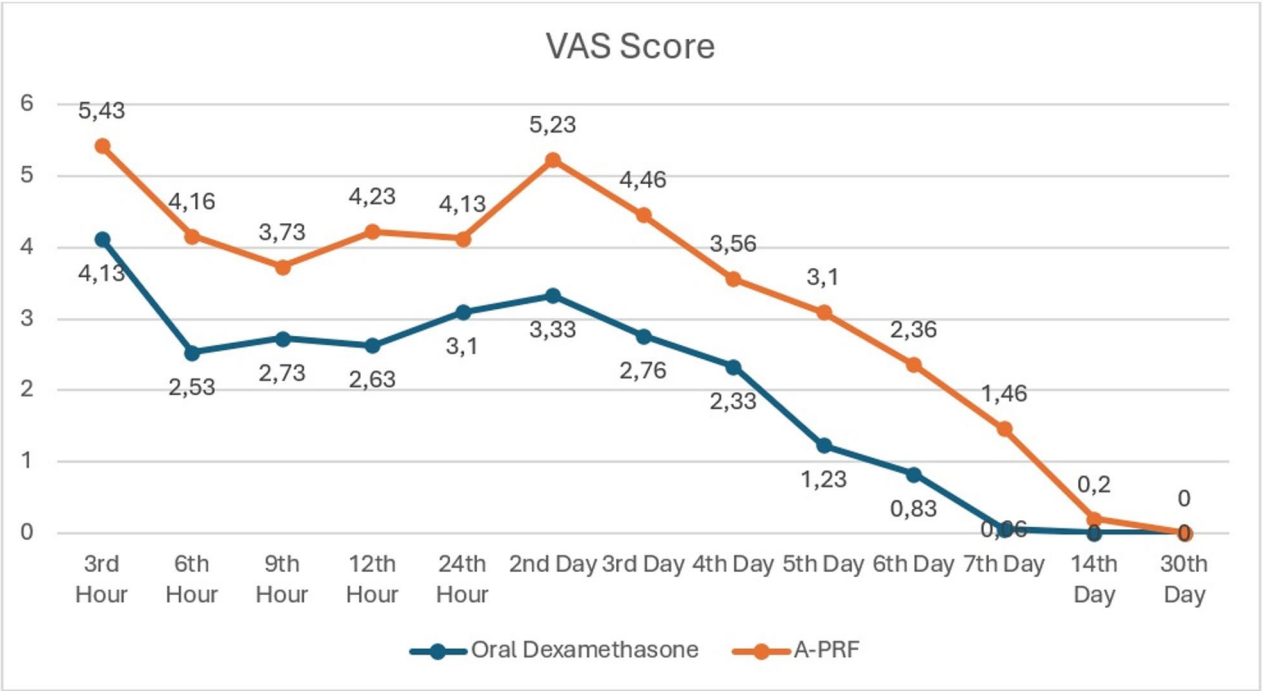


Fig. 7 VAS score follow-ups of cases treated with A-PRF and oral dexamethasone

Table 1 Comparisons of analgesic consumption for groups

Number	Oral Dexamethasone				A-PRF				p
	0	1	2	3	0	1	2	3	
Analgesic 3rd hour	6 (20,0)	24 (80,0)	0 (0,0)	0 (0,0)	4 (13,3)	26 (86,7)	0 (0,0)	0 (0,0)	^a 0,157
Analgesic 6th hour	25 (83,3)	5 (16,7)	0 (0,0)	0 (0,0)	24 (80,0)	6 (20,0)	0 (0,0)	0 (0,0)	^a 0,655
Analgesic 9th hour	19 (63,3)	11 (36,7)	0 (0,0)	0 (0,0)	16 (53,3)	14 (46,7)	0 (0,0)	0 (0,0)	^a 0,366
Analgesic 12th hour	17 (56,7)	13 (43,3)	0 (0,0)	0 (0,0)	9 (30,0)	21 (70,0)	0 (0,0)	0 (0,0)	^a 0,005**
Analgesic 24th hour	12 (40,0)	18 (60,0)	0 (0,0)	0 (0,0)	5 (16,7)	23 (76,7)	2 (6,7)	0 (0,0)	^a 0,029*
Analgesic 2nd day	5 (16,7)	11 (36,7)	14 (46,7)	0 (0,0)	1 (3,3)	6 (20,0)	15 (50,0)	8 (26,7)	^a 0,001**
Analgesic 3th day	7 (23,3)	12 (40,0)	10 (33,3)	1 (3,3)	3 (10,0)	7 (23,3)	16 (53,3)	4 (13,3)	^a 0,001**
Analgesic 4th day	9 (30,0)	17 (56,7)	4 (13,3)	0 (0,0)	3 (10,0)	9 (30,0)	16 (53,3)	2 (6,7)	^a 0,001**
Analgesic 5th day	16 (53,3)	13 (43,3)	1 (3,3)	0 (0,0)	6 (20,0)	9 (30,0)	14 (46,7)	1 (3,3)	^a 0,001**
Analgesic 6th day	21 (70,0)	8 (26,7)	1 (3,3)	0 (0,0)	11 (36,7)	12 (40,0)	6 (20,0)	1 (3,3)	^a 0,001**
Analgesic 7th day	29 (96,7)	1 (3,3)	0 (0,0)	0 (0,0)	15 (50,0)	13 (43,3)	2 (6,7)	0 (0,0)	^a 0,001**
Analgesic 14th day	30 (100)	0 (0,0)	0 (0,0)	0 (0,0)	29 (96,7)	0 (0,0)	1 (3,3)	0 (0,0)	^a 0,317
Analgesic 30th day	30 (100)	0 (0,0)	0 (0,0)	0 (0,0)	30 (100)	0 (0,0)	0 (0,0)	0 (0,0)	^a 1,000

Wilcoxon Signed Ranks Test

*p<0,05

