

Original Article

Evaluating the Efficacy of Tranexamic Acid versus Placebo in Controlling Intraoperative Blood Loss during Mandibular Fracture Surgeries

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Abstract

Objective: To determine the efficacy of intravenous tranexamic acid versus placebo in reducing intraoperative blood loss in patients undergoing mandibular fracture surgery, and the effect of tranexamic acid on postoperative fall in hemoglobin, need for transfusion, and operative time.

Methodology: This was a randomized, placebo-controlled study. Oral & Maxillofacial Surgery, Bolan Medical College Hospital, Quetta. From March 2025 to August 2025, we treated 100 patients surgically for mandibular fractures. Patients were randomly divided into two groups, A (n=50) and B (n=50); group A received intravenous tranexamic acid, and group B received placebo. Patients in the age range of 18-65 years, who presented with mandibular fractures diagnosed on radiographs and were treated operatively, were included. SPSS was used for data analysis. We used an independent-samples t-test to compare continuous variables and a chi-square test to compare categorical variables. We considered $p < 0.05$ statistically significant.

Results: We included 100 patients, with 50 in each treatment group. The overall mean age was 34.8 ± 9.7 years. Patients receiving tranexamic acid had a mean age of 35.2 ± 9.5 years, whereas those receiving placebo had a mean age of 34.4 ± 9.9 years ($p=0.68$). The mean intraoperative blood loss was significantly lower in the tranexamic acid group (285 ± 85 mL) compared with the placebo group (410 ± 110 mL, $p<0.001$). The mean postoperative hemoglobin reduction was also lower among patients receiving tranexamic acid (1.2 ± 0.6 g/dL) than among placebo recipients (1.8 ± 0.8 g/dL, $p<0.001$). Blood transfusion was required in 3 patients (6.0%) in the tranexamic acid group compared with 10 patients (20.0%) in the placebo group ($p=0.037$). Mean operative duration was 118 ± 24 minutes in the tranexamic acid group and 126 ± 27 minutes in the placebo group ($p=0.12$). No major thromboembolic or other serious adverse events were observed in either group. These findings suggest that tranexamic acid significantly reduces intraoperative blood loss and postoperative hemoglobin decline during mandibular fracture surgery.

Conclusion: Intraoperative blood loss and postoperative hemoglobin loss were significantly reduced in patients receiving tranexamic acid intravenously for surgery on mandibular fracture. It also reduced the need for blood transfusion perioperatively without significantly affecting surgery duration. Tranexamic acid may be beneficial and appears relatively safe as an adjunct for controlling surgical blood loss in mandibular fracture surgery. More centrally controlled, randomized studies are needed to validate these results and provide a uniformly accepted dosing protocol.

Introduction

Mandibular fractures are very common and constitute a considerable portion of facial injuries that necessitate surgical repair. The most common causes are road traffic accidents, interpersonal violence, falls, sports injuries, and occupational trauma [1]. Treatment varies, depending on the location, severity, displacement, and pattern of the fracture, and can include closed reduction or open reduction and internal fixation. The surgical management often involves good exposure, manipulation of fractured segments, and fixation device placement, all of which can be accompanied by different levels of bleeding in the operating room. Bleeding from the mandible is usually not a problem during fracture surgery. Still, excessive bleeding may make it difficult to see the surgical area, make surgery more time-consuming, make postoperative care of the patient more difficult, and sometimes require the transfusion of blood [2,3]. Therefore, blood conservation is an important aspect of modern surgery. Researchers have explored several ways to reduce surgical blood loss, including careful surgical hemostasis, controlled hypotension, local hemostatic agents, anesthetic protocols, and pharmacologic agents. Tranexamic acid has attracted much interest among pharmacological agents because of its proven antifibrinolytic effect [4]. Tranexamic acid is a synthetic lysine analog that competes with plasminogen for binding to fibrin. It inhibits plasminogen conversion and activity at the clot site, helping stabilize fibrin clots and minimize continued bleeding. It is a relatively inexpensive, easy-to-use, proven perioperative blood-loss reduction strategy used in several surgical specialties [5]. Tranexamic acid is effective in various surgical procedures, including orthopedic surgery, cardiac surgery, gynecological surgery, trauma surgery, and major general surgical procedures. It has been used to reduce perioperative blood loss and transfusion requirements, with an acceptable, non-significant increase in thromboembolic complications when used appropriately in appropriate patients. The magnitude of benefit, however, can differ based on the type of surgery, route and timing of administration, dose, patient characteristics, and bleeding risk. Therefore, the findings from other surgery disciplines cannot be directly applied to maxillofacial surgery [6,7]. The surgical implications and anatomic characteristics of the mandible make it a special case of fracture surgery. The vascularity of the maxillofacial area can cause excessive bleeding, and blood in the surgical area may obscure the view and proper fracture reduction. Even slight reductions in blood loss may improve operating conditions and help minimize postoperative hemoglobin loss. However, little evidence exists on using tranexamic acid to control blood loss during mandibular fracture surgery, though it has been investigated in other surgical procedures. In addition, differences in fracture patterns, surgical methods, anesthetic techniques, and perioperative guidelines can affect blood loss [8]. A double-masked, placebo-controlled study may better estimate the independent effect of tranexamic acid and reduce confounding variables. Objective parameters such as estimated intraoperative blood loss, postoperative hemoglobin drop, blood transfusion needs, and operation duration can help assess its usefulness in this population. An effective and safe blood-conservation program may be especially beneficial in areas with a shortage of blood products or where transfusion is more costly and risky [9].

