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A RANDOMISED CLINICAL TRIAL COMPARING THE TOPICAL TRANEXAMIC ACID WITH CONVENTIONAL ANTERIOR NASAL PACKING IN THE MANAGEMENT OF EPISTAXSIS

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Abstract

BACKGROND

Epistaxis is a common problem in the emergency department (ED). There are different kinds of treatment for epistaxis. We included those patients whose bleeding that persists after simple first aid measures, followed by standardised topical vasoconstrictor therapy will be randomised to receive either TXA or ANP .This study intended to evaluate the topical use of injectable form of tranexamic acid vs anterior nasal packing with Vaseline ribbon gauge.

Methods

Topical application of injectable form of tranexamic acid (500 mg in 5 mL) was compared with anterior nasal packing in 100 patients with anterior epistaxis presented to an ED in a randomized clinical trial. The time needed to arrest initial bleeding, hours needed to stay in hospital, need for blood products and any rebleeding during 24 hours and 1 week later were recorded, and finally, the patient satisfaction was rated by a 0-10 scale.

Results

Time needed to arrest the bleeding was noted about 5-10 minutes of treatment in tranexemic acid group with mild to moderate epistaxis. Anterior nasal packing was done for moderate epistaxsis and were arrested in 100% of population. In addition, average stay in the hospital was noted 2days or less in 94% of the tranexamic acid group, whereas anterior nasal packing group minimum stayed for 5 days and maximum was 8 days.Rebleeding was noted in 9 % of patients, where 1 % seen after treatment with tranexemic acid and 8% after removal of anterior nasal packing group patient. Patient satisfaction is better in tranexamic acid group.

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Conclusions

Topical application of injectable form of tranexamic acid was better than anterior nasal packing in the initial treatment of anterior mild to moderate epistaxis in terms of hospital stay patient satisfaction and rebleeding .

KEY WORDS : ANTERIOR NASAL PACKING, TRANEXEMIC ACID, REBLEED, HOSPITAL STAY.

Statements and Declarations

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Competing Interests-The authors declare that they have no conflicts of interest to declare that are relevant to the contents of this article.

Availability of Data and Material- Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

Ethical Approval–Ethical approval was waived by the Institutional Research Committee VIMS in view of retrospective nature of study and all procedures being performed were part of routine care.

Code Availability- Not Applicable

Author Contributions-All authors contributed to the study conception and design. Material preparation and analysis were performed by Dr. ABHILASH A M and Dr. VINAYA KUMAR S M. Data collection was done by Dr. VINAYA KUMAR S M. The first draft of manuscript was done by Dr. Pooja N and all authors commented on previous version of manuscript. All authors read and approved the final manuscript.

Introduction :

Epistaxis is a common presentation to the department of otorhinolaryngology, accounting for about 1 in every 200 ENT visits and affecting up to 60% of the population at some point in their lives. Local trauma or low ambient humidity are the most common causes of epistaxis, while a range of other reasons have been suggested. Epistaxis is a self-limiting issue in the vast majority of cases, but it can be lethal in certain populations. Depending on personal physician choice, a range of therapeutic techniques are currently used in the ED: local pressure, cauterization, use of topical vasoconstrictor drugs, or nasal packing.

Both systemic and local causes can cause epistaxis. Inflammatory, infective, traumatic, anatomical (deviated nasal septum, septal spur), chemical, or climatic changes, neoplasm, and foreign bodies are some of the local reasons.Hematological illnesses that produce coagulopathy, cardiovascular diseases such as hypertension and vascular heart disease, liver disease, renal disease, and anticoagulant medications are also systemic causes of epistaxis. Its etiology is unknown in 70% to 80% of cases.[3]

The epistaxis is aggravated by nose blowing, severe coughing in chronic obstructive pulmonary disease (COPD), straining in constipation and benign prostatic hyperplasia (BPH), and moving heavy objects.

