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Original Article

Does intravenous tranexamic acid reduce bleeding during mastoidectomy?

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Abstract: Mastoidectomy is one of the important head and neck surgeries which is mostly performed due to complications of otitis media. This procedure is performed under microscopic surgery and as a result, a clean visual field is required for surgeons. Bleeding is one of the important issues during microscopic surgeries which reduces visualization. In this clinical trial, we aimed to examine effects of tranexamic acid in reducing bleeding during mastoidectomy. Here we investigated 69 patients who were candidates of mastoidectomy. Patients were randomized into two groups. In group 1, patients received tranexamic acid (10 mg/kg) at the beginning of surgeries along with other anesthetic drugs. In group 2, patients received normal saline as placebo with the same volume. Data regarding to bleeding, duration of surgeries, heart rate and blood pressure of patients were collected and analyzed. We indicated that administration of tranexamic acid is associated with significant reduced bleeding and also reduced blood pressure during surgeries (P<0.001). Taken together, we suggest that otolaryngologists should administer tranexamic acid during microscopic surgeries in order to reduce bleeding and provide a better visual field.

Keywords: Mastoidectomy, bleeding, tranexamic acid, microscopic surgeries

Introduction

Mastoidectomy are considered as important surgical procedures for otitis media with complications [1]. Mastoidectomy was introduced as a successful surgical method for drainage after otitis media and its complications [2, 3]. The most important indication for mastoidectomy is cholesteatoma formation [4]. Mastoidectomy could also be performed along with tympanoplasty with is reported to improve ostrich horn function [5, 6]. Mastoid air cells are removed in simple mastoidectomy which is performed under microscopic fields [7]. This procedure requires continuous suctions of blood in surgical field so that the surgeon will have a better visual field [8]. In this regard, different studies have tried to utilize new medical or non-medical mechanisms of reducing blood loss during surgery. Nowadays, different pre-operation laboratory tests are performed in order to examine patients' blood and assess its tendency of bleeding through coagulation tests [9].

On the other hand, variable clinical methods and medications have been used in order to reduce bleeding during mastoidectomy. Controlled hypotension using different medications such as nitroglycerin, remifentanil and labetalol has been used in different studies which brought promising results [10-12]. While this methods might also result in some serious complication including: sever bradycardia and reduced perfusions in vital organs (brain, heart, kidneys and etc.) [13]. Furthermore, anesthetic medications might also cause post-operation bleeding. These issues resulted in increased requirements for improving new methods of reducing bleeding during mastoidectomy.

Tranexamic acid is known as a useful medication in reducing bleeding in variable situations such as epistaxis, tooth extraction and during rhinoplasty in patients with hemophilia [14, 15]. Studies have also shown that tranexamic acid has better therapeutic results compared to similar medication like aprotinin [16]. Tran-

