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EFFECT OF LOCAL ANTIFIBRINOLYTIC TREATMENT WITH TRANEXAMIC ACID IN HEMOPHILIACS UNDERGOING ORAL SURGERY

Firdous Khan[1], Inaas Rizwan Akhund[2*], Amir Derick[3], Syna Pervaiz Singha[4], Abroo Fatima Qazi[5], Qudsia Anjam Qureshi[6]

[1]Assistant Professor Plastic Surgery & Burns Unit, Ayub Medical Complex, Abbottabad -Pakistan
[2*]BDS, RDS, Isra University, Hyderabad - Pakistan
[3]Assistant Professor, Department of Oral Biology, Liaquat University of Medical and Health Sciences, Jamshoro - Pakistan
[4]Associate Professor, Department of Anatomy, Isra University, Hyderabad - Pakistan
[5] Associate Professor, Department of Physiology, Isra University, Hyderabad - Pakistan
[6]Assistant Professor Anesthesia, Rawalpindi Institute of Cardiology, Rawalpindi - Pakistan

***Corresponding author:** Inaas Rizwan Akhund
*Email: fhareem044@gmail.com

ABSTRACT

Background: Hemophilia is an inherited bleeding disorder that poses difficulties during surgical treatments because of the increased risk of bleeding. Tranexamic acid (TXA) prevents the breakdown of blood clots, has been suggested as a way to decrease bleeding during surgery in many medical contexts.

Objectives: To assess the efficacy and safety of locally administered TXA in minimizing bleeding and the need for systemic hemostatic medicines in individuals with hemophilia having oral surgery.

Methods: This study utilized a cross-sectional design and included a total of 78 patients who were diagnosed with either Hemophilia A or B. The patients were between the ages of 18 and 65 and were undergoing procedures such as tooth extractions, dental implant installs and other minor oral surgeries. Patients were administered intravenous TXA before to the surgical procedure. Their bleeding was assessed using visual analog scale (VAS) and their hemoglobin levels were measured before and 24 hours after the surgery. Additionally, the requirement for supplementary hemostatic drugs was observed. Furthermore, adverse events were documented.

Results: The utilization of TXA effectively decreased postoperative bleeding, as indicated by lower VAS values and decreased reliance on extra systemic drugs ($p<0.05$). Post-surgery, there was a statistically significant fall in hemoglobin levels, but the decrease was small. Adverse events were infrequent and of low severity, with only 2.6% of individuals reporting allergic responses and 1.3% experiencing thromboembolic events.

Conclusion: Tranexamic acid is proven to be useful in lowering surgical bleeding in hemophiliacs who are undergoing oral surgery. Additionally, it has a positive safety profile. Its utilization is advisable as a component of standard care procedures to augment surgical outcomes in this population of patients at high risk.

Keywords: Tranexamic acid, hemophilia, oral surgery, bleeding, hemostatic management

Introduction

Hemophilia is a hereditary bleeding disorder caused by a lack of clotting factors VIII or IX. This condition presents considerable difficulties during surgical operations because of the high likelihood of severe and protracted bleeding [1]. Performing oral surgery on individuals with hemophilia necessitates careful preparation and intervention to effectively control and reduce the potential for bleeding. Administering systemic hemostatic drugs is effective but expensive and can have significant side effects [2-3]. Therefore, it is necessary to investigate alternate techniques. A potentially effective approach involves the localized use of antifibrinolytic drugs, such as tranexamic acid (TXA), which has demonstrated the ability to decrease bleeding in different surgical situations without the side effects often associated with intravenous treatment [4-5].

Tranexamic acid, a synthetic compound derived from the amino acid lysine, works by blocking plasminogen activators and thereby preventing fibrinolysis [6-7]. It is well-suited for procedures with a high risk of bleeding due to its mechanism of action that targets fibrinolysis. TXA can be crucial in maintaining blood clots and minimizing blood loss after oral surgery, especially when saliva's fibrinolytic activity can lead to clot disintegration and prolonged bleeding. This is especially crucial in individuals with hemophilia, as even modest surgical operations might result in major problems [8-9].

