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Original Research Article

Effect of Tranexamic Acid on Perioperative Blood Loss and Hematoma Formation in Hypospadias Repair

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Abstract: ***Background:*** Hypospadias repair remains one of the most commonly performed paediatric urological procedures. Intraoperative bleeding can obscure the operative field, prolong operative time, and predispose to hematoma formation, wound infection, and urethrocutaneous fistula. Tranexamic acid (TXA), a synthetic lysine analogue, has demonstrated efficacy in reducing surgical blood loss in multiple surgical specialties, but its perioperative use in hypospadias repair has not been well studied. Objective: To evaluate the effect of perioperative administration of tranexamic acid on perioperative blood loss and hematoma formation in children undergoing primary hypospadias repair. ***Methods***: A randomized controlled trial was conducted at the Department of Paediatric Surgery, Shaikh Zayed Hospital Lahore, from January 2024 to December 2025. Sixty male children aged 1–10 years undergoing primary hypospadias repair were enrolled and randomly allocated to two equal groups: Group A (received IV TXA 15 mg/kg 10 min before induction and continued 8-hourly for 72 h postoperatively) and Group B (control, received no pre-operative TXA). Peri-operative blood loss was quantified by gauze-weight method; post-operative hematoma was assessed clinically within 48 h. Data were analyzed with SPSS v26 using Student's t-test and Chi-square test ($p < 0.05$ significant). ***Results:*** Mean peri-operative blood loss was 22.4 ± 6.1 mL in the TXA group vs 37.8 ± 8.5 mL in controls ($p < 0.001$). Hematoma formation occurred in 1 (3.3%) child in Group A vs 6 (20%) in Group B ($p = 0.045$). No TXA-related adverse events were recorded. ***Conclusion:*** Pre-operative tranexamic acid significantly reduces peri-operative blood loss and post-operative hematoma formation in hypospadias repair without added risk of thrombosis or other adverse effects. Routine use of TXA as an adjunct to pediatric hypospadias surgery is recommended to enhance hemostasis and improve surgical outcomes.

Keywords: Hypospadias, Tranexamic acid, Pediatric urology, Blood loss, Hematoma, Hemostasis

INTRODUCTION

Hypospadias is one of the most frequent congenital anomalies of the male external genitalia, characterized by ectopic placement of the urethral meatus on the ventral surface of the penis, often accompanied by ventral curvature (chordee) and an incomplete prepuce [1–3]. It is the second most common congenital anomaly in males after

undescended testis [4]. Globally, its incidence is estimated at 1 in 150–300 live male births, with a rising trend in industrialized nations [5]. Although the exact etiology remains multifactorial, a combination of genetic predisposition, hormonal disruption during fetal development, and environmental influences has been implicated [6,8].

Surgical correction is the mainstay of management, aiming to achieve a straight penis, a glanular meatus, and satisfactory cosmetic outcome [11]. Techniques such as tubularized incised-plate urethroplasty (TIP Snodgrass) and Bracka two-stage repair are commonly used depending on the site and severity [12–14]. Despite significant advances in surgical methods, post-operative complications remain frequent; these include bleeding, hematoma, infection, urethrocutaneous fistula, and dehiscence, each of which may compromise the final outcome [17]. Among these, peri-operative bleeding is a critical yet often under-addressed factor influencing surgical visibility and healing.

Adequate hemostasis during hypospadias surgery is essential for precise dissection and layered reconstruction. Conventional methods such as penile tourniquets, diluted epinephrine infiltration, and bipolar diathermy have been employed to achieve a bloodless field [16]. However, each technique has drawbacks — tourniquets may cause ischemic injury if used for prolonged period of time, epinephrine can induce systemic absorption and tachyarrhythmia, and excessive diathermy may lead to thermal damage of delicate tissues [17]. Hence, the search for safe pharmacological adjuncts to enhance hemostasis continues.

Tranexamic acid (TXA) is a synthetic derivative of lysine that exerts antifibrinolytic effects by competitively inhibiting the binding of plasminogen and plasmin to fibrin [18,19]. By stabilizing the fibrin matrix and preventing premature clot breakdown, TXA effectively reduces diffuse capillary bleeding. It has been proven beneficial in major orthopedic, cardiac, and craniofacial surgery, with documented reductions in blood loss and transfusion requirements [20–23]. Its safety profile in pediatric patients is well established, with low risk of thromboembolic complications [24].

