



# Non - traumatic Epistaxis Management Using Celox<sup>®</sup> Dressing: A Randomized Clinical Trial

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## Abstract

**Background:** Epistaxis is the most common otolaryngologic emergency.

**Objectives:** The current study aimed at evaluating the therapeutic effect of the Celox<sup>®</sup> bandage to manage non - traumatic epistaxis in the emergency department.

**Methods:** In the current randomized, clinical trial, 150 patients with non - traumatic epistaxis admitted to the emergency department in Imam Reza and Sina hospitals affiliated to Tabriz University of Medical Sciences, Tabriz, Iran, during years 2015-2016. The patients were randomly divided into two groups: group 1 dressing with the Celox<sup>®</sup> band and group 2 dressing with the anterior nasal tampon. The convenient sampling method was employed. Bleeding control (minute), patients' satisfaction, and lack of rebleeding within the first 24 hours of administration were compared between the two groups.

**Results:** There was no statistically significant difference between the two groups in terms of demographic variables, vital signs, and paraclinical testing results ( $P > 0.05$ ). With respect to the control of bleeding in the first 5 minutes after management, 93.3% of the bleeding was controlled in the Celox<sup>®</sup>, and 96% of the bleeding was controlled in the anterior tampon groups ( $P = 0.467$ ). The satisfaction level of the patients in the Celox<sup>®</sup> group was greater than that of the tampon group, and the difference was statistically significant ( $P < 0.001$ ). Lack of rebleeding within 24 hours after management had the most significant effect on the patient satisfaction [odds ratio (OR) = 3.969].

**Conclusions:** Based on the results of the current study, there was no significant difference in bleeding control and the success rate between the two groups in the study. Ease of usage, however, makes Celox<sup>®</sup> a better alternative to control epistaxis. Furthermore, the treatment of epistaxis with Celox<sup>®</sup> leads to higher satisfaction levels.

**Keywords:** Epistaxis, Treatment, Chitosan, Emergency Department, Hospital

## 1. Background

Epistaxis refers to any bleeding originates from the nose, the sinuses, or the paranasal cavities of the nostril or mouth (1). Epistaxis usually occurs in 7% - 14% of the total population each year (2). Although most epistaxis cases are mild (3), it is usually self-limited, and the external pressure on the nose is controlled (4).

Currently, the treatments available for epistaxis include direct nasal pressure, chemical cauterization, thrombogenic reticulated foams, and anterior/posterior nasal packs (1, 5, 6). At present, the anterior nasal pack is one of the routine procedures to control epistaxis (7) performed after applying local anesthesia with lidocaine and a vasoconstrictor drug such as epinephrine (1, 8, 9) and subsequently, a band stained with the tetracycline ointment or petroleum jelly is placed in the nose. This

method has some prerequisites, such as the requirement for antibiotic prophylaxis, the need to preserve the pack for a long time, and essentiality of an anesthetic. Fulfillment of these prerequisites allows physicians to follow easier ways to control simple epistaxis (9).

One of the newest products used to control different types of bleeding is the Celox<sup>®</sup> coagulation powder. This product is used to control external bleeding quickly; the main constituent of this product is chitosan. Celox powder and tampon are certified by FDA (Food and Drug Administration of America), CE (Europe Union), and IRC (the Iran Registration Code) of the Iranian Ministry of Health and Medical Education (10-12).

## 2. Objectives

The current study aimed at comparing Celox® with conventional topical therapy (shrink + tampons) to manage epistaxis in patients referred to the emergency department.

## 3. Methods

### 3.1. Study Design

The current randomized, clinical trial was conducted at the emergency department of Imam Reza and Sina hospitals affiliated to Tabriz University of Medical Sciences, Tabriz, Iran, from July 2015 to December 2016.

### 3.2. Setting and Selection of Participants

The inclusion criteria were the age range 18 - 65 years and referring to the emergency department for non-traumatic epistaxis. The exclusion criteria were coagulation disorders (international normalized ratio (INR) > 1.5) and taking anticoagulant and antiplatelet drugs, systolic blood pressure > 140 mmHg, history of cardiovascular diseases, need for hospitalization, multiple trauma, isolated nose trauma, shock, and not willing to participate in the study.