Resuscitating patients with epistaxis of any age group, determining the source of the bleed, controlling the bleeding, and treating the underlying cause come first. There is no set strategy for treating epistaxis, although a variety of treatment options are available, including local pressure, topical vasoconstrictor, nasal packing, cauterization (chemical/electric), and vascular embolization or ligation.

Squeezing the nose, utilising vasoconstrictor agents, chemical (silver nitrate) or electrical cauterization, and nasal packing with ribbon gauze or nasal tampon are currently used to treat epistaxis [5]. Nasal packing is commonly done after a local anaesthetic like lidocaine and a

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vasoconstrictor like adrenaline [6], which causes mucosal shrinking and makes it easier to insert pledgets filled in petroleum jelly or ointments like tetracycline and inflating balloons or packs [4].
Anterior nasal packing, albeit one of the most common treatments for epistaxis, has certain drawbacks, such as the pack's extended duration, the necessity for prophylactic antibiotics, and the need for analgesics [4].
Epistaxis has been treated with a variety of locally administered haemostatic drugs, including tranexamic acid [7] and aminocaproic acid [8].

Tranexamic acid has been used orally [9], topically [7], and locally as gels [10], however systemic tranexamic acid is not recommended in thromboembolic patients.
The goal of this trial was to see how effective topical use of tranexamic acid, an injectable form of the drug, was at treating epistaxis.
TXA is found to be a successful adjuvant in the treatment of mild and moderate epistaxis, it may be able to eliminate the requirement for nasal packing in those patients who benefit from it, as well as lessen the need for hospitalisation. This would be a significant result for patients and healthcare systems alike.

Materials and methodology:
This is a randomized study, conducted from March 2020- August 2021 in the Department of ENT, Vijayanagara Institute of Medical Sciences, Ballari, Karnataka, India. Ethical committee clearance was obtained before the study was conducted.
100 patients included in the study who are presented to the ENT department with anterior mild and moderate epistaxis that persists after simple first aid measures, followed by standardised topical vasoconstrictor therapy. All eligible patients were randomised into two groups, 50 in the tranexemic acid group and 50 in the anterior nasal packing group. After 15 minutes of initial measures, if bleeding still persists, tranexemic acid group received a cotton pledget of 15 cm that had been soaked in the injectable form of tranexemic acid (500 mg in 5 mL) and inserted into the affected nostril and observed for 15minutes, if bleeding stops, time required to stop the bleeding was noted. Patient was followed up for re-bleeding or adverse events at 24 hours and 1week. The patient for follow up to document any re-bleeding or adverse events at 24 hours and 1 week. Also evaluate satisfaction rate on a numerical rating scale at the time of emergency department discharge. Also patient was evaluated for satisfaction rate on a numerical rating scale. If bleeding persist after 15 minutes in tranexamic acid group, then anterior nasal packing was considered.
The anterior nasal packing group received a ribbon gauge that had been soaked in Vaseline inserted into the affected nostril and left in place for 15 minutes. if bleeding stops keep note the time required to stop the bleeding . The packs were left in situ for 2 days before removal. If the assigned treatment failed, we evaluated anterior nasal packing and cautery (if indicated) for the tranexemic acid group and cautery alone for the anterior nasal packing group.
Inclusion criteria : All patients with mild and moderate anterior epistaxsis,

