Archives of Anesthesiology and Critical Care (Autumn 2024); 10(Supplement 1): 493-498.

Available online at http://aacc.tums.ac.ir

Research Article

Comparison Between Oral and Intravenous Tranexamic Acid in Endoscopic Sinus Surgery

Majid Razavi, Mohammad Alipour, Leila Mashhadi, Mehryar Taghavi Gilani*

Cardiac Anesthesia Research Center, Imam-Reza Hospital, School of Medicine, Mashhad University of Medical Science, Mashhad, Iran.

ARTICLE INFO

Article history:
Received 15 January 2024
Revised 09 February 2024
Accepted 26 February 2024

Keywords:
Bleeding;
Anesthesia;
Endoscopic sinus surgery;
Tranexamic acid

ABSTRACT

Background: The goal of this study is to assess oral and intravenous administration of tranexamic acid's (TXA) on intra-operative bleeding during endoscopic sinus surgery and to compare with control group.

Methods: Forty-eight patients who were scheduled for endoscopic sinus surgery were chosen and randomly assigned to three groups. In first group 20mg/kg intravenous tranexamic acid, in second group 1000 mg 4 times daily for 48 hours and in third group 10 ml of normal saline were administered. The quality of the surgical field was estimated every 15 minutes by Boezaart scale. Volume of bleeding, pre and postoperative hematocrit, surgeon's satisfaction by likert scale and duration of the surgical procedure were evaluated. Data was analyzed by SPSS v21 and P<0.05 was significant.

Results: Demographic parameters were not different among three groups. The surgical field quality at 15th minute was grade I-II in 25, 68.75 and 75 percent of the patients in the control, intravenous and oral groups, respectively. And also, no patients in the intervention groups and 42% of the patients in the control group were in grade IV. At 15 minute following surgery, there was a significant difference between the tranexamic groups and the control group (P = 0.002). at 30th minute 25, 50 and 56% of the patients in the control intravenous and oral groups, respectively were in grade I-II and difference was significant (P = 0.003). But at 45th minutes quality of surgical field was not different significantly (P = 0.163). The intraoperative average bleeding was 95.46, 94.32 and 190.64 ml for intravenous, oral and control patients that difference was significant (P = 0.001). The satisfaction of the surgeon was higher in the intravenous and oral TXA groups than the control group (P = 0.012). In comparison to the control group, the tranexamic group's surgical time were considerably lower (P 0.001). Hematocrits and drug side effects did not differ significantly among groups.

Conclusion: Systemic tranexamic acid (intravenous or oral) during endoscopic sinus surgery enhances surgical field quality, decreases intra-operative hemorrhage, and shortens operation duration.

Introduction

Bleeding during surgery causes surgical problems and complications during and after surgery [1-2]. Even small bleeding, in closed and small spaces such as sinus and middle ear surgery, causes malfunction of the surgeon, reduced surgeon's vision, as well as complications such as visual impairment, vascular damage, and hearing loss [3-5]. Bleeding causes hemodynamic disorder in patients and if not controlled, it is associated with increased morbidity and mortality [6]. Therefore, the control and management of intraoperative bleeding by the anesthesiologist improves the surgery, shortens the duration of the operation, and causes fewer complications for the patients [4, 6-7].

The authors declare no conflicts of interest.

*Corresponding author.
E-mail address: taghavim@mums.ac.ir

There are several methods to control and manage bleeding during surgery. The use of antihypertensive drugs such as vasodilators and remifentanil are routine methods to control bleeding. Changing the patient's position as well as antifibrinolytic drugs are also used to control bleeding. In recent studies, anti-fibrinolytic medications like tranexamic acid have been administered systemically to decrease bleeding during a variety of surgical procedures, including major orthopaedic surgery, adenotonsillectomy, and endoscopic sinus surgery [8-10].

A synthetic antifibrinolytic substance called tranexamic acid (TXA) binds to the lysine binding sites of plasmin and plasminogen and stopping fibrinolysis. Each surgical procedure involves some degree of tissue damage, which can result in the release of enzymes like tissue plasminogen activator, which turns plasminogen into plasmin and initiates the fibrinolysis process. TXA inhibits the activity of this enzyme and fibrinolysis subsequently [11-12].