To determine the sample volume, a comparison test was performed. The basic information about the success of epistaxis control raised from the study by Zahed was used (8); thereafter, using the software G power version 3.1.2, a total of 75 subjects was calculated for each group.

The current study was approved by the Ethics Committee of Tabriz University of Medical Sciences (registration code: TBZMED.REC.1394.201) on 13 May, 2016. It was also registered in the Iranian registry of clinical trial (IRCT) (code IRCT2015053112592N1).

### 3.3. Randomization and Blinding

The patients were divided into two individual blocks using random allocation software. The analysis strategy in the current study was as per protocol. Figure 1 shows the flowchart of the study.

### 3.4. Intervention

The primary outcome variables were the bleeding control and patient satisfaction. The secondary outcome variables included a lack of rebleeding within the first 24 hours after the management. In the method including the tampon with Celox® band (MedTrade Products Ltd., Crewe, UK), after unloading each of the blood clots from the nostrils, the band available in each product pack -the Celox® band- was placed inside bleeding nostrils with bayonet pins. The patient was then asked to press his nostrils. The control

of nose bleeding was evaluated, and the bleeding control was recorded in minutes using a stopwatch. After bleeding control, the Celox® band was removed. In the control group, to control bleeding, the conventional method, i.e., the shrinkage of the nostril was performed using a 3-band cotton soaked with epinephrine and lidocaine; then, an anterior nasal tampon was embedded into the nostril using a band mesh stained with 3% tetracycline ointment. All the listed variables were evaluated in the first group.

### 3.5. Methods of Measurement

Control of bleeding was defined as the stopping of bleeding from the nostrils and the lack of bleeding in the back of the throat after embedding Celox® band or the nasal tampons. The length of stay (LOS) of the patient in the emergency department was also recorded. The patient was followed up for 24 hours after the treatment in case of recurrent bleeding and the results were recorded. To assess patient satisfaction among different treatment methods, 24 hours after discharge from the emergency department, the 0 - 10 numerical rating scale (NRS) was used, in which score 1 means least, and 10 refers to the highest satisfaction.

### 3.6. Statistical Analysis

The collected data were transferred into STATA statistical software version 11.0 (STATA Corp., Texas, USA). First, the normal distribution of the data was evaluated using the Kolmogorov - Smirnov test. The descriptive statistics were to express data as frequency (in percentage) qualitatively. To compare the 2 groups in terms of qualitative variables, the Chi - square test was used. To analyze the non-normal distribution of the quantitative data, the median (first and third quartiles) was used. The quantitative data were analyzed using the Mann - Whitney U test was used. To determine the factors affecting patient satisfaction, the ordinal regression was used.  $P < 0.05$  was considered the level of significance.

## 4. Results

The current study evaluated 150 patients with epistaxis (75 patients in each group) referred to the emergency department. In terms of gender 84 males (56%) and 66 females (44%) were included in the investigation. The mean age of the subjects in the Celox and tampon groups was 49 and 41 years, respectively. Table 1 shows the demographic characteristics and the medical history of the patients in the two groups.

In terms of the success rate in controlling epistaxis in the two groups of patients under study, the epistaxis was controlled with the measures taken, and the rate was 100%

