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Comparison of the therapeutic efficacy of topical tranexamic acid, epinephrine, and lidocaine in stopping bleeding in non-traumatic epistaxis: a prospective, randomized, double-blind study

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Abstract. – OBJECTIVE: Nasal packing is used to stop bleeding in cases of epistaxis. Different topical drugs are preferred to these packs in the emergency department. In this study, we aimed to compare the efficacy of lidocaine, epinephrine and tranexamic acid (TXA) in stopping bleeding in patients with epistaxis.

PATIENTS AND METHODS: Patients with non-traumatic epistaxis were evaluated in three treatment groups as topical lidocaine, epinephrine, and TXA. These treatments were applied prospectively in a double-blind manner and randomized manner. The bleeding stop times of the patients were recorded with bleeding time parameters.

RESULTS: A total of 108 patients were included in the study. The mean age of the patients was 55.7±17.7 years. When the bleeding stop times were compared between the groups, there was no statistically significant difference (lidocaine *vs.* epinephrine, p=0.870; lidocaine *vs.* TXA, p=0.502; and epinephrine *vs.* TXA, p=0.242). The systolic blood pressure value statistically significantly differed between the lidocaine and epinephrine groups (p=0.034) and between the epinephrine and TXA groups (p=0.003). There was also a statistically significant difference between the diastolic blood pressure values of the epinephrine and TXA groups (p=0.020).

CONCLUSIONS: We found that nasal packing with lidocaine, epinephrine and TXA was not superior to each other in terms of stopping bleeding time.

Key Words:
Epistaxis, Nasal packing, Tranexamic acid, Epinephrine, Lidocaine.

Introduction

Epistaxis is very common among emergency hemorrhagic cases, constituting approximately one-third of otolaryngological emergencies[1]. The majority (90%) of these cases are anterior nosebleeds, and the remainder (10%) are posterior nosebleeds[2]. Bleeding is usually self-limiting[3], but as with other bleeding cases, compression works in managing epistaxis for patients requiring treatment[4]. Nasal packing is also recommended for the basic management of epistaxis. If bleeding still does not stop, topical agents, such as oxymetazoline, phenylephrine hydrochloride, epinephrine, and lidocaine, can be used[5,6]. In addition, tranexamic acid (TXA), an anti-fibrinolytic agent used in major trauma and surgery, can also be applied to increase hemostasis[7]. However, the use of phenylephrine, oxymetazoline, and epinephrine is neither recommended nor indicated in hypertensive patients with epistaxis[8].

Based on the hemorrhagic properties of the above-mentioned agents, the preferred topical applications may show clinical differences in emergency departments (EDs). Studies have been conducted to evaluate topical agents, their efficacy, and bleeding time[9,10]. Studies on the efficacy, hemodynamic effects, and safety of these agents in epistaxis have mostly focused on facilitating nasotracheal intubation in operating rooms[11,12]. However, to our knowledge, no study has yet compared the efficacy of topical TXA, epinephrine, and lidocaine in controlling epistaxis. In

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our study, we evaluated the efficacy of the topical applications of TXA, lidocaine, and epinephrine in a prospective, double-blind, and randomized manner in patients admitted to the ED with non-traumatic anterior epistaxis.

Patients and Methods

Ethical Approval and Patient Selection

The study started after obtaining the Ethical Approval from the Clinical Research Ethics Committee of Atatürk University Faculty of Medicine (meeting number 3, decision number 6, dated 4/15/2021). The study was conducted in a prospective, randomized, double-blind, and controlled manner with a sample of randomly selected patients over a 6-month period.

Patients were selected from cases of non-traumatic nosebleeds admitted to the ED of a university hospital. The exclusion criteria were as follows: not agreeing to participate in the study, bleeding having stopped by the time the patient presented to the ED, age under 18 years, presence of post-traumatic nosebleed or bleeding disorders, use of blood thinners, history of hypertension (HT), drug abuse, and allergy to one of the treatment agents. In addition, patients with septal perforation and a recent history of nasal surgery were also excluded from the study.