Oral, intravenous and topical tranexamic acid have been used in studies but there is not still agreement on its efficacy and its effective dose and low study comparing its oral versus intravenous administration in sinus surgery [8, 13-14]. This study was aimed to compare the effects of oral with intravenous tranexamic acid and control group on surgical field visualization, quality, bleeding and adverse events in patients undergoing endoscopic sinus surgery.

Methods

The current study is a prospective randomized clinical trial that was conducted on sixty patients with grade three bilateral obstruction due to severe sinonasal polyposis. After approved of ethical committee of university, this study performed from August 2019 to December 2021 in educational hospital.

Patients with ASA class I-II aged 16-60 years old, after written informed consent were chosen. Exclusion criterias were cardiovascular, hepatic and renal disease, haemoglobin < 10 mg/dl, and also haematological and coagulative abnormalities. Complete blood cell, urea, creatinine, prothrombin and partial thromboplastin time were done for all patients. One speciality surgeon performed all surgeries. All patients received prednisolone tablets 20 mg daily for 7 days plus intranasal corticosteroid spray for 10 days before surgery.

The patients were classified into three groups randomly. First group received no medication (control group), the second group received tranexamic acid capsules orally, 250 mg 4 times daily for 48 hours before the procedure, and third group received 20mg/kg intravenous tranexamic acid over 15mins prior to surgery.

On operation room, the patients monitored for noninvasive blood pressure, heart rate, O2 saturation and electrocardiography. After preoxygenation, the patients were anesthetized by 0.03 mg/kg midazolam, 2 µg/kg fentanyl, 1 mg/kg lidocaine, 5 mg/kg thiopental Na, and 0.5mg/kg atracurium. Tracheal intubation was performed after 3 minutes and anesthesia was maintained by propofol and remifentanil infusion (50 ml – 1 mg), with oxygen and nitric oxide 50-50 percent, and also 10 mg atracurium was administered every 30 mins. After intubation the patients were positioned with head up 30 degrees. One ml lidocaine 1% combined with 1/100000 adrenaline solution was applied to outer surface of nasal cavity by surgeon.

Mean arterial pressure is maintained between 65-75 mm-Hg during surgery and nitroglycerin was infused if necessary. Systolic, diastolic blood pressure and heart rate was measured every 5min during surgery. Primary outcomes were quality of surgical field and bleeding that were evaluated at 15, 30, 45 minutes. The quality of surgical field was evaluated with Boezaart score (table 1), and also surgical field bleeding was calculated with bloody sponges and the amount of blood in suction drain after subtracting the washing serum. Secondary outcomes were surgeon's satisfaction that was assessed by 5-point likert scale for agreement (1 = Strongly disagree; 2 = Disagree; 3 = Neutral; 4 = Agree; 5 = Strongly agree) and duration of surgery.

The eligible patients were assigned to the intravenous, oral and control groups using the balance block randomization method. We prepared three sheets of paper. The sheets were placed in a container and randomly drawn out for each patient. The random allocation was conducted by anesthesiologist (1:1:1). Thus, the surgeon and evaluator the effect of interventions, were not aware of the administered drugs. The statistical analyst was unaware of the trial groups either, until the data were analyzed and the labels were decoded.

Statistical methods

According to the research of Alimian et al. (8) in 2011 and the significant level of alpha = 0.05% and the confidence level of 80%, the number of 16 patients in each group was obtained and 20 patients in each group were considered for possible dropout. All data were analyzed by SPSS version 20 statistical software. The ANOVA and Mann Whitney test was used for analysis of continuous variables, the chi-square test and Fisher exact test for nominal variables. $P<0.05$ was meaningful.

Table 1- 6-point Boezaart grading scale

Grade	Assessment
0	No bleeding (cadaveric conditions)
1	Slight bleeding, no suctioning required
2	Slight bleeding, occasional suctioning required
3	Slight bleeding, frequent suctioning required; bleeding threatens surgical field a few seconds after suction is removed

4	Moderate bleeding, frequent suctioning required, and bleeding threatens surgical field directly after suction is removed
5	Severe bleeding, constant suctioning required; bleeding appears faster than can be removed by suction; surgical field severely threatened and surgery usually not possible

Results

Ten of the 60 patients were unsuitable, and two patients declined to participate (Figure 1). Forty-eight patients were divided randomly to three groups, of whom 16 were assigned to the intravenous TXA group, 16 to the oral TXA group, and 16 to the control group. The analysis was based on information from 48 patients because no patient was dropped to analysis. There were 18 female patients and 30 male patients. There was no significant statistical difference between the three groups for demographic parameters (Table 2).

