Original Article

A NOVEL TRANEXAMIC ACID PROTOCOL ENHANCES RECOVERY AFTER LOWER THIRD MOLAR SURGERY: A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Effective control of pain, edema, trismus, and fluid loss is critical for optimal postoperative recovery following third molar extractions. This study aimed to evaluate the effects of tranexamic acid on inflammatory and biophysical parameters after such procedures. A randomized clinical trial with a split-mouth design was conducted, in which patients underwent bilateral lower third molar extractions on separate hemifaces, with a minimum interval of 15 days. One side received oral tranexamic acid (1.5 g/day for 3 days, starting 8 hours prior to surgery), while the other side received a placebo, ensuring blinding. Postoperative assessments included pain (Visual Analogue Scale), edema (tragus to labial commissure distance), trismus (interincisal distance), and body composition via bioimpedance at immediate, 2-, 4-, and 7-day intervals. Results demonstrated a significant reduction in pain, edema, and trismus on postoperative days 2 and 4 in the tranexamic acid group. Additionally, a smaller variation in body composition was observed, suggesting reduced fluid loss. It is concluded that tranexamic acid offers meaningful benefits in postoperative recovery, representing a promising strategy for the surgical management of third molars.

Key words: Tranexamic acid, Tooth extraction, Recovery of function, Molar surgery.

Introduction

The extraction of impacted mandibular third molars is one of the most common surgical procedures in dental and maxillofacial practice. Although generally considered a low-complexity intervention, it is frequently associated with various postoperative adverse events, including pain, edema, trismus, bleeding, and localized inflammation. These signs and symptoms can significantly impair the patient's quality of life in the days following surgery and may prolong the functional recovery of the affected tissues [1-3].

Surgical trauma triggers an acute inflammatory response characterized by vasodilation, plasma fluid extravasation, and cellular infiltration, mediated by pro-inflammatory cytokines such as interleukins (IL-1, IL-6), tumor necrosis factor-alpha (TNF-α), and prostaglandins. Simultaneously, activation of the fibrinolytic system contributes to the degradation of the blood clot formed in the post-extraction socket, predisposing the site to persistent bleeding and potential complications such as dry socket, infection, and delayed bone healing. Clot stability is therefore essential not only for immediate hemostasis but also for proper subsequent tissue regeneration [4].

By competitively blocking lysine binding sites on plasminogen, tranexamic acid (TXA), a synthetic lysine analog, prevents plasminogen from being converted to plasmin and the consequent breakdown of fibrin. Recent research has indicated that TXA may be useful in controlling local inflammatory responses, which could lead to less postoperative pain and swelling, in addition to its proven effectiveness in reducing bleeding in various surgical contexts, such as orthopedic, gynecological, cardiovascular, and trauma surgery. Although TXA has been investigated for use in implant and periodontal operations, its usage in more involved oral surgery, such as third molar extractions, is still not well understood. The majority of existing studies have methodological shortcomings, such as small sample numbers, a lack of suitable control groups, or a dependence on subjective outcome measures. Furthermore, the effect of TXA on objective parameters such as observable biophysical and metabolic changes after surgery is unknown, limiting understanding of its systemic and local effects [5, 6].

Given the clinical relevance of clot stability in preventing complications, enhancing postoperative healing, and the possible anti-inflammatory action of TXA, it is essential to investigate its applicability in oral surgery through more rigorous study designs. Well-structured clinical trials with intraindividual control and quantitative variable assessment are crucial to validate its use as an adjunct in postoperative management [7].

In this context, the present study aimed to investigate the effects of local administration of tranexamic acid on postoperative recovery in patients undergoing lower third molar extraction. Through a randomized, double-blind, split-mouth clinical trial with intraindividual control, we assessed biophysical, inflammatory, and clinical

parameters, including volume of anesthetic infiltration, surgical time, mouth opening amplitude, pain perception, body composition via bioelectrical impedance, and weight variation. This approach seeks to broaden the understanding of TXA's therapeutic potential in dentistry and provide evidence to support its rational use based on objective data.