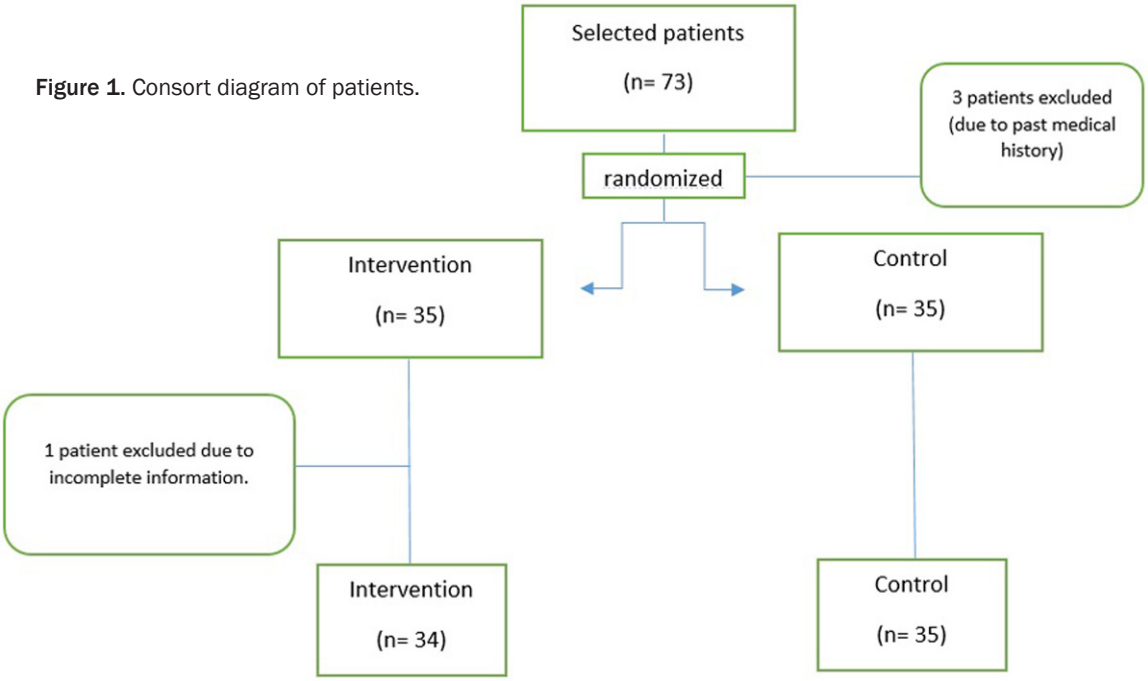

Figure 1. Consort diagram of patients.

examic acid has antifibrinolytic characteristics and inhibits transformations of plasminogen into plasmin [17]. It also acts by impacting on fibrin and forming hemostasis. As a result, tranexamic acid might be an appropriate medication in reducing bleeding during surgeries. In a meta-analysis by Ker and colleagues, they had a survey on effects of tranexamic acid in reducing bleeding during different surgeries. They included 129 studies with 10488 patients and indicated that tranexamic acid decreases the need for blood transfusion 33% during surgeries and also decreases bleeding [18]. To the best of our knowledge, no previous study has evaluated effects of tranexamic acid in reducing bleeding during mastoidectomy in Tehran. As a result, we aimed to investigate this issue in the current paper.

Methods and material

This study is a randomized double-blinded clinical trial performed in 2018 in Imam Khomeini hospital and Ordibehesht clinic in Tehran. The present study was approved ethically by ethical committee of Tehran University of Medical Sciences. Our study population was consisted of all patients who were candidates of mastoidectomy referred to Imam Khomeini hospital and Khordad clinic. We conducted sample size evaluations and 33 patients were calculated in each group. Overall, we included 70 patients in both groups and 35 in each group. Our inclusion criteria were: age between 20-70 and being a candidate for mastoidectomy by decision of an expert otolaryngologist. Our exclusion criteria were: patient's refusal, having hypertension, previous history of ischemic heart diseases and any allergies to tranexamic acid. It should also be noted that any changes of surgical procedures or medications was considered as an exclusion criteria. All patients signed informed consent and surgical approaches and procedures were explained for each patient.

Demographic data of patients including age and sex were collected. All information regarding to past medical history such as diabetes, hypertension, cardiovascular diseases and smoking were also gathered. All patients divided into two groups each containing 35 patients. This procedure was performed using computed randomization. The study was double-blinded meaning that surgeon, patients and the collector of information were not aware of the groups of patients and medications.

Patients underwent mastoidectomy under the same condition. Anesthetic medications were sodium thiopental (5 mg/kg), atracurium (0.5 mg/kg) and fentanyl (2 μg/kg). Anesthetic pro-

Table 1. Demographic data of patients

Variable		Group		*p*-value
		Tranexamic acid	Control	
Age (year) (mean ± SD)		32.87±7.9	33.20±6.25	0.52
Sex (number (%))	Male	20 (58.8)	18 (51.4)	0.74
	Female	14 (41.2)	17 (48.6)	

Table 2. Heart rate of patients during surgeries in different times (mean ± SD)

