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Original article

Effect of single-dose intravenous tranexamic acid on postoperative nasal bleed in septoplasty



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ABSTRACT

Objective: Postoperative nasal bleeding is a common complication of septoplasty and may lead to painful procedure of nasal packing to stop bleeding. Since Tranexamic acid (TXA) has been reported to reduce bleeding, the purpose of this study is to investigate the effect of single dose of intravenous TXA on postoperative nasal bleed associated with septoplasty.

Materials and methods: This prospective randomized, double-blinded clinical trial consisted of 176 patients aged 18–55 years who underwent septoplasty for symptomatic deviated nasal septum. These participants were randomly divided into 2 groups; 88 patients were given normal saline (Control group) and 88 patients were administered a single shot of intravenous TXA 10 mg/kg (TXA group). Operative technique applied was same in all cases. At the end of surgery nasal packs, nasal splints or trans-septal suturing were not done. Nasal bleeding was monitored after surgery and up to 2 weeks postoperatively.

Results: Patients receiving TXA showed significantly less postoperative nasal bleeding compared with controls. Extensive bleeding in terms of number of gauze pads used and duration was also higher in placebo with a statistically significant difference (all $P < 0.05$). Seven patients required nasal packing in control group to stop bleeding as compared to one patient in TXA group. Adverse reactions to TXA were minimal, and these were easily managed conservatively.

Conclusion: Single intravenous dose of TXA is shown to be effective and safe agent in preventing post-operative nasal bleeding after septoplasty therefore avoiding additional techniques of nasal packing, intranasal splint or trans-septal suturing during surgery.

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1. Introduction

Septoplasty is a common nasal elective surgical procedure that is done to improve nasal airway function in patients having deviated nasal septum (DNS), and it is the third most frequent otorhinolaryngological procedure performed [1]. Postoperative epistaxis is considered a common complication of this procedure with as high as 35% bleeding rate including minor and major hemorrhages [2]. This not only leads to morbidity of the patient with different conservative measures to stop bleeding which also includes the painful procedure of nasal packing in case of severe hemorrhage but also raises the question on safety of septoplasty without nasal packing.

An antifibrinolytic agent, Tranexamic acid (TXA) which is a synthetic derivative of amino acid lysine, blocks lysine binding sites on plasminogen molecules reversibly [3], and thus controls bleeding in

various cardiac, orthopedic, spinal, dental and prostatic surgeries [4–7]. Although TXA has been used in both intravenous (IV) and per oral forms, and earlier studies have also confirmed its favorable effects on nasal bleeding in patients undergoing elective nasal procedures like functional endoscopic sinus surgery (FESS), rhinoplasty and adenoidectomy [8–11], to the best of our knowledge no one tried its use in preventing epistaxis associated with septoplasty alone, specifically with single intravenous shot given in postoperative recovery phase. The aim of this study is to investigate the effect of single-dose intravenous tranexamic acid on postoperative nasal bleed associated with septoplasty.

2. Materials and methods

Patients aged 18–55 years who had symptomatic deviated nasal septum (DNS) without history of allergy and underwent septoplasty were included in the study. This prospective randomized, double-blinded clinical trial was carried out at Liaquat National Hospital Karachi from June 2015 to May 2017. Patients were

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randomly allocated into one of the two groups via computer-generated random-number tables. Tranexamic acid group (TXA group) included 88 subjects who received a single dose of intravenous TXA 10 mg/kg. The control group included 88 subjects who received normal saline as placebo. Both tranexamic acid or normal saline solutions were prepared in identical 50 ml normal saline intravenous bags by hospital pharmacy with labels indicating only patient's name and medical record number so that they appeared indistinguishable. These solutions were delivered to recovery room nursing staffs who in the presence of one of the co-authors of the study administered drug to the patient in postanesthesia recovery room, 30 min after the procedure finished and administered within 10–15 min. Neither the surgeon, nor the patient or nursing staff knew the composition of the solution administered. All patients were in the anesthetic risk group ASA (American Society of Anesthesiologists) physical status I and II. All surgical procedures were performed under general anesthesia by the same surgeon i.e. of Assistant Professor level. Operative technique applied was same i.e. Killian procedure (Submucous resection with preservation of dorsal and caudal portion of septal cartilage through closed approach) in all cases, and there were no changes in the technique during the study period. Mucosal tears occurred in 21 patients during surgery, all of which were small and closed by interrupted absorbable suture. At the end of surgery, no nasal packs were used. Also, nasal splints or trans-septal suturing were not employed.