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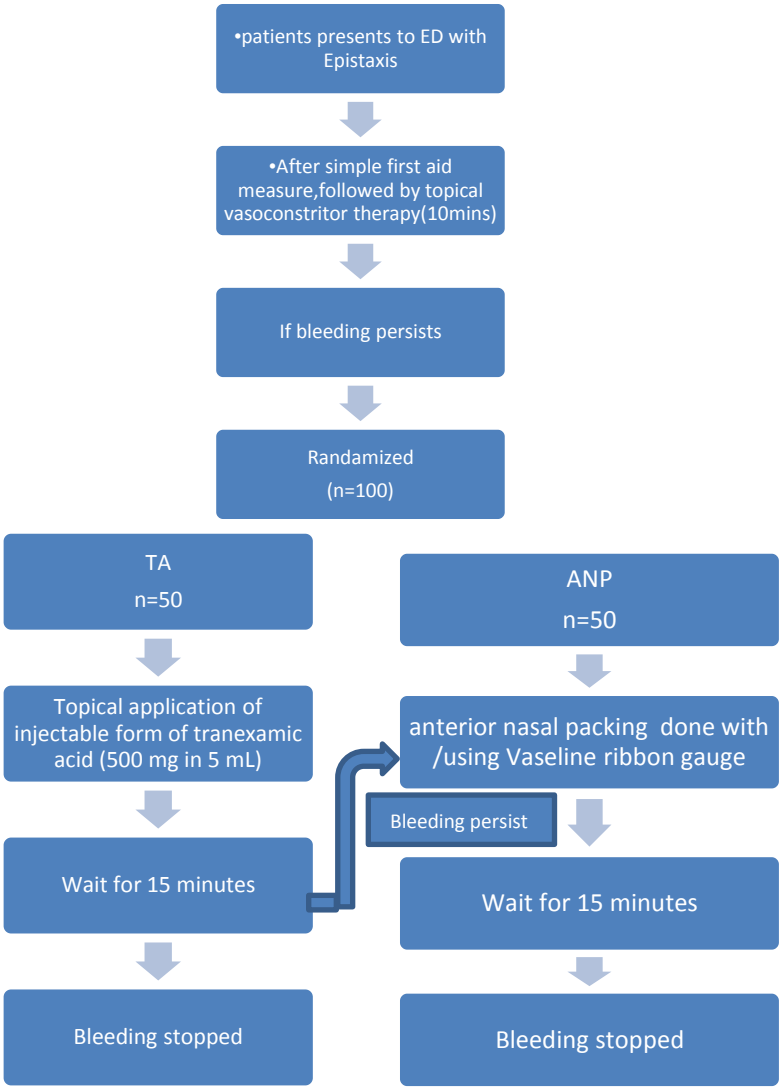
Exclusion criteria: severe epistaxsis
Posterior epistaxsis
Patients with haemophilia / bleeding disorders

All 100 patients were selected randomly and grouped into two groups on simple random basis, 50 each patients were subjected to topical tranexamic acid treatment and anterior nasal packing treatment and we followed below flow chart for the treatment .



ANTERIOR NASAL PACKING:

This entails packing the nasal cavity with vasaline-impregnated gauze. Adult gauze size 25mm broad, while children's gauze size 12mm wide and one metre long on each side.The use of vasaline facilitates insertion, inhibits drying, and allows the pack to be removed without causing extra stress.

(I) Bismuth tribromophenate

(ii) Calcium sodium alginate (kaltostat)

(iii) Oxytetracycline base) are the additional components utilised for impregnation.

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When calcium sodium alginate comes into touch with blood, it absorbs quickly and creates a thick hydrophilic gel. This gel adheres easily to the contours of any lesion and promotes platelet activation and blood coagulation by releasing calcium ions. We used petroleum jelly based vasaline anterior nasal packing cottons.

Outcomes

The primary outcome was the proportion of patients in each group whose bleeding had stopped at 10 - 15 minutes.

Secondary outcomes were: 1) frequency of epistaxis recurrence at 24 hours in tranexemic acid group and 2 days after pack removal, 2) length of stay, 3) Patient satisfaction is measured on a scale of 0–10, with a higher score signifying higher satisfaction.

Data Analysis

Frequency and percentage are used to convey qualitative data.

The mean and standard deviation were used to represent continuous variables.

To compare mean values between groups, an unpaired t test was utilized. To assess the association between variables Chi Square test was used. And Fisher's exact test was used. Mean comparison between groups done with unpaired t test.