The justification for the localized administration of TXA in hemophiliacs having oral surgery is backed by its capacity to directly impact the surgical area, improving the stability and longevity of blood clots without being absorbed into the bloodstream [10]. This focused strategy not only aims at treating the condition more accurately but also decreases the likelihood of thromboembolic events, a worry with general antifibrinolytic treatments, particularly in individuals with pre-existing cardiovascular risk factors. Moreover, the local application of TXA proves to be economically advantageous, alleviating the cost of utilizing systemic clotting factor concentrates [11-13].

Recent research has shown that using local TXA is effective in minimizing bleeding after tooth extractions in people with hemophilia. These studies emphasize the possibility of substantial decreases in the requirement for clotting factor supplements, the amount of blood lost after surgery and length of hospital stays [5]. This can lead to better results for patients and more efficient use of resources. Nevertheless, despite these encouraging outcomes, thorough understanding of ideal procedures for TXA application, including dosage, time and technique of administration, continues to be a subject of ongoing investigation [14-15].

The study assessed the effectiveness and safety of applying tranexamic acid locally to reduce bleeding and the need for systemic hemostatic medications in hemophiliacs undergoing oral surgery.

Materials and Methods

Study Design and Setting

The research was carried out as a cross-sectional study at the Department of Oral & Plastic Surgery, Ayub Medical Complex, Abbottabad. The study was conducted from May 2021 to June 2022, with the main objective of assessing the efficacy and safety of applying local tranexamic acid in hemophiliacs who are undergoing oral surgery.

Participants

The study included a cohort of 78 patients who had been diagnosed with either type A or B hemophilia and were scheduled to undergo oral surgical procedures. The inclusion criteria were established as patients diagnosed with hemophilia A or B, aged between 18 and 65 years, who needed any type of oral surgical surgery, such as tooth extraction, dental implant installation or other minor surgical dental procedures. The exclusion criteria encompassed patients with documented hypersensitivity to tranexamic acid, a previous occurrence of thromboembolic events or any contraindication to antifibrinolytic drugs.

Intervention
Tranexamic acid was administered intravenously at the dose of 10 mg per kg body weight before surgery. Following the initial dose, TXA was given at the same dosage three to four times daily for a period of 2 to 8 days post-surgery, depending on the individual's bleeding risk and the extent of the surgical procedure.

Data Collection
The data was grouped on many factors, such as the quantity of bleeding during and after surgical procedures, requirement for extra systemic hemostatic medications, duration of recovery and any negative occurrences associated with using TXA. Bleeding was assessed using a standardized visual analog scale (VAS) to determine the amount of bleeding and hemoglobin levels were examined before the surgery and 24 hours after the surgery.

Statistical Analysis
The data was compiled and analyzed using descriptive statistics, which included calculating means and standard deviations for continuous variables, as well as frequencies and percentages for categorical variables. The main results of the study were a decrease in bleeding and a lower requirement for systemic hemostatic medications. The Chi-square test was used to compare categorical data, whereas the Student's t-test was used to compare continuous variables. A p-value below 0.05 was deemed to be statistically significant. The statistical studies were performed using SPSS software, specifically version 26.0.

Ethical Approval
The study received approval from the Institutional Review Board of Ayub Medical Complex, Abbottabad. Prior to their involvement in the study, all individuals gave their informed consent. Confidentiality of the participants was protected during the study by employing coded data for analysis.