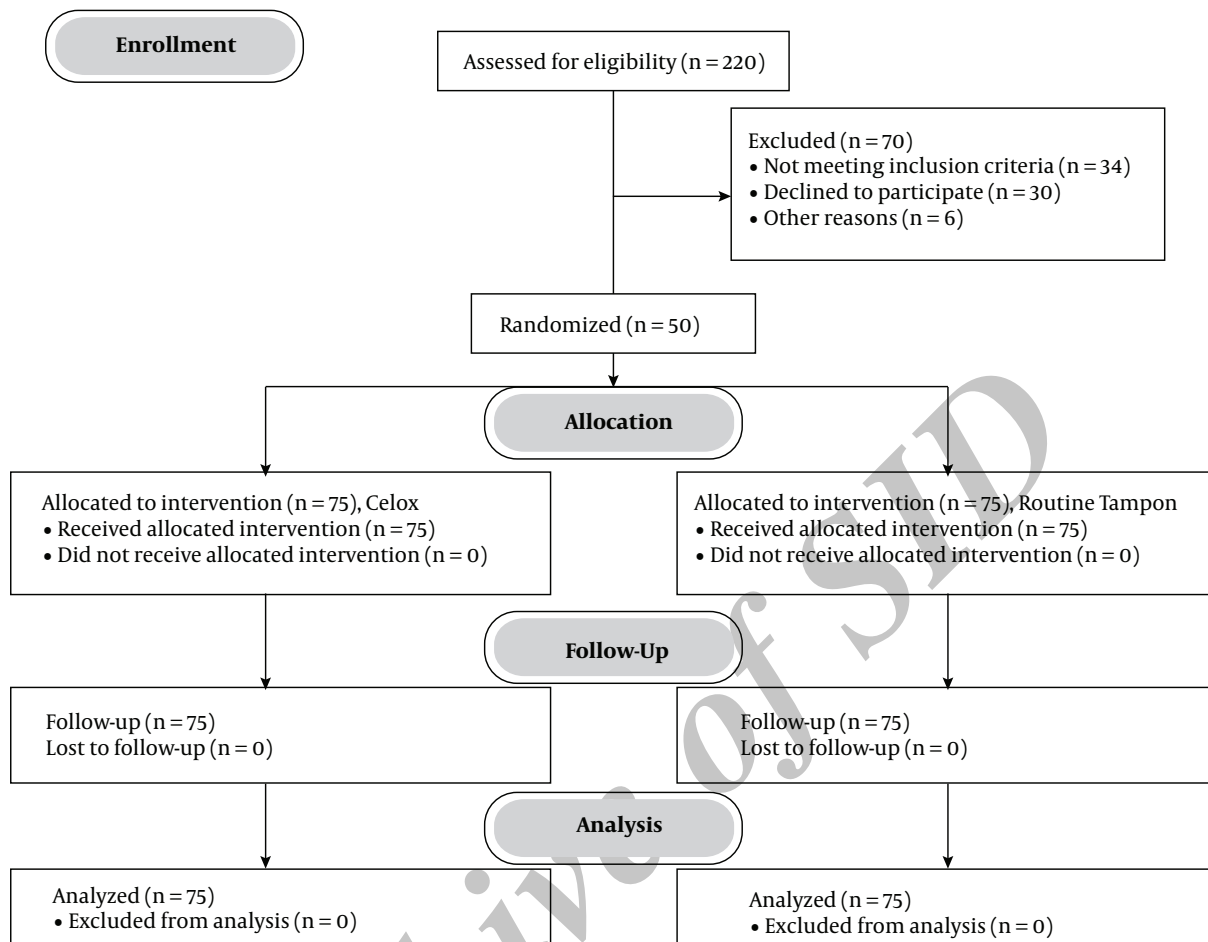


Figure 1. The Flowchart of the Study

in the two groups; there was no significant difference between the groups in terms of the success rate ( $P > 0.05$ ).

The patients were divided into two groups regarding the history of epistaxis and rebleeding within 24 hours after discharge; these two aspects were compared in the two groups. Among the study subjects, 47 patients (31.3%) had a history of epistaxis. Out of the patients with a history of epistaxis, 10 (21.3%) patients experienced rebleeding within 24 hours after the management; out of the patients without a history of epistaxis, 7 (6.8%) experienced rebleeding within 24 hours after the management. There was a significant difference between the 2 groups in terms of the recurrence of epistaxis ( $P = 0.013$ ) demonstrating that the relapse rate was higher in patients with the history of epistaxis. The mean of bleeding control (in minutes) and length of stay (in minutes) of the patients under study in the Celox group were 3 and 60 minutes, respectively; in the tampon group, the bleeding control, and the

length of stay were 3 and 60 minutes, respectively. Table 2 shows the results of the two groups in terms of bleeding control, length of stay, rebleeding within the next 24 hours, and patient satisfaction.