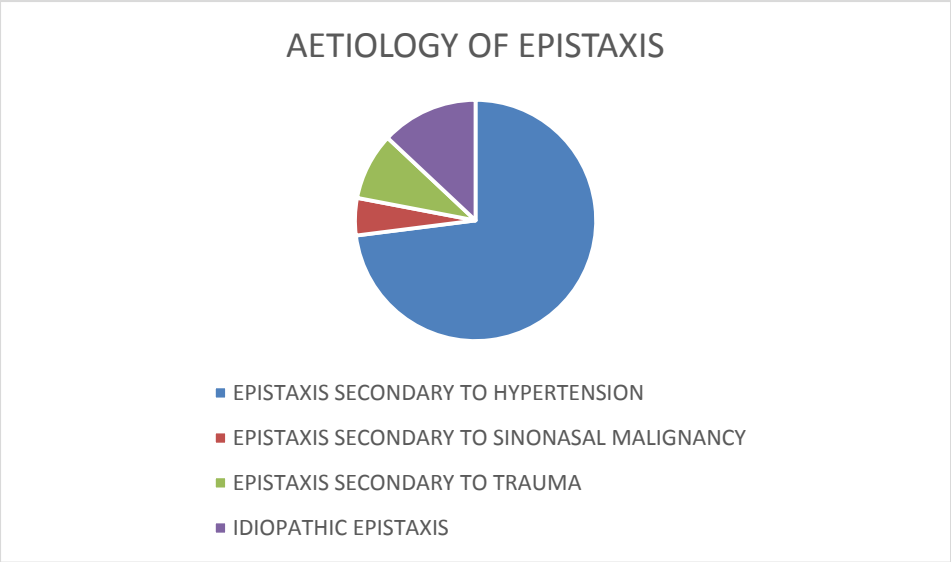
P value of <0.05 was considered statistically significant.

IBM SPSS Version 28 for windows was used to do statistical analysis.

RESULTS

A total of 100 patients (74 men and 26 women) were enrolled in this randomized clinical trial. A total of 100 eligible patients were randomized and included in the study: 50 in the TXA group and 50 in the ANP group. The patients were then subjected to all routine haematological and radiological investigations.

All patients were treated according to above protocol . 26% of both the groups has arrested the bleeding in 5 minutes, 24% in 10 minutes and 25% each in 15 and 20 minutes.



GRAPH 1: PIE CHART SHOWING THE VARIOUS ETIOLOGY OF EPISTAXIS IN BOTH GROUPS.