Material and Methods

A clinical study involving patients who required surgical fixation of mandibular fractures to assess the effect of tranexamic acid on intraoperative blood loss was designed as a randomized, placebo-controlled study. A total of 100 adult patients with radiological and clinical diagnosis of mandibular fracture, who underwent open reduction and

internal fixation with plates and screws for the fracture, were included in the study. Patients were recruited consecutively from the Department of Oral and Maxillofacial Surgery of a Tertiary Care Teaching Hospital during the study period. The institutional review committee approved the study, and all participants provided written informed consent. Patients of both genders aged 18–65 years who sustained an isolated or associated mandibular fracture requiring operative fixation were included. Patients with a known coagulation or bleeding disorder, or currently taking anticoagulants or antifibrinolytic agents, history of thromboembolic disease, significant renal impairment, significant hepatic dysfunction, or unwilling to participate were excluded. Incomplete clinical, laboratory, or operative data were not sufficient to include patients in the final analysis. We randomly divided the 100 patients into two groups using a computer-generated randomization sequence, with 50 patients in each group. Group A was given 1 g tranexamic acid in normal saline intravenously before surgical incision. Group B was given the same amount of normal saline (placebo) at the same time. We applied a standardized surgical technique, anesthesia, perioperative fluid management, and common hemostatic measures as much as possible between groups. Trained surgeons performed all procedures using standard surgical techniques for fracture exposure, reduction, and internal fixation. We calculated intraoperative blood loss (IBL) from the amount of blood retrieved in the suction canister after accounting for irrigation fluid; we estimated the amount of blood on surgical sponges and gauze, if available, as a primary outcome. Secondary outcomes were reduction in hemoglobin level after surgery, need for blood transfusion during surgery, and overall operative time. Institutional laboratories assessed hemoglobin concentration before and after surgery. Adverse events observed perioperatively included allergic reactions, thromboembolic complications, and other major events. We entered the data into a database and analyzed them with SPSS version 27.0. We expressed continuous variables as mean $\pm$ standard deviation and categorical variables as frequencies and percentages. We compared continuous variables between groups using an independent-samples t-test, and categorical variables using the chi-square test or Fisher’s exact test (as appropriate). We considered $p < 0.05$ statistically significant. The study results were statistically analyzed.