In pediatric reconstructive urology, literature on TXA remains scarce. The delicate vascular anatomy of penile tissues and the small operative field make even minimal bleeding significant. Moreover, postoperative hematoma compromises graft take, increases infection risk, and predisposes to fistula [25]. Therefore, interventions that safely reduce peri-operative bleeding are of substantial clinical importance. This study was designed to quantitatively evaluate the effect of tranexamic acid in reducing peri-operative blood loss and hematoma formation during hypospadias repair in children under controlled conditions.

Materials and Methods

This randomized controlled trial was conducted in the Department of Paediatric Surgery, Federal Postgraduate Medical Institute (FPGMI) / Shaikh Zayed Hospital, Lahore, between January 2024 and December 2025. The study protocol was approved by the Institutional Review Board, and written informed consent was obtained from parents or guardians of all participants. A total of 60 male children aged 1–10 years fulfilling inclusion criteria were enrolled using simple random sampling. Based on previous literature demonstrating a mean intraoperative blood loss difference of ≈15 mL between TXA and control groups with a standard deviation of 15 mL [24], a sample of 30 per group achieved 95% confidence and 80% power. Patients were randomly allocated into two equal groups (A and B) using computer-generated numbers and sealed opaque envelopes. The inclusion criteria for this study comprised all male children aged between 1 and 10 years who presented with primary hypospadias, irrespective of the type or location of the meatal opening. Children with anterior (glanular, coronal, or subcoronal), middle (distal or mid-penile), and posterior (penoscrotal or perineal) varieties were all eligible for enrollment, provided they were undergoing their first surgical correction. Only patients who were clinically stable, had normal coagulation profiles, and whose parents provided informed written consent were included. All participants were required to have no prior surgical intervention for hypospadias, ensuring a uniform cohort for evaluating peri-operative blood loss and hematoma formation following tranexamic acid administration. Group A received intravenous tranexamic acid 15 mg/kg 10 minutes before induction of anesthesia, followed by 8-hourly maintenance doses for 72 hours postoperatively. Group B received no pre-operative TXA but similar post-operative analgesia and antibiotic regimens. All patients underwent repair by the same surgeon using standardized technique appropriate to the meatal position (TIP Snodgrass for distal types, Bracka two-stage for proximal types). Peri-operative blood loss was measured using the gauze-weight method. Ten-by-ten-centimeter gauze pads were pre-weighed dry and then re-weighed post-use in sealed polythene bags to prevent evaporation. The difference in weight (grams) was considered equal to blood volume in milliliters (1 g = 1 mL). No tourniquet was used; hemostasis was achieved with bipolar diathermy only. Post-operative hematoma was defined as a painless, fluctuant swelling detected within 48 hours of surgery. All patients were examined by the same observer unaware of group allocation. Data was entered into IBM SPSS v26.0. Quantitative variables (age, blood loss) were expressed as mean ± SD and

compared using independent-sample t-test. Qualitative variables (hematoma formation, hypospadias type) were compared using Chi-square test. Stratified analysis was performed for age and hypospadias type. A p-value < 0.05 was considered statistically significant.

RESULTS

Baseline Characteristics

A total of 60 children aged 1–10 years (mean ± SD = 5.1 ± 2.4 years) were enrolled and randomized equally into Group A (TXA) and Group B (Control). Baseline demographic and clinical characteristics were comparable between the two groups (Table 1). The mean duration of surgery was also statistically similar (p = 0.41), ensuring that operative time did not confound intraoperative blood loss.