**p<0,01

surgery [16, 17]. The findings of the present study are in agreement with this observation, as 76.7% of the patients were female and 23.3% were male. This disparity may be attributed to sex-based differences in health-seeking behavior, pain perception, or referral practices, which tend to favor earlier diagnosis and treatment in female patients [18].

In the present study, the mean duration of surgery was 23.33 ± 6.73 min in patients who received oral dexamethasone and 25.00 ± 6.15 min in those treated with A-PRF, indicating no statistically significant difference between the two groups. Although blood collection and centrifugation were additionally required for the A-PRF application, this did not result in a significant increase in surgical duration. Therefore, the use of A-PRF did not pose a disadvantage in terms of surgical duration. This finding suggests that the incorporation of A-PRF into clinical practice seems to be feasible from a procedural standpoint and does not impose a time-related disadvantage in routine surgical workflows.

Pain, edema, and trismus are among the most common complications of impacted third molar surgery and significantly affect patient comfort and quality of life. The VAS is a reliable method for evaluating pain [19–21]. In the current study, the mean VAS scores at 3, 6, 9, 12, and 24 h, and on postoperative Days 2 to 7 were significantly higher in cases where A-PRF was applied compared to those who received oral dexamethasone ($p < 0.05$). In addition, the amount of analgesic consumption following A-PRF application was found to be statistically significantly higher than in the oral dexamethasone group. These findings suggest that oral dexamethasone is more effective than A-PRF in managing postoperative pain. In the literature, A-PRF has been reported to