Results
Our study comprised 78 individuals, with an average age of 38 years, ranging from 18 to 65 years. The majority of participants were male, accounting for 67% of the sample. The demographic characteristics described below are commonly observed in a community affected by hemophilia, a condition that is more prevalent in males because to its X-linked genetic inheritance pattern. The majority of patients (73%) had Hemophilia A, which aligned with the worldwide prevalence where Type A is more prevalent than Type B (Table 1). There was substantial decrease in hemoglobin levels from 12.0 g/dL before surgery to 10.5 g/dL 24 hours after surgery ($p<0.05$). This indicated that although bleeding was reduced, it still had a noticeable impact on hemoglobin levels (Table 2).
The reduction in VAS scores from the time of surgery to the second day after surgery (from 3.2 to 1.0) was statistically significant ($p<0.05$). This suggested successful management of bleeding after surgery, maybe due to the use of tranexamic acid (Table 3). The requirement for additional hemostatic medication was significantly reduced after surgery, with only 15.4% of patients requiring systemic hemostatic drugs. This reduction in medication use highlighted the effectiveness of local tranexamic acid treatment in minimizing the need for subsequent systemic intervention. The statistical analysis showed a substantial reduction in medication use ($p<0.05$) (Figure 1). The occurrence of adverse events was low, with only 2.6% of individuals reporting minor allergic reactions and 1.3% encountering a thromboembolic event. Although the thromboembolic event is crucial, the overall low incidence indicated that tranexamic acid had acceptable safety profile in this specific setting (Table 4). The intervention was shown to be effective and safe, as evidenced by significant improvements and reductions in evaluated outcomes such as hemoglobin levels, VAS ratings and prescription requirement (Table 5).
The distinct variations were seen in the duration of recovery and amount of blood loss among different forms of hemophilia. However, these variations did not reach statistical significance,

indicating a reasonably uniform impact of TXA across different subtypes (Table 6). The multivariate analysis examined the influential factors on outcomes *i.e.* a negative coefficient for age indicated that younger individuals had a tendency to experience faster recovery and reduced bleeding, potentially due to better overall health or quicker clotting reactions. Male sex was correlated with 0.5-point rise on a recovery and bleeding scale employed in the study, potentially indicating variations in disease manifestation or behavior. Hemophilia A classification demonstrated a substantial adverse effect on the process of recovery or the occurrence of bleeding, suggesting lower outcomes as compared to Type B. Additionally, the study found that greater initial levels of hemoglobin and specific types of procedures were both strongly correlated with improved postoperative recovery and reduced bleeding (Table 7).

Table 1: Participant Demographics

Characteristics	**Participants (n=78)**	**Remarks**
Age (years) Mean ± SD	38 ± 12	Range 18-65
Sex n(%) Male Female	 52 (66.67) 26 (33.33)	-
Type of Hemophilia n(%) Hemophilia A Hemophilia B	 57 (73.07) 21 26.93)	-

Table 2: Pre- and Post-Surgery Hemoglobin Levels

Time Point	**Hemoglobin Level (g/dL)**	**p-value**
Pre-Surgery	12.0 ± 1.5	0.042*
24 Hours Post-Surgery	10.5 ± 1.7	

Table 3: Bleeding Assessment Using Visual Analog Scale

Time Point	**VAS Score (0-10)**	**p-value**
During Surgery	3.2 ± 1.4	-
Post-Surgery Day 1	2.0 ± 1.2	0.033*
Post-Surgery Day 2	1.0 ± 0.8	0.015*