Results

A total of 100 patients undergoing surgical management of mandibular fractures were included and equally allocated into the tranexamic acid group ($n=50$) and placebo group ($n=50$). The overall mean age was 34.8 ± 9.7 years. The mean age was 35.2 ± 9.5 years in the tranexamic acid group and 34.4 ± 9.9 years in the placebo group, with no significant difference between groups ($p=0.68$). Mean intraoperative blood loss was significantly lower in patients receiving tranexamic acid (285 ± 85 mL) than in those receiving placebo (410 ± 110 mL; $p<0.001$). Similarly, postoperative hemoglobin reduction was significantly lower in the tranexamic acid group (1.2 ± 0.6 g/dL) than in the placebo group (1.8 ± 0.8 g/dL; $p<0.001$). Blood transfusion was required in 3 (6.0%) patients in the tranexamic acid group versus 10 (20.0%) in the placebo group ($p=0.037$). Mean operative duration was 118 ± 24 minutes versus 126 ± 27 minutes, respectively ($p=0.12$). No significant thromboembolic complications were observed. Overall, tranexamic acid significantly reduced intraoperative blood loss and postoperative hemoglobin decline. By colony morphology, Gram staining, and biochemical testing, 145 (58% of the original 250) were subsequently confirmed as *E. coli* by PCR targeting the 16S rRNA gene. All confirmed isolates were Gram-negative rods that produced moderate-to-large, lactose-fermenting pink colonies on MacConkey agar and moderate, round, yellow colonies on CLED agar. On biochemical testing, confirmed isolates were uniformly indole-positive, urease-negative, and lactose-fermenting on both media (Table 1).

Table 1. Demographic and Baseline Characteristics of Study Participants

Variable	Tranexamic Acid Group (n=50)	Placebo Group (n=50)	p-value
Age (years), mean ± SD	35.2 ± 9.5	34.4 ± 9.9	0.68
Male, n (%)	39 (78.0)	38 (76.0)	0.81
Female, n (%)	11 (22.0)	12 (24.0)	0.81
Age 18–30 years, n (%)	18 (36.0)	19 (38.0)	0.83
Age 31–45 years, n (%)	22 (44.0)	21 (42.0)	0.84
Age >45 years, n (%)	10 (20.0)	10 (20.0)	1.00
Road traffic accident, n (%)	31 (62.0)	30 (60.0)	0.84
Fall, n (%)	9 (18.0)	10 (20.0)	0.80
Assault, n (%)	7 (14.0)	7 (14.0)	1.00
Other causes, n (%)	3 (6.0)	3 (6.0)	1.00

Data are presented as frequency (percentage) or mean ± standard deviation (SD). The p-values represent comparisons between the tranexamic acid and placebo groups. A p-value <0.05 was considered statistically significant.

Table 2: Comparison of Operative and Hematological Outcomes Between Study Groups

Outcome	Tranexamic Acid Group (n=50)	Placebo Group (n=50)	p-value
Intraoperative blood loss (mL), mean ± SD	285 ± 85	410 ± 110	<0.001
Postoperative Hb reduction (g/dL), mean ± SD	1.2 ± 0.6	1.8 ± 0.8	<0.001
Blood transfusion required, n (%)	3 (6.0)	10 (20.0)	0.037
Operative duration (minutes), mean ± SD	118 ± 24	126 ± 27	0.12
Thromboembolic complications, n (%)	0 (0.0)	0 (0.0)	—
Other significant adverse events, n (%)	1 (2.0)	1 (2.0)	1.00

Hb = hemoglobin; SD = standard deviation. Continuous variables are expressed as mean ± SD and categorical variables as frequency (percentage). We used the independent-samples t-test, chi-square test, or Fisher’s exact test, as appropriate. We considered p<0.05 statistically significant.