Materials and Methods

Study design

This study was designed as a randomized, double-blind, split-mouth clinical trial involving patients undergoing bilateral extraction of impacted mandibular third molars. Each participant underwent surgery on both sides, with a minimum interval of 15 days between procedures. One side received tranexamic acid, while the contralateral side received a placebo, ensuring blinding and standardization of the intervention. The study was conducted in full accordance with the ethical principles outlined in the Declaration of Helsinki and was approved by the institutional Research Ethics Committee. Prior to data collection, a pilot study was conducted to evaluate the feasibility of the instruments and the participants' comprehension of the questionnaires and applied tests.

Inclusion and exclusion criteria

Eligible participants were adults over 18 years of age with a clinical indication for bilateral extraction of mandibular third molars, with teeth presenting similar positions and levels of impaction. Exclusion criteria included a history of hematologic disorders, allergy to any medication used in the protocol, continuous use of anticoagulants or anti-inflammatory drugs, and any systemic condition that could interfere with wound healing.

Data collection and instruments

Data were collected using a structured form completed by the investigator based on clinical evaluations and patient-reported outcomes [8-15]. The form included information on age, sex, operative time (in minutes), and postoperative variables such as pain, edema, trismus, and body composition. Pain was assessed using a Visual Analogue Scale (VAS); edema was measured as the distance from the tragus to the labial commissure; and trismus was evaluated by the interincisal distance between teeth 11 and 41. Body composition and estimated blood volume loss were assessed using a bioelectrical impedance scale (InBody® 120, Biospace Co. Ltd., Seoul, South Korea). Measurements were recorded at five distinct time points: T1 = preoperative, T2 = immediate postoperative (day 0), T3 = 2 days postoperative, T4 = 4 days postoperative, and T5 = 7 days postoperative.

Intervention protocol

Tranexamic acid was administered according to the manufacturer's guidelines. In this study, the dosage was set at 1.5 g per day, divided into three 500 mg doses every 8 hours for three consecutive days, starting 8 hours before surgery. In the control group, a placebo tablet with identical organoleptic properties was administered at the same intervals to maintain blinding. Postoperative medications were standardized for all participants and included amoxicillin 500 mg every 8 hours for seven days, ibuprofen 400 mg every 12 hours for four days, and paracetamol 500 mg every 6 hours for three days.

Results and Discussion

Statistical methods

The data was analyzed descriptively, using absolute and relative frequencies for categorical variables and means, standard deviations (mean ± SD), medians, and interquartile ranges (median [P25; P75]) for numerical variables. Comparisons between sides at each time point were made using the paired Student's t-test or the Wilcoxon signed-rank test, as applicable. For comparisons over many time points, the repeated measures ANOVA (F test) or Friedman test was used. When the F test revealed significance, Bonferroni's multiple comparison tests were used for pairwise evaluations. If the Friedman test revealed significant differences, appropriate post-hoc multiple comparisons were performed.

The choice between the paired *t*-test and the Wilcoxon test was based on the distribution of the difference variable between sides: the paired *t*-test was used when the difference followed a normal distribution, while the Wilcoxon test was applied when normality was rejected or when dealing with ordinal data. Repeated measures ANOVA was conducted when data were normally distributed at all time points; otherwise, the Friedman test was used. Normality was assessed using the Shapiro-Wilk test.
A significance level of 5% was adopted for all statistical tests. Data entry was performed using Microsoft Excel, and statistical analyses were conducted with IBM SPSS Statistics, version 27.

Sociodemographic characteristics

The majority of participants were female (75.0%), while males comprised 25.0% of the sample. The mean age was 23.42 years (SD = 3.29), with a median of 23.00 years and an interquartile range of 21.25 to 26.50 years. The mean height was 165.33 cm (SD = 10.01), with a median of 162.00 cm, ranging from 157.75 to 176.25 cm.

Operative parameters

The mean surgical time was longer on the side treated with tranexamic acid (test side), averaging 52.08 minutes, compared to 46.58 minutes on the control side; however, this difference was not statistically significant ($p = 0.154$). Regarding the volume of anesthetic solution administered, the mean was 7.33 mL on the test side and 7.40 mL on the control side, also without statistical significance ($p = 1.000$).

Data analysis

As shown in **Table 1**, statistically significant differences

between sides were observed for protein levels (at T2, T3, T4, and T5) and mineral content (at T1 and T4). Across time points, significant variations were identified in nearly all variables on both sides, except for total body water on the test side, which remained stable.