According to Table 2, there are no significant differences between the two groups in terms of the LOS in the emergency department and rebleeding within 24 hours after discharge ( $P > 0.05$ ). In addition, in terms of the success rate in controlling nasal bleeding in less than 5 minutes, there was no significant difference between the two groups ( $P > 0.05$ ). The satisfaction of the patients was, however, length of stay in the Celox® group than the tampon group, which was statistically significant ( $P < 0.001$ ).

Table 3 shows the median (first and third quartiles) of patient satisfaction based on patients' age, type of treatment, bleeding control, LOS, and rebleeding within 24 hours after the management. The patients' satisfaction was high when patients were younger, experienced a short

**Table 1.** Demographic Status and the Laboratory Findings of the Study Groups

Variable	Celox® Group	Control Group	P Value
<b>Age (year)</b>			0.805 <sup>a</sup>
First quartile	28	27	
Median	49	41	
Third quartile	60	60	
<b>Gender</b>			0.511 <sup>b</sup>
Male	44 (58.7%)	40 (53.3%)	
Female	31 (41.3%)	35 (46.7%)	
<b>History of epistaxis</b>			0.379 <sup>b</sup>
Yes	21 (28%)	26 (34.7%)	
No	54 (72%)	49 (65.3%)	
<b>MAP (mmHg)</b>			0.090 <sup>a</sup>
First quartile	80	75	
Median	80	80	
Third quartile	85	83.3	
<b>Laboratory</b>			
<b>Platelet (/mm<sup>3</sup>)</b>			0.985 <sup>a</sup>
First quartile	190000	185000	
Median	235000	235000	
Third quartile	297000	310000	
<b>INR</b>			0.101 <sup>a</sup>
First quartile	1	1	
Median	1	1	
Third quartile	1.1	1.1	

Abbreviations: INR, international normalized ratio; MAP, mean atrial pressure.

<sup>a</sup>Mann - Whitney U test<sup>b</sup>Chi-square test

bleeding control and length of stay, and had no rebleeding in 24 hours after the management. To determine the correlation between the mentioned variables and the satisfaction rate, the ordinal regression was used. Table 4 shows the coefficient and the OR between age, type of treatment (Celox® and tampon), bleeding control, length of stay of patients in the emergency department, and the relapse of epistaxis and patients' satisfaction. The study results showed that all the mentioned variables except the relapse of epistaxis after 24 hours of management had an inverse relationship with the satisfaction rate. With an increase in the duration of these variables and a change in the type of treatment with the tampon, the patients' satisfaction reduced. Relapse of epistaxis after 24 hours of management had a direct relationship with the satisfaction rate; the OR of this variable was higher than those of the others. By way of example, this variable had the most potent effect on de-

**Table 2.** Comparison of the Study Groups in Terms of Bleeding Control, Rebleeding Within 24 Hours, and Patient Satisfaction Level

Variable	Celox® Group	Control Group	P Value
<b>Bleeding control, min</b>			0.467 <sup>a</sup>
≤ 5	70 (93.3%)	72 (96%)	
> 5	5 (6.7%)	3 (4%)	
<b>Length of hospital stay, min</b>			0.597 <sup>a</sup>
≤ 60	50 (66.7%)	53 (70.7%)	
> 60	25 (33.3%)	22 (29.3%)	
<b>Rebleeding in 24 h</b>			0.440 <sup>a</sup>
Yes	10 (13.3%)	7 (9.3%)	
No	65 (86.7%)	68 (90.7%)	
<b>Satisfaction</b>			< 0.001 <sup>b</sup>
First quartile	9	8	
Median	10	9	
Third quartile	10	9	

Abbreviations: m, minutes

<sup>a</sup>Chi-square test<sup>b</sup>Mann - Whitney U test

termining the satisfaction of patients.