Study Protocol

Written consent was obtained from all patients. Neither the patient nor the physician applying the nasal packing knew what treatment would be applied to each patient. Research Randomizer (https://www.randomizer.org/#randomize) was used to generate a randomized ordered list of patients to be administered nasal packing. A physician placed the agents to be used for nasal packing in colorless, transparent, indistinguishable boxes. The tops of the boxes were numbered 1, 2, and 3. Only the physician who prepared them knew their contents. The TXA (Transamine 50 mg/ml intravenous), epinephrine (Adrenalin 1 mg 1:1000 1 ml intramuscular, intravenous, subcutaneous) and lidocaine (Lidocaine HCl 1% 10 mg/ml intramuscular, intravenous, subcutaneous) agents reserved for the study were checked weekly for the possibility of expiration or spoilage. Nasal packing applications were performed by another physician, who did not know the agent contained in the pack. The physician applied the nasal packing treatments accompanied by a nurse in a double-blind and randomized manner. For the procedure, the patient's head was positioned at a 45° angle under appropriate lighting. The agents were absorbed onto cotton strips. After the nasal packing was placed, a chronometer was started by a healthcare professional who assisted the physician. The moment when bleeding stopped was evaluated based on the absence of salivary bleeding in the nasopharynx and the absence of any bleeding in the form of leakage on the packing. When this was achieved, the chronometer was stopped, and the bleeding stop time was recorded.

At the time of admission, the patients' arterial blood pressure and heart rate values were measured before the nasal packing application. The serum platelet count, prothrombin time, activated partial thromboplastin time and international normalized ratio values, and bleeding stop times were recorded. The packing was checked frequently. The patients included in the study were evaluated in three separate groups: topical lidocaine, epinephrine, and TXA. For patients whose bleeding continued for 20 minutes despite nasal packing, consultation from an otolaryngologist was requested. For these patients, bleeding was stopped by cauterization.

Statistical Analysis

Statistical analysis was performed using SPSS software, version 25.0 (IBM Corp., Armonk, NY, USA). The distribution of variables was evaluated for normality using the Kolmogorov-Smirnov test. Descriptive statistics were given as frequency (n) and percentage (%) for categorical variables. In the comparison of continuous variables with more than two independent groups, analysis of variance (ANOVA) was used when the normal distribution condition was met, and the Kruskal-Wallis test otherwise. Following the ANOVA test, post-hoc tests were performed using the Tukey test when variances were homogeneous and Tamhane's T2 test when variances were not homogeneous. The statistical significance level was set at $p<0.05$.

G-Power 3.1 software was used to calculate the sample size for the study. During this process, the medium effect size was set at 0.5, type 1 error at 0.05, and power at 0.8. Considering 10% missing data, the sample size for the study was calculated at 36 patients for each group (108 patients with an allocation ratio of 1:1:1).

Results

The study was initially planned with 293 patients. However, 185 patients were excluded due

to a history of HT (n=91), anticoagulant use (n=42), traumatic nosebleed (n=23), bleeding that did not stop despite nasal packing (n=13), refusal to participate in the study (n=9), and bleeding occurring after nasal surgery (n=7). As a result, the study was conducted with 108 patients who met the inclusion criteria (Figure 1). 13 patients' bleeding did not stop. In these patients, lidocaine (n=5), TXA (n=4), and epinephrine (n=4) were used. The mean patient age was 55.7 ± 17.7 years. When evaluated according to the group, the mean age was 56.0 ± 18.1 years for the lidocaine group (n=36), 52.5 ± 15.5 years for the epinephrine group (n=36), and 59.0 ±19.0 years for the TXA group (n=36). Fifty-one (47.2%) patients included in the study were female, and 57 (52.8%) were male. Eight (7.5%) of the 108 patients had a previous history of epistaxis. The detailed demographic data of the patients are given in Table I.

The mean bleeding stop times were 9.9 ± 3.2 min for the lidocaine group, 10.3 ± 4.5 min for the epinephrine group, and 8.9 ± 3.4 min for the TXA group. These parameters were not statistically significantly different between any of the groups (lidocaine *vs.* epinephrine: p=0.870; lidocaine *vs.* TXA: p=0.502; epinephrine *vs.* TXA: p=0.242) (Table II) (Figure 2).