Table 1(a). Baseline characteristics of study participants (n = 60)

Variable	Group A (TXA, n = 30)	Group B (Control, n = 30)	*p* value
Mean age (years) ± SD	5.2 ± 2.3	5.0 ± 2.5	0.79
Weight (kg) ± SD	18.1 ± 5.4	17.6 ± 5.1	0.67
Duration of surgery (min) ± SD	93 ± 17	96 ± 19	0.41
Type of hypospadias			
Anterior (glanular/coronal/subcoronal)	14 (46.7%)	13 (43.3%)	0.79
Middle (distal/mid penile)	10 (33.3%)	11 (36.7%)	0.79
Posterior (penoscrotal/perineal)	6 (20%)	6 (20%)	–
Pre-op Hb (g/dL) ± SD	11.9 ± 0.7	11.8 ± 0.6	0.48

No statistically significant differences were noted between the groups at baseline, indicating successful randomization.

Table 1(b). Stratification of study participants according to age (n = 60)

Age Group (years)	n (TXA)	n (Control)	Blood Loss TXA (Mean ± SD)	Blood Loss Control (Mean ± SD)	p-value (Blood Loss)	Hematoma TXA n (%)	Hematoma Control n (%)	p-value (Hematoma)
1–4 years	10	10	19.6 ± 5.0	33.4 ± 7.1	< 0.001	0 (0%)	2 (20%)	0.147
5–7 years	11	11	22.7 ± 5.8	38.1 ± 8.2	< 0.001	1 (9.1%)	2 (18.2%)	0.530
8–10 years	9	9	26.9 ± 6.2	42.9 ± 8.7	< 0.001	0 (0%)	2 (22.2%)	0.136
Overall	30	30	22.4 ± 6.1	37.8 ± 8.5	< 0.001	1 (3.3%)	6 (20%)	0.045

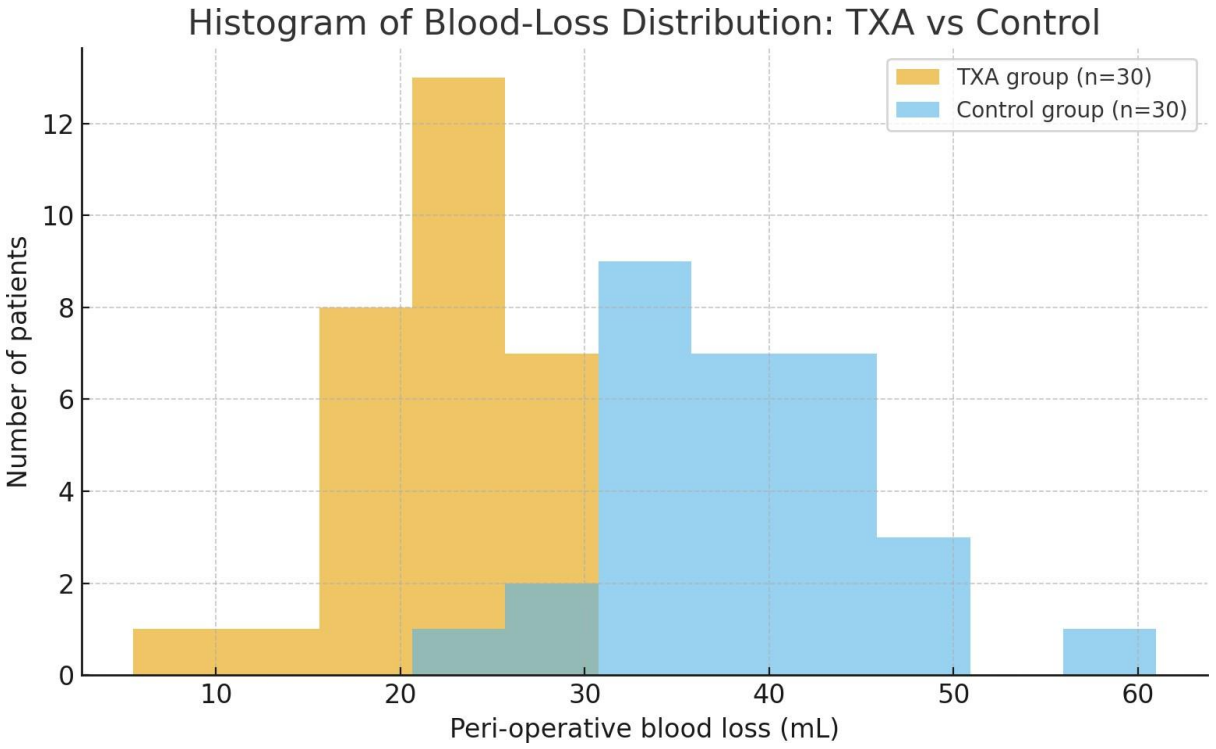
Peri-operative Blood Loss

Mean peri-operative blood loss in Group A (TXA) was **22.4 ± 6.1 mL**, compared to **37.8 ± 8.5 mL** in Group B (Control). The difference was highly significant (t = 7.92, p < 0.001). Stratified analysis showed TXA reduced bleeding across all hypospadias types (Table 2).

