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Topical tranexamic acid for the treatment of acute epistaxis in the emergency department☆

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ABSTRACT

Objective: To evaluate the effectiveness and potential benefits of topical tranexamic acid (TXA) in the management of acute epistaxis.
Methods: Retrospective review was performed among all patients presenting to the institution's emergency department (ED) with epistaxis between September 2014 and August 2016. Patients achieving hemostasis with standard of care agents, such as oxymetazoline, lidocaine, or epinephrine were excluded. The primary outcome was the ED length of stay (LOS). Secondary outcomes included the incidence of hospital admission, otolaryngologist consultation, nasal packing, prophylactic antibiotic use, and ED visit for rebleeding within seven days of treatment.
Results: Among 122 patients, 30 received topical TXA (500 mg injectable solution soaked onto packing material and applied to the affected nostril) and 92 were managed with standard care. Nearly half (46.7%) of TXA-treated subjects received TXA either alone or in combination with standard of care agents as their initial treatment strategy. No significant difference was observed in the ED LOS (272 vs 232 min in TXA and standard care arms, respectively, $p = 0.26$). However, TXA was associated with a significant reduction in otolaryngologist consults (30.0% vs 65.2%, $p = 0.002$) and nasal packing (16.7% vs 23.9%, $p = 0.003$).
Conclusions: This investigation did not demonstrate a significant difference in ED LOS among patients with acute epistaxis treated with topical TXA or standard care. However, this data does add to existing evidence that TXA may be associated with a reduction in resource utilization, suggesting it may provide more effective bleeding control. Overall, more data is needed to confirm the potential benefits of this practice.

1. Introduction

It is estimated that 60% of the world's population will experience epistaxis throughout their lifetime [1]. Most nosebleeds are self-limiting and can be managed in an outpatient setting, but approximately 6% of cases require medical attention, making epistaxis a common chief complaint in the emergency department (ED).

Initial management of epistaxis includes application of topical vasoconstrictors and local anesthetics, such as phenylephrine, oxymetazoline, epinephrine, and lidocaine, in combination with nostril compression [2]. Refractory bleeds require alternative methods, such as nasal packing, cauterization, or surgical ligation which may require involvement of an otolaryngologist. Nasal packing and balloon systems are often kept in place for 1 to 5 days, can cause patient discomfort, and may require prophylactic antibiotics and a follow-up visit for removal. The need for removal can be avoided with some absorbable products, such as oxidized cellulose or topical thrombin. However, these methods can be costly compared to some first line medications [1,3]. Complications of nasal packing can include increased bleeding from traumatic packing, infection, tissue necrosis, or toxic shock syndrome with prolonged packing [2]. Thus, avoidance of these methods using adjunct therapies is preferable.

The use of some topical hemostatic agents, including tranexamic acid (TXA), chitosan, and aminocaproic acid have been reported in the literature for the management of epistaxis [4-7]. TXA, in particular, has been used topically in gel and injectable forms for epistaxis treatment, as well as orally and as intranasal administration for the prevention of rebleeding [4-7]. In one randomized, single-center, parallel group study among 216 patients with idiopathic anterior epistaxis, topically

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applied injectable TXA was associated with a higher portion of patients achieving cessation of bleeding within 10 min compared to topical epinephrine and lidocaine followed by anterior nasal packing [4]. Secondary outcomes also demonstrated significantly fewer rebleeding events within 24 h or seven days and shorter ED length of stay (LOS) after treatment with TXA. Topical TXA's comparatively low cost, ease of administration, and avoidance of follow-up visits compared to conventional nasal packing techniques make it an attractive option for treatment of epistaxis in the ED. It also has the potential to decrease resource utilization by minimizing the need for specialist consultation and reducing ED LOS. The objective of this retrospective cohort study was to assess the effectiveness and potential benefits of the addition of topical TXA to the standard of care compared to standard care alone for the treatment of epistaxis in the ED.

2. Methods

2.1. Setting

This single center, retrospective chart review was conducted at Oregon Health & Science University (OHSU), a 573-bed academic medical center and Level 1 trauma center in Portland, Oregon. It was approved by the institutional review board and informed consent was waived.

2.2. Selection of subjects

Subjects were identified for eligibility if they had visited the ED between September 2014 and August 2016 with a primary diagnosis of epistaxis, as identified by ICD9/10 codes. Included patients must have received the entirety of their epistaxis care at the same institution; those receiving initial treatment at outside facilities before transfer to OHSU were excluded. Those with significant traumatic etiologies who were sent directly to the OR and those with minor bleeds not requiring any interventions were excluded. All patients were treated according to provider discretion. In order to ensure a comparable severity of epistaxis between the comparator groups, patients achieving hemostasis solely with traditional first line therapies including oxymetazoline, lidocaine, or epinephrine were also excluded from the study. Patients with any allergies to the study medications were excluded.