When the arterial blood pressure was evaluated, the mean systolic blood pressure was 142.8 ± 21.2 mmHg for the lidocaine group, 132.3 ± 10.6 mmHg for the epinephrine group, and 146.5 ± 19.4 mmHg for the TXA group. The systolic blood pressure values were statistically significantly different between the lidocaine and epinephrine

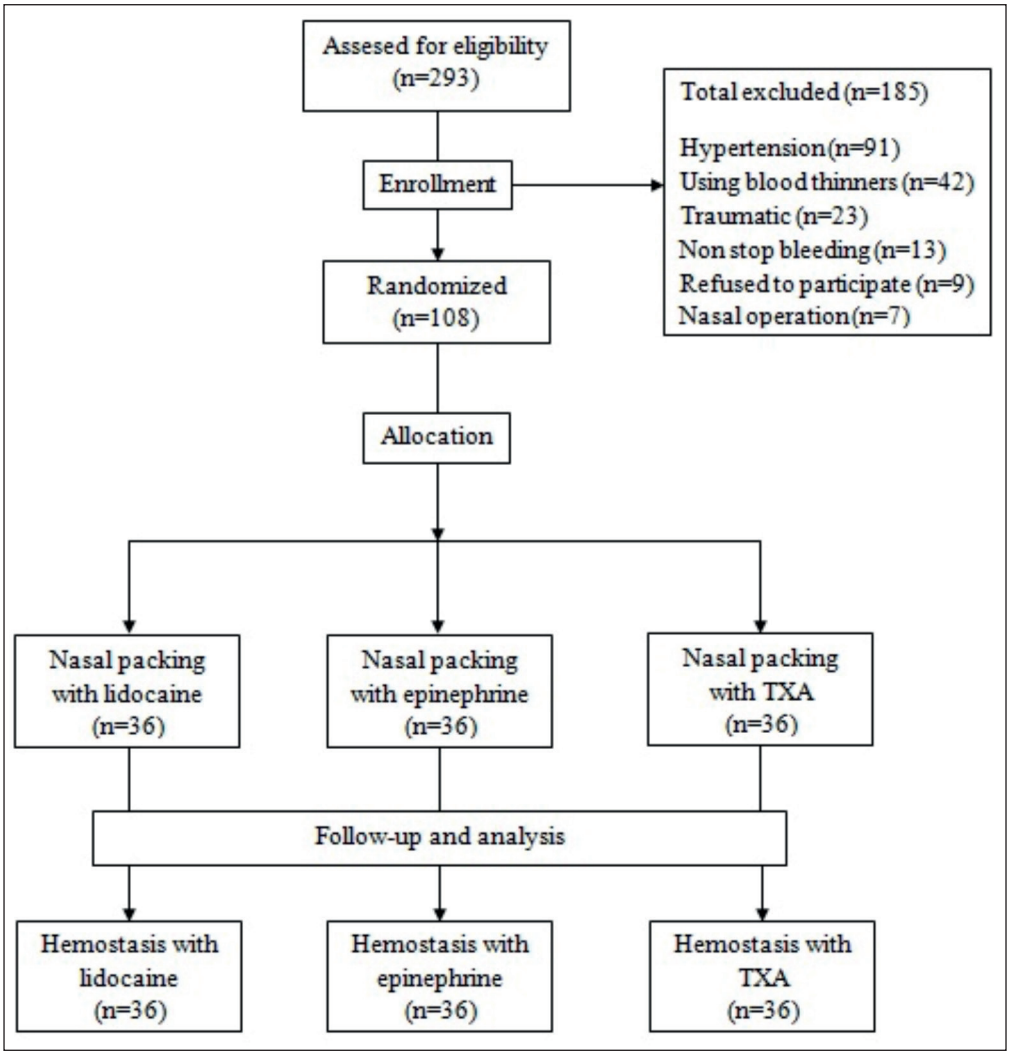

Figure 1. Patient allocation flowchart.

