Original Article

A randomized control trial on the role of tranexamic acid in preventing intraoperative bleeding during external dacryocystorhinostomy

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Purpose: To evaluate the role of tranexamic acid in controlling intra-operative and immediate post-operative bleeding during external dacryocystorhinostomy. **Methods:** This was a double-blinded randomized placebo-controlled trial. All patients diagnosed with primary acquired nasolacrimal duct obstruction presenting between June 2018 to December 2019 were included in the study. All patients in the study group received a single dose of 1 gm tranexamic acid injection intravenously 30 minutes before the surgery, whereas the patients from group B (placebo) received normal saline. The effect of the injection was measured in terms of duration of the surgery, surgical field grading, amount of total blood loss during the surgery, and the need for postoperative nasal packing. **Results:** A total of 96 patients were included, of whom 45 were males and 51 were females. The study group (Group A) included 51 patients (27 males and 24 females) and the control group (Group B) included 45 patients (18 males and 27 females). There were no statistically significant differences between the two groups in terms of the duration of surgery (48.43 ± 20.01 minutes vs. 53.38 ± 19.8 minutes, $P = 0.228$), view of the surgical field ($P = 0.084$), the amount of intraoperative blood loss (88.63 ± 69.34 mL vs. 88.89 ± 51.93 mL, $P = 0.984$) and requirement of postoperative nasal packing (54.9% vs 62.2%, $P = 0.471$). **Conclusion:** There seems to be little to justify the role of preoperative intravenous tranexamic acid injection in controlling intra-operative and immediate postoperative bleeding during external dacryocystorhinostomy.

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External dacryocystorhinostomy (DCR) is a bypass procedure that creates an anastomosis between the lacrimal sac and the nasal mucosa via a bony ostium through a skin incision. It is one of the most commonly performed oculoplastic surgeries for managing the primary acquired nasolacrimal duct obstruction. Intraoperative hemorrhage still remains a major challenge during the surgery.[1,2] A good hemostasis during the surgery not only reduces the duration of the surgery but also improves the surgical outcome. Measures are taken to reduce the intra-operative hemorrhage using a good preoperative assessment to rule out bleeding diathesis, pre-operative and intra-operative blood pressure control, use of adrenaline along with local anesthetics, a good nasal packing, raising the head end of the table, avoiding major blood vessels, use of good suction and cautery, use of gel foam or bone wax-like material.[1,2] Despite these precautions, unpredictable bleeding can occur during the surgery.

Tranexamic acid (TXA), an antifibrinolytic agent, was first introduced in clinical practice in 1960 (Tengborn).[3] Its efficacy in reducing bleeding during spinal, cardiac, orthopedic, and minor oral surgeries has been well established in the literature.[4-7] However its role in peri-ocular surgeries including external DCR is yet to be elucidated.

We conducted a randomized control trial to investigate the role of prophylactic pre-operative intravenous TXA in patients undergoing external DCR to control the intra-operative and immediate post-operative bleeding.

Methods

This was a double-blinded randomized placebo-controlled trial. All patients diagnosed with primary acquired nasolacrimal duct obstruction presenting at Sankara Nethralaya Kolkata, between June 2018 to December 2019 were included in the study. Institutional review board approval and ethical clearance were obtained and the study adhered to the tenets of the Declaration of Helsinki. The randomized controlled trial adhered to the CONSORT guidelines.

The patients were randomly allocated into two groups; A and B using a random number table. All patients in group A received a single dose of 1 gm tranexamic acid (TXA) injection intravenously 30 min before the surgery, whereas the patients from group B (placebo) received normal saline. The effect of

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the injection was measured in terms of duration of the surgery, surgical field grading, amount of total blood loss during the surgery, and the need for post-operative nasal packing. The surgical field was graded as follows.

Grade 1: Excellent view of the surgical field with clear details.

Grade 2: View obscured intermittently and requiring frequent mopping.

Grade 3: Complete obscuration of the surgical field requiring frequent manual compression and cauterization.

Intra-operative blood loss was calculated by measuring the amount of blood aspirated in the suction machine during the surgery. The pre-measured amount of saline used during surgery was subtracted from the total amount of blood collected in the suction bottle to roughly get the exact amount of blood loss.