In side-by-side comparisons, protein concentrations were consistently higher on the test side: at T2, the means were 9.09 and 8.63; at T3, 8.86 and 8.18; at T4, 9.13 and 8.23; and at T5, 9.18 and 8.32, respectively. For mineral content, mean values were higher on the control side at T1 (3.46 vs. 3.06) and T4 (3.23 vs. 3.04), indicating an inverse trend compared to protein levels.

In the temporal analysis, key findings included the following: for total body water on the control side, the highest mean was recorded at T1 (37.03), followed by a decline at subsequent time points (ranging from 36.28 to 36.53), with T1 differing significantly from T2, T3, and T5. On the test side, protein levels peaked at T1 (9.28) and reached their lowest at T3 (8.86), with intermediate values between 9.09 and 9.18; significant differences were observed between T1 and T3, as well as between these and the remaining time points. On the control side, the highest protein levels were at T1 (9.08) and T2 (8.63), while means ranged from 8.18 to 8.32 at later times; T1 and T2 differed from each other and from subsequent evaluations.

Regarding minerals on the test side, the highest mean was at T5 (3.22), with values at other time points ranging from 2.91 to 3.06. T5 was significantly different from all other time points, and T2 differed from both T1 and T4. On the control side, the highest mineral means were at T1 (3.46) and T5 (3.40), with the lowest at T2 (2.95) and intermediate values ranging from 3.09 to 3.23. Significant differences were found between T2 and all other times, as well as between T1 and T5 compared to T3 and T4.

Table 1. Descriptive Statistics of Body Water, Protein, and Mineral Content by Time Point and Side Evaluated

		Test Side		
	Time	**(n = 12)**	**Control Side (n = 12)**	
Variable		Mean± SD Median (P25; P75)	Mean ± SD Median (P25; P75)	**p-value**
Body Water (ml)	T1	35,71 ± 6,82 35,40 (29,28; 42,83)	37,03 ± 5,29 **(A)** 35,75 (32,30; 42,78)	**$p^{(1)}$ = 0,146**
	T2	35,43 ± 6,82 35,15 (28,55; 42,65)	36,39 ± 5,24 **(B)** 35,40 (31,90; 42,30)	**$p^{(1)}$ = 0,277**
	T3	35,22 ± 6,17 35,40 (28,40; 41,38)	36,28 ± 5,17 **(B)** 35,55 (31,80; 42,10)	**$p^{(1)}$ = 0,196**
	T4	35,25 ± 6,07 35,45 (28,90; 42,00)	36,39 ± 5,16 **(AB)** 35,90 (32,10; 42,00)	**$p^{(1)}$ = 0,145**
	T5	35,53 ± 6,44 35,70 (29,13; 42,65)	36,53 ± 5,20 **(B)** 35,70 (32,10; 42,10)	**$p^{(1)}$ = 0,239**
	p-value	**$p^{(3)}$ = 0,245**	**$p^{(3)}$ < 0,001***	
Protein (Kg)	T1	9,28 ± 2,26 **(A)** 8,40 (7,95; 11,05)	9,08 ± 2,08 **(A)** 8,30 (7,50; 11,08)	**$p^{(1)}$ = 0,264**
	T2	9,09 ± 2,30 **(B)** 8,20 (7,78; 10,93)	8,63 ± 1,99 **(B)** 8,10 (6,98; 10,43)	**$p^{(1)}$ = 0,035***
	T3	8,86 ± 2,17 **(C)** 8,20 (7,28; 10,70)	8,18 ± 1,39 **(C)** 7,70 (7,03; 9,75)	**$p^{(1)}$ = 0,042***
	T4	9,13 ± 2,19 **(B)** 8,50 (7,83; 10,98)	8,23 ± 1,46 **(C)** 7,80 (6,98; 9,88)	**$p^{(2)}$ = 0,004***
	T5	9,18 ± 2,22 **(B)** 8,20 (7,83; 10,95)	8,32 ± 1,92 **(C)** 7,55 (6,88; 9,88)	**$p^{(1)}$ = 0,002***

