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Research Article

A NEW METHOD OF EPISTAXIS MANAGEMENT USING NASAL GEL: A SINGLE CENTER, RANDOMIZED CLINICAL TRIAL

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ABSTRACT

Objective: Epistaxis is one of the common causes of patients' referral to the emergency departments. In the majority of cases, epistaxis is managed by traditional methods. We investigated the efficacy of nasal gel (NG) in comparison to anterior nasal packing (ANP) to stop mild-to-moderate anterior nasal bleeding.

Methods: In this prospective, randomized clinical trial, patients were divided into two groups of ANP (n=60) and NG (n=40). We determined and compared the efficacy of treatment (bleeding stop time and recurrence), patients' satisfaction at discharge (length of stay in the hospital, pain during the procedure, and procedural time), and safety (less side effects) in both groups.

Results: The procedural time ≤2 min was observed in 90% and 58.33 % of NG group and ANP group, respectively (p<0.001). Pain score during procedure ≤4 and patients' satisfaction ≥7 were, respectively, seen in 87.5% and 65% of NG group, but it was 43.33% and 41.7% in ANP group, respectively (p<0.001, p=0.02). The side effects in ANP group were 35%; however, no side effects were observed in NG group.

Conclusion: In the management of mild-to-moderate anterior nasal bleeding although NG efficacy is equivalent to ANP, using NG may be more convenient and satisfactory for patients. In addition, the use of this gel may result in more safety and fewer side effects.

Keywords: Epistaxis, Patient satisfaction, Visual analog scale.

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INTRODUCTION

Epistaxis is the second cause of patients' referral with Ear, Nose, and Throat (ENT) problems to the emergency departments (ED) and nearly 60% of people experience epistaxis during their life cycle. Epistaxis has two age peaks (<10 and >60 years), two origins (anterior and posterior), and two types of primary (70–80% with no cause) and secondary (due to underlying diseases and anticoagulant medicines) [1,2]. Evidence shows that epistaxis in most cases is self-limiting, but it can be life-threatening, especially in elderly with underlying diseases [3].

Today, on account of using anticoagulant drugs, the prevalence of epistaxis is on a rise [4]. However, therapeutic strategies are very different, and no defined guideline exists in epistaxis management [5,6]. A preferable procedure to control bleeding is nasal endoscopy, but since it is not available in all centers, nasal packing is still the most common applied technique [7]. This mechanical treatment causes some problems. Low-risk side effects such as pain and discomfort to high-risk side effects such as toxic shock syndrome can occur. This is inevitable as the nasal mucosa is a common site for infection and hospital environment, as well as devices, are often resistant to disinfectants [5-9]. Furthermore, in most hospitals, nasal bleeding control is done by general physicians who might not have the expertise to do this procedure [10]. Besides this traditional mechanical technique, the use of more convenient local medicines such as pig thrombin (floseal) and herbal drugs are increasing [11-14]. One of these convenient methods is using nasal gel (NG). Nozohaem for epistaxis treatment is easy and has the fast effect. This gel increases vasoconstriction in the nasal mucosa and activates coagulation system. Platelets aggregation to collagen forms a plug. Then, fibrin threads and clots are made. This gel contains glycine and calcium (www.nozohaem.com). Glycine is an amino acid which is used in the production of protein and collagen. Collagen causes efficient platelets function to decrease bleeding. Glycine helps to control bleeding through absorbing water and increasing the concentrations of coagulant factors and platelets [15]. Meantime, calcium promotes coagulation through inducing coagulation process and activating coagulant factors such as factor 13 [16]. In addition, platelets induce the process of clot repair by increasing calcium [17,18].

The aim of this study was to compare NG with anterior nasal packing (ANP) in mild-to-moderate anterior nasal bleeding management. The primary outcome was NG efficacy (bleeding stop time and recurrence). The secondary outcomes were patients' satisfaction at discharge (length of stay in the hospital, pain during the procedure, and procedural time) and safety (less side effects) of using NG.

METHODS

Study period

The study was conducted over a period of 6 m from November 2015 to April 2016.

Study design

This prospective, randomized clinical trial was performed on patients with anterior nasal bleeding referred to Shafa Hospital in Kerman. Shafa hospital is the referral center for ENT patients in the southeast of Iran. In this study, the efficacy and safety of ANP and NG procedures, and patients' satisfaction in these two groups were compared with each other. Treatment procedures were done by a trained general physician, and data were gathered by an emergency medicine

specialist. Another emergency medicine specialist supervised data collection.

Ethics committee approval

The study was approved by the Ethical Committee of Kerman University of Medical Sciences and also Iranian registry of clinical trials (Irct ID: IRCT 2016121222181N2). Oral consent was obtained from each patient.