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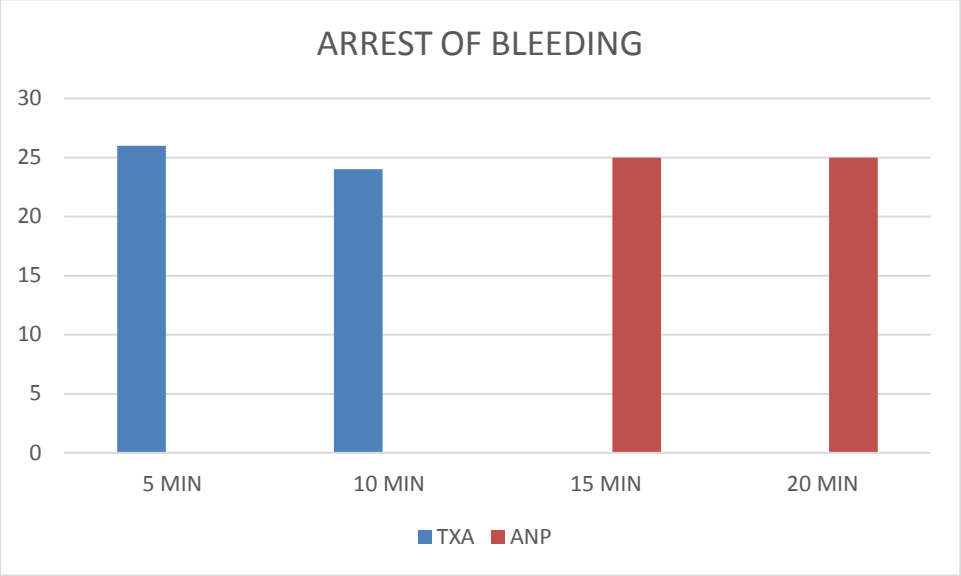
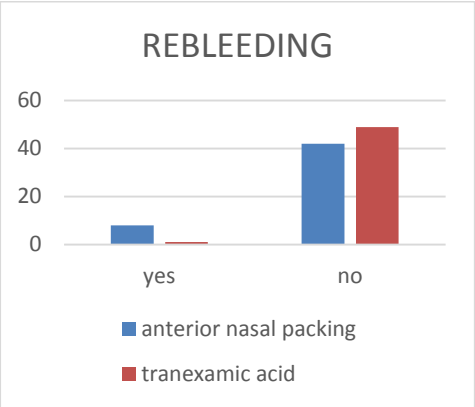
In our study the epistaxis was categorized into mild, moderate and severe epistaxis, depending on the amount of bleeding from nose, mild is considered when bleeding in the form of droplets, moderate when bleeding is intermittent free flow and severe when there is continuous flow of stream of bleeding. In our study we considered mild and moderate epistaxis, we found that 73% patients had epistaxis secondary to hypertension, 13% idiopathic, 9% epistaxis secondary to trauma and 5% epistaxis secondary to Sino nasal malignancies. Graph 1 pie chart showing the various etiology of epistaxis in both groups.



GRAPH 2 : SHOWING ARREST OF BLEEDING IN BOTH GROUPS

In our study we found the following results, both the groups the bleeding was stopped within 20 minutes of initiation of treatment .in case of tranexemic acid group, maximum of bleeding was controlled within 5 minutes in 52% of patients, where as in case of anterior nasal packing patients, maximum of patients had controlled within 15 minutes and 20 minutes in 50%. The statistical analysis showed that p value <0.0001 that is statistically significant. Graph 2 showing the duration of bleeding in both groups.



GRAPH 3 : BAR DIAGRAM SHOWING REBLEEDING IN BOTH GROUPS.

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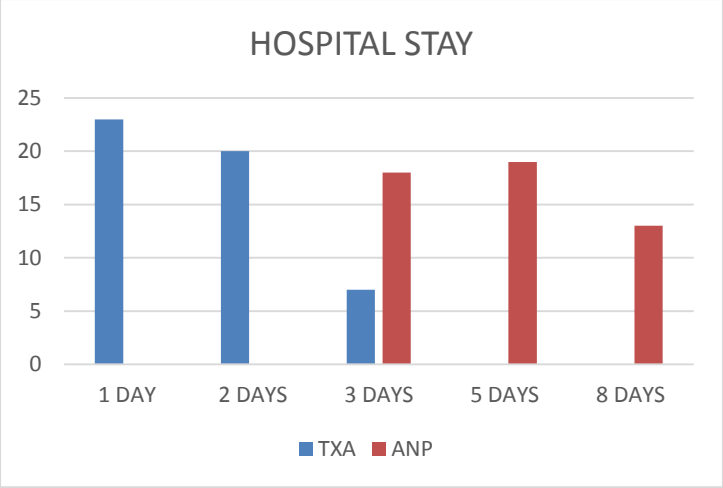

GRAPH 4 : BAR DIAGRAM SHOWING HOSPITAL STAY IN BOTH GROUPS

In our study over all 9 patients had re-bleeding .which included both the groups. Only 1 patient had re bleeding in tranexemic acid group whereas 8 patients 16% patients had re-bleeding in anterior nasal packing group after the pack has been removed after 48 hours within 24 hours. The p value was <0.0001 which is statistically significant. When compared to anterior nasal packing group there was much lesser incidence of re-bleed in anterior nasal packing group. Graph 3: bar diagram showing re-bleeding in both groups.