The surgical field quality according to Boezaart grading scale in the three groups at 15, 30, and 45mins after the commencement of surgery were shown in table 3. Only 25% of the patients in the control group were in grade II at 15th minute following the start of operation, and also 68.75% and 75% of the patients in the intervenous and oral TXA groups were in grade II, respectively. None of the patients in the intervenous and oral TXA groups were in grade IV, while 43.75% of the patients in the control group were in grade IV (P= 0.002). At 15th minute, there was no difference between the oral and intervenous TXA groups, but there was a significant difference between the TXA groups and the control group (p value= 0.002).

Twenty-five percent of the patients in the control group, and also 50% of oral TXA patients and 56% of intravenous TXA patients were in grade I and II at 30th minute. Seventy-five percent of the control group were in grade III and difference was significant (P = 0.003). Before 45 minutes, the surgery was complete on two, one and two patients in the intravenous TXA, the oral TXA, and the control group subsequently. The majority of the patients in the control group were in grade III at 45th minute following the commencement of surgery (64.29%), and also 57.14% and 60% of the intravenous and oral TXA groups were in grade II, however this difference was not statistically meaningful (P= 0.163) (Table 3).

The control group had significantly more bleeding than the intervention groups during 15, 30, 45 minutes. The amount of bleeding for the entire surgery time was 95.46±15.2 ml for intravenous TXA patients, 94.32±17.31 ml for oral patients, and 190.64±35.62 ml for the control group (P = 0.001) (Table 2). The smallest bleeding was 20 ml in intravenous TXA group and the greatest bleeding was 330 ml in the control group. Hematocrite after surgery was 38% in intervention groups and 36% in control group which was not statistically significant (P = 0.1).

The duration of surgery was 52.36±8.12 minutes in intravenous TXA group, 59.68±7.62 minutes in oral TXA group and 80.74±8.65 minutes in control group. There was a significant difference between intervention and control groups (P = 0.001) but not significant between intravenous and oral TXA group (P = 0.76) (Table2).

Surgeon's satisfaction was evaluated by likertt grading system and is shown in (Table 4). The satisfaction of the surgeon was higher in the intravenous TXA group than in the oral TXA group, but there was no statistically significant difference (P= 0.23). But in the control group, the satisfaction of the surgeon was less than the two intervention TXA groups (P= 0.012). TXA may have side effects such as regurgitating, nausea and poor color vision that were evaluated at 6 hours, and no complications were reported in three groups.

Table 2- demographic and hemodynamic parameters.

Parameters	IV TXA group	oral TXA group	control group	P value
Sex (F/M)	6/10	7/9	5/11	0.23
Age	32.13±12.65	29.23±11.28	30.11±10.59	0.45
Bleeding (ml)	95.46±15.2	94.32±17.31	190.64±35.62	0.001
Surgery time (min)	52.36±8.12	59.68±7.62	80.74±8.65	0.001

Table 3- Boezaart grading scale at 15, 30 and 45 minutes after the start of surgery in three goups n (%).

Boezaart grading scale	15 minutes assessment			30 minutes assessment			45 minutes assessment		
	IV TXA group	oral TXA group	control group	IV TXA group	oral TXA group	control group	IV TXA group	oral TXA group	control group
0	-	-	-	-	-	-	-	-	-
1	3(18.75%)	4(25%)	-	2(12.5%)	2(12.5%)	-	-	-	-
2	8(50%)	8(50%)	4(25%)	7(43.75%)	6(37.5%)	4(25%)	8(57.14%)	9(60%)	5(35.71%)
3	5(31.25%)	4(25%)	5(31.25%)	7(43.75%)	8(50%)	12(75%)	6(42.86%)	6(40%)	9(64.29%)

4	-	-	7(43.75%)	-	-	-	-	-	-
5	-	-	-	-	-	-	-	-	-

Table 4- Likert grading system for surgeon satisfaction in three groups n (%)

Likert grading scale	IV TXA group	oral TXA group	control group
1	-	-	3 (18.75%)
2	3 (18.75%)	2 (12.5%)	5 (31.25%)
3	4 (25%)	4 (25%)	5 (31.25%)
4	6 (37.5%)	8 (50%)	2 (12.5%)
5	3 (18.75%)	2 (12.5%)	1 (6.25%)