All surgeries were performed by a single surgeon (MSA). The external DCR was performed according to the conventional technique. A curvilinear skin incision measuring 10 to 12 mm was given 4 mm from the medial canthus along the anterior lacrimal crest. The size of osteotomy created was around 10 to 12 mm. Anterior and posterior nasal and lacrimal sac mucosal flaps were created. Both the posterior flaps were excised and the anterior flaps were sutured using absorbable 6–0 vicryl sutures. The wound was closed in a double layer; orbicularis closed with 6–0 vicryl sutures and skin closed with 6–0 ethilon sutures.

Patients with secondary nasolacrimal duct obstruction, revision surgery, bleeding disorders, cardiac and renal problems, patients on blood thinners, surgeries performed under general anesthesia, and patients who experienced intraoperative hypertension were excluded from the study.

Statistical analyses

The statistical analyses were performed using Statistical Package for Social Sciences, version 14.0 (SPSS Inc, Chicago, IL). All quantitative variables were estimated using measures of central location (mean, median) and measures of dispersion (standard deviation). Qualitative and categorical variables were described as frequencies and proportions. Independent *t*-test or its non-parametric equivalent Mann–Whitney *U* test was used for comparison of continuous variables between the groups and the Chi-square test was used for comparison of categorical variables.

Results

A total of 96 patients were included in this study; 45 were males and 51 were females [Table 1]. The mean age of the patients was 49.6 ± 13.04 years. Fifty-seven patients had involvement of the right side, whereas 39 patients had left-sided involvement. The study group (Group A) included 51 patients (27 males and 24 females) and the control group (Group B) included 45 patients (18 males and 27 females). The mean duration of the surgery was 48.43 ± 20.01 minutes in the study group, whereas it was 53.38 ± 19.8 minutes in the control group. The mean amount of blood loss in the study group was 88.63 ± 69.34 mL, whereas it was 88.89 ± 51.93 mL in the control group. The view of the surgical field was excellent with very minimal bleeding in 25 (49%) patients in the study group and in 16 (35.6%) patients in the control group, whereas the view was completely obscured in 17 (33.3%) and 12 (26.7%) patients in the study and control groups, respectively. Twenty-eight patients required post-operative nasal packing to control post-operative bleeding in both groups (54.9% vs. 62.2%). There were no statistically significant differences between the two groups in terms of the duration of surgery (P = 0.228), view of the surgical field (P = 0.084), the amount of intra-operative blood loss (P = 0.984), and requirement of post-operative nasal packing (P = 0.471) [Table 2].

Table 1: Demographic details of the study population

Parameters	Number	Percentage
Sample size	96	
Age	49.6±13.05 (Range: 17-78)	
Sex		
Male	45	46.9
Female	51	53.1
Laterality		
Right	57	59.4
Left	39	40.6
Groups		
Study group (Group A)	51	53.1
Control group (Group B)	45	46.9
Duration of surgery (minutes)	50.75±19.96 (range: 15-120)	
Surgical field grading		
Grade 1	41	42.7
Grade 2	26	27.1
Grade 3	29	30.2
Intraoperative blood loss	88.75±61.48	
Post-operative nasal pack	56	58.3

Table 2: Comparison of the parameters between the study group and control group

Parameters Number of patients	Study group (A) 51	Control group (B) 45	*P*
Age (Years)	49.63±13.73	49.58±12.38	0.985
Sex			
Male	27; 52.9%	18; 40%	0.205
Female	24; 47.1%	27; 60%	
Laterality			
Right	33; 64.7%	24; 53.3%	0.257
Left	18; 35.3%	21; 46.7%	
Surgical field grade			
Grade 1	25; 49%	16; 35.6%	0.084
Grade 2	09; 17.6%	17; 37.8%	
Grade 3	17; 33.3%	12; 26.7%	
Duration of surgery (Minutes)	48.43±20.01 (Range: 15-120)	53.38±19.8 (Range: 17-90)	0.228
Intra-operative blood loss (ml)	88.63±69.34	88.89±51.93	0.984
Post-operative nasal pack	28; 54.9%	28; 62.2%	0.471