Time (minute)	Group		*p*-value
	Tranexamic acid	Control	
0	74.2±5.1	75.0±4.5	0.344
15	71.4±7.2	77.5±5.6	0.227
30	74.3±6.9	77.8±4.0	0.712
45	72.4±5.8	75.1±5.7	0.616
60	74.1±6.4	74.2±6.2	0.224
75	73.2±7.2	73.8±5.4	0.257
90	73.4±5.0	74.2±4.8	0.662
105	73.7±6.2	72.9±5.2	0.389
120	73.9±4.5	75.3±5.2	0.455

Table 3. Systolic blood pressure of patients during surgeries in different times (mean ± SD)

Time (minute)	Group		*p*-value
	Tranexamic acid	Control	
0	117.7±6.6	119.1±6.3	0.144
15	117.4±6.2	117.5±6.0	0.130
30	115.5±5.8	116.8±5.4	0.110
45	111.2±5.4	113.3±5.0	0.039
60	110.5±4.7	112.5±4.9	0.007
75	108.4±4.0	110.8±4.6	<0.001
90	106.9±3.5	110.4±4.4	<0.001
105	106.3±3.1	109.6±3.9	<0.001
120	104.9±2.9	108.2±3.8	<0.001

cedure continued using isoflurane, N_2O and oxygen along with morphine (0.1 mg/kg). In order to reduce bleeding during surgery, the first group of patients received remifentanil (0.1 μg/kg/min) with tranexamic acid (10 mg/kg) at the beginning of surgeries. The control group received only remifentanil (0.1 μg/kg/min) with normal saline with equal volume as placebo. All of the mastoidectomy procedures were performed by a single surgeon. Data regarding to heart rate, systolic and diastolic blood pressure and mean blood pressure of patients were collected in 30, 45, 60, 75, 90, 105, 120 minutes during surgeries. Blood pressures and heart rates were assessed by operation room monitors. Total bleeding volume in both groups were also noted in cc and analyzed. Duration of surgeries was another evaluated parameter which was measured by our research team.

Statistical analysis

Data analysis was performed using SPSS software version 20. Qualitative variables were analyzed using X^2 tests and independent t test was used for quantitative variables. Mann-Whitney test was also used for further analysis. Multiple time points between the two groups were performed using ANOVA test.

Results

A total of 73 patients were included in this study but 3 patients excluded due to their past medical history. 1 patient was also excluded during the study due to incomplete information. Consort diagram of patients is presented in **Figure 1**. Our study population consisted of 38 (55%) males and 31 (45%) females. Mean age of patients was 33±6.8. Initial analysis showed that there was no significant difference between two groups of patients regarding to age and sex (**Table 1**).

Analysis of hemodynamic index showed that no significant differences were observed between two groups regarding to heart rate, systolic and diastolic and mean blood pressure of patients before surgeries (P>0.05).

No significant differences were also observed between heart rate of two groups during surgeries (P>0.05) (**Table 2**). Evaluating systolic blood pressure during surgeries showed a lower blood pressure in patients receiving tranexamic acid. This reduction was initiated after 30 minutes after surgery initiation (**Table 3**). Diastolic blood pressure of patients who received tranexamic acid were also significantly lower after 30 minutes after surgery initiation (**Table 4**). Same results were observed for mean arterial blood pressure of patients who were treated with tranexamic acid. The results regarding to mean arterial blood pressure are summarized in **Table 5**.

We also showed a significant lower bleeding volume during surgeries in tranexamic acid group compared with control group (P<0.001)

Table 4. Diastolic blood pressure of patients during surgeries in different times (mean ± SD)

Time (minute)	Group		*p*-value
	Tranexamic acid	Control	
0	77.8±8.8	79.6±8.1	0.751
15	76.2±8.4	78.3±7.5	0.334
30	73.5±7.9	77.5±6.4	0.007
45	71.2±6.5	77.0±6.0	<0.001
60	68.5±5.4	75.6±5.6	<0.001
75	66.4±5.0	74.2±5.3	<0.001
90	65.3±4.3	73.2±5.0	<0.001
105	65.0±3.5	72.0±4.8	<0.001
120	63.1±2.6	71.2±4.2	<0.001