	p-value	**$p^{(4)} < 0,001$***	**$p^{(4)} < 0,001$***	
Minerals (Kg)	T1	3,06 ± 0,78 (A)	3,46 ± 0,78 (A)	**$p^{(1)} = 0,004$***
		2,90 (2,40; 3,85)	3,25 (2,75; 4,33)	
	T2	2,91 ± 0,73 (B)	2,95 ± 0,64 (B)	**$p^{(1)} = 0,773$**
		2,70 (2,30; 3,75)	2,90 (2,30; 3,50)	
	T3	2,93 ± 0,99 (AB)	3,09 ± 0,69 (C)	**$p^{(2)} = 0,125$**
		2,40 (2,25; 4,18)	2,70 (2,60; 3,98)	
	T4	3,04 ± 0,73 (A)	3,23 ± 0,70 (C)	**$p^{(1)} = 0,005$***
		2,70 (2,70; 3,93)	3,10 (2,55; 4,05)	
	T5	3,22 ± 0,68 (C)	3,40 ± 0,72 (A)	**$p^{(1)} = 0,184$**
		3,10 (2,68; 3,84)	3,50 (2,60; 4,18)	
	p-value	**$p^{(4)} < 0,001$***	**$p^{(4)} < 0,001$***	

*) Statistically significant difference at the 5.0% level
(1) Paired Student's t-test
(2) Paired Wilcoxon test
(3) Repeated measures ANOVA (F test) with Bonferroni post-hoc comparisons
(4) Friedman test with corresponding post-hoc comparisons
Note: If all letters in parentheses differ, statistically significant differences are confirmed between the corresponding assessments.

Body composition variables

As shown in **Table 2**, statistically significant differences between sides were observed for fat percentage and body weight at time point T1. In both cases, mean values were higher on the control side compared to the test side: for fat percentage, the means were 21.88% and 20.04%, respectively; for body weight, they were 71.44 kg and 68.09 kg, respectively.

Regarding temporal variations, significant changes were identified in fat percentage, body weight, and lean mass on both sides, as well as in body fat percentage specifically on the test side. For fat percentage on the test side, the highest mean was recorded at T1 (20.04%), while the lowest values occurred at T4 (19.50%) and T3 (19.58%). At the other time points, means ranged from 19.85% to 19.88%. Statistical analyses revealed that T1 differed significantly from all other time points; T2 was different from T4, and T3 and T4 differed from T5.

As for body fat percentage on the control side, the highest mean was observed at T1 (21.88%), followed by values between 21.43% and 21.45% at T2 and T5, and between 20.98% and 21.08% at T3 and T4. In this comparison, T1 differed significantly from all other time points, while T2 and T5 differed from T3 and T4.

Regarding body weight on the test side, the highest mean was at T1 (68.09 kg) and the lowest at T3 (66.58 kg), with intermediate values ranging from 66.92 kg to 67.81 kg. Statistical testing indicated that T1 was significantly different from T2 and T3, while T3 and T4 differed from T5. On the control side, the highest mean weight was also observed at T1 (71.44 kg), followed by T2 (69.68 kg), while the lowest values were at T3 (68.53 kg) and T4 (68.93 kg); means ranged from 69.43 kg to 69.68 kg at the remaining times. Multiple comparisons demonstrated that T1 was significantly different from all subsequent time points, T2 differed from T3, and T3 and T4 differed from T5.

For fat percentage on the test side, the highest mean was at T2 (30.03%) and the lowest at T4 (29.55%), with intermediate values between 29.78% and 29.95% at the other time points. Analyses indicated that T4 was significantly different from all other time points, and T2 differed from T3 and T5.

Regarding lean mass on the test side, the highest means were observed at T5 (23.88 kg) and T1 (23.60 kg), while the other time points ranged from 23.26 kg to 23.53 kg. Statistical comparisons showed that T1 and T5 differed significantly from the intermediate time points, and T3 differed from T4. On the control side, the highest lean mass values were recorded at T1 (24.40 kg) and T5 (24.16 kg), with values ranging from 23.84 kg to 24.01 kg at the remaining points. Analyses revealed that T1 differed significantly from the other time points, T2 from T4, and T3 and T4 from T5.