Table I. Demographic characteristics of the patients.

Characteristic	Treatment			Total (n = 108)
	Lidocaine (n = 36)	Epinephrine (n = 36)	TXA (n = 36)	
Age (years)	56.0 ± 18.1	52.5 ± 15.5	59.0 ± 19.0	55.7 ± 17.7
Gender				
Female	20 (55.6%)	16 (44.4%)	15 (41.7%)	51 (47.2%)
Male	16 (44.4%)	20 (55.6%)	21 (58.3%)	57 (52.8%)
Epistaxis history				
Present	0 (0%)	2 (5.6%)	6 (16.7%)	8 (7.5%)
Absent	36 (100%)	34 (94.4%)	30 (83.3%)	100 (92.5%)

TXA: Tranexamic acid. Statistics are given as either n (%) (for categorical variables) or mean ± SD (for continuous variables).

group (p=0.034) and between the epinephrine and TXA group (p=0.03). The mean diastolic blood pressure value was 84.5 ± 11.6 mmHg for the lidocaine group, 79.1 ± 8.0 mmHg for the epinephrine group, and 85.5 ± 9.4 mmHg for the TXA group. A statistically significant difference was found between the diastolic blood pressure values of the epinephrine and TXA groups (p=0.020). There was no statistically significant difference between the three groups in relation to their heart rate values (p>0.05) (Table II).

When the hemostasis parameters of the patients were evaluated, the mean platelet count was 273.6 ± 43.3 10^3/μL for the lidocaine group, 240.6 ± 47.8 10^3/μL for the epinephrine group, and 288.1 ± 92.4 10^3/μL for the TXA group.

All patients included in the study were kept under observation in the ED for 60 minutes, due to the possibility of bleeding recurrence after the bleeding stopped. Since none of the patients whose bleeding stopped had re-bleeding, all patients were discharged from the ED. In addition,

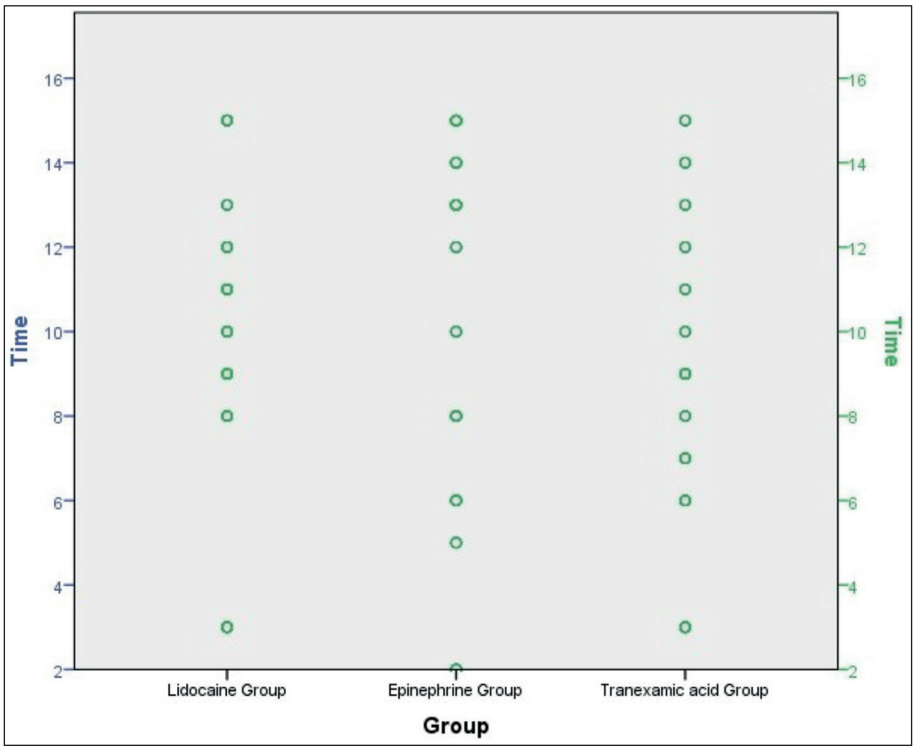

Figure 2. Comparison of the groups according to the bleeding stop time.

