Effect Of TXA On Intraoperative Blood Loss In Mandibular Fracture Surgeries A Prospective, Double Blinded Randomized Clinical Trial

Dr. Zibran Khan*, Dr. Darshan Patel, Dr. Bhagavandas Rai***, Dr. Mandeepsinh Gohil****, Dr. Mayur Mishra*****, Dr. Parth Parekh******

*Reader, Pacific Dental College And Hospital, Udaipur, **Assistant Professor, Ananta Institute Of Medical Sciences, Udaipur, ***Professor, Pacific Dental College And Hospital, Udaipur, ****Reader, *****Senior Lecturer, College Of Dental Sciences Amargadh, Bhavnagar, ******Senior Lecturer, Geetanjali Dental And Research Institute, Udaipur

Abstract: Background: The aim of this double blind prospective study was to determine whether administering 1 gm Tranexamic Acid (TXA) would the intraoperative blood loss during the Open Reduction and Internal Fixation (ORIF) surgery of mandibular fracture via the intraoral approach operated under local anesthesia (LA). Material And Methods: 20 patients who underwent ORIF surgery of mandibular fractures under LA were randomly allocated to two groups. Study group was administered 1 gm TXA diluted in a 500 ml Ringer Lactate solution one hour before the surgery. Control group did not receive any such IV infusion. All the surgeries were performed by the same surgeon. Result: Mean difference in Intraoperative blood loss between the two groups was found out to be statistically insignificant. Effect of age, gender or site of fracture was also found out to be insignificant. Conclusion: There is not much effect of TXA on intraoperative blood loss during ORIF of a mandibular fracture via the intraoral approach. Even without tranexamic, if area is infiltrated with adrenaline, proper flap reflection and tissue handling technique is used, and vital structures avoided; blood loss will be minimal. [Khan Z Natl J Integr Res Med, 2021; 12(5):36-41]

Key Words: Mandibular fractures, Tranexamic Acid, Open reduction and internal fixation, Blood loss

Author for correspondence: Dr. Mayur Mishra, Senior Lecturer, College Of Dental Sciences Amargadh, Bhavnagar. E-mail:Mayurnm21@gmail.com

Introduction: While treating a mandibular fracture, every surgeon aims to return the patients' original function and appearance. Bone fractures are either managed by closed reduction or open reduction and internal fixation (ORIF).

Closed reduction, using Inter-Maxillary Fixation (IMF) or Circum-mandibular wiring, has the drawbacks like Immobilized Jaw for a longer duration leading to noncompliance, Restricted dietleading to weight loss, Poor Oral Hygiene, Communication Problem, Social embarrassment, Malunion or delayed union & in case of Condyle fracture in Children it may lead to Ankylosis. In addition to these, closed reduction cannot be used in cases of patient with severe seizure disorders, sleep apnea, brittle diabetes, coagulopathies where a second procedure to remove the IMF is not desired[1].

However, ORIF can overcome these difficulties, especially is cases with wider displacement of fracture segments and inability to stabilize the occlusion. In some cases (where fractured fragment is avulsed requiring reconstruction or in comminuted fractures where fractured fragments needs to be fixed using Micro or Mini plates), closed reduction fails to yield desired results and ORIF is the only option[2]. As the orofacial region is highly vascularized, it is normal to experience profuse bleeding during any surgical procedure in this region and same goes for ORIF for mandibular fractures. This causes decrease in visibility of surgical field leading to increased duration of the surgery[3].

Blood (for transfusion) is a finite resource with a limited shelf life and is associated with considerable processing costs[4]. To reduce the risk of transmission of various blood borne diseases or transfusion related complications, it needs critical review of its usage. Nowadays, blood conservation is the priority in all types of surgery[5].

Various measures are developed to conserve blood, like acute normovolemi - chemodilution, hypotensive anesthesia, positioning the surgical field above the level of heart, cell saving, preoperative autologous blood donation[6,7]. All

these techniques require special knowledge, training, and skill of the individual.