Table 2. Descriptive Statistics of Body Weight, BMI, Body Fat Mass, Body Fat Percentage, and Lean Mass by Time and Evaluated Side.

		Test Side	
	Time	**(n = 12)**	**Control Side**

			(n = 12)	
Variable		Mean± SD	Mean ± SD	**p-value**
		Median (P25; P75)	Median (P25; P75)	
Fat (Kg)	**T1**	20,04 ± 3,46 **(A)**	21,88 ± 4,05 **(A)**	**$p^{(1)}$ = 0,018***
		18,90 (17,63; 21,05)	19,10 (18,80; 27,20)	
	T2	19,85 ± 3,43 **(BD)**	21,45 ± 4,30 **(B)**	**$p^{(1)}$ = 0,194**
		18,70 (17,35; 20,85)	18,30 (18,30; 27,10)	
	T3	19,58 ± 3,82 **(BC)**	20,98 ± 4,22 **(C)**	**$p^{(1)}$ = 0,461**
		18,60 (17,03; 20,75)	18,30 (17,40; 26,50)	
	T4	19,50 ± 3,71 **(C)**	21,08 ± 4,23 **(C)**	**$p^{(1)}$ = 0,228**
		18,30 (16,88; 20,43)	18,20 (17,98; 26,60)	
	T5	19,88 ± 3,60 **(D)**	21,43 ± 4,17 **(B)**	**$p^{(1)}$ = 0,380**
		18,80 (17,35; 20,75)	18,70 (18,33; 26,90)	
	p-value	**$p^{(3)}$ < 0,001***	**$p^{(3)}$ < 0,001***	
Weight (Kg)	**T1**	68,09 ± 7,34 **(AD)**	71,44 ± 5,30 **(A)**	**$P^{(2)}$ = 0,015***
		65,40 (62,55; 75,15)	69,55 (66,63; 77,20)	
	T2	67,28 ± 7,39 **(BC)**	69,43 ± 4,89 **(BD)**	**$p^{(2)}$ = 0,126**
		64,70 (61,80; 74,63)	68,20 (64,83; 74,85)	
	T3	66,58 ± 6,68 **(B)**	68,53 ± 4,14 **(C)**	**$p^{(2)}$ = 0,159**
		64,60 (62,53; 72,33)	67,70 (64,68; 73,50)	
	T4	66,92 ± 6,33 **(BD)**	68,93 ± 4,34 **(CD)**	**$p^{(2)}$ = 0,099**
		64,80 (62,80; 73,53)	67,90 (65,15; 73,73)	
	T5	67,81 ± 6,63 **(AC)**	69,68 ± 4,66 **(B)**	**$p^{(2)}$ = 0,117**
		65,80 (62,98; 74,61)	68,40 (66,20; 74,35)	
	p-value	**$p^{(4)}$ = 0,001***	**$p^{(4)}$ < 0,001***	
BMI	**T1**	24,92 ± 1,78	26,38 ± 3,61	**$p^{(2)}$ = 0,259**
		24,22 (23,88; 26,32)	26,65 (23,05; 29,45)	
	T2	24,93 ± 4,38	25,67 ± 3,73	**$p^{(2)}$ = 0,548**
		25,23 (19,97; 28,83)	25,42 (22,02; 28,77)	
	T3	24,52 ± 4,94	25,29 ± 3,13	**$p^{(2)}$ = 0,558**
		23,29 (20,64; 28,30)	25,99 (22,70; 27,21)	
	T4	24,70 ± 3,40	25,50 ± 3,68	**$p^{(2)}$ = 0,527**
		25,55 (23,40; 27,16)	25,76 (22,57; 28,30)	
	T5	25,07 ± 3,97	25,73 ± 3,44	**$p^{(2)}$ = 0,589**
		24,34 (21,83; 28,89)	25,26 (23,22; 27,65)	
	p-value	**$p^{(4)}$ = 0,989**	**$p^{(4)}$ = 0,933**	
Fat percentage (%)	T1	29,95 ± 7,22 **(AB)**	30,87 ± 6,59	**$p^{(1)}$ = 0,446**
		28,72 (23,60; 33,92)	28,51 (24,20; 38,89)	