2.3. Data collection

Retrospective chart review of each epistaxis-related hospital encounter was performed. Subjects treated at any point during their stay with topically-applied TXA solution for injection were categorized into the treatment arm. All other subjects with sustained bleeding after the previously-mentioned first line therapies were categorized into the control arm. The primary outcome was the ED LOS among subjects not admitted to the hospital. This was originally designed to be measured from the time of first epistaxis treatment to discharge; however, due to a lack of accurate records for time of administration, the primary outcome was later revised to total ED LOS. Secondary outcomes included the incidence of hospital admission, otolaryngologist consultation, nasal packing, prophylactic antibiotic use, and ED visit for rebleeding within seven days of treatment.

2.4. Statistical analysis

The primary outcome was assessed by use of the Mann-Whitney *U* test. Categorical data were compared with Chi-Square or Fisher Exact tests, as appropriate, using a significance level of 0.05.

3. Results

3.1. Population

Among patients receiving treatment for epistaxis in the ED during the study period, 41 achieved hemostasis with first line agents alone and were excluded. Another five were excluded for receipt of initial treatment at an outside facility and 4 eloped before any treatment was administered. A remaining 122 patients met inclusion criteria; 30 received TXA and 92 were treated with standard care alone. Among 74 patients with the location of epistaxis recorded, 78.3% were anterior bleeds. Notably, patients in the TXA group showed higher rates of antiplatelet therapy, anticoagulant therapy, and disorders associated with risk of bleeding compared to the standard care group, though only the use of left ventricular assist devices (LVADs) was statically significant (Table 1).

3.2. Interventions and outcomes

The majority of subjects in either study arm received initial therapy with a traditional first line agent, though this was less common in the TXA arm (Table 2). Nearly half (46.7%) of patients in the TXA arm received TXA as their initial treatment, either alone or concomitantly with traditional standard of care agents. Among those receiving TXA, administration consisted of 500 mg injectable TXA solution per nostril, soaked onto cotton pledgets or nasal tampons ($n = 29$) or 100 mg aerosolized ($n = 1$).

The number of patients admitted to the hospital did not differ between TXA and standard care arms (Table 3). After removing those admitted to the hospital, the primary outcome was available in 24 TXA and 68 standard care subjects, and was not significantly different between groups (median ED LOS 272 vs 232 min, respectively, $p = 0.26$).

During the entirety of their ED or hospital stay, fewer patients treated with TXA received chemical cauterization (13.3% vs 28.3%, $p = 0.099$) or surgical intervention (3.3% vs 7.6%, $p = 0.450$) compared to those in the standard care arm, though these were not statistically significant. There was a significant reduction observed in the number of otolaryngologist consultations and use of nasal packing among patients treated with TXA (Table 3). Four and 13 patients received transfusions in the TXA and standard care arms, respectively, and no thrombotic events were recorded up to 10 days after treatment.

4. Discussion

Identification of new treatment strategies for epistaxis could have numerous advantages with regards to cost, resource utilization, patient discomfort, and risk for complications. An alternative treatment strategy, such as the addition of topical TXA to standard care, could provide a significant improvement in the current management of epistaxis.

One randomized, single-center, parallel group trial has compared the effect of topical TXA to usual anterior nasal packing [4]. Study subjects ($n = 216$) presenting to the ED with anterior nosebleeds received either a 15 cm cotton pledget soaked in 500 mg of injectable TXA, or a pledget soaked in epinephrine (1:100000) and lidocaine 2% for 10 min followed by anterior packing with tetracycline-soaked pledgets. In this study, cessation of bleeding was achieved within 10 min in more patients treated with TXA than nasal packing (71% vs 31.2%, odds ratio [OR] 2.28, 95% confidence interval [CI] 1.68–3.09, $p < 0.001$) and TXA-treated subjects were more likely to have short ED lengths of stay (discharge in ≤2 h 95.3% vs 6.4%, OR 14.8, 95% CI 7.2–30.4, $p < 0.001$). Additionally, TXA was associated with a reduction in rebleeding events within 24 h (4.7% vs 12.8%, OR 0.36, 95% CI 0.14–0.98, $p = 0.034$) and seven days (2.8% vs 11%, OR 0.26, 95% CI 0.07–0.88, $p = 0.018$). No complications or adverse events were observed, and patients in the TXA group reported higher satisfaction rates than the anterior packing group. However, the control group in this study was treated with

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