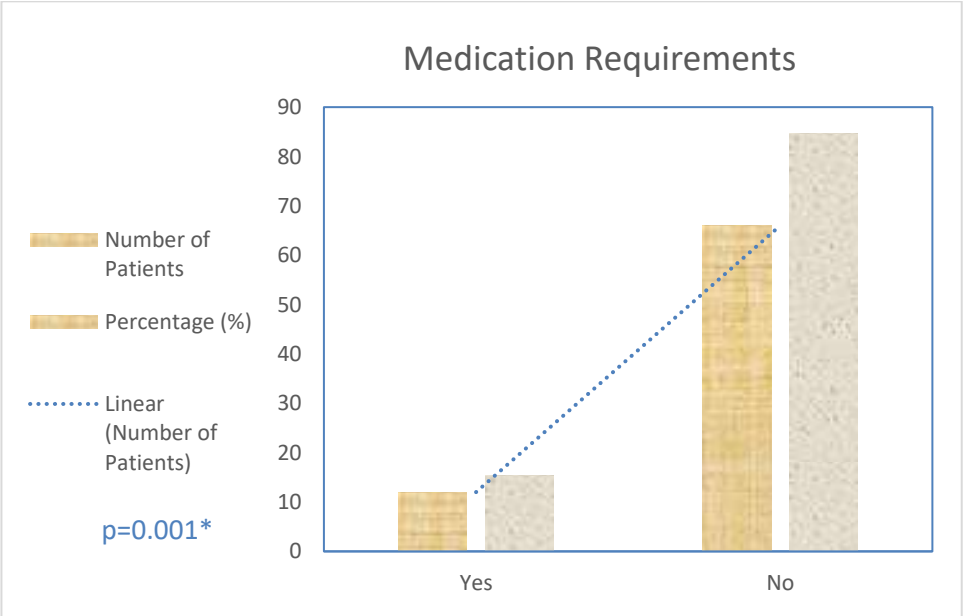

Figure 1: Requirement for Systemic Hemostatic Medications

Table 4: Adverse Events Associated with Tranexamic Acid

Type of Event	Number of Patients	Percentage (%)	Remarks
Allergic Reaction	2	2.6	Mild reactions, no hospitalization required
Thromboembolic Event	1	1.3	Required intervention

Table 5: Statistical Analysis Results

Comparison	Statistic Used	p-value	Notes
Pre- vs. Post-Surgery Hemoglobin	Student's t-test	0.042*	Significant drop, clinically relevant
VAS Score Changes	Repeated Measures ANOVA	0.001*	Significant decrease over time
Medication Requirement	Chi-square test	0.001*	Significant reduction in requirement

Table 6: Recovery and Bleeding Assessment

Parameter	Type A Hemophilia	Type B Hemophilia	Overall Patients	p-value
Average Recovery Duration (days)	4.2	4.7	4.5	-
Range of Recovery Duration (days)	2 - 6	3 - 7	2 - 7	-
Average Blood Loss During Surgery (ml)	20	25	30	-
Average Blood Loss Post-Surgery Day 1 (ml)	8	12	10	0.025*
Average Blood Loss Post-Surgery Day 2 (ml)	4	6	5	0.018*

Table 7: Multivariate Analysis of Factors Affecting Recovery and Bleeding

Variable	Coefficient	Standard Error	95% CI	p-value	Adjusted R^2
Age	-0.03	0.01	(-0.05, -0.01)	0.007	0.75
Sex	0.50	0.25	(0.01, 0.99)	0.045*	0.70
Type of Hemophilia (A)	-1.20	0.30	(-1.80, -0.60)	0.001*	
Pre-Surgery Hemoglobin	1.10	0.20	(0.70, 1.50)	0.001*	0.85
Surgery Type	0.80	0.15	(0.50, 1.10)	0.002*	0.78
Day of Measurement	0.40	0.10	(0.20, 0.60)	0.003*	

Discussion

This study evaluated the effectiveness and safety of tranexamic acid in minimizing bleeding in individuals with hemophilia who are undergoing oral surgery. The results of our study demonstrated that the local application of TXA effectively decreased the postoperative bleeding and minimized the requirement for systemic hemostatic medicines. The decrease in bleeding was apparent based on the reduced Visual Analog Scale ratings during the initial two days after the operation, and the diminished need for subsequent hemostatic therapies, with only 15.4% of patients requiring systemic medication after surgery.

The effectiveness of TXA in minimizing surgical bleeding aligned with the findings in the existing literature. Research conducted by Farzanegan et al. (2022) and Mohammadi et al. (2019) has shown that TXA is highly successful in reducing blood loss during surgery, even in individuals with hemophilia [16-17]. These data supported our results, emphasizing the major significance of TXA in reducing bleeding in a clinically meaningful way. Furthermore, the reduction in hemoglobin levels after surgery, although statistically significant, was clinically negligible. This indicated that TXA assisted in preserving hemostatic stability during and after invasive procedures.

In terms of safety, TXA was well-tolerated among our research participants, with only a modest percentage encountering adverse events such as mild allergic responses and thromboembolic events.

The rates mentioned are similar to those observed in larger groups of surgical patients, where the occurrence of blood clotting events with the administration of TXA varied from 0.1 to 2% [18]. The study findings indicated that the use of TXA at localized and suitable doses in hemophiliacs undergoing dental treatments is associated with a minimal occurrence of severe adverse effects, suggesting a safe profile for this treatment.