	T2	30,03 ± 7,24 (A)	31,13 ± 6,95	**p(2) = 0,505**
		28,79 (23,73; 34,05)	28,46 (24,16; 39,56)	
	T3	29,84 ± 7,38 (BD)	30,81 ± 6,79	**p(1) = 0,420**
		28,79 (24,16; 33,94)	28,48 (23,68; 39,00)	
	T4	29,55 ± 7,16 (C)	30,78 ± 6,80	**p(1) = 0,326**
		28,18 (24,41; 33,39)	28,00 (24,14; 38,98)	
	T5	29,78 ± 7,19 (D)	30,99 ± 6,79	**p(2) = 0,424**
		28,42 (23,93; 33,88)	28,59 (24,12; 39,17)	
	p-value	**p(3) < 0,023***	**p(3) = 0,056**	
Lean mass (Kg)	T1	23,60 ± 5,55 (A)	24,40 ± 6,26 (A)	**p(1) = 0,082**
		21,70 (19,90; 29,83)	22,00 (19,50; 31,75)	
	T2	23,34 ± 5,21 (BC)	24,01 ± 6,21 (BD)	**p(1) = 0,210**
		21,20 (19,78; 29,00)	21,55 (19,10; 31,33)	
	T3	23,26 ± 5,19 (B)	23,90 ± 6,30 (BC)	**p(1) = 0,239**
		21,30 (19,43; 29,25)	21,50 (18,90; 31,30)	
	T4	23,53 ± 5,51 (C)	23,84 ± 6,18 (C)	**p(1) = 0,488**
		21,50 (19,45; 29,88)	21,30 (19,10; 31,13)	
	T5	23,88 ± 5,58 (A)	24,16 ± 5,97 (D)	**p(1) = 0,543**
		21,50 (20,00; 30,25)	22,35 (19,20; 30,83)	
	p-value	**p(3) < 0,001***	**p(3) < 0,001***	

(*) Statistically significant difference at the 5.0% level
(1) Paired Student's t-test
(2) Paired Wilcoxon test
(3) Friedman test with post hoc comparisons
(4) Repeated measures ANOVA (F test) with Bonferroni post hoc comparisons
Note: If all letters in parentheses are different, significant differences are confirmed between the corresponding evaluations.

Facial swelling and mandibular mobility

Statistically significant differences between sides were identified for mouth opening and tragus–labial commissure distance. For mouth opening, between-side differences were observed at all time points except T1, while for tragus–labial commissure distance, significant differences were present at all time points evaluated.

In the side-by-side comparisons, mean mouth opening values were consistently higher on the test side compared to the control side: at T2, means were 36.78 mm and 34.75 mm, respectively; at T3, 36.83 mm and 33.08 mm; at T4, 38.50 mm and 34.24 mm; and at T5, 39.83 mm and 37.17 mm. Conversely, for tragus–labial commissure distance, the control side consistently showed higher mean values: at T1, 12.65 mm versus 11.97 mm on the test side; at T2, 13.28 mm and 12.37 mm; at T3, 13.56 mm and 12.48 mm; at T4, 12.84 mm and 11.95 mm; and at T5, 12.72 mm and 11.87 mm.

Regarding temporal variations, significant changes were observed across time points for both variables on each side. For mouth opening on the test side, the highest mean values were recorded at T5 (39.83 mm), T1 (39.17 mm), and T4 (38.50 mm), while the remaining time points ranged from 36.78 mm to 36.83 mm. Statistical analyses demonstrated that T1 differed significantly from T2 and T3; T2 and T3 differed from T4 and T5; and T4 differed from T5.

On the control side, the highest mean mouth opening values were observed at T1 (39.50 mm) and T5 (37.17 mm), while the other time points ranged from 33.08 mm to 34.75 mm. Multiple comparisons indicated that T1 and T5 differed significantly from each other and from all other time points, while T2 differed from T3.

As shown in **Figure 1**, for tragus–labial commissure distance on the test side, the highest means occurred at T3 (12.48 mm) and T2 (12.37 mm), while values at the remaining time points ranged between 11.87 mm and 11.97 mm. Significant differences were detected between T2 and T3, which also differed from all other time points. On the

control side, the highest means were recorded at T3 (13.56 mm) and T2 (13.28 mm), with remaining values ranging from 12.65 mm to 12.84 mm. Statistical analyses confirmed that T2 and T3 were significantly different from all other time points.

