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Comparison of topical tranexamic acid versus traditional anterior nasal packing for the treatment of epistaxis

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Abstract: Introduction: Epistaxis is a common condition witnessed in the Emergency department. Due to the discomfort patients experience, the likelihood of complications, and the necessity of following up with their treating physician to remove the nasal packing, it may be reasonable to utilize other drugs to treat epistaxis before nasal packing. It is well-recognized that the antifibrinolytic drug tranexamic acid (TXA) is helpful in various therapeutic contexts where uncontrolled bleeding may be an issue. There is anecdotal data that suggests topical TXA may be helpful for acute epistaxis, but more research is needed.
Material and Method: The Patients were divided into two groups- Group T- A cotton pledget soaked in 5ml of Tranexamic acid (prefilled syringe) and 10 ml of Phenylephrine with 5ml of 2% Lignocaine with 1:1000 adrenaline and Group C- A cotton pledget soaked in 10ml of Phenylephrine with 5ml of 2% Lignocaine with 1:1000 adrenaline with 5ml Normal saline (prefilled syringe). Outcomes recorded were the proportion of patients in both groups who needed anterior nasal packing after 20 minutes of pack removal, the number of patients whose bleeding stopped within ten minutes, the length of stay in the ED, the necessity of cauterization, and a telephonic follow-up conducted by an independent ENT resident using a structured questionnaire to record any episode of rebleeding within 24 hours to five days. Any drug-related side effects were recorded, such as thrombosis, nausea, and hypersensitivity.
Result: Patients requiring anterior nasal packs were less in the Tranexamic acid group (P<0.038). The length of hospital stay was decreased in Group T (P <0.045), and the proportion of patients whose bleeding was stopped within 10 mins was more in Group T (P< 0.04). The incidence of rebleeding within 24 hours decreased in Group T (P< 0.038), but no significant difference was found in rebleeding number within 1-5 days. No minor/major complications to the drug were noted in Group T.
Conclusion: Topical TXA is safe and effective for the cessation of anterior nasal bleeding, thus preventing the use of anterior nasal packing, which is tedious for the patient and medical staff. TXA has been shown to decrease the rate of packing significantly.

Keywords: Epistaxis; Tranexamic acid; Intranasal; Topical; Atraumatic.

1. Introduction

Epistaxis is a frequent cause of a visit to the emergency department whose severity could be from self-limiting to life-threatening [1]. At least 60% of the population has a minimum of one episode of epistaxis during their lifetime, out of which 6% require medical aid [1] and can be life-threatening. Most bleedings can be stopped with just a few simple first aid techniques, like squeezing the anterior tip of the nose, placing an ice pack on the nasal bridge, and assuming a forward lean posture of head [2]. Next in line are vasoconstrictors and electrical cauterization, and the ultimate solution for consistent bleeding has been nasal packing, which is required to be kept for 24 to 48 hours [3–5]. Nasal packs insertion and removal result in mean pain scores (4.5/10) comparable to acute myocardial infarction [6,7]. They have also been shown to lengthen hospital stays by at least two days and increase the risk of complications like infection, airway obstruction,

sleep apnea, and tissue necrosis. The intermediate step between the first aid measures and packing was recently introduced using intravenous tranexamic acid to be placed intranasally for cessation of epistaxis and clot stabilization. Almost 90% of hemorrhaging is anterior in origin. Blood loss is reduced by the competitive inhibition of plasminogen and plasmin8 by TXA, leading to a decrease in fibrinolysis and the formation of fibrin degradation products, thus resulting in clot stability. It is affordable, safe, and easily accessible.

A meta-analysis [9] comprising at least 10,488 patients has shown TXA to decrease the mortality rate and the frequency of blood transfusion. The side effects with 200mg of topical TXA are assumed to be negligible compared to 1gm TXA given intravenously as the plasma concentration is meant to be 1/10 of that of the intravenous route [10]. Being quite a common presentation, an affordable yet effective method must be devised for its control.

Intranasal use of Tranexamic acid will lead to increased intensity of local effects rather than systemic effects [11]. This study aimed to examine the role of intranasal tranexamic acid in patients with atraumatic anterior epistaxis because the findings of earlier multicenter RCTs did not consistently demonstrate its therapeutic effects [12,13].

Our study's main goal was to ascertain if our strategy was beneficial in lowering the rate of anterior nasal packing in persons with spontaneous atraumatic nasal bleeding. The secondary goals are the length of hospital stay, acute rebleeding (within 24 hours), late rebleeding (1-5 days), and the necessity for electrical cauterization. After the first cessation, rebleeding is described as the appearance of blood on the upper lip.