Whereas in anterior nasal packing group, all patients were admitted and pack was removed after 48 hours, maximum of patients were stayed for 5 days 38% patients, 3 days in 36% of patients, and 8 days in case of 26% of patients. The stay was maximum in anterior nasal packing group when compared to tranexemic acid group. The p value is <0.000 which is statistically significant. Graph 4: bar diagram showing hospital stay in both groups

In our study sepsis was seen in 2 patients of anterior nasal packing accounting for 4% of group. No sepsis was seen in tranexamic acid group. The p value is <0.0001 which is statistically significant. No deaths were noted in the study.

All patients were given a visual analogue patient satisfaction score from 0-10. Most of the patients of tranexemic acid group given a score of 8-9 whereas in case of anterior nasal packing group most of the patients were given a score of 6-7. There was better patient satisfaction in case of tranexemic acid group when compared to anterior nasal packing group.

Discussion

Patients who present with epistaxis are a common occurrence in our everyday procedures.

It affects people of all ages.

Epistaxis can be classified as anterior or posterior depending on where it occurs.

Children and young adults are more likely to experience anterior epistaxis.

The bleeding point is anteriorly positioned and easily identifiable, therefore it is rarely dangerous.

It usually has an arterial (kiesselbach's plexus) or venous origin (retrocolumellar vein).

Posterior epistaxis is more common in the elderly, and because the site of bleeding is more posteriorly placed, it is difficult to approach, making it difficult to stop bleeding.

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The prolonged duration of bleeding is most likely due to angiopathy changes caused by age and cardiovascular disease. [1]

Although the majority of cases are self-limiting, some do not resolve without help. In the last decade, new therapeutic choices and procedures have emerged, particularly with the introduction of nasal endoscopy.

To control epistaxis, a variety of therapy procedures have been utilised, ranging from nose pinching to vascular ligation. Treatment for epistaxis is determined on the location, severity, and origin of the bleeding. Nonsurgical and surgical treatments are the two primary categories of treatment options. Digital nasal compression, topical vasoconstrictor, local cauterization (chemical or electric), and nasal packing (anterior or posterior) are some of the nonsurgical/conservative options. If the bleeding point is visible, it can be cauterised using silver nitrate, chromic acid, or trichloroacetic acid, or it can be sealed with electrocautery utilising bipolar diathermy.

Other recent therapy options for reducing bleeding include fibrin glue, which is made from human plasma cryoprecipitate and binds to injured arteries to stop bleeding. In a randomised controlled trial, fibrin glue was found to have less local problems than electrocautery, chemical cautery, or nasal packing. Laser therapy has also been used to treat epistaxis, which has proven to be effective in situations of recurrent bleeds caused by vascular anomalies such as hereditary haemorrhagic telangiectasia.

Tranexemic acid is considered an important medicine by the World Health Organization.[16]It's an antifibrinolytic medication and a synthetic derivative of the amino acid lysine that lowers plasmin concentration by blocking plasminogen's lysine binding sites, which prevents plasminogen from binding to fibrin and then converting to plasmin[17].Plasmin may inhibit platelet adhesion and aggregation by interfering with platelet function via the complement system[18,19].Tranexemic acid has been examined for several types of bleeding, including epistaxis, using multiple routes of administration, including oral, intravenous, and topically.

Topical tranexemic acid has also been proven to reduce postoperative haemorrhage after adenoidectomy, as well as establishing haemostasis and enhancing the surgical field in endoscopic sinus surgery.[10.12]

In our study we found the topical application of the injectable formulation of tranexemic acid to be more effective than anterior nasal packing with Vaseline ribbon gauge with 73% of patients in the former group achieving bleeding cessation within 10 minutes compared with 29% in the latter group.

In patients taking antiplatelet medicines, topical use of the injectable version of tranexemic acid appears to be a superior treatment option for anterior epistaxis than anterior nasal packing.