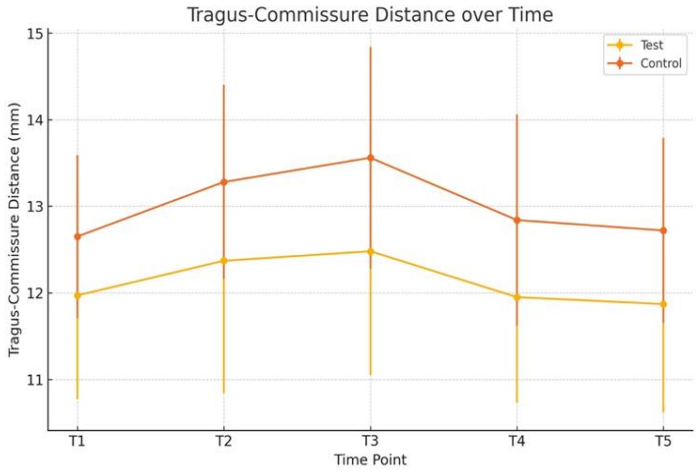

Figure 1. Tragus–Commissure Distance Over Time (Mean ± SD) for Test vs. Control Side

Pain assessment

Statistically significant differences between sides were identified for pain scores at all time points, except at T1 and T5. Whenever differences were detected, mean pain scores were consistently higher on the control side compared to the test side. Specifically, at T2, mean scores were 3.75 on the control side and 2.75 on the test side; at T3, 3.42 and 2.25, respectively; and at T4, 1.58 and 0.33.

In terms of pain progression over time, both sides showed null mean scores at T1. Pain peaked at T2, followed by a gradual reduction to T5. On the test side, mean pain levels varied from 2.75 at T2 to 0.00 at T5. On the control side, the mean score was 3.75 at T2 and dropped to 0.67 at T5. Multiple comparisons demonstrated that, on the test side, all time point pairs had statistically significant differences, with the exception of T1 and T5. On the control side, all comparisons were significant, except at T3 (3.42) and T4 (1.58), which did not differ substantially.

As we can observe in **Figure 2**, when pain was categorized by intensity, all participants reported no pain on either side at T1. At T2, all individuals on the control side experienced moderate pain, whereas on the test side, 75% reported moderate pain and 25% reported mild pain. At T3, on the test side, 66.7% of participants reported mild pain and 33.3% reported moderate pain. Conversely, on the control side, 91.7% reported moderate pain and only 8.3% reported mild pain, representing a statistically significant difference between sides.

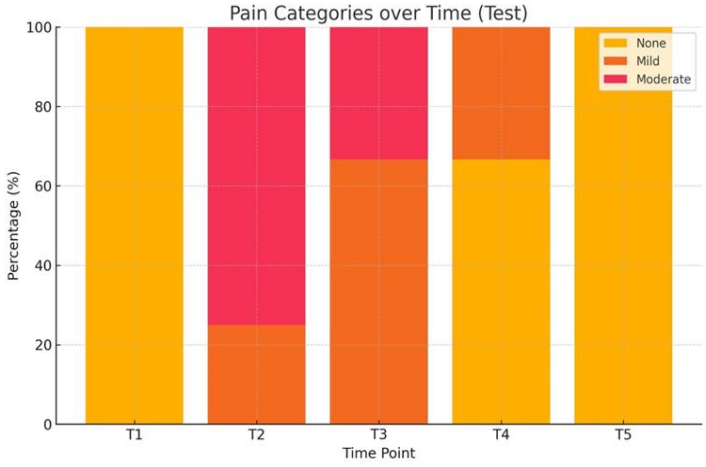

Figure 2. Stacked Bar Chart of Pain Category Distribution Over Time for Test vs. Control Sides

At T4, 66.7 % of participants on the test side reported no pain and 33.3 % reported mild pain, whereas all participants on the control side experienced mild pain; this inter-side difference was statistically significant. At T5, participants on the test side again reported complete absence of pain [16-21]. In contrast, 66.7 % of the control side were pain-free and 33.3 % reported mild pain. Intra-side comparisons revealed statistically significant differences between all time points except between T1 and T5 on the test side and between T2 and T3 on the control side.