Table II. Comparison of the blood parameters, vital signs, and bleeding stop times between the groups.

Variable	Lidocaine	Epinephrine	TXA	*p1**	*p2**	*p3**
Bleeding's stop time (min)	9.9 ± 3.2	10.3 ± 4.5	8.9 ± 3.4	0.870	0.502	0.242
Systolic blood pressure (mmHg)	142.8 ± 21.2	132.3 ± 10.6	146.5 ± 19.4	**0.034**	0.666	**0.003**
Diastolic blood pressure (mmHg)	84.5 ± 11.6	79.1 ± 8.0	85.5 ± 9.4	0.056	0.900	**0.020**
Heart rate (min)	86.3 ± 9.5	88.7 ± 9.9	88.0 ± 10.5	0.701	0.864	0.958
Prothrombin time (sec)	12.9 ± 2.2	12.5 ± 1.7	12.2 ± 1.1	0.595	0.208	0.736
aPTT (sec)	27.1 ± 6.9	25.4 ± 3.7	24.7 ± 3.3	0.310	0.102	0.810
INR	1.08 ± 0.20	1.05 ± 0.60	1.02 ± 0.90	0.633	0.196	0.680

p1: lidocaine *vs.* epinephrine, *p2*: lidocaine *vs.* TXA, *p3*: epinephrine *vs.* TXA. TXA: Tranexamic acid, aPTT: Activated partial thromboplastin time, INR: International normalized ratio. Data are presented as mean ± SD. *Analysis of variance.

no drug-related side effects were observed for any of the three treatments applied.

Discussion

Epistaxis affects 60% of people during their lifetime, and 70-80% of epistaxis cases are idiopathic[13]. This bleeding can also occur due to various other causes, such as trauma and coagulopathy[13]. In epistaxis cases presenting to the ED, the efficacy of the agents used in anterior nasal packing to stop the bleeding remains a matter of debate. Among the most common treatment methods are direct nasal compression, application of topical agents including vasoconstrictors, cauterization of the bleeding site, and packing with various absorbable or non-absorbable materials[14]. The current literature supports that topical oxymetazoline, cautery, nasal packing, and topical TXA may be effective for epistaxis[15]. However, no studies have yet compared the efficacy of topically applied lidocaine, epinephrine, and TXA in epistaxis. Therefore, our study is the first to investigate the efficacy of these three agents in epistaxis.

Amini et al[16] conducted a study investigating patients using aspirin or clopidogrel who were admitted to the ED with anterior epistaxis. The authors compared the effectiveness of topical TXA and anterior nasal packing with phenylephrine-lidocaine to treat epistaxis in these patients. The mean bleeding stop time was 6.70 ± 2.35 minutes in the TXA group and 11.50 ± 3.64 minutes in the phenylephrine-lidocaine group. The authors suggested that TXA was an effective treatment option in stopping bleeding, reducing re-bleeding, and decreasing hospital stay in patients with epistaxis taking antiplatelet agents[16]. In the current study, we also examined the effects of topical TXA and lidocaine in patients with epistaxis. We observed that the two agents had similar bleeding stop times, with neither being superior to the other. One reason why our results diverged from those of Amini et al[16] may be that we excluded all patients who were using antiplatelets or anticoagulants. In order to obtain more reliable data, these patients were excluded from our study since there would have been a difference in the coagulation cascade of patients using antiplatelets or anticoagulants.

TXA has been shown to be beneficial in various hemorrhagic conditions, including traumatic hemorrhage, post-adenoidectomy, and endoscopic sinus surgery[7,17,18]. In a study comparing TXA with oxymetazoline in 38 patients, it was found that TXA was more effective than oxymetazoline in providing hemostasis in anterior epistaxis[9]. Recent studies have shown that the topical use of intravenous TXA is effective in the emergency treatment of epistaxis. For example, one study found that the topical application of intravenous TXA was superior to anterior nasal packing in anterior epistaxis[19]. In another study, hemostasis was achieved in 71% of patients treated with topical TXA and 31.2% of patients treated with only anterior nasal packing[20]. In our study, TXA packing was applied to one group of patients with anterior epistaxis, and hemostasis was achieved in all these cases. In addition, concerning the bleeding stop times of lidocaine, epinephrine, and TXA in epistaxis, we found that they had similar values with no significant differences.