Table 5. Mean blood pressure of patients during surgeries in different times (mean ± SD)

Time (minute)	Group		*p*-value
	Tranexamic acid	Control	
0	93.1±6.4	94.2±5.6	0.366
15	89.8±6.1	92.4±5.2	0.201
30	87.0±5.3	91.0±4.7	0.003
45	85.2±5.0	88.8±4.7	<0.001
60	82.5±4.7	88.2±4.4	<0.001
75	80.3±4.0	87.0±4.1	<0.001
90	79.6±3.2	86.5±4.0	<0.001
105	77.0±2.6	84.7±3.9	<0.001
120	75.2±2.4	83.1±3.7	<0.001

Table 6. Bleeding, surgery duration and recovery time in groups (mean ± SD)

Variable	Group		*p*-value
	Tranexamic acid	Control	
Bleeding volume (ml)	60.2±17.5	90.4±26.4	<0.001
Surgery duration (min)	161.3±16.6	157.0±14.9	0.264
Recovery time (min)	47.8±6.6	44.8±8.1	0.227

but no significant difference was observed between two groups regarding to duration of surgeries or recovery time (**Table 6**).

Discussion

In the present study, we evaluated effects of tranexamic acid in reducing bleeding during mastoidectomy and indicated that using tranexamic acid is associated with less bleeding. We also showed that patients who receive tranexamic acid have lower blood pressures during surgeries. So far, no previous study has evaluated effects of tranexamic acid on bleeding during mastoidectomy in Tehran. Different studies have evaluated impacts of tranexamic acid on bleeding during variables surgeries in head and neck regions [14, 19]. Evidence indicated that the use of tranexamic acid is associated with lower bleeding during surgeries such as sinus endoscopy, rhinoplasty and tonsillectomy [20, 21]. In a by Das and colleagues, they evaluated the effect of tranexamic acid on intra-operative bleeding and surgical field visualization during endoscopic tympanoplasty, endoscopic atticotomy or mastoidectomy, endoscopic ossiculoplasty, and endoscopic stapedotomy. They reported that the use of tranexamic acid is associated with less bleeding and better visual fields during microscopic surgeries [22]. These results are in line with the results of our study. Godier and others also had a survey on characteristics of tranexamic acid and showed that early administration of this drug especially in traumatic patients is associated with reduced bleeding and mortality events. They also supported the idea that tranexamic acid has acceptable antithrombotic effects which make this drug suitable for systematic use during operations [23].

In another study by Guerriero and others in 2011, they evaluated cost effectiveness of tranexamic acid administration in traumatic patients and indicated that this drug is highly cost effective. They also suggested that intra-operative use of tranexamic acid should be evaluated [24]. These reports support this idea that tranexamic acid is a proper drug for reducing intra-operation bleeding as well as other clinically important situations. The use of tranexamic acid has also been proven in reducing blood loss during menstruation in women with heavy menstrual bleeding [25]. In another study by Ker and others in 213, topical usage of tranexamic acid has been investigated. They declared that systemic usage of tranexamic acid might be associated with thromboembolic events and as a result, topical usage of tranexamic acid could be a better option. They concluded that topical administration of this drug is also efficient and causes

reduction in surgical site bleeding however, its effects on the risk of thromboembolic events is uncertain [26]. There have been also studies that evaluated effects of systemic administration of tranexamic acid after cardiac [27] and orthopedic [28] surgeries and also in traumatic patients [29]. These studies indicated efficacy of tranexamic acid in reduction of bleeding in different situations. Here we showed that tranexamic acid could also be used in microscopic surgeries of head and neck area which require a clean visual field. As a result, we suggest that this method should be used by otolaryngologists and especially in microscopic surgeries.

Conclusion

Here we evaluated effects of systemic administration of tranexamic acid in reducing intraoperative bleeding during mastoidectomy. This survey along with previous data put emphasis on efficacy of tranexamic acid for variable surgeries especially microscopic surgeries which require a clean visual field.

Disclosure of conflict of interest

None.

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