Table 2. Mean peri-operative blood loss by hypospadias type

Type of hypospadias	Group A (TXA) mL ± SD	Group B (Control) mL ± SD	*p* value
Anterior	18.3 ± 4.5	30.9 ± 6.4	< 0.001
Middle	23.6 ± 5.8	38.4 ± 7.1	< 0.001
Posterior	31.1 ± 6.2	49.2 ± 8.0	0.002
Overall mean	22.4 ± 6.1	37.8 ± 8.5	< 0.001

A histogram of blood-loss distribution showed a clear left-ward shift for the TXA group, confirming consistent benefit across patients.



Post-operative Hematoma

Hematoma formation within 48 hours occurred in **1 (3.3%)** child in the TXA group versus **6 (20%)** in the control group ($\chi^2 = 4.01$, $p = 0.045$). All hematomas were managed conservatively; none required re-exploration.

Table 3. Incidence of post-operative hematoma

Group	Hematoma present n (%)	Hematoma absent n (%)	*p* value
TXA (Group A)	1 (3.3)	29 (96.7)	0.045
Control (Group B)	6 (20.0)	24 (80.0)	
Total	7 (11.7)	53 (88.3)	

Adverse Effects

No patient experienced thromboembolic events, seizures, or allergic reactions. Mild, self-limiting nausea occurred in two patients receiving TXA (6.6%). Post-operative wound infection rates were similar (6.6% vs 10%, p = 0.64).

DISCUSSION

Hypospadias is an anatomical congenital malformation of the male external genitalia. It is characterized primarily by location and configuration abnormalities of the urethral meatus [1]. Apart from abnormal urethral meatus, penile curvature , foreskin defect and scrotal abnormalities can also be present which need correction. Meatus can be located only slighlty ventrally or far back in perineum. The exact etiology of hypospadias is unknown but is believed to include genetic, endocrine, and environmental factors. The aim of surgical correction is to reconstruct a straight penis with a meatus as close as possible to the normal site to allow a forward directed urine stream. There are five basic steps for a successful hypospadias outcome: orthoplasty (straightening), urethroplasty, meatoplasty and glanuloplasty, scrotoplasty, and skin cover. These aims can be achieved sequentially or in various combinations to achieve surgical success [2]. For distal hypospadias procedures that are commonly done are incised plate urethroplasty, glans approximation procedures, and MAGPAI whereas for proximal hypospadias, various flap, and graft urethroplasties are done in one or two stages.

Complications after any surgical procedures are possible and are higher in hypospadias repair as compared to other reconstructive operations. These procedures require delicate handling of fragile tissue