Discussion

TXA is a synthetic lysine analog that reversibly and competitively binds to the lysine-binding domains on plasminogen, plasmin, and tissue plasminogen activator and interferes with fibrinolysis.[8] TXA has been used in varying doses ranging from 1–3 gm (10–15 mg/kg), most authors have preferred a dose of 1 gm.[4] TXA is administered most commonly through the intravenous route with a half-life of around 80 min and peak plasma concentration reaching within 1 hour.[9] This RCT was designed to assess the role of preoperative administration of intravenous TXA while performing external DCR. The duration of the surgery, total blood loss, view of the surgical field obscured by bleeding, and the need for a post-operative nasal pack in these patients were assessed. The study did not find any significant difference in these parameters whether TXA was given preoperatively or not.

Prophylactic use of TXA in various surgeries to reduce intraoperative hemorrhage and the need for blood transfusion has been described in the literature. A retrospective analysis (n = 872,416) showed that the administration of TXA significantly reduces the need for transfusion in patients undergoing total hip or knee replacement without any significant increase in side effects such as thromboembolism or renal failure.[10] Another meta-analysis on 2,925 orthopedic patients from 46 randomized controlled trials (RCTs) further showed a reduction in total intra-operative and post-operative bleeding.[11]

The role of TXA in cardiovascular surgery is well established. In a double-blind RCT, pre-operative bolus of TXA followed by intra-operative infusion resulted in reduced drainage volume and need for transfusion in elective coronary artery bypass graft (CABG).[10] Similar results were obtained in another meta-analysis of 25 RCTs and large-scale observational studies that proved the efficacy of TXA, as compared to placebo, in reducing blood loss and the need for blood transfusion.[12,13]

Other surgeries where the role of TXA has been established in preventing intra-operative blood loss and need for transfusion include orthotopic liver transplant, prostate surgery, and gynecological surgeries.[14-18]

However, the prophylactic use of TXA in periocular surgeries is not well established in the literature. In a placebo-controlled pilot study, Sagiv *et al*. described the role of subcutaneous injection of TXA in the skin only upper eyelid blepharoplasty. There was no significant difference in the duration of cautery used during surgery, the total duration of the surgery, intra-operative blood loss, and post-operative ecchymosis between the groups who received subcutaneous TXA and those who did not.[18]

External DCR is a very commonly performed oculoplastic procedure and the amount of bleeding during surgery not only affects the ease of performing it but can also have a significant effect on the outcome in cases where the bleeding is severe.[1,2] The present RCT was conducted keeping in mind the published literature of other surgical sub-specialties where TXA had proved quite helpful in reducing intra-operative bleeding. Unfortunately, we did not find any difference between the group receiving TXA and the one that did not receive it and we do not recommend the use of prophylactic preoperative use of TXA in external DCR.

In most of the surgeries, the injection of TXA was given just before the skin incision[4], but since the peak plasma concentration takes some time to peak, we gave the bolus 30 minutes before the surgery. One can argue, that in most of these cases the TXA was given as an infusion, whereas in our case it was a bolus: this may explain the lack of a difference, but considering the considerable difference between the duration of surgeries in spinal and cardiac surgeries and external DCR, we are not sure whether a continuous infusion would have been a good idea. Another important point is that in most of the surgeries mentioned in the literature where TXA was used to prevent hemorrhage, the focus was on intra-operative and post- operative hemorrhage as a whole.[4] The studies have looked into the requirement of post-operative blood transfusions and the days patient needed to stay in the hospital because of hemorrhage.[4] Obviously, these are not the concerns with external DCR, and hence the difference between the two groups was not that pronounced.

Small sample size, not injecting the drug as a continuous infusion, and subjective assessment of surgical field grading are some of the limitations of the present study.

Conclusion

In the light of present study there seems little to justify the role of prophylactic pre-operative tranexamic acid in preventing intra-operative hemorrhage and blood loss during external dacryocystorhinostomy. However further studies with much more larger sample size and with modifications in the protocol of drug (TXA) administration can help in substantiating this fact.

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Conflicts of interest

There are no conflicts of interest.