In our research population, the benefits of topical tranexemic acid treatment included faster haemostasis, a shorter hospital stay, a decreased recurrence rate, and higher patient satisfaction.

It's also a straightforward approach that's simple to teach and learn.

Furthermore, the rate of recurrent bleeding in the tranexemic acid group was considerably lower than in the anterior nasal group during the first week after therapy. The tranexemic acid

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group had a much shorter stay in the hospital. One possible explanation for the decreased re-bleeding rate observed in the tranexamic acid group in our study is that tranexamic acid, as an antifibrinolytic medication, could minimise enhanced fibrinolytic activity described in epistaxis patients [9].Tranexamic acid, like aminocaproic acid, is an antifibrinolytic agent; however, it is nearly 10 times more effective and has a longer half-life; both medications work by binding to plasminogen and inhibiting its binding to fibrin, preventing plasminogen activation and transformation into plasmin. [14, 15]

This is in line with the findings of a research by Zahed R et al, which looked at the use of topical tranexemic acid to treat idiopathic epistaxis. [7]

As a result, at centres where anterior nasal packing is routinely used to treat epistaxis, adopting this treatment strategy may increase patient flow through the emergency department. Patient satisfaction was also higher in the tranexemic acid group. More likely to be implemented into clinical practice are treatments that are more comfortable for patients and easier to administer for physicians.

This ease and convenience has been confirmed in studies by Zahed R et al (7) and Tibbelin et al. [25] in the treatment of epistaxis with tranexamic gel. Tranexemic acid could be used to treat chronic epistaxis if it is found to be effective.

If tranexemic acid was found to be a useful adjunct to the management of persistent epistaxis, it could obviate the need for nasal packing in those patients where it is effective and reduce the need for hospital admission. This would be an important finding for the benefit of patients and healthcare systems. (17)

Anterior nasal packing is an effective, although unpleasant, means of treating recurrent epistaxis, which usually necessitates admission to the hospital. Toxic shock syndrome has been documented following anterior nasal packing. Nasal carriage of Staphylococcus aureus is common, and these bacteria create exotoxin when they pack. Fever, rash, hypotension, mucosal hyperaemia, vomiting, and diarrhoea are all symptoms of the condition. Packing should be avoided in patients with blood dyscrasias. If packing is required, calcium sodium alginate or microfibrillar collagen should be used. With packing, there is a risk of increased bleeding and infection. In a sleeping adult, swallowing occurs once per minute, but in an awake adult, it occurs five times each minute. Patients wearing nasal packs experience excruciating discomfort as a result of this.

There are many other modalities of treatment of epistaxsis. Refractory epistaxis that does not respond to conservative treatment, such as anterior and posterior nasal packing, is usually treated using surgical/interventional procedures as a last resort. Selective arterial embolization or arterial ligation are two surgical therapeutic options. Coils, gel foam, or polyvinyl alcohol are used to embolise the bleeding vessel in angiographic embolization. Cerebrovascular accident, hemiplegia, ophthalmoplegia, facial nerve palsy, and soft tissue necrosis are all possible sequelae of arterial embolization. No surgical procedures were performed on any of our patients.

Topical tranexemic acid has been demonstrated to be safe and effective in a variety of contexts, and there is some indication that it may be beneficial in certain epistaxis patients, however more research is needed.

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The findings of this study could possibly lead to a decrease in the requirement for anterior nasal packing and, as a result, hospitalisation for patients with epistaxis, as well as a decrease in an unpleasant operation with known dangers. (17)

When compared to anterior nasal packing, topical application of the injectable version of tranexemic acid appears to be a better therapeutic option for anterior epistaxis in mild to moderate cases.

In our research population, the benefits of topical tranexemic acid treatment included faster haemostasis, a shorter hospital stay, a decreased recurrence rate, and higher patient satisfaction.