The frequency of nosebleeds generally begins to increase after the age of 20 years. This rate further increases with age, peaking in adults ages 70-79 years[21]. It has been shown that patients presenting to the ED with epistaxis often have high blood pressure[22]. It is known that topical vasoconstrictor agents are contraindicated in patients with HT. However, a previous study reported that these agents did not cause an increase in blood pressure

during treatment[8]. Even so, we excluded hypertensive patients with epistaxis from our study.

Newton et al[23] evaluated 353 patients with epistaxis, of whom 180 (51%) were male and 173 (49%) were female, with a mean age of 70 years. When the patients' comorbidities were examined, HT was present in 198 (56%), diabetes mellitus in 67 (19%), coronary artery diseases in 97 (28%), atrial fibrillation in 94 (27%), hereditary hemorrhagic telangiectasia in 3 (1%), and other blood disorders in 12 (3%) patients. In our study, the mean age of the patients was lower (55.7±17.7 years). However, the gender ratio [51 female (47.2%) and 57 male (52.8%)] was similar to the previous study[23]. The lower mean age of our sample can be attributed to our exclusion of patients with HT and of those using anticoagulant medication.

A previous study[10] compared the efficacy of nasal compression with TXA, simple nasal compression, and nasal packing with a normal saline solution in stopping nosebleeds in 135 patients. The success rates of these applications were 91.1%, 93.3%, and 71.1%, respectively. The authors concluded that nasal compression with TXA was more comfortable for patients with epistaxis than anterior nasal packing. In addition, the mean systolic blood pressure values of the patients were 146 mmHg in the nasal compression with TXA group, 145 mmHg in the simple nasal compression group, and 150 mmHg in the compression with saline group. The mean diastolic blood pressure values were 83 mmHg, 80 mmHg, and 80 mmHg, respectively, and the heart rate values were 88/min, 86/min, and 86/min, respectively. Our study showed similar arterial blood pressure values as the patients in that study.

Studies[24,25] on the use of epinephrine in epistaxis have compared epinephrine and xylometazoline in reducing bleeding in nasotracheal intubation, which is mostly undertaken in maxillofacial surgery. Different topical vasoconstrictors (cocaine, epinephrine, phenylephrine, xylometazoline, and oxymetazoline) have been used to reduce the incidence of epistaxis[26]. In a study conducted by Song[24] with 80 patients (40 treated with xylometazoline spray and 40 with epinephrine packing), the two treatments had similar efficacy in reducing bleeding during nasotracheal intubation. Furthermore, the author found no significant differences between the two methods regarding complications related to nasotracheal intubation. In a similar study[25] evaluating 110 patients (55 in the xylometazoline packing group and 55 in the epinephrine packing group) during nasotracheal intubation, Patel et al[25] observed no statistically significant difference between the two groups. In the current study, hemostasis was achieved in all patients who received epinephrine packing. In addition, we determined that TXA, epinephrine, and lidocaine had very similar efficacy in stopping bleeding.

There were some limitations to the content of our study. The first was the small sample size of 108 patients. Second, patients with posterior epistaxis were excluded from the study, due to the inability to perform interventions in these cases under ED conditions. Third, we did not use absorbable and inflatable sponges that are commonly used in practice because these are non-drug methods of stopping nosebleeds. Fourth, the severity of bleeding was lower in some of the patients due to their late arrival times, thus affecting the efficacy of treatment, albeit partially. Fifth, we excluded patients who used blood thinners or had a history of HT.