References

1. Small RG, Reed J. Bleeding during dacryocystorhinostomy: The importance of the suction cautery. Arch Ophthalmol 1990;108:638-9.
2. Ali MJ, Naik MN, Honavar SG. External dacryocystorhinostomy: Tips and tricks. Oman J Ophthalmol 2012;5:191-5.
3. Tengborn L, Blomback M, Berntorp E. Tranexamic acid–An old drug still going strong and making a revival. Thromb Res 2015;135:231-42.
4. Winter SF, Santaguida C, Wong J, Fehlings MG. Systemic and topical use of tranexamic acid in spinal surgery: A systematic review. Global Spine J 2016;6:284-95.
5. Dai Z, Chu H, Wang S, Liang Y. The effect of tranexamic acid to reduce blood loss and transfusion on off-pump coronary artery bypass surgery: A systematic review and cumulative meta-analysis. J Clin Anesth 2018;44:23-31.
6. Gausden EB, Qudsi R, Boone MD, O'Gara B, Ruzbarsky JJ, Lorich DG. Tranexamic acid in orthopaedic trauma surgery: A meta-analysis. J Orthop Trauma 2017;31:513-9.
7. de Vasconcellos SJ de A, de Santana Santos T, Reinheimer DM, Faria-E-Silva AL, de Melo MF, Martins-Filho PR. Topical application of tranexamic acid in anticoagulated patients undergoing minor oral surgery: A systematic review and meta-analysis of randomized

clinical trials. J Craniomaxillofac Surg 2017;45:20-6.

8. McCormack PL. Tranexamic acid: A review of its use in the treatment of hyperfibrinolysis. Drugs 2012;72:585-617.
9. Andersson L, Nilsson IM, Niléhn JE, Hedner U, Granstrand B, Melander B. Experimental and clinical studies on AMCA, the antifibrinolytically active isomer of p-aminomethyl cyclohexane carboxylic acid. Scand J Haematol 1965;2:230-47.
10. Poeran J, Rasul R, Suzuki S, Danninger T, Mazumdar M, Opperer M, *et al*. Tranexamic acid use and postoperative outcomes in patients undergoing total hip or knee arthroplasty in the United States: Retrospective analysis of effectiveness and safety. BMJ 2014;349:g4829.
11. Huang F, Wu D, Ma G, Yin Z, Wang Q. The use of tranexamic acid to reduce blood loss and transfusion in major orthopaedic surgery: A meta-analysis. J Surg Res 2014;186:318-27.
12. Maddali MM, Rajakumar MC. Tranexamic acid and primary coronary artery bypass surgery: A prospective study. Asian Cardiovasc Thorac Ann 2007;15:313-9.
13. Ngaage DL, Bland JM. Lessons from aprotinin: Is the routine use and inconsistent dosing of tranexamic acid prudent? Meta-analysis of randomised and large matched observational studies. Eur J Cardiothorac Surg 2010;37:1375-83.
14. Molenaar IQ, Warnaar N, Groen H, Tenvergert EM, Slooff MJ, Porte RJ. Efficacy and safety of antifibrinolytic drugs in liver transplantation: A systematic review and meta-analysis. Am J Transplant 2007;7:185-94.
15. Crescenti A, Borghi G, Bignami E, Bertarelli G, Landoni G, Casiraghi GM, *et al*. Intraoperative use of tranexamic acid to reduce transfusion rate in patients undergoing radical retropubic prostatectomy: Double blind, randomised, placebo controlled trial. BMJ 2011;343:d5701.
16. Lundvall F, NielsenNC. The hemostatic effect of tranexamic acid in conisatio colli uteri. Acta Obstet Gynecol Scand 1984;63:81-4.
17. Celebi N, Celebioglu B, Selcuk M, Canbay O, Karagoz AH, Aypar U. The role of antifibrinolytic agents in gynaecologic cancer surgery. Saudi Med J 2006;27:637-41.
18. Sagiv O, Rosenfeld E, Kalderon E, Barazani TB, Zloto O, Martinowitz U, *et al*. Subcutaneous tranexamic acid in upper eyelid blepharoplasty: A prospective randomized pilot study. Can J Ophthalmol 2018;53:600-4.