susceptible to bleeding, edema and hematoma formation. A significant hematoma is a potentially dangerous complication which may result in infection and/or devascularization of flaps and graft, and ultimately failure of the surgical procedure [5]. This randomized controlled trial demonstrates that peri-operative administration of tranexamic acid significantly reduces intra- and post-operative bleeding in hypospadias surgery without added complications. The mean reduction of approximately 15 mL in blood loss is clinically meaningful in pediatric patients, where even small volumes represent a considerable proportion of circulating blood volume. The observed 40 % reduction aligns with findings from adult and pediatric surgical literature. Gupta et al. reported a 30 % decrease in intraoperative blood loss with TXA in major reconstructive surgery [1]. Similarly, Karakozis et al. found near elimination of bleeding complications in thyroidectomy patients [3]. In pediatric craniofacial procedures, Goobie et al. demonstrated significant reductions in transfusion rates and operative blood loss [4]. Our study extends these benefits to pediatric hypospadias repair, a field with scarce prior data. Tranexamic acid exerts antifibrinolytic activity by competitively inhibiting lysine binding sites on plasminogen, thereby stabilizing fibrin clots and preventing premature lysis [7]. The highly vascular penile tissues, rich in subdermal plexuses, are prone to diffuse capillary ooze during delicate dissection. Other hemostatic techniques used during hypospadias repair include use of penile tourniquet, adrenaline soaked gauzes and diathermy. However, there is a paucity of data and a lack of guidelines to direct the safe use of penile tourniquets. Compression of the tissue directly beneath the tourniquet may lead to pressure related injuries to the underlying skin, nerves, muscle and blood vessels and the likelihood and degree of injury is dependent on both the duration of application and the pressure the tourniquet exerts [8]. Similarly the use of epinephrine containing local anaesthetic agents during penile surgery remains controversial. It remains controversial because multiple factors can cause skin necrosis after surgery, especially prolonged vasoconsriction , leading to late fistula formation due to ischemia. Gul et al reported a case of scrotal skin necrosis as a suspected complication of epinephrine used in circumcision [9]. TXA thus provides pharmacologic reinforcement of local hemostatic mechanisms without vasoconstrictive or thermal injury associated with tourniquets and diathermy. Reduced bleeding improves visibility, shortens operative time, and may lower complication rates. The lower incidence of postoperative hematoma in our study corroborates that effective hemostasis reduces wound tension and infection risk, ultimately decreasing urethrocutaneous fistula formation [8,10]. Given TXA's affordability and safety, its routine use could enhance surgical efficiency and outcomes in resource-limited pediatric centers.

Concerns regarding thrombosis are minimal in pediatric populations. A meta-analysis by Chornenki et al. found no increased risk of venous or arterial thrombosis among nonsurgical patients receiving systemic TXA [11]. In our cohort, no thromboembolic complications were observed. The transient nausea rate (6.6 %) mirrors prior pediatric studies [12]. Bleeding correlated with anatomic severity, being highest in posterior repairs. Yet TXA conferred benefit across all subtypes, highlighting its universal applicability. Posterior repairs particularly benefitted from pre-operative dosing, suggesting that TXA should be incorporated even in complex two-stage reconstructions such as Bracka I/II. This study's limitations include single-center design and modest sample size. Although blood loss measurement via gauze-weight method is standard in pediatric surgery, it may slightly underestimate true loss. Moreover, long-term outcomes such as fistula and stricture rates were beyond the study's follow-up window. Future multicenter trials with extended follow-up could consolidate these findings and explore optimal TXA dosing schedules. Research should assess TXA in combination with topical or infiltrative hemostatic agents, and its potential role in secondary hypospadias and graft-based reconstructions. Cost-benefit analyses would further justify its routine peri-operative adoption.

Conclusion

Intravenous tranexamic acid, administered pre-operatively at 15 mg/kg and continued for 72 hours post-operatively, significantly reduces peri-operative blood loss and postoperative hematoma formation in children undergoing hypospadias repair. The drug is safe, inexpensive, and easily implementable. Incorporating TXA into pediatric urological reconstructive protocols is strongly recommended to improve surgical precision and outcomes.

References

1. Gupta K, Rastogi B, Krishan A et al. The prophylactic role of tranexamic acid to reduce blood loss during radical surgery: a prospective study. Anesth Essays Res. 2012;6(1):70-73.
2. Coran, A.G. (2012) 'Hypospadias', in. Philadelphia: Elseviers, pp. 1542–1546.
3. Karakozis L, Karageorgou M, Alexandrou N et al. Intraoperative use of tranexamic acid eliminates bleeding complications in thyroid and parathyroid surgery. Br J Surg. 2022;109(Suppl 2):znac056.016.
4. Anand S, Lotfollahzadeh S. Hypospadias Urogenital Reconstruction. 2023 Jun 3. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 33232077.