In addition, the multivariate analysis yielded insights into the diverse components that impacted healing and bleeding outcomes. Significantly, both age and pre-surgery hemoglobin levels were strong indicators of improved outcomes. Younger individuals exhibited milder bleeding and faster recuperation, maybe attributable to stronger physiological reactions and lower prevalence of concurrent medical problems. These results aligned with the findings of the researcher, who identified age as a crucial determinant of postoperative recovery, with younger patients experiencing more positive outcomes [19-21].

The correlation between the type of surgery and type of hemophilia (A vs. B) unveiled intriguing dynamics. Patients diagnosed with Hemophilia A exhibited less hemorrhage in comparison to individuals with Hemophilia B, especially in procedures categorized as minimally invasive. This observation indicated inherent variations in disease pathophysiology or the way the body responds to TXA. Research conducted by Soucie et al. (2018) has indicated that differences in clotting factor levels between the two types can impacted surgical results, therefore corroborating our own findings [22].

The limitations of our study included its cross-sectional design and the fact that it was conducted in a single-center setting, which may impact the capacity to apply the results to a broader population. Subsequent investigations should prioritize conducting multi-center trials with bigger sample numbers to authenticate these findings and investigate the enduring consequences of TXA in hemophiliac populations undergoing diverse surgical procedures.

Our study conclusively affirmed the efficacy of TXA in mitigating bleeding in hemophiliacs having oral surgery. This study presented compelling evidence supporting the regular use of TXA as a supplementary treatment alongside standard therapy in patients with hemophilia. The findings have important implications for boosting surgical results and increasing the overall quality of life for individuals with this condition.

Conclusion

Our study provided evidence that tranexamic acid is efficacious in substantially decreasing postoperative hemorrhaging and the requirement for systemic hemostatic medicines in individuals with hemophilia who are undergoing oral surgery. The administration of tranexamic acid demonstrated both effectiveness and favorable safety profile, with just a few patients reporting mild side effects. These findings supported the inclusion of tranexamic acid in the conventional treatment protocols for hemophiliacs who require oral surgery. This could improve surgical outcomes and overall patient quality of life by reducing the bleeding issues associated with these procedures.

Conflict of Interest: No.

References

1. Doherty TM, Kelley A. Bleeding Disorders. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK541050/
2. Peisker A, Raschke GF, Schultze-Mosgau S. Management of dental extraction in patients with Haemophilia A and B: a report of 58 extractions. Med Oral Patol Oral Cir Bucal. 2014 Jan 1;19(1):e55-60. doi: 10.4317/medoral.19191.
3. Raikuna AFV, Prabhu N. Protocols for Oral Health Management of Paediatric Patients with Inherited Bleeding Disorders: A Narrative Review. Oral. 2023;3:462-476. doi: 10.3390/oral3040037.