Tranexamic Acid (TXA), a synthetic derivative of the amino acid lysine, is a competitive inhibitor of plasminogen activation and at much higher concentrations a noncompetitive inhibitor of plasmin, thus implying that TXA interferes with the fibrinolytic processin the same way as aminocaproic acid. TXA is 6-10 times more potent in vitrothan aminocaproic acid[8].

It has been shown to reduce blood loss and need for blood transfusion in cardiacsurgery, knee arthroplasty surgery, spine surgery and orthopedic surgery[9,10,11,12]. Topical TXA has been used in treatment of post-operative bleeding in anticoagulated patients after oral surgery procedures[13,14]. The present study evaluates the efficiency of TXA in reducing the intraoperative blood loss while performing open reduction and internal fixation in mandibular fracture.

Material & Methods: The study population consisted of 20 patients with trauma induced mandibular fracture, who visited the deptartment of Oral and Maxillofacial Surgery in Pacific Dental College and Hospital (Udaipur, Rajasthan, India). Only the patients who could be treated with ORIF by intraoral approach, had physical status classification of ASA-1 and age range of 17-40 years were included in this study.

The protocol was reviewed and approved by the ethical committee of Pacific Dental College and Hospital. Consent forms were signed by the patients participating in this study after informing them about the purpose and design of the study
The fractures were further classified based on Dingman and Natvig classification[15].

Patients included in the study group received 1 gm. TXA diluted in 500 ml Ringer Lactate (RL) solution intravenously one hour before the surgery whereas the control group patient were not given any such IV infusion.

All the surgeries were performed by the same surgeon. Patients with adequate mouth opening were administered mandibular nerve block or in case of reduced mouth opening, Inferior nerve block along with lingual nerve block and buccal nerve block (if required) were administered. The surgical site was infiltrated with 4.mg + 0.02 mg Adrenaline diluted in 3 ml Normal Saline.

The blood loss during the ORIF was calculated by Volumetric and Gravimetric method[16,17]. In Volumetric Method, the volume of saline and povidone iodine irrigation used during the surgery was carefully measured and noted down. The volume of solution present in the suction bottle at the completion of the surgery was measured. Weight of the empty suction chamber was measured and then the weight of suction chamber filled with suctioned fluid was measured. The difference between the weight of suction chamber with fluid and that of empty suction chamber is the amount of suctioned fluid. The difference between the volume of fluid in the suction bottle and volume of irrigation used was the amount of blood sucked by the suction apparatus.

In gravimetric Method, gauzes used were of uniform size. Hence all the gauzes had the same weight. Collective weight of the blood-soaked gauzes (Wt) used during the surgery was determined using a highly sensitive weighing machine. Also, the number of gauzes used was determined. Multiplying the number of gauzes with the weight of a single gauze gave us the collective weight of the number of dry gauzes used (Wn). Subtracting collective weight of dry gauze used from the collective weight of blood-soaked gauzes gave us the amount of blood soaked (Wb) inthe gauze (Wb = Wt - Wn). As the density of blood is similar to that of water(1000ml = 1000gm) 18, the weight of blood-soaked during surgery can be used to calculate the volume of the blood soaked in the gauze.

Total blood loss was obtained by adding the figures from the volumetric and gravimetric method.

Duration of surgery was measured in minutes. Fromme's Ordinal scale was used to assess the surgical field quality.

Fromme's Ordinal Scale 19

- Grade 0: No bleeding; virtually bloodless field.
- Grade1: Minimal bleeding; not a surgical nuisance.
- Grade2: Mild bleeding, a nuisance but does not compromises dissection.
- Grade3: Moderate bleeding slightly compromises dissection.

- Grade4: Severe bleeding; significantly compromises dissection.
- Grade5: Massive bleeding; cannot carry out dissection.

Pre-operative Hemoglobin (Hb) and Post-operative Hb of the patient was also recorded.