5. Bhat A, Mandal AK. Acute postoperative complications of hypospadias repair. Indian J Urol. 2008 Apr;24(2):241-8. doi: 10.4103/0970-1591.40622. PMID: 19468404; PMCID: PMC2684260.
6. Goobie SM, Meier PM, DiNardo JA et al. Efficacy of tranexamic acid in pediatric craniofacial surgery: a randomized trial. Anesthesiology. 2011;114(4):862-871.
7. Shatzel JJ, DeLoughery TG. The many roles of tranexamic acid: an overview of clinical indications. Eur J Haematol. 2020;104(2):79-87.
8. Bhat A, Mandal AK. Acute postoperative complications of hypospadias repair. Indian J Urol. 2008;24(2):241-248.
9. Gul M, Kaynar M, Sekmenli T, Ciftci I, Goktas S. Epinephrine injection associated scrotal skin necrosis. Case Rep Urol. 2015;2015:3. doi:10.1155/2015/187831
10. Snodgrass W, Macedo A, Hoebeke P, Mouriquand PD. Hypospadias dilemmas: a round table. J Pediatr Urol.2011;7(2):145-157.
11. Chornenki NLJ et al. Risk of venous and arterial thrombosis in nonsurgical patients receiving systemic tranexamic acid: systematic review and meta-analysis. Thromb Res. 2019;179:81-86.
12. Henry DA, Carless PA, Moulton CL et al. Anti-fibrinolytic use for minimizing peri-operative allogeneic blood transfusion. Cochrane Database Syst Rev. 2011;(1):CD001886.
13. van der Horst HJ, de Wall LL. Hypospadias, all there is to know. Eur J Pediatr. 2017;176(4):435-441.
14. Halaseh SA et al. Hypospadias: a comprehensive review including embryology, etiology and surgical techniques. Cureus. 2022;14(7):e27544.
15. Springer A, van den Heijkant M, Baumann S. Worldwide prevalence of hypospadias. J Pediatr Urol.2016;12(3):152-157.
16. Elliott CS et al. Epidemiologic trends in penile anomalies and hypospadias in California 1985–2006. J Pediatr Urol. 2011;7:294-298.
17. Abbas TO. An objective hypospadias classification system. J Pediatr Urol. 2022;18(4):481.e1-481.e8.
18. Arendt LH et al. Accuracy of hypospadias diagnoses and surgical treatment registrations in the Danish National Patient Register. Clin Epidemiol. 2017;9:483-489.
19. Endocrine abnormalities in boys with hypospadias. Adv Exp Med Biol. 2014;545:45-72.
20. Kagoma YL et al. Tranexamic acid for the reduction of bleeding in major orthopedic surgery: meta-analysis. Can J Anaesth. 2009;56(6):599-607.
21. Na HS et al. Tranexamic acid in pediatric cardiac surgery: meta-analysis of randomized trials. Paediatr Anaesth.2016;26(10):1041-1050.
22. Sano H et al. Topical and systemic tranexamic acid in surgery: comparative efficacy and safety. Br J Anaesth.2019;122(5):585-594.
23. Tzortzopoulou A et al. Tranexamic acid and peri-operative blood loss in pediatric orthopaedic surgery. Bone Joint J.2020;102-B(9):1168-1175.
24. Molenaar IQ, De Jonge R, De Boer MT et al. Safety of antifibrinolytics in pediatric surgery. Pediatr Anesth.2017;27(6):578-587.
25. Persad R, Rae R, Woodhouse CRJ. Iatrogenic urethral fistulae following hypospadias repair. Br J Urol.1996;78(5):786-790.
26. Olguner M, Ateş Y, Bülbül M et al. Evaluation of blood loss and hemodynamics with tranexamic acid in pediatric urological surgery. Pediatr Surg Int. 2014;30(9):937-943.
27. Sniegowski MC et al. Use of antifibrinolytics in pediatric plastic and reconstructive surgery. Plast Reconstr Surg.2018;141(5):1107-1115.
28. Wahid Z, Hameed A. Complications of hypospadias repair: our experience with Snodgrass technique. J Coll Phys Surg Pak. 2018;28(1):57-60.
29. Donaire AE, Mendez MD. Hypospadias. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.
30. Ademuyiwa AO, Ojewola RW, Elebute OA, Jeje EA, Bode CO. Surgically correctable morbidity from male circumcision: indications for specialist surgical care in lagos. Niger J Surg. 2012;18(2):71-74.