Conclusions

In cases of epistaxis, it is important for the nosebleed to be stopped as soon as possible after the arrival at the ED for the patient's comfort. Nasal packing with topical lidocaine, epinephrine, or TXA can be used to control epistaxis in these patients. When we examined which agent provided hemostasis earlier, we did not find any nasal packing application to be superior to the others in terms of bleeding stop time. Therefore, we can conclude that all the three agents can be safely used to stop bleeding in patients presenting nosebleeds, according to the physician's preference.

Conflict of Interest

The authors declare no conflicts of interest.

Financial Supports

This research did not receive any financial support.

Ethical Approval

This study started after obtaining the ethical approval from the Clinical Research Ethics Committee of Atatürk University Faculty of Medicine (meeting number 3, decision number 6, dated 4/15/2021).

All procedures performed in studies involving human participants were done in accordance with the ethical standards of the Institutional and/or National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent
Informed consent was obtained from all participants included in the study.

Authors' Contribution
ME, LS and AG: Concept and design of study or acquisition of data or analysis and interpretation of data, drafting the article or revising it critically for important intellectual content, final approval of the version to be published.

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References

1) Cohen O, Shoffel-Havakuk H, Warman M, Tzelnick S, Haimovich Y, Kohlberg GD, Halperin D, Lahav Y. Early and later ecurrent epistaxis admissions: patterns of incidence and risk factors. Otolaryngol Head Neck Surg 2017; 157: 424-431.
2) Krulewitz NA, Fix ML. Epistaxis. Emerg Med Clin North Am 2019; 37: 29-39.
3) Viehweg TL, Roberson JB, Hudson J. Epistaxis: diagnosis and treatment. J Oral Maxillofac Surg 2006; 64: 511-5118.
4) Corbridge R, Djazaeri B, Hellier W, Hadley J. A prospective randomized controlled trial comparing the use of merocel nasal tampons and BIPP in the control of acute epistaxis. Clin Otolaryngol Allied Sci 1995; 20: 305-307.
5) Tangbumrungtham N, Hwang PH, Maul X, Borchard NA, Dholakia SS, Patel ZM, Nayak JV, Choby G. The effect of topical epinephrine 1:1000 with and without infiltration of 1% lidocaine with epinephrine 1:100,000 on endoscopic surgical field visualization: a double-blind randomized controlled study. Int Forum Allergy Rhinol 2020; 10: 147-152.
6) Barnes ML, Spielmann PM, White PS. Epistaxis: a contemporary evidence based approach. Otolaryngol Clin North Am 2012; 45: 1005-1017.
7) Roberts I, Shakur H, Coats T, Hunt B, Balogun E, Barnetson L, Cook L, Kawahara T, Perel P, Prieto-Merino D, Ramos M, Cairns J, Guerriero C. The CRASH-2 trial: a randomised controlled trial and economic evaluation of the effects of tranexamicacid on death, vascular occlusive events and transfusion requirement in bleeding trauma patients. Heal Technol Assess 2013; 17: 1-79.
8) Bellew SD, Johnson KL, Nichols MD, Kummer T. Effect of Intranasal Vasoconstrictors on Blood Pressure: A Randomized, Double-Blind, Placebo-Controlled Trial. J Emerg Med 2018; 55: 455-464.
9) Whitworth K, Johnson J, Wisniewski S, Schrader M. Comparative Effectiveness of Topically Administered Tranexamic Acid Versus Topical Oxymetazoline Spray for Achieving Hemostasis in Epistaxis. J Emerg Med 2020; 58: 211-216.
10) Akkan S, Çorbacıoğlu ŞK, Aytar H, Emektar E, Dağar S, Çevik Y. Evaluating effectiveness of nasal compression with tranexamicacid compared with simple nasal compression and merocel packing: a randomized controlled trial. Ann Emerg Med 2019; 74: 72-78.
11) Kameyama K, Watanabe S, Kano T, Kusukawa J.Effects of nasal application of an epinephrine and lidocaine mixture on the hemodynamics and nasal mucosa in oral and maxillofacial surgery. J Oral Maxillofac Surg 2008; 66: 2226-2232.
12) Saif AM, Farboud A, Delfosse E, Pope L, Adke M. Assessing the safety and efficacy of drugs used in preparing the nose for diagnostic and therapeutic procedures: a systematic review. Clin Otolaryngol 2016; 41: 546-563.
13) Bridwell RE, April MD, Long B. Does Oral or Topical Tranexamic Acid Control Bleeding From Epistaxis? Ann Emerg Med 2019; 74: 300-302.
14) Tunkel DE, Anne S, Payne SC, Ishman SL, Rosenfeld RM, Abramson PJ, Alikhaani JD, Benoit MM, Bercovitz RS, Brown MD, Chernobilsky B, Feldstein DA, Hackell JM, Holbrook EH, Holdsworth SM, Lin KW, Lind MM, Poetker DM, Riley CA, Schneider JS, Seidman MD, Vadlamudi V, Valdez TA, Nnacheta LC, Monjur TM. Clinical Practice Guideline: Nosebleed (Epistaxis). Otolaryngology Head Neck Surg 2020; 162: 1-38.
15) Kamhieh Y, Fox H. Tranexamic acid in epistaxis: a systematic review. Clin Otolaryngol 2016; 41: 771-776.
16) Amini K, Arabzadeh A, Jahed S, Amini P. Topical Tranexamic Acid versus Phenylephrine-lidocaine for the Treatment of Anterior Epistaxis in Patients Taking Aspirin or Clopidogrel; a Randomized Clinical Trial. Arch Acad Emerg Med 2020; 9: e6.
17) Alimian M, Mohseni M. The effect of intravenous tranexamic acid on blood loss and surgical field quality during endoscopic sinus surgery: a placebocontrolled clinical trial. J Clin Anesth 2011; 23: 611-615.
18) Albirmawy OA, Saafan ME, Shehata EM, Basuni AS, Eldaba AA. Topical application of tranexamic acid after adenoidectomy: a double-blind, prospective, randomized, controlled study. Int J Pediatr Otorhinolaryngol 2013; 77: 1139-1142.
19) Zahed R, Moharamzadeh P, Alizadeharasi S, Ghasemi A, Saeedi M. A new and rapid method for epistaxis treatment using injectable form of tranexamic acid topically: a randomized controlled trial. Am J Emerg Med 2013; 31: 1389-1392.
20) Zahed R, Mousavi Jazayeri MH, Naderi A, Naderpour Z, Saeedi M. Topical Tranexamic Acid Compared With Anterior Nasal Packing for Treatment