Results: Mean Intraoperative blood loss was compared between the study (32.12±17.982) and control group (49.57±33.591) (Table1).

Table 1: Group Statistics

	Group	Sample Size	Mean	Std. Deviation	Std. Error Mean
Age	Control	10	31.20	12.709	4.019
	Study	10	24.70	8.015	2.534
Weight	Control	10	59.27	6.869	2.172
	Study	10	57.36	9.381	2.967
Allowable Blood Loss	Control	10	935.03	480.057	151.807
	Study	10	972.01	543.923	172.004
Total Blood Loss	Control	10	49.57	33.591	10.622
	Study	10	32.12	17.982	5.686
Duration of Surgery	Control	10	57.50	18.143	5.737
	Study	10	52.00	16.193	5.121
Pre HB	Control	10	12.03	2.019	.639
	Study	10	12.66	1.546	.489
Post HB	Control	10	11.31	2.213	700
	Study	10	12.22	1.797	.568

The mean difference was found out to be17.443±12.049 (Table 2). This seems to be a notable difference at first, but as the standard deviation in the total intraoperative blood loss was high the p-value came out to be 0.165 (Table2). Hence the difference is statistically insignificant.

Table 2: Independent Sample t-Test

	Mean Difference	Std. Error Difference	t	df	P
Age	6.500	4.751	1.368	18	.188
Weight	1.910	3.677	.519	18	.610
Allowable Blood Loss	-36.984	229.414	-.161	18	.874
Total Blood Loss	17.443	12.049	1.448	18	165
Duration of Surgery	5.500	7.690	715	18	.484
Pre HB	-.630	.804	- .783	18	444
Post HB	-.910	.902	-1.009	18	.326

Both the group consisted of 10 patients each with control group having the mean age of 31.20±12.709 years and study group having the mean age of 24.70±8.015 years (Table 1). Independent sample t-Test was applied to find out the effect of age of the patient on the blood loss in the surgery (Table 2). The p value was found to be 0.188. This shows that age of the patient did not have any effect on the amount of blood loss during surgery. The control group had 8 cases of single site of fracture and 2 cases of double sites of fracture whereas study group had 5 cases of both (single site and double sites of fracture) (Table3).

Table 3: No. Of Fracture Sites

		Control Group	Study Group	Total
No. Of Fracture Sites	**1 Site**	8	5	13
	2 Sites	2	5	7
Total		10	10	20

Chi-square tests (Pearson Chi-Square, p=0.160 and Fisher's Exact Test, p=0.350) were performed to find out the effect of number of fracture sites on the amount of blood loss. Number of fracture sites did influence the amount of blood loss

during surgery, but it was statistically insignificant. The control group had the mean preop and postop Hb level of 12.03±2.019 and11.31±2.213 respectively whereas the study group had the mean preop and postop Hb level of12.66±1.546 & 12.22±1.797 (Table1). Independent sample t-Test was applied to find out the effect of pre-operative Hb level of the patient on the blood loss in the surgery (Table2). The p value was found to be 0.444. This shows that preop Hb level of the patient did not have any effect on the amount of blood loss during surgery. Assessment of surgical field quality according to Fromme's Ordinal Scale revealed that majority of the [cases] in Study group were given score 1 whereas score 2 was common in control group (Table 4).

Table 4: Surgical Field Quality (SFQ)

	Grade	Control Group	Study Group	Total
SFQ	1	2	7	9
	2	8	3	11
Total		10	10	20

Test applied for Surgical Field Quality were Chi-square tests (Pearson Chi-Square, p=0.025 and Fisher's Exact Test, p=0.070). One of the two tests stated that there was no significant difference in surgical field quality between the study and control groups. Hence even the difference between the two groups based on surgical field quality is statistically insignificant.

Comparison of the duration of the surgery between the two groups showed that the mean duration of surgery was 5.5 minutes less in study group (Table 1 & 2). But this difference is statistically insignificant. It was also observed that longest duration of surgery and highest amount of blood loss was observed in control group.