Patient data collection form

The patients were selected randomly from those who presented to the ED with epistaxis. At first, the patients were examined by a trained general physician. Medication allocation was done based on simple random sampling, and the patients were allocated randomly to one of the two mentioned treatment approaches. Random codes were obtained by SPSS software. Both treatment procedures were performed by the same trained general physician, and data gathering was done by an emergency medicine specialist. Considering the different nature of the two procedures, emergency medicine specialists, and the general physician were not blinded to the study.

Plan of work

A total of 100 patients were randomized (60 patients underwent ANP, and 40 patients received NG). In the ANP group, first, a cotton ball, previously soaked in a mixture of 2% lidocaine and 1:100 000 epinephrine, was placed in the anterior nostril after clearing of the clots by nasal blowing. The emergency medicine specialist examined the patients every 2 min until the bleeding stoppage. Finally, the nose was packed with tetracycline-impregnated gauze. The nasal pack was removed after 2–3 days. All nasal packing procedures were performed by the same trained general physician. In the second group, after blowing the nose, the trained physician entered NG tube (Fig. 1) into the patient's nose about 1–1.5 cm and emptied the contents of tube (2 ml gel) with fast pressure while getting the nose with thumb and point fingers. In the case of bleeding continuation, the second tube was used. Concerning no response to the treatment in the ANP group, chemical cauterization with silver nitrate and in the NG group, ANP was used. In resistant to treatment, bilateral nasal packing was performed.

During and after the intervention, the patients were evaluated every 2 min to determine bleeding stop time. After the bleeding stopped, the designed questionnaire was completed by an emergency medicine specialist. The variables including bleeding severity grading to exclude severe nasal bleeding [19], bleeding stop time after the intervention, pain score during the procedure and patient's satisfaction at discharge using visual analog scale (VAS) [20,21], discharge time, procedural time, and side effects in each group were determined and compared. Bleeding recurrence in patients (24 h and 1 week after discharge) was followed up by telephone.

Fig. 1: Nasal gel tube

Inclusion and exclusion criteria

The patients with mild-to-moderate anterior nasal bleeding were enrolled into the study. We excluded other epistaxis patients. From 146 patients, 100 patients were selected and divided randomly into two groups of ANP (n=60) and NG (n=40) (Fig. 2).

Sample size calculation

This was a parallel-group randomized controlled trial. In 30% of patients with epistaxis treated with ANP, the bleeding stopped <8 min [2]. In the current study, we aimed whether a new treatment (NG) could achieve 60% success (Δ=30%). We set 2-sided α of 0.05 and power of 80%, and sample size in each group was calculated to be 40 according to the formula (80 in total) [22].

$$n = \frac{\left[Z1-\frac{\pm}{2}\sqrt{2\bar{P}\left(1-\bar{P}\right)}+Z1-\beta\sqrt{P0\left(1-P0\right)+P1\left(1-P1\right)}\right]^2}{\left(P1-P0\right)^2}=40$$

During the study period, 20 more patients were referred to the hospital. Therefore, in total 100 patients were enrolled.

Statistical analysis

Data analysis was done through IBM SPSS statistics version 20 using independent-sample *t*-test and χ^2 to compare basal characteristics between the two groups. Efficacy of interventions was evaluated using χ^2 test. Results are presented in terms of odds ratio (OR) (95% confidence interval [CI]).

RESULTS

A total of 100 patients were recruited in this study, 51 patients were male, and 49 were female. The mean ± standard deviation age was 43.63±20.78 and 39.48±19.03 in ANP and NG groups, respectively. As contrary to sex, there was no significant difference between the two groups concerning age, history of epistaxis, history of anticoagulants consumption, underlying diseases, and the results of prothrombin time and platelet count (Table 1).

NG group was superior to ANP treatments in terms of almost all outcomes. The procedural time ≤2 min was observed in 36 patients (90%) of NG group and 35 patients (58.33%) of ANP group (OR, 0.15; 95% CI 0.04–0.92, p<0.001). This indicates that those in ANP group were 85% less likely to experience procedural duration of ≤2 min. The bleeding stop time ≥8 min was less in the ANP group compared to the NG group (50% vs. 67.5%), which was of marginal significance (p=0.08). In addition, discharge time ≤55 min was higher in the NG group (62.5% vs. 43.33%) giving a p=0.06. Pain score during procedure ≤4, determined based on VAS, was observed in 87.5% of NG group and 43.33% of ANP

Table 1: Patient characteristics

Group	ANP[1]	NG[2]	p
Age (mean±SD)	43.63±20.78	39.48±19.03	0.54
Sex (%) (male/female)	58.33/41.67	35.00/65.00	0.02
History of epistaxis (% of yes)	61.67	70.00	0.39
History of anticoagulant (% of yes)	38.33	35.00	0.73
Underlying disease (% of yes)	37.29	52.50	0.13
PLT[3]×10^3/µl (mean±SD)	287.70±40.31	275.14±40.4	0.22
PT[4] (s)	11.94±1.89	12.51±0.70	0.14
Intensity of bleeding (%)	43.33/56.67	70.00/30.00	