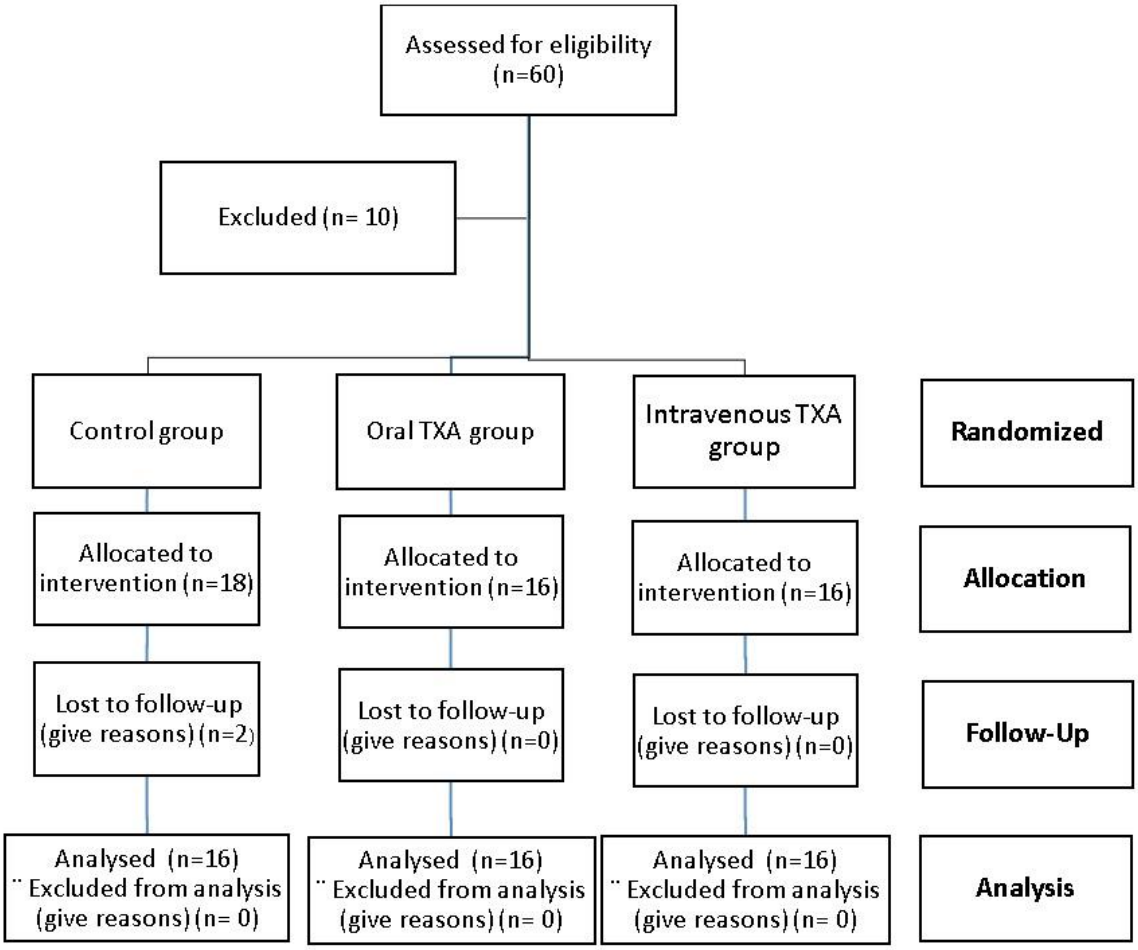

Figure 1- Flow chart of the process

Discussion

Intraoperative bleeding is a surgical problem and bleeding control is a challenge for anaesthesiologists. In the small surgical field such as endoscopic sinus surgery the amount of bleeding is so important because it distorts the field vision, lengthen the operation time and complicate its performance. Antifibrinolytic drugs administered systemically, and effectively lessen bleeding during and following surgery [8-9, 16]. A synthetic antifibrinolytic agent called tranexamic acid (TXA) is available in an oral formulation that is much less expensive than the IV preparation.