reduce postoperative pain compared to control groups (e.g., physiological saline) [17, 22]. In a study by Gupta and Agarwal [22], A-PRF was evaluated against a control group in terms of postoperative complications following impacted third molar surgery. They found no significant difference between the test and control groups on the first postoperative day; however, as of the third day, pain was significantly reduced in the A-PRF group compared to controls. On Days 3 and 7, pain intensity was also lower in the A-PRF-treated sites than in the control group. In a recent study by Starzynska et al. [17], the use of A-PRF following third molar surgery was associated with a significant reduction in pain on postoperative Days 3 and 7. Analgesic consumption was also lower in the A-PRF group. Kumar et al. [23] evaluated postoperative complications in A-PRF and control groups after third molar surgery. Their results indicated that the A-PRF group experienced less pain on the first postoperative day compared to control group. Furthermore, in a study by Caymaz and Uyanık [24], the effect of A-PRF on postoperative pain after mandibular third molar surgery was compared to leukocyte-PRF (L-PRF). The authors concluded that A-PRF significantly reduced postoperative pain and resulted in a lower need for analgesics in the A-PRF group. However, there are also studies in the literature which report conflicting results regarding the effects of A-PRF. In a study by Özgül et al. [25], no significant difference in pain was found between the PRF-treated group and the control group following impacted third molar extraction. This discrepancy may be due to limitations in the study design. In the aforementioned study, both third molars were extracted in a single session, potentially affecting the pain outcomes due to crossover effects. Similarly, a study by Asutay et

al. [13] reported that PRF had no significant positive effect on postoperative pain after third molar surgery. In another study by Gülşen and Şentürk [26], the use of PRF did not result in a significant improvement in swelling or pain compared to natural healing after mandibular third molar surgery. Torul et al. [27] also reported no statistically significant effect of PRF application on pain intensity following surgical extraction of third molars. The discrepancies among these studies are likely due to differences in study designs, sample sizes, and the inherently subjective nature of pain evaluation methods. In the current literature, A-PRF appears to be effective in reducing postoperative pain complications. Therefore, we compared the autologous product A-PRF with oral dexamethasone in the current study.

In our study, measurements showed that on postoperative Day 2, the severity of edema was statistically significantly lower in patients who received oral dexamethasone compared to those who received A-PRF. By Day 7, no significant difference was observed between the groups in terms of edema levels. On Days 14 and 30, edema levels were found to be similar in both groups, and the differences between the measurements were not statistically significant. These results indicate that A-PRF is less effective than oral dexamethasone in controlling edema during the early postoperative period. Although a reduction in edema was also observed in the A-PRF group, this effect was not statistically significant compared to dexamethasone. However, considering the potential local and systemic side effects of dexamethasone, A-PRF may still be considered a viable clinical option for reducing postoperative complications, particularly since it is an autologous product and, thus, less likely to cause adverse effects [17, 22]. In the literature, Gupta and Agarwal [19] reported a marked improvement in edema in the A-PRF group. Similarly, Starzynska et al. [17] found that edema was lower in the A-PRF-treated group. Although they found no significant effect of A-PRF on postoperative pain, Özgül et al. [25] demonstrated its effectiveness in reducing edema. Zahid and Nadershah [16], in their study, suggested that A-PRF might be a viable option for reducing postoperative swelling following the surgical extraction of impacted third molars. Nevertheless, there are also studies which examining the efficacy of A-PRF on edema or report no significant differences. To illustrate, in a study conducted by Gülşen and Şentürk [26], PRF had no significant effect on postoperative edema.

Trismus is commonly assessed by measuring the distance between the upper and lower central incisors at maximum mouth opening [17, 22, 27]. In our study, mouth opening was found to be significantly greater in patients who received oral dexamethasone compared to those who received A-PRF ($p < 0.05$). Measurements showed that on postoperative Days 2 and 7, oral

dexamethasone was significantly more effective than A-PRF in reducing trismus ($p = 0.001$ and $p < 0.01$). On Days 14 and 30, the mean mouth opening remained higher in the dexamethasone group compared to the A-PRF group, although the difference was not statistically significant ($p > 0.05$). These findings indicate that dexamethasone is more effective in reducing trismus during the early postoperative period, whereas both groups reached similar levels of recovery in the later stages. In a study by Gupta and Agarwal [22], trismus was reported to be reduced in the A-PRF group compared to the control group. The authors associated the observed improvements in pain, soft tissue healing, and edema in the A-PRF group with the release kinetics of growth factors and inflammatory mediators contained in A-PRF. Similarly, Starzynska et al. [17] found a significant relationship between A-PRF application and the development and severity of trismus on postoperative Days 3 and 7. In their study group, the absence of trismus or its limitation to a mild degree was observed more frequently than in the control group. Kumar et al. [23] also reported that patients in the A-PRF group experienced less trismus on the first postoperative day compared to the control group. Additionally, they observed enhanced periodontal healing and faster recovery in the A-PRF group. However, the literature on the effects of A-PRF on trismus presents inconsistent findings. While some studies report a significant reduction in trismus, others have found no meaningful difference [13]. These conflicting results in the literature can be attributed to variations in surgical techniques, timing of evaluations, measurement methods, and individual biological response differences.