[1]Anterior nasal packing (n=60), [2]nasal gel (n=40), [3]Platelet, [4]Prothrombin time. SD: Standard deviation

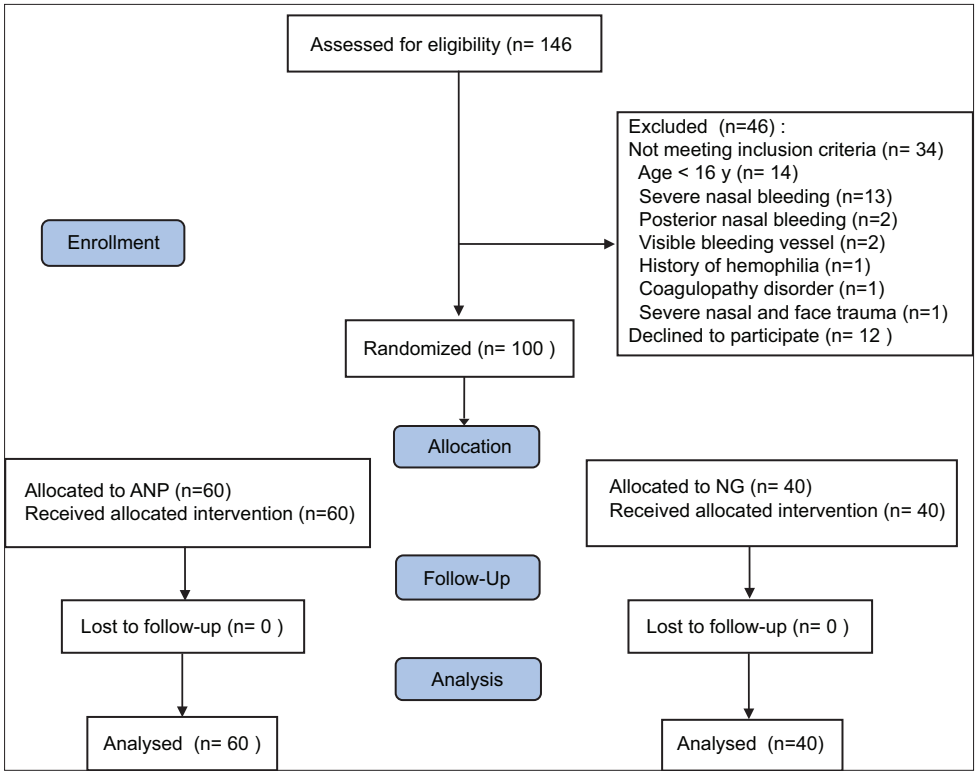

Fig. 2: Consolidated Standards of reporting trials flow diagram

group (OR, 0.1; 95% CI, 0.30–0.31, p<0.001). This indicates that those in ANP group were 90% less likely to have pain score ≤4. While 41.7% of ANP patients were satisfied, corresponding figure in NG group was 65%, (OR, 0.38; 95% CI, 0.16–0.88, p=0.02). In regard to the observed side effects (nausea, intolerance), it was 35% in ANP group, but no side effects were observed in NG group. ANP group was only better than NG in terms of recurrence. In the NG group, 25% of patients experienced the recurrence. Corresponding figure in the ANP group was about 12% (OR=0.40, p=0.08) (Table 2).

Table 2: Effect of ANP compared with NG on efficacy variables

Group	ANP[1]	NG[2]	OR (95% CI)	p
Procedural time ≤2 min (%)	58.33	90.00	0.15 (0.04–0.49)	<0.001
Bleeding stop time ≥8 min (%)	50.00	67.50	0. 48 (0.20–1.10)	0.08
Discharge time ≤55 min (%)	43.33	62.50	0. 45 (0. 20–1.04)	0.06
VAS[3] of pain during procedure ≤4 (%)	43.33	87.50	0.1 (0.03–0.31)	0.001
VAS of satisfaction ≥7 (%)	41.70	65.00	0.38 (0.16–0.88)	0.022
Side effects in the ED (%)	35.00	0		
Recurrence (%)	11.67	25.00	0.40 (0.14–1.15)	0.08

[1]Anterior nasal packing (n=60), [2]Nasal gel (n=40), [3]Visual analog scale.
ED: Emergency department, CI: Confidence interval, OR: Odds ratio

DISCUSSION

Although ANP, as a mechanical procedure, is still a common procedure in the management of epistaxis, there are more convenient procedures for this purpose. Since there was no significant difference in bleeding stop time and recurrence in NG and ANP groups, this study showed similar efficacy for both procedures in epistaxis treatment. There was no significant difference in discharge time in both groups; however, pain during the procedure and procedural time were lower in NG group compared to ANP group. In addition, patients' satisfaction at discharge was higher in NG group. The safety use of NG was more than ANP due to fewer side effects.