Discussion: Due to the high vascularity in the orofacial region, it is normal to experience profuse bleeding during any surgical procedure and the same goes for ORIF. This causes decreased visibility of the surgical field leading to increased duration of the surgery.

Pharmacological therapies to decrease bleeding (and in turn decrease blood transfusions) are important for medical and economic reasons.

Another advantage of using pharmacologic therapies to reduce blood loss is that they do not require any special skills. Several drugs including aprotonin, TXA, epsilon amino caproic acid, desmopression, prostacycline, dipyridamole, recombinant factor VIIa and erythropoietin have been investigated for reducing intraoperative blood loss. In this study, the antifibrinolytic agent TXA was used as a hemostatic agent.

TXA, a synthetic derivative of the amino acid lysine, reversibly blocks the lysine binding sites on plasminogen molecules and exerts its antifibrinolytic property.Plasminogen is an enzyme that causes degradation of a fibrin clot, fibrinogen, and coagulation factors V, VIII. TXA reduces conversion of plasminogen to plasmin by inhibiting activation of plasminogen. It is 6–10 times more potent than epsilon amino caproic acid. The strength with which TXA binds to plasminogen molecule is notably higher than that of amino caproic acid[8].

Andersson et al.[2] observed that TXA at a therapeutic plasma concentration of 10 mg/ml reduced tissue plasminogen activity by 80%[20]. There are several adverse effects of rapid infusion of TXA. These include increased chances of a Thrombo-embolic event, hypotension, nausea &vomiting[8,21.] Thrombo-embolic event is the most serious complication as it poses a threat to the patient's life[12]. In the present study, TXA was administered intravenously in a diluted form (1 gm TXA in 500 ml Ringer Lactate solution) for slow infusion over a period of one hour preoperatively.

Although there was a slight difference in the mean total blood loss during surgery between the two groups (17.443±12.049), the difference was not enough to be considered statistically significant. Difference in duration of surgery and surgical field quality was statistically insignificant.

These could be attributed to the skills of the operating surgeon. Proper technique and avoiding vital structures (such as facial artery or mental neurovascularbundle) would reduce

chances of profuse bleeding drastically. Use of sharp blade, placement of a proper incision, proper mucoperisoteal reflection and proper soft tissue retraction also plays a major role in avoiding any soft tissue injury that may lead to increase in amount of blood loss.

In this study no patient developed drug (thromboembolism) or anaesthesia related complications. The gravimetric method was used to measure blood loss, but blood on surgical drapes, gowns and instruments was difficult to quantify accurately. The suction bottle contained not only the irrigation fluid and blood, but also saliva and bone powder produced during the bone drilling for screws. All these uncertainties contributed to the inaccuracy of blood loss estimation, although these would apply uniformly to all cases.

There are no studies on the effectiveness of antifibrinolytic agents during Open Reduction & Internal Fixation surgery.

This lack of studies mandates, further studies involving not only mandibular fracture but also the midface fractures with a larger population size to assess the effectiveness of various antifibrinolytic agents during open reduction and internal fixation surgery.

Conclusion: According to this study, there is not much effect of TXA on intraoperative blood loss during ORIF of a mandibular fracture via the intraoral approach. Even without tranexamic, if area is infiltrated with adrenaline, proper flap reflection and tissue handling technique is used, and vital structures avoided; blood loss will be minimal.

There are no studies on the effectiveness of antifibrinolytic agents during Open Reduction & Internal Fixation in maxillofacial region. Further studies with a larger population size are required to assess the effectiveness of various antifibrinolytic agents during ORIF surgery.

Studies are required not only in mandibular fracture surgeries but also in the midface region.