In a study, Lou et al. [28] investigated the efficacy of dexamethasone injection administered to different anatomical sites in reducing postoperative sequelae following the extraction of impacted mandibular third molars. In Group 1, patients received a submucosal injection of 4 mg of dexamethasone on the buccal side of the adjacent second molar. In Group 2, the same dose was injected on the buccal side of the extraction socket. The control group received a submucosal injection of physiological saline on the buccal side of the adjacent second molar. According to the results, submucosal dexamethasone injection on the buccal side of the adjacent second molar significantly reduced postoperative edema and trismus. On postoperative Day 3, edema and trismus levels in Group 1 were significantly lower compared to Group 2. However, no significant differences were observed among the three groups at any time point regarding VAS pain scores or the amount of analgesic consumption. The authors concluded that dexamethasone effectively alleviated postoperative swelling and mouth opening limitation, and injection on the buccal side of the adjacent second molar was found to be more effective than

injection on the buccal side of the extraction socket [28]. In another study, Majid [29] compared the effects of a 4 mg of submucosal dexamethasone injection to a 4 mg of intramuscular injection and a control group in terms of postoperative sequelae and quality of life after impacted third molar surgery. The study found that while intramuscular dexamethasone reduced swelling and pain compared to the control group, its effect on trismus was limited. On the other hand, submucosal injection led to significant improvements in swelling, pain, and trismus. The study concluded that submucosal dexamethasone provided notable improvements in swelling, pain, trismus, and postoperative quality of life after extraction of impacted lower third molars, and yielded comparable results to the intramuscular route. Similarly, Shad et al. [30] evaluated the effect of preoperative submucosal dexamethasone on postoperative pain, swelling, and trismus compared to a control group. The authors found that preoperative administration of submucosal dexamethasone significantly reduced postoperative pain, swelling, and trismus, thereby enhancing patients' quality of life. In a study conducted by Khosraviani et al., intraoral dexamethasone injection or placement of dexamethasone into the alveolar socket was reported to be more effective than ibuprofen in controlling postoperative pain, swelling, and trismus following impacted third molar extraction. The authors also emphasized that local dexamethasone applications may represent a practical and effective alternative that could reduce the potential adverse effects associated with systemic corticosteroid use [6]. Similarly, in our study, oral dexamethasone demonstrated a more pronounced clinical effect than A-PRF in reducing postoperative pain, analgesic consumption, edema, and trismus following impacted third molar surgery. However, considering that A-PRF is a biologically safe, naturally derived, and locally applicable biomaterial, it may represent a safe and effective alternative, particularly in clinical situations where corticosteroid use is limited or less preferred. In another systematic review, Khosraviani et al. reported that meloxicam demonstrated analgesic effects equal or superior to several NSAIDs, salicylates, tramadol, and the corticosteroid methylprednisolone in controlling pain following third molar extraction. The authors concluded that meloxicam may be considered an effective alternative anti-inflammatory and analgesic agent for postoperative pain management after third molar surgery [31]. Although corticosteroids demonstrated superior clinical efficacy compared to A-PRF in our study, the literature suggests that some agents may exhibit effects comparable or even superior to corticosteroids.