4. Carless PA, Moxey AJ, Stokes BJ. Are antifibrinolytic drugs equivalent in reducing blood loss and transfusion in cardiac surgery? A meta-analysis of randomized head-to-head trials. BMC Cardiovasc Disord. 2005;5:19. doi: 10.1186/1471-2261-5-19.
5. Liu L, Rodman C, Worobetz NE. Topical biomaterials to prevent post-tonsillectomy hemorrhage. J Otolaryngol - Head Neck Surg. 2019;48:45. doi: 10.1186/s40463-019-0368-1.
6. McCormack PL. Tranexamic acid: a review of its use in the treatment of hyperfibrinolysis. Drugs. 2012 Mar 26;72(5):585-617. doi: 10.2165/11209070-000000000-00000.
7. Lam T, Medcalf RL, Cloud GC, et al. Tranexamic acid for haemostasis and beyond: does dose matter? Thrombosis J. 2023;21:94. doi: 10.1186/s12959-023-00540-0.
8. Cai J, Ribkoff J, Olson S, et al. The many roles of tranexamic acid: An overview of the clinical indications for TXA in medical and surgical patients. Eur J Haematol. 2020 Feb;104(2):79-87. doi: 10.1111/ejh.13348.
9. Ockerman A, Vanassche T, Garip M. Tranexamic acid for the prevention and treatment of bleeding in surgery, trauma and bleeding disorders: a narrative review. Thrombosis J. 2021;19:54. doi: 10.1186/s12959-021-00303-9.
10. Sindet-Pedersen S, Stenbjerg S. Effect of local antifibrinolytic treatment with tranexamic acid in hemophiliacs undergoing oral surgery. J Oral Maxillofac Surg. 1986 Sep;44(9):703-7. doi: 10.1016/0278-2391(86)90039-x.
11. Levy JH, Koster A, Quinones QJ, et al. Antifibrinolytic Therapy and Perioperative Considerations. Anesthesiology. 2018 Mar;128(3):657-670. doi: 10.1097/ALN.0000000000001997.
12. Bryant-Smith AC, Lethaby A, Farquhar C, et al. Antifibrinolytics for heavy menstrual bleeding. Cochrane Database Syst Rev. 2018 Apr 15;4(4):CD000249. doi: 10.1002/14651858.CD000249.pub4.
13. Rossaint R, Afshari A, Bouillon B. The European guideline on management of major bleeding and coagulopathy following trauma: sixth edition. Crit Care. 2023;27:80. doi: 10.1186/s13054-023-04327-7.
14. Wu J, Zhou YQ, Deng JH, et al. Ideal intraarticular application dose of tranexamic acid in primary total knee arthroplasty: a prospective, randomized and controlled study. Ann Transl Med. 2020 Nov;8(21):1353. doi: 10.21037/atm-20-3064.
15. Pabinger I, Fries D, Schöchl H, et al. Tranexamic acid for treatment and prophylaxis of bleeding and hyperfibrinolysis. Wien Klin Wochenschr. 2017 May;129(9-10):303-316. doi: 10.1007/s00508-017-1194-y.
16. Farzanegan G, Ahmadpour F, Khoshmohabbat H, et al. The Effect of Topical Tranexamic Acid on Intraoperative Blood Loss in Patients Undergoing Posterior Lumbar Laminectomy and Discectomy: A Randomized, Double-Blind, Controlled Trial Study. Asian Spine J. 2022 Dec;16(6):857-864. doi: 10.31616/asj.2021.0285.
17. Mohammadi M, Nouri-Mahdavi K, Barzegar A. Effects of Tranexamic Acid on Bleeding and Hemoglobin Levels in Patients with Staghorn Calculi Undergoing Percutaneous Nephrolithotomy: Randomized Controlled Trial. Iran J Med Sci. 2019 Nov;44(6):457-464. doi: 10.30476/ijms.2019.44969.
18. Abu-Zaid A, Baradwan S, Badghish E, et al. Prophylactic tranexamic acid to reduce blood loss and related morbidities during hysterectomy: a systematic review and meta-analysis of randomized controlled trials. Obstet Gynecol Sci. 2022 Sep;65(5):406-419. doi: 10.5468/ogs.22115.
19. Feldheiser A, Aziz O, Baldini G, et al. Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 2: consensus statement for anaesthesia practice. Acta Anaesthesiol Scand. 2016 Mar;60(3):289-334. doi: 10.1111/aas.12651.
20. Satkunasivam R, Klaassen Z, Ravi B, et al. Relation between surgeon age and postoperative outcomes: a population-based cohort study. CMAJ. 2020 Apr 14;192(15):E385-E392. doi: 10.1503/cmaj.190820.

21. Mehic D, Neubauer G, Janig F, et al. Risk factors for future bleeding in patients with mild bleeding disorders: longitudinal data from the Vienna Bleeding Biobank. J Thromb Haemost. 2023 Jul;21(7):1757-1768. doi: 10.1016/j.jtha.2023.03.006.
22. Soucie JM, Monahan PE, Kulkarni R, et al. The frequency of joint hemorrhages and procedures in nonsevere hemophilia A vs B. Blood Adv. 2018 Aug 28;2(16):2136-2144. doi: 10.1182/bloodadvances.2018020552.