2. Material and Method

The study was conducted after approval from the IRB in our hospital under the Department of Emergency Medicine. It is a randomized, double-blinded study. The inclusion criteria [14] were patients aged 18-65 years presenting to the ED with atraumatic spontaneous epistaxis, bleeding not controlled by conventional emergency care protocols. Patients who were hemodynamically unstable, allergic to tranexamic, known oropharyngeal, nasal, or nasopharynx malignancy, refused to participate, with a known bleeding disorder or on anticoagulation drugs, posterior nasal bleeding, traumatic epistaxis, pregnancy, bleeding controlled by standard emergency protocols and anterior nasal packing had to be used as the first step according to Surgeons clinical acumen was excluded from the study [14]. The baseline demographics and hemodynamic parameters measured included sex, age, blood pressure, and history of recent use of NSAIDs.

The sample size was calculated based on a study conducted on 30 patients keeping into consideration [14], the power of the study to be 80% with a confidence interval of 95%, i.e., type 1 error of 5%. This resulted in a minimum sample size of 80 in each study arm. Taking into account a 10% dropout, 90 patients were enrolled in each study arm. Thus a total of 180 patients were taken into the study.

The ENT surgeons examined the patients, and after their inclusion in the study, each surgeon was given a random medical kit box through computer-generated allocation. Each patient was given resuscitation and first aid measure according to a standardized institutional protocol.

The Patients were divided into two groups- **G**roup T A cotton pledget soaked in 5 ml of Tranexamic acid (injectable form, prefilled syringe) and 10 ml of Phenylephrine with 5 ml of 2% Lignocaine with 1:1000 adrenaline.

Group C A cotton pledget soaked in 10ml of Phenylephrine with 5ml of 2% Lignocaine with 1:1000 adrenaline with 5ml Normal saline (prefilled syringe). It was a double-blind trial in which the physician inserted the pledget and watched the outcomes while the patient was unaware of the intervention. Pledget was introduced into the nostril using bayonet forceps and nasal speculum. The cotton was removed from the nostril after 20 minutes in both groups. If bleeding occurred, either cauterization or nose packing was done, depending on whether the bleeding site was visible.

The following results were noted: the proportion of patients whose bleeding was under control within 10 minutes, the proportion of patients in both groups who needed anterior nasal packing after 20 minutes of pledget removal, the length of stay in the emergency department, the need for cauterization, and a telephonic follow-up conducted by an independent ENT resident using a structured questionnaire to record any episode of rebleeding within 24 hours to five days and patient satisfaction score on a scale of 10 was noted. Any drug-related side effects were recorded, such as thrombosis, nausea, and hypersensitivity.

3. Statistical Analysis

Data analysis was done using Statistical Package for social sciences (SPSS), version 20. X^2 and Fischer's exact test were used for the categorical variables as appropriate. For the Continuous variable, the Mann-Whitney U test was used. P value<0.05 was considered significant. The statistician who assessed the records was also blinded to the groups.

4. Results

40 patients out of 220 eligible patients registered for the study did not meet the inclusion criteria, thus, were excluded from the study. The remaining 180 patients were randomized into the two study groups. The consort flow diagram is given below. (Figure 1)

Demographics and baseline hemodynamic parameters were comparable in both groups. In comparison, Group C patients who required anterior nasal packs were less in Group T (P<0.038). The number of days of hospital stay was also significantly decreased in Group T (P <0.045), Proportion of patients where the bleeding was stopped within 10 mins was more in Group T (P< 0.04).

Rebleeding incidence within 24 hours was decreased in Group T (P< 0.038), but significantly no difference was found in rebleeding number within 1- 5 days. No minor/major complications to the drug were seen in Group T. In our study, the Patient satisfaction score was almost similar (P>0.128) (Table 1)

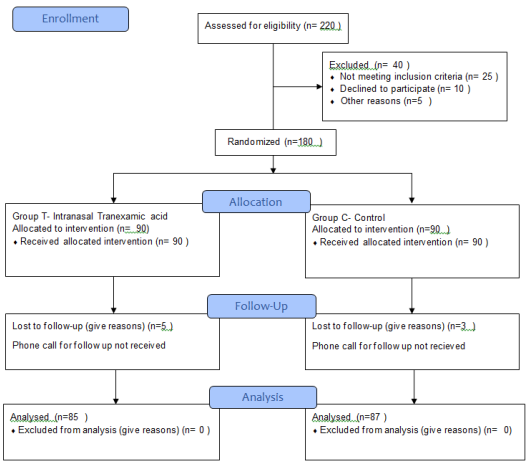

Figure 1. Flow Diagram

Table 1. Frequency of clinical outcomes in two groups

Parameter	Group T (85)	Group C (87)	P value
Patients whose bleeding stopped within 10 mins	45 (52.9%)	35 (41.1%)	0.042
No. of Patients requiring Nasal Pack after 20 mins.	40 (47.05%)	50 (57.4%)	0.038
No. of patients stay more than 2 hours in ED.	10 (11.7%)	15 (17.2%)	0.045
Re-bleeding within 24hrs-5 days.	15 (17.6%)	17 (19.5%)	0.8
Patient satisfaction score	8.7±1.3	7.4±2.3	0.128
Side effects	nil	nil	0

5. Discussion

Considering the percentage of occurrence of anterior epistaxis [15], various methods have been devised to not only control the bleed but also to prevent the likelihood of future recurrence. The sought-after modalities must be practical, affordable, and resource-friendly [16]. The goal of pragmatic design is to facilitate the patient's journey rather than impede it.