In our study systemic tranexamic acid had a significant effect on reducing blood loss and surgical field bleeding and improves the surgical field vision. The intraoperative blood loss was on average 95.46 ml in the intravenous group, 94.32 ml in oral group and 190.64 ml in the control group. There was a significant difference between intervention and control group but there was not a significant difference between oral and intravenous

group. The quality Boezaart score was much less in intervention groups 1-2 vs 3-4 for control group, and also the surgeon's satisfaction was significantly better in patients receiving tranexamic acid (3-4 vs 4-5). This randomized controlled trial aims to establish whether oral TXA reduces blood loss during endoscopic sinus surgery in a manner comparable to that of intravenous TXA.

There are many studies assessing the efficacy of intravenous and topical use, but their results were controversial [14, 17-19]. In one study, twenty-eight patients with rhinosinusitis with and without polyposis were compared in a double-blinded, randomized, controlled trial. Blood loss did not decrease statistically significant with the use of tranexamic acid (201 vs 231 mL). Also, there were no negative outcomes or complications [20]. Mottaghi el al. conducted a similar study and evaluated TXA between the two groups. They concluded that adjunctive intravenous tranexamic acid did not seem to reduce blood loss during endoscopic sinus surgery or improve surgical field visibility [21].

On the contrary, in one study by Alimian, patients received either sterile water 0.1 mL/kg or intravenous tranexamic acid 10 mg/kg. Blood loss was almost 312.75 mL in the placebo group and 184.64 mL in the TXA group. And also, In the TXA group compared to the placebo group, the surgeon was more pleased with the surgical environment [8]. In other study, the effectiveness of TXA was shown and blood loss was 174 vs 229 ml in intervention group compared to placebo group respectively [14].

Athanasiadis et al studied the effect of TXA on 30 patients undergone endoscopic sinus surgery. Patients were divided into three groups. First group received topical epsilon aminocaproic acid EACA, second group received 100 mg TXA and the third group received 1 g TXA by nasal spray. Reduced blood loss was not significant by EACA at 2, 4, and 6 mins, and also TXA significantly improved surgical field quality [13]. Also, the other studies were shown that TXA was significantly effective for blood loss and surgeon's satisfaction [8-10].

In our study, hematocrite change was less in intervention groups but was not significantly different (3.2 vs 2.5). Also in SaeedollahNuhi,s study, that pre- and postoperative hematocrit (38.81 4.20 vs. 36.60 3.35) and pre- and postoperative hemoglobin (12.51 2.5 vs. 11.64 1.9) levels did not differ significantly in the TXA and control group, and also between two groups [22].

We didn't find any adverse effects from the use of tranexamic acid. Side effects of TXA are usually gastrointestinal, but we and other studies, results have no obvious complications. In our study, the duration of surgery was also significantly less in intervention groups, especially intravenous group than control group. But results in other studies were controversial [20-23] that can be due to drug dosage.

The main limitation of our study was the small sample size and also no evaluation of the patients with or without polyposis that can be effective on surgical bleeding. Therefore, we recommand that randomized controlled trials are designed to evaluate with more sample size and assessment of sinositis ethiology.

Conclusion

The tranexamic acid can effectively reduce the blood loss and enhance the surgeon's satisfaction, and also lower the duration of surgery but we didn't find significant difference between oral and intravenous rout of use. We recommend the use of oral tranexamic acid instead of its intravenous form, because oral rout is effective same as intravenous TXA with low costs for health system.

Acknowledgment

We sincerely thank Research Council of Mashhad University of Medical Sciences. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. This study was taken from thesis no: 922422.

References

[1] Bajwa SJS, Bajwa SK, Bindra GS. The anesthetic, critical care and surgical challenges in the management of craniopharyngioma. Indian J Endocrinol Metab. 2011; 15(2):123-6.

[2] Bajwa SJS, Sehgal V. Anesthesia and thyroid surgery: The never ending challenges. Indian J Endocrinol Metab. 2013; 17(2):228-34.

[3] Schaefer SD. Endoscopic Sinus Surgery: Anatomy, Three-Dimensional Reconstruction, and Surgical Technique. Plastic and Reconstructive Surgery. 2009;124(2):658.

[4] Stammberger H, Posawetz W. Functional endoscopic sinus surgery. Eur Arch Otorhinolaryngol. 1990;247(2):63-76.

[5] Stammberger H. Endoscopic Endonasal Surgery—Concepts in Treatment of Recurring Rhinosinusitis. Part II. Surgical Technique. Otolaryngol Head Neck Surg. 1986; 94(2):147-56.