To the best of our knowledge, no previous studies in the literature have evaluated the use of oral dexamethasone for reducing postoperative complications following impacted third molar surgery. In this context, this is to

first study to address this topic, which can be regarded as a strength of the study. Nonetheless, there are several limitations to this study. First, the study lacks a placebo/sham control group. As the study was designed using a split-mouth model to minimize individual variability such as differences in pain threshold, the control group could only consist of the patient's maxillary third molars. However, since surgical parameters such as extraction difficulty would not be comparable in such cases, we determined that including a non-treatment control group would not be appropriate. In addition, the inclusion of an independent third control group (i.e., a true placebo or no-treatment group) was not feasible within the current study design. This is because such a group would not be directly comparable within the split-mouth framework, as it would involve conditions that differ significantly from the study interventions in terms of surgical exposure, healing environment, and clinical context. Introducing such a group could lead to substantial variability and confounding factors, thereby potentially compromising the internal validity of the study, which was specifically designed to minimize inter-individual differences. Second, despite oral dexamethasone being compared to an autologous blood-derived product such as A-PRF, it is already considered one of the most effective methods for reducing postoperative edema and pain in the literature. Therefore, dexamethasone could be anticipated to demonstrate superior results. An additional limitation is the use of the oral formulation of dexamethasone, which exerts its effects more slowly compared to its intramuscular or submucosal forms. However, to minimize bias, the study was designed as a split-mouth model and all surgical procedures were performed by a single surgeon. Further multi-center, large-scale, prospective, randomized-controlled studies are warranted to confirm these findings.

Conclusion

In conclusion, although A-PRF has been shown to reduce pain, analgesic consumption, postoperative edema, and trismus, it seems to be statistically less effective than oral dexamethasone in achieving these outcomes. Oral dexamethasone demonstrates a more pronounced clinical effect, particularly in situations where rapid and strong suppression of the inflammatory response is required compared to A-PRF. However, A-PRF has several advantages, such as being a natural biomaterial, having no additional cost, ease of application, and high biological safety, which may make it preferable to dexamethasone in certain clinical situations. In particular, A-PRF may be considered a preferred option in patients for whom steroid use may be associated with potential risks and in cases where lower surgical trauma is anticipated. On the other hand, due to the potential systemic side effects

of dexamethasone, A-PRF may be considered as a safer alternative. In clinical situations where corticosteroid use is limited or less preferred, A-PRF provides a meaningful advantage as a biologically based local treatment option. Therefore, shared decision-making between the patient and clinician is essential while choosing the most appropriate method. In complex extractions involving significant surgical trauma, clinicians may prefer dexamethasone in collaboration with the patient, whereas, in simpler and minimally invasive procedures, A-PRF may be sufficient and preferable. Moreover, our study demonstrated that the oral form of dexamethasone, rather than the injectable form, is still effective. Taken together, future studies, including comparative groups such as A-PRF, dexamethasone, and a control group tailored to different clinical scenarios, are warranted to contribute significantly to the body of knowledge in the literature.

Abbreviations

A-PRF	Advanced Platelet-Rich Fibrin
CONSORT	Consolidated Standards of Reporting Trials
PRF	Platelet-Rich Fibrin
VAS	Visual Analog Scale
NCSS	Number Cruncher Statistical System
L-PRF	Leukocyte Platelet-Rich Fibrin

Supplementary Information

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Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

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Not applicable.

Authors' contributions

All authors contributed to the study's conception, design, intellectual content, and literature search. Y.E managed recruitment, informed consent, adherence to ethical guidelines, and treatment implementation. Y.E conducted clinical procedures, ensured participant safety, and addressed adverse events. Y.E and S.K.T documented processes and monitored participant compliance. All authors participated in data acquisition and analysis, manuscript drafting and editing, reviewing and approving the version to be published. All authors are responsible for the work integrity and act as 'guarantors'. All authors read and approved the final manuscript.

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Data availability

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the Van Yuzuncu Yil University Clinical Research Ethics Committee (YYU/13/20.09.2021) and conducted in accordance with the principles of the Declaration of Helsinki.

All the patients in the study provided their informed consent to share their clinical data for research purposes.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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