of Epistaxis in Patients Taking Antiplatelet Drugs: Randomized Controlled Trial. Acad Emerg Med 2018; 25: 261-266.

21) Pallin DJ, Chng YM, McKay MP, Emond JA, Pelletier AJ, Camargo CA Jr. Epidemiology of epistaxis in US emergency departments, 1992 to 2001. Ann Emerg Med 2005; 46: 77-81.

22) Kikidis D, Tsioufis K, Papanikolaou V, Zerva K, Hantzakos A. Is epistaxis associated with arterial hypertension? A systematic review of the literature. Eur Arch Otorhinolaryngol 2014; 271: 237-243.

23) Newton E, Lasso A, Petrcich W, Kilty SJ. An outcomes analysis of anterior epistaxis management in the emergency department. J Otolaryngol Head Neck Surg 2016; 45: 24.

24) Song J. A comparison of the effects of epinephrine and xylometazoline in decreasing nasal bleeding during nasotracheal intubation. J Dent Anesth Pain Med 2017; 17: 281-287.

25) Patel S, Hazarika A, Agrawal P, Jain D, Panda NK. A prospective randomized trial of xylometazoline drops and epinephrine merocele nasal pack for reducing epistaxis during nasotracheal intubation. J Dent Anesth Pain Med 2020; 20: 223-231.

26) El-Seify ZA, Khattab AM, Shaaban AA, Metwalli OS, Hassan HE, Ajjoub LF. Xylometazoline pretreatment reduces nasotracheal intubation-related epistaxis in paediatric dental surgery. Br J Anaesth 2010; 105: 501-505.