Patients who had known allergy to TXA, those who had bleeding diathesis, had physical status of ASA (American Society of Anesthesiologists) stages III or more before surgery, those who were using anticoagulant drugs, history of previous nasal surgery, those who underwent concomitant rhinoplasty or turbinectomy or endoscopic sinus surgery, pregnant women, and those who did not sign the informed consent were excluded from the study. We did not do routine screening for thromboembolic event related to TXA in postoperative period in our study. The study was approved by the Liaquat National Hospital Ethics Committee and written informed consent was obtained from all eligible patients.

Postoperative blood loss during the initial admission or during the follow-up period was estimated by the amount of gauze pads (4" × 4") used. Complete soakage of 1 gauze pad with blood was taken as approximately 10 ml of blood loss. Patients stayed in the hospital for at least 24 h, and then returned home if there was no adverse event postoperatively. At discharge, all patients were instructed to report all episodes of nasal bleeding for up to 2 weeks

postoperatively. So all bleeding episodes, which occurred after the procedure till 2 weeks, were assessed for each case.

Patient's data were compiled and analyzed through Statistical Package for Social Sciences (SPSS) Version 21. Frequency and percentage were reported for qualitative variables, and mean ± standard deviation was reported for quantitative variables. Chi² and Fisher's exact tests were applied to see the association of nasal bleeding between two groups. *P*-value ≤ 0.05 was considered statistically significant.

Normal seepage: any episode of discharge from one or both nostrils after septoplasty which is intermittent and stopped by nasal pinching. It is a normal reaction from trauma during surgery.

Postoperative nasal bleed: any episode of bleeding from one or both nostrils after septoplasty which is continuous, not stopped by nasal pinching and requires other methods for control. It is considered as a complication of surgery.

Amount of nasal bleed: complete soakage of one 4" × 4" gauze pad was taken as 10 ml of blood loss. Similarly 5 ml and 2.5 ml amount was taken when soakage of gauze pad was half or quarter respectively.

Frequency of nasal bleed: number of episodes of bleeding from one or both nostrils after septoplasty.

3. Results

The control group consisted of 46 males and 42 females (mean age = 9.66 ± 8.76 years), while TXA group consisted of 59 males and 29 females (mean age = 33.31 ± 8.90 years). Fig. 1 shows the age distribution of patients for each group. Age distribution between 2 groups was not significant.

Functional outcome was good with 88% patients in both groups were relieved of their nasal obstruction complaint postoperatively with no significant difference.

Postoperative nasal bleeding was noted in 26 patients out of 176 (Table 1). Bleeding was found less in TXA group as compared to the control group with a statistically significant difference (*P* = 0.018).

Extensive bleeding in terms of number of gauze pads used and duration was higher in the control group with a statistically significant difference (*P* < 0.05). Nasal packing was required to stop bleeding more in patients who received normal saline in contrast to tranexamic acid (36.8% vs. 14.3%). Similarly, three subjects in the control group had more than one episode of nasal bleed as compare to only one subject in TXA group. However, these two factors