The findings of this study demonstrate that tranexamic acid has significant beneficial effects on postoperative recovery following lower third molar extractions, exerting a positive influence on key clinical parameters such as pain, edema, trismus, and estimated body volume loss. The methodology employed—particularly the split-mouth design with administration of the drug to only one hemiface—enabled greater control of individual variables and allowed for a more accurate comparative assessment between the treated and untreated sides [22].

Pain is one of the main morbidity factors in dental surgical procedures, and its reduction is a central goal of any postoperative therapeutic approach. The statistically significant reduction in pain among patients who received tranexamic acid suggests a potential indirect analgesic effect of the drug, likely resulting from decreased release of inflammatory mediators secondary to clot stabilization. Previous studies had already pointed to this effect, particularly in surgeries involving bone manipulation or highly vascularized tissues, reinforcing the data found in the present study [23].

With regard to edema, the literature indicates that tranexamic acid may reduce fluid extravasation by limiting fibrin degradation and plasminogen activation, thereby resulting in reduced tissue inflammation. This is reflected in the significant reduction in swelling observed on postoperative days 2 and 4 on the treated sides [24-31]. This favorable response is consistent with findings from other surgical specialties such as orthopedics, cardiovascular surgery, and oral and maxillofacial surgery, where tranexamic acid has demonstrated substantial reductions in edema and local inflammatory response. Although the application of the drug in dental settings is still considered emerging, the results support its potential inclusion in inflammatory control protocols for oral surgeries [32, 33].

Trismus, characterized by limited mouth opening, is frequently associated with postoperative pain and edema. The improvement in this parameter on the sides treated with tranexamic acid suggests that, by controlling inflammation and swelling, the drug may contribute to faster and more comfortable functional recovery, especially during the early postoperative days, which are clinically more critical for the patient. This effect is particularly relevant for patients who need to return quickly to their daily or professional activities, thereby expanding the practical applicability of this therapeutic approach [34, 35].

Another relevant point concerns the estimation of total body volume loss using body composition analysis via bioelectrical impedance. Although this tool is not commonly used in dental studies, its inclusion in the present protocol enabled an indirect yet valid estimate of fluid shifts and blood loss, indicating that tranexamic acid may indeed contribute to more efficient local hemostasis. This property, already well-documented in major medical surgeries, is demonstrated here in outpatient dental contexts as well, expanding the scope of the drug's application [36, 37].

Although the results are encouraging, some limitations should be taken into account. The use of a placebo in the control group allowed for proper study blinding, minimizing assessment bias and guaranteeing that the observed effects could in fact be attributed to tranexamic acid. Additionally, the use of a standardized pharmacological protocol among all participants—including antibiotics, anti-inflammatory agents, and analgesics—ensured that the only independent variable was the administration of the experimental drug, strengthening the internal validity of the research. Even though the number of participants is suitable for an initial clinical trial, the data's generalizability is still constrained. Additionally, the evaluation of delayed outcomes, like the emergence of dry sockets, infections, or other adverse events, is impossible in the absence of long-term follow-up. It's also critical to stress that, although being novel, the use of a bioimpedance scale needs controlled settings, such as adequate hydration and the absence of significant metabolic swings, to guarantee data dependability [38, 39].

Future studies with larger sample sizes and evaluation of different routes of tranexamic acid administration—such as oral rinses, direct topical application, or intravenous administration in more complex cases—may clarify the drug's efficacy with greater precision and optimize its clinical use [40-45]. Additionally, it would be valuable to investigate whether the combined use of tranexamic acid with specific suturing techniques or tissue regeneration agents could further enhance the outcomes observed [46, 47].

Conclusion

In conclusion, the data from this study indicate that tranexamic acid, when administered orally following an adjusted protocol, can promote a more comfortable, effective, and functionally favorable postoperative recovery after lower third molar extractions. Its antifibrinolytic activity, combined with its ability to reduce inflammatory parameters, positions the drug as a promising alternative in contemporary dental surgical practice, with the potential to be incorporated into clinical protocols for high-risk patients

or more complex surgical procedures.

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