## 5. Discussion

Epistaxis is one of the common complaints in the emergency department (13). The exact prevalence of epistaxis is unknown; the most common cases of epistaxis are self-limiting and self-remitting cases. When medical intervention is needed, it is mostly required due to recurrent bleeding or the severe nature of epistaxis (14-16).

Various studies are conducted on the treatment of epistaxis. Granville - Chapman et al., concluded that such a treatment plays an essential role in the prevention, but it seems that new products such as wound state, Celox®, and combat gauze are more effective (14). The results of the study by Ozlem Koksall et al., demonstrated that Celox® had an effective influence on controlling bleeding in normothermic and hypothermic situations, or during the use of an anticoagulant (17).

Moharamzadeh et al., recommended adding 2% citric acid to the routine management of epistaxis (18). Zahed et al., concluded that the addition of tranexamic acid during the treatment with the anterior nasal tampon in epistaxis was more effective in controlling bleeding than the other methods (9). Chhapola et al., showed that tranexamic acid, without complications, led to a significant reduction of nasal bleeding during the endoscopic surgery of the nose (19).

**Table 3.** Mean Patient Satisfaction in the Study Groups

Variable	First Quartile	Median	Third Quartile	P Value <sup>a</sup>
<b>Age (y)</b>				0.005
18 - 40	9	10	10	
41 - 65	8	9	10	
<b>Type of treatment</b>				< 0.001
Celox	9	10	10	
Anterior tampon	8	8	9	
<b>Bleeding control ≤ 5 min</b>				0.002
Yes	8	9	10	
No	5	5.5	8.75	
<b>Length of hospital stay (min)</b>				< 0.001
≤ 60	9	9	10	
> 60	7	8	10	
<b>Rebleeding in 24 hours</b>				< 0.001
Yes	5	8	9	
No	8	9	10	

<sup>a</sup>Mann - Whitney U test, P < 0.05 was considered significant

**Table 4.** Coefficient and OR of the Variables for Patient Satisfaction

Variable	Coefficient	Odds Ratio	95% Confidence Interval of Odds Ratio	P Value
Age	- 0.289	0.972	0.950 - 0.994	0.001
Type of treatment	- 2.762	0.063	0.028 - 0.142	< 0.001
Bleeding control time	- 0.854	0.425	0.280 - 0.647	< 0.001
Length of hospital stay	- 0.007	0.993	0.986 - 1.000	< 0.001
Relapse	1.378	3.969	1.283 - 12.276	< 0.001

Statistically, the satisfaction of the patients in the group treated with the Celox<sup>®</sup> band was higher than the tampon group. In addition, regarding the evaluation of patient satisfaction, factors such as younger age, control of bleeding in a short time, and early discharge from the emergency department, using the Celox<sup>®</sup> band for the treatment, and no rebleeding increased patient satisfaction. It can be concluded that the quick and easy embedded Celox<sup>®</sup> band had a stronger effect on patient satisfaction and a reduced LOS in the emergency department in comparison to the anterior nasal tampon. In addition, the lack of rebleeding within 24 hours after the management had the most powerful impact on patient satisfaction (OR = 3.969).

The small sample size and the lack of long-term follow - up of the studied patients were among the notable limitations.

Based on the results of the current study, it can be concluded that considering the lack of a significant difference

in the discharge time and recurrence within 24 hours between the two methods, owing to the ease of use of Celox<sup>®</sup> and the higher patient satisfaction, the Celox<sup>®</sup> band can provide a better alternative to control epistaxis. Future studies should consider more influential factors such as the types of used anticoagulant drugs, medication dosage, the potential impact of previous diseases, and the causes of epistaxis.

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### Footnotes

**Authors' Contribution:** All authors read and approved the final copy of the manuscript. Alireza Ala, Sahar Shirzadegan, and Haniyeh Ebrahimi Bakhtavar: data collection, writing and critical revision of the manuscript; Farzad Rahmani and Robab Mehdizadeh Esfanjani: study design and performing the statistical analyses and interpretation of data.

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