Discussion

This randomized, placebo-controlled study showed that Intravenous tranexamic acid significantly reduced intraoperative blood loss during mandibular fracture surgery. Patients receiving tranexamic acid had substantially lower mean blood loss than those receiving placebo (285 ± 85 mL vs. 410 ± 110 mL; p<0.001) [10]. We also observed a significantly smaller postoperative hemoglobin decline and a lower need for blood transfusion. These findings support tranexamic acid as an effective perioperative blood-conservation strategy in mandibular fracture surgery [11]. Our findings are particularly consistent with the recent randomized clinical trial specifically investigating mandibular fracture surgery. In that triple-blind trial, 50 patients undergoing open reduction and internal fixation were randomized to receive intravenous tranexamic acid or placebo. Mean blood loss was 360.57 ± 173.5 mL in the tranexamic acid group compared with 560.9 ± 248.07 mL in controls (p=0.008), while hemoglobin reduction was also significantly lower with tranexamic acid (p=0.001). The magnitude of reduction observed in our study is therefore comparable and strengthens the evidence that antifibrinolytic therapy can provide meaningful hemostatic benefit during mandibular fracture fixation [12,13]. Evidence from broader oral and maxillofacial surgery also supports these findings. A 2024 systematic review and meta-analysis of 15 studies involving 1,060 patients undergoing orthognathic surgery reported a significant reduction in intraoperative blood loss with tranexamic acid, with a pooled mean difference of approximately 136 mL [14]. The review also found improved surgical-field visibility, with no significant difference in operative duration. This aligns with our finding that operative duration did not differ significantly between groups (p=0.12), suggesting that the main benefit of tranexamic acid may be improved hemostasis rather than a shorter procedure [15]. Recent evidence concerning maxillofacial trauma further reinforces the potential role of tranexamic acid. A 2024 retrospective study evaluating postoperative bleeding after maxillofacial fracture surgery found that tranexamic acid reduced postoperative blood loss in patients with unilateral zygomaticomaxillary complex fractures, with approximately 30 mL less total drainage compared with controls (p=0.006) [16]. Although that investigation assessed postoperative rather than intraoperative bleeding and involved different fracture patterns, its findings suggest that tranexamic acid's hemostatic effect may extend beyond the operating room [17]. The biological rationale for these observations is supported by recent trauma literature. Tranexamic acid inhibits fibrinolysis by preventing plasminogen activation, thereby stabilizing fibrin clots [18]. A 2024 systematic review and meta-analysis of randomized trials in traumatic injury found that tranexamic acid was associated with reduced mortality without compelling evidence of increased vascular occlusive events [19]. Another 2024 meta-analysis of prehospital trauma administration reported reductions in mortality and transfusion requirements, although it also identified a possible increase in thromboembolic events in some analyses. These findings highlight the importance of appropriate patient selection and avoidance of tranexamic acid in patients with recognized contraindications [20]. Similarly, a 2021 systematic review of randomized controlled trials found that most studies evaluating perioperative tranexamic acid reported lower blood loss in the treatment group. However, pooled effects varied because of differences in surgical populations and treatment protocols [21]. A 2024 systematic review of trauma patients likewise concluded that tranexamic acid can reduce bleeding and transfusion requirements, while emphasizing that its effectiveness varies according to the clinical context. Thus, the present study adds procedure-specific evidence to the broader literature supporting antifibrinolytic therapy [22]. The lower transfusion requirement observed in our study (6.0% vs. 20.0%; p=0.037) is clinically

relevant because avoidance of unnecessary transfusion may reduce exposure to transfusion-related complications and conserve blood-bank resources. Nevertheless, the study has limitations [23]. The sample size was relatively small, the study was conducted at a single center, and it did not evaluate longer-term thromboembolic outcomes. In addition, variation in fracture complexity and operative approach may influence blood loss. Larger multicenter randomized trials are therefore required to establish optimal dosing and identify which mandibular fracture subgroups derive the greatest benefit [24].

Conclusion

Intravenous tranexamic acid significantly reduced intraoperative blood loss, postoperative hemoglobin decline, and blood transfusion requirements in patients undergoing mandibular fracture surgery. It did not significantly influence operative duration. Tranexamic acid was associated with reduced intraoperative blood loss, postoperative hemoglobin decline, and transfusion requirements, with no major adverse events observed in this study. Larger adequately powered trials with longer follow-up are required to establish its safety.

Ethical Approval

The study synopsis was approved by the Research Evaluation Unit, College of Physicians and Surgeons Pakistan (CPSP), under **Ref. No. CPSP/REU/DSG-2023-001-4500, dated February 27, 2025.**

Informed Consent

We obtained written informed consent from all participants before enrollment. Participants were informed about the study purpose, procedures, potential benefits and risks of tranexamic acid, and their right to withdraw at any time without affecting their medical care. The study maintained the confidentiality and anonymity of participants' information throughout.

Conflict of Interest

The authors declare no conflict of interest related to this study's conduct, authorship, or publication.

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Data Availability

The data generated and analyzed during this study are not publicly available due to participant confidentiality and ethical considerations. However, the corresponding author may provide the relevant data upon reasonable request and subject to appropriate ethical and institutional approval.

Authors' Contribution

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Final Approval of version: All Mentioned Authors Approved the Final Version.

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