There are several medical procedures for epistaxis management. Different anticoagulants and vasoconstrictors medicines have shown more effective in comparison to mechanical procedures in the control of anterior and even posterior nasal bleeding [12,13,23,24]. Some medicines, such as bismuth, in combination with other and even some herbal medicines, have shown good efficiency in bleeding control [25,26]. In the absence of severe bleeding and high-risk conditions, local medical treatments are preferable in comparison to surgical procedures [12], unless no response to them is seen [27-29]. These methods are a better tolerated, more safe, and easy alternative to nasal packing in patients presenting with acute anterior epistaxis [12,23,24]. In the present study, there was no significant difference in bleeding stop time between NG and ANP procedure, in regard to their efficiency in the control of mild-to-moderate anterior nasal bleeding (Grades I and II). This can be due to good NG efficacy in controlling Grades I and II epistaxis through reabsorption of water and concentrating coagulation factors and platelets in the bleeding site. In addition, the two studied groups indicated no significant difference in bleeding recurrence during the first 24 h and the 1st week after the intervention. However, the underlying conditions in the two groups were not significantly different. Therefore, the efficacy of this method in epistaxis control including bleeding stop time and recurrence is similar to ANP and may be of considerable importance, although there is little evidence of the effectiveness of this gel.

Patients' satisfaction is a pivotal factor concerning hospital service quality. Patients are too expectant about the quality and speed of received treatments in the ED. Several factors affect patients' satisfaction in the ED. Among these factors, pain control has a role regarding the satisfaction rate [30-32]. In our study, use of NG caused significantly increased patients' satisfaction. In addition, there are several supportive medications to control epistaxis in spite of various invasive surgical

procedures [13,14,33]. These nonsurgical procedures are preferred to control mild-to-moderate bleedings [27]. Using these methods, due to their convenience and less pain, are increasing in comparison to painful surgical methods and chemical cauterization [6]. In the present study, NG group showed lower pain during the procedure and higher patients' satisfaction in comparison to ANP group. In nasal packing, as a traumatic, painful procedure, both insertion and removal of the packs are painful and cause great suffering. Moreover, it needs a second refers to the hospital for pack removal while NG, after being swallowed, is easily exerted through the digestive system. However, it is important that the use of either of these procedures should be according to the physician opinion or even patient's preference. Moreover, due to the overcrowding conditions in the ED and its outcomes, short hospital stay and early discharge are very significant [34]. In our study, two groups showed no significant difference in this term that can be attributed to the small sample size; however, procedural time in NG group was significantly shorter. This time-saving procedure could result in more satisfaction and improved ED management. In this study, pain score during the procedure and procedural time were lower in NG group that cause patients' satisfaction at discharge.

The mechanical procedure of nasal packing has some side effects which compromise patients' health. This technique can cause some problems such as pain and discomfort, septum necrosis, local infection, toxic shock syndrome, and the need for using antibiotics or analgesics. Some of these can cause irreversible and dangerous side effects [5,6]. Although in this study, all these side effects were not seen in the hospital or patients' follow up, some side effects such as intolerance and nausea were significantly more in ANP group. Therefore, NG using has more safety and fewer side effects.

In our randomization process, we used a random number generator to divide subjects into two groups. This method does not guarantee the matching of baseline characteristics and potential confounders between two arms. In addition, the sample size at two arms might be different. However, here, fortunately, distribution of almost all baseline characteristics was the same in the two groups. In future studies, we recommend using better randomization methods such as minimization.

Limitations

The present study had the following limitations: The sample size was small due to the lack of access to NG, patients with severe (Grade III) or posterior nasal bleeding and those younger than 16 years were excluded, and the study subjects were selected from only one center. None of the patients and general physician and emergency medicine specialists were blinded to the study.

CONCLUSION

It seems that use of NG can be safe and efficient in mild-to-moderate anterior epistaxis management. Increasing patients' satisfaction resulting from less pain during the procedure, shorter procedural time, and fewer side effects are some of the desirable characteristics of this procedure in comparison to ANP. Due to the small sample size, another study is recommended with a larger sample size. In particular, there is little evidence of the benefits and effectiveness of this gel.

AUTHORS CONTRIBUTION

Study concept, design and supervision: MT; acquisition of data: AR and SHM; analysis and interpretation of data: MRB; drafting of the manuscript, technical and material support: MT.

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CONFLICTS OF INTERESTS

None declared.

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