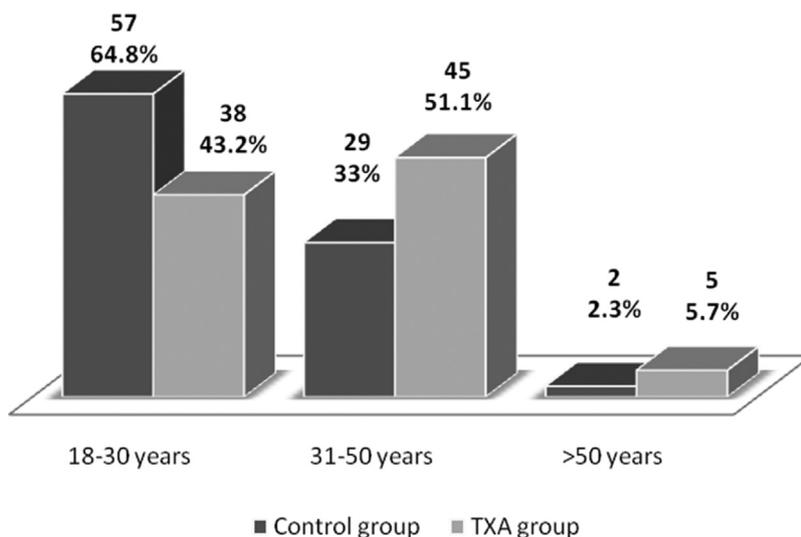


Fig. 1. Age distribution of patients in the two groups (*n* = 176).

Table 1
Association of nasal bleeding in the two groups (n = 176).

	n (%)		P-Value
	Control group (n = 88)	TXA group (n = 88)	
Nasal Bleeding			
Yes	19(21.6)	7(8)	0.018
No	69(78.4)	81(92)	

Chi² test applied. P-value ≤ 0.05 considered as significant.

Table 2
Comparison of nasal bleeding variables between the groups (n = 26).

Variable	Control group n = 19	TXA group n = 7	P-value
Number of gauze pads			
0–3	2(10.5)	5(71.4)	0.006
4–6	4(21.1)	1(14.3)	
> 6	13(68.4)	1(14.3)	
Duration of bleeding (minutes)			
≤ 10	5(26.3)	6(85.7)	0.021
> 10	14(73.7)	1(14.3)	
Packing done			
Yes	7(36.8)	1(14.3)	0.375
No	12(63.2)	6(85.7)	
Frequency			
1	16(84.2)	6(85.7)	1.000
> 1	3(15.8)	1(14.3)	

Fisher exact test applied. P-Value ≤ 0.05 considered as significant.

were not statistically significant (Table 2). There was no difference in delay of bleeding occurrence after the end of the procedure between 2 groups.

All patients who developed epistaxis in both groups either in initial admission or follow-up period were managed conservatively with different methods, which included topical nasal decongestant, chemical cautery with silver nitrate sticks or nasal packing. No patient required blood transfusion or control of nasal bleeding in the operating theatre under general anesthesia.

Mucosal tears were observed in 11 (12.5%) cases of TXA group and 10 (11.3%) cases of control group. They were source of epistaxis in three patients in the control group as opposed to one in TXA group. Similarly, septal hematoma was developed in 3 (3.4%) and 1 (1.1%) cases in the control and TXA group respectively. All these cases were managed by incision and drainage.

None of the study patient had a thromboembolic event (e.g. deep vein thrombosis, pulmonary embolism, cerebral thrombosis) or an allergic reaction to TXA. Six patients reported headache and four had nausea without vomiting, both these complications were easily managed conservatively. There were no other side effects of the drug.

4. Discussion

Researches from the past showed a beneficial effect of using tranexamic acid to control intraoperative and postoperative bleeding in different elective procedures. Casati et al. [4] reported favorable outcomes of TXA in reducing perioperative bleeding in patients undergoing thoracic aortic surgery while Cheriyan et al. [7] found positive results in decreasing surgical bleeding and transfusion requirements in spine surgery. In the last 10 years, its widespread role in rhinological procedures was also documented especially in endoscopic sinus surgery in which it significantly reduced estimated blood loss and improved surgical field quality for the operator during surgery [8,9].

Nasal bleeding is the most common complication of nasal surgery [12,13]. The rate of hemorrhage after septoplasty is variable

with 2.3% [14] to 35% [2]. In our study, the rate was 14.7% in both groups combined, comparable to the study done by Al-Raggad et al. [15].