It's also a straightforward approach that's simple to teach and learn..

Finally, although commercially available nasal sponges, tampons, and balloon tamponade devices are meant to treat epistaxis, we did not compare them to tranexemic acid in this study and hence cannot comment on their relative efficacy or tolerability.

Conclusion

In our study topical tranexamic acid group add advantage of shorter hospital stay, less re-bleeding and patient satisfaction compared to anterior nasal packing group in mild to moderate cases of epistaxis , and being simple for health care providers.

Topical tranexamic acid can be used as adjuvant therapy in mild to moderate anterior epistaxis cases.

References

1) Evaluation of Etiology and Treatment Methods for Epistaxis: A Review at a Tertiary Care Hospital in Central Nepal Ramesh Parajuli
2) 16. Kamhieh Y, Fox H. Tranexamic acid in epistaxis: a systematic review. Clin Otolaryngol 2016;41:771–6.
3) 17. Shi J, Ji H, Ren F, et al. Protective effects of tranexamic acid on clopidogrel before coronary artery bypass grafting: a multicenter randomized trial. JAMA Surg 2013;148:538–47.
4) 18. Weber CF, Gorlinger K, Byhahn C, et al. Tranexamic acid partially improves platelet function in patients treated with dual antiplatelet therapy. Eur J Anaesthesiol 2011;28:57–62.
5) 19. Putnam JB, Royston D, Chambers AF, et al. Evaluating the role of serine protease inhibition in the management of tumor micrometastases. Oncology (Williston Park) 2003;17:9–30; quiz 31–2.
6) 7. 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;31:1389–92.
7) 8. Sanchez-Palomino P, Sanchez-Cobo P, Rodriguez-Archilla A, et al. Dental extraction in patients receiving dual antiplatelet therapy. Med Oral Patol Oral Cirugia Bucal 2015;20:e616.
8) 20. Sindet-Pedersen S, Stenbjerg S, Ingerslev J. Control of gingival hemorrhage in hemophilic patients by inhibition of fibrinolysis with tranexamic acid. J Periodontal Res 1988;23:72–4.

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9) 21. Shakur H, Elbourne D, Gulmezoglu M, et al. The WOMAN Trial (World Maternal Antifibrinolytic Trial): tranexamic acid for the treatment of postpartum haemorrhage: an international randomised, double blind placebo controlled trial. Trials 2010;11:40.
10) 22. Roberts I, Edwards P, Prieto D, et al. Tranexamic acid in bleeding trauma patients: an exploration of benefits and harms. Trials 2017;18:48.
11) 10. Athanasiadis T, Beule AG, Wormald PJ. Effects of topical antifibrinolytics in endoscopic sinus surgery: a pilot randomized controlled trial. Am J Rhinol 2007;21:737–42.
12) 12. 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;77:1139–42.
13) 9] White A, O'reilly B. Oral tranexamic acid in the management of epistaxis. Clin Otolaryngol Allied Sci 2007;13(1):11–6.
14) [14] Thorsen S. Differences in the binding to fibrin of native plasminogen and plasminogen modified by proteolytic degradation. Influence of omega-aminocarboxylic acids. Biochim Biophys Acta 1975;393(1):55–65.
15) [15] Hoylaerts M, Lijnen HR, Collen DS. Studies on the mechanism of the antifibrinolytic action of tranexamic acid. Biochimica et Biophysica Acta 1981;673: 75–85.
16) 25. Tibbelin A, Aust R, Bende M, et al. Effect of local tranexamic acid gel in the treatment of epistaxis. ORL J Otorhinolaryngol Relat Spec 19.
17) Novel use of tranexamic acid to reduce the need for Nasal Packing in Epistaxis (NoPac) randomised controlled trial: research protocol Adam Reuben,1 Andrew Appelboam,1 Andy Barton,2 Patricia Jane Vickery,3 Richard Body,4 Malcolm Hilton,5 Jason Coppell,6 Paul Ewing