In our study, an intravenous formulation of TXA has been used intranasally. Tranexamic acid is an effective antifibrinolytic drug for nasal bleeding compared to standard care. A study was conducted by Asha R Birmimgham [17], where out of 122 patients, 30 patients were treated with Topical TXA, concluded that 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). Still, contrary to our study, the hospital stay days were relatively high.

A recent meta-analysis conducted by Janapal et al. [18] using PubMed and Scopus databases on around 1299 patients supported our observation by concluding that patients treated with TXA were 3.5 times (OR 3.5, 95% CI 1.3-9.7) more likely to achieve bleeding cessation at the time of the first consultation. Patients treated with TXA had 63% (OR 0.37, 95% CI 0.20-0.66) less likelihood of returning due to rebleeding at 24-72 h. A meta-analysis by Jonathan et al. [19] found moderate quality evidence that locally applied TXA, along with standard care, is better for stopping bleeding within 10 mins, and the risk of re-bleeding is also low compared to standard care alone.

Zahed et al. [20] conducted a study comparing the topical application of injectable TXA with anterior nasal packing using tetracycline. The author observed success in the TXA group after ten minutes of treatment i.e., the Odds ratio was 2.28, meaning the TXA group showed 2.28 times better control in comparison to the anterior pack group (odds ratio, 2.3; confidence interval- 95% (1.7-3.1); P < .001) which was similar to our study results. Moreover, supporting our results, 95.34% of patients in the TXA group were discharged in less than 2 hours vs. 6.4% in the nasal packing group (P < .001). In contrast, according to our observations rebleeding within 24 hours was significantly less in the TXA group than in the control group. Still, as their comparison group was that of nasal packing, thus P value was insignificant. Patient satisfaction score was significantly higher in the TXA group as anterior nasal packs are highly inconvenient (P < .001). In our study, the Patient satisfaction score was almost similar (P>0.128) as both groups had the topical application of drugs.

Reuben et al. [21] study in which groups were randomly assigned to receive topical tranexamic acid or a placebo, revealed that there was no statistically significant difference between the two (odds ratio 1.107; 95% confidence interval 0.769 to 1.594; P=.59). Logan [22] compared the effectiveness of cotton pledgets put into the bleeding naris while being soaked in the intravenous version of tranexamic acid with conventional nasal packing therapy. The bleeding stopped in 71% of the tranexamic acid group and 31.2% of the control group within 10 minutes (odds ratio, 2.28; 95% confidence range, 1.68-3.09; p 0.001).

In contrast to our findings, Gottlieb Met al23; found that topical TXA was not linked with a statistically significant difference in the cessation of bleeding after 30 minutes when comparing intranasal tranexamic acid with the control group. Similar to our study, more patients were discharged within 2 hours of arrival, there were fewer episodes of rebleeding within the first 24 hours and at one week, and patient satisfaction was higher in the TXA group. These differences may be because patients were taking anticoagulants in this study. The most recent nonblinded trial by Whitworth et al. [24] on 38 patients with anterior epistaxis showed that topical tranexamic acid administration is superior to topically spray vasoconstrictor oxymetazoline in reducing anterior epistaxis.

Given the financial advantages and ease of usage, this procedure is efficient and is worth the inclusion as standard protocol in emergency rooms for the cessation of epistaxis. Therefore, topical TXA for persistent epistaxis may be advantageous for the patient (less nasal packing and decreased hospital admission) and the healthcare system (saving on bed occupancy and providing an economical alternative to packing and admission).

6. Strengths and Study Limitations

The study's strength is the frequent presentation of atraumatic nasal bleeding to the emergency room. Moreover, it is a double-blind, randomized study. Our study's limitation is the large range of methods available for stopping nasal bleeding, which makes standardization difficult; comparing results from different studies can be challenging.

7. Conclusion

Topical TXA has been demonstrated to be safe and effective for stopping anterior nasal bleeding, avoiding the need for anterior nasal packing, which is time-consuming for patients and medical personnel. TXA has been demonstrated to lower the rate of packing considerably.

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Conflicts of Interest: "Authors declare no conflict of interests."

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