[6] Wormald PJ, Van Renen G, Perks J, Jones JA, Langton-Hewer CD. The effect of the total intravenous anesthesia compared with inhalational anesthesia on the surgical field during endoscopic sinus surgery. Am J Rhinol. 2005; 19(5):514-20.

[7] Jacobi KE, Böhm BE, Rickauer AJ, Jacobi C. Moderate controlled hypotension with sodium nitroprusside does not improve surgical conditions or decrease blood loss in endoscopic sinus surgery. J Clin Anesth. 2000; 12(3):202-7.

[8] Alimian M, Mohseni M. The effect of intravenous

tranexamic acid on blood loss and surgical field quality during endoscopic sinus surgery: a placebo-controlled clinical trial. J Clin Anesth. 2011; 23(8):611-5.

[9] Ralley FE, Berta D, Binns V, Howard J, Naudie DD. One intraoperative dose of tranexamic Acid for patients having primary hip or knee arthroplasty. Clin Orthop Relat Res. 2010; 468(7):1905-11.

[10] Brum MR, Miura MS, Castro SFd, Machado GM, Lima LH, Neto JFL. Tranexamic acid in adenotonsillectomy in children: A double-blind randomized clinical trial. Int J Pediatr Otorhinolaryngol. 2012; 76(10):1401-5.

[11] Longstaff C. Studies on the mechanisms of action of aprotinin and tranexamic acid as plasmin inhibitors and antifibrinolytic agents. Blood Coagul Fibrinolysis. 1994; 5(4):537-42.

[12] Wang W, Boffa MB, Bajzar L, Walker JB, Nesheim ME. A Study of the Mechanism of Inhibition of Fibrinolysis by Activated Thrombin-activable Fibrinolysis Inhibitor. J Biol Chem. 1998; 273(42):27176-81.

[13] Athanasiadis T, Beule AG, Wormald PJ. Effects of topical antifibrinolytics in endoscopic sinus surgery: a pilot randomized controlled trial. Am J Rhinol. 2007; 21(6):737-42.

[14] Jabalameli M, Zakeri K. Evaluation of Topical Tranexamic Acid on Intraoperative Bleeding in Endoscopic Sinus Surgery. Iran J Med Sci. 2006; 31(4) 221-223.

[15] Boezaart AP, van der Merwe J, Coetzee A. Comparison of sodium nitroprusside- and esmolol-induced controlled hypotension for functional endoscopic sinus surgery. Can J Anaesth. 1995; 42(5):373-6.

[16] 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.

[17] Abrishami A, Chung F, Wong J. Topical application of antifibrinolytic drugs for on-pump cardiac surgery: a systematic review and meta-analysis. Can J Anaesth. 2009; 56(3):202-12.

[18] Tang YMJ, Chapman TWL, Brooks P. Use of tranexamic acid to reduce bleeding in burns surgery. J Plast Reconstr Aesthet Surg. 2012; 65(5):684-6.

[19] Kaewpradub P, Apipan B, Rummasak D. Does Tranexamic Acid in an Irrigating Fluid Reduce Intraoperative Blood Loss in Orthognathic Surgery? A Double-Blind, Randomized Clinical Trial. J Oral Maxillofac Surg. 2011; 69(6):e186-e9.

[20] Langille MA, Chiarella A, Côté DW, Mulholland G, Sowerby LJ, Dziegielewski PT, et al., editors. Intravenous tranexamic acid and intraoperative visualization during functional endoscopic sinus surgery: a double-blind randomized controlled trial. International forum of allergy & rhinology; 2013; 3(4):315-8.

[21] K. Mottaghi FS, A. Salimi, S. Malek, N. Rahimi. Evaluation of intravenous Tranexamic acid effects on bleeding, duration of surgery and surgeon satisfaction in endoscopic sinus surgery. J Iran Anesth Crit Care Med Assoc Iran. 2010; 72: 14–29.

[22] Nuhi S, Goljanian Tabrizi A, Zarkhah L, Rashedi Ashrafi B. Impact of Intravenous Tranexamic Acid on Hemorrhage During Endoscopic Sinus Surgery. Iran J Otorhinolaryngol. 2015; 27(82):349-54.

[23] Eldaba AA, Amr YM, Albirmawy OA. Effects of tranexamic acid during endoscopic sinsus surgery in children. Saudi J Anaesth. 2013; 7(3):229-33.