Nasal packing with different materials or trans-septal suturing is still usually performed by most surgeons at the end of septal surgery in order to maintain hemostasis and prevent postoperative nasal bleed. The negative impacts of these techniques especially nasal packing on quality of life have been reported in previous studies [16–18]. We administered intravenous tranexamic acid post procedure to prevent epistaxis without doing nasal packing, trans-septal suturing and nasal splinting. Our findings confirm that the administration of IV TXA according to bodyweight can significantly reduce postoperative hemorrhage compared with placebo. Similar results were observed by Yaniv et al. [19], by giving 1 g of oral TXA to the patients who underwent elective nasal surgery. Their results showed considerably less operative and postoperative bleeding in the study group compared with the control group. But as compared to our study, which includes patients with DNS undergoing septoplasty only, their subjects underwent FESS as a primary modality of treatment for chronic rhinosinusitis in combination with septoplasty and conchotomy for concomitant DNS and hypertrophy of turbinates. In contrast, some other studies found no significant difference for using TXA in elective procedures [20,21].

Eftekharian et al. [10] and Albirmawy et al. [11], comparing the administration of 1000 mg of TXA with that of placebo in rhinoplasty and adenoidectomy respectively, found a favorable effect of the drug in the amount of bleeding between the 2 groups. These findings are consistent with the result of our study.

Nasal packing was done to stop active bleeding in 7/19 cases in the control and 1/7 case in TXA group. The remaining fifteen patients required topical nasal decongestant and three cases needed chemical cautery with silver nitrate. None of the patients required thermocoagulation or angioembolization.

A study from Turkey [22] reported less postoperative bleeding and other complications with the trans-septal suturing technique as compared to nasal packing while a work from Iran [23] opposed it. Similarly, a study from Turkey by Bingol et al. [24] indicated that nasal splint was more effective in terms of causing lesser bleeding in contrast to nasal packing as opposed to a work from Iran by Ardehali et al. [25] We did not apply any of these methods in our subjects.

Mucosal tears are also another important factor of epistaxis in septal surgery. Several methods including continuous quilting suture and using curved needle technique have been described in the literature in order to lessen the complication rate from these wounds [26,27]. Mucosal tears were seen in 21(12%) cases in our series, which was almost half as reported by Sathyaki et al. (i.e. 24%) [28] of their conventional septoplasty cases. These breaches were a source of epistaxis more in the control group than TXA but the difference was insignificant.

In a study conducted by Rajguru et al. [29], internal bleeding in the form of a septal hematoma was reported more (4%) as compared to our results (2%). Multiple management options ranging from nasal splinting, trans-septal suturing and nasal packing with different materials were described in literature to avoid hematoma [25,30,31]. We did not employ any of these methods and although TXA group had least cases in which septal hematoma formed, it was not statistically significant.

Functional outcome in terms of relief of nasal obstruction, which is one of the main goals of surgery was reported as 70% [32] and 81% [29] in two previous works. Our results showed the 88% patients got benefit from procedure, which was higher than both previous studies.

Common side effects of tranexamic acid include nausea, vomiting, and possibly arterial or venous thrombosis. Less than 10% cases of our TXA group developed early postoperative nausea and

vomiting, which did not differ significantly from the control group. Arterial or venous thrombosis was not detected in any of our patients clinically. Although there is a theoretical risk of thrombosis, none of the published randomized controlled studies [3] proved it and only isolated case reports showed a thromboembolic event with the use of multiple higher doses of tranexamic acid in the postoperative period, rather than as a single dose treatment [3].

The limitations of our study were its small sample size. In addition, amounts of blood loss were estimated by visual assessment of gauze pads and not by any quantitative method like gravimetric analysis, photospectrometry etc.

5. Conclusion

A single intravenous dose of tranexamic acid is shown to be effective and safe agent in preventing postoperative nasal bleeding after septoplasty therefore avoiding additional techniques of nasal packing, intranasal splint or trans-septal suturing during surgery. However, further clinical trials using larger number of patients are required to confirm these findings.

Ethical approval

This prospective study was in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all eligible patients in the study.

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Disclosure of interest

The authors declare that they have no competing interest.

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