References:

1. Blitz M, Notarnicola K, Closed Reduction of the Mandibular Fracture - Atlas Oral Maxillofacial Surg Clin N Am 17 (2009) 1–13
2. Koshy J C, Pearls of Mandibular Trauma Management, seminars in plastic surgery/volume 24, number 4 - 2010
3. Gray's Anatomy: The Anatomical Basis of Clinical Practice Elsevier / Churchill Livingstone, 2005, ISBN 0-443-06676-0
4. Blaudszun G, Butchart A, Klein AA. Blood conservation in cardiac surgery. Transfus Med. 2018 Apr;28(2):168-180
5. Mc Swiney MM, O'Farrell D, Joshi GP, et al. Blood transfusion in total hip athroplasty: guidelines to eliminate overtransfusion [J]. Can J Anaesth 1993;40(3):222-6
6. Shah A, Strategies to minimize intraoperative blood loss during major surgery - BJS 2020; 107: e26–e38
7. Rivera D, Antonio P F. Blood-Saving Techniques in Surgery ,Colombian Journal of Anestesiology 2011;39(4):545-559
8. Satyavathi K, Vemu N. J, Mohammed S. TXA: A proven antifibrinolytic agent (A review). Oriental Journal of Chemistry 2009;25(4), 987-992
9. Shore-Lesserson L, Reich DL, Vela-Cantos F. TXA reduces transfusions and mediastinal drainage in repeat cardiac surgery 1996;83(1):18-26
10. Singh J, Ballal M. S, Mitchell P. Effects of TXA on blood loss during total hip arthroplasty. Journal of Orthopaedic Surgery, 2010;18(3):282-6
11. Kazemi SM, Mosaffa F, Eajazi A. The effect of TXA on reducing blood loss in cementless total hip arthroplasty under epidural anesthesia. Orthopedics. 2010 Jan;33(1):17
12. Gonclaves FD, Novaes FR, Maja MA. Influence of TXA in postoperative bleeding of cardiac surgery with cardiopulmonary bypass. Revista Brasileira de Cirurgia Cardiovascular 2002; 17(4): 331-338
13. Gaspar R, Brenner B, Ardekian L. Use of TXA mouthwash to prevent postoperative bleeding in oral surgery patients on oral anticoagulant medication. Quintessence International 1997 Jun; 28(6):375-9
14. Carter G, Goss A. TXA mouthwash--a prospective randomized study of a 2-day regimen vs 5 day regimen to prevent postoperative bleeding in anticoagulated patients requiring dental extractions. International Journal of Oral & Maxillofacial Surgery 2003 Oct;32(5):504-7
15. Dingman R O, Natvig P. Surgery of Facial Fractures,Philadelphia, PA: WB Saunders; 1964.

16. Sebastian Jaramillo, Mar Montane-Muntane Agreement of surgical blood loss estimation methods - - Transfusion. 2019 Feb;59(2):508-515.
17. Holmes AA.Clinical Evaluation of a Novel System for Monitoring Surgical Hemoglobin Loss - Anesth Analg. 2014 Sep; 119(3): 588–594.
18. Vitello D J, Ripper RM, Vitello J.Blood Density Is Nearly Equal to Water Density: A Validation Study of the Gravimetric Method of Measuring Intraoperative Blood Loss - - Journal of Veterinary Medicine Volume 2015:152730
19. Fromme GA, MacKenzie RA, Gould AB, Lund BA, Offord KP. Controlled hypotension for orthognathic surgery. Anesth Analg. 1986;65(6):683–686.
20. Andersson L, Nilsoon IM, Colleen S et al. Role of urokinase and tissue activator in sustaining bleeding and the management thereof with EACA and AMCA. Ann N Y Acad Sci 1968;146:642–58.
21. Chauncey JM, Wieters JS. Tranexamic Acid. [Updated 2020 Aug 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 (ASSESSED ON DEC 2020)

Conflict of interest: None
Funding: None
Cite this Article as: Khan Z, Patel D, Rai B, Gohil M, Mishra M, Parekh P. Effect Of TXA On Intraoperative Blood Loss In Mandibular Fracture Surgeries A Prospective, Double Blinded Randomized Clinical Trial. Natl J Integr Res Med 2021; Vol.12(5): 36-41