J Surg Med. 2024;8(10):159-162.
https://doi.org/10.28982/josam.7852

JOSAM

Research article
https://jsurgmed.com/

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Comparison of traditional and next-generation oral anticoagulants in the etiology of epistaxis

Süheyla Kandemir [1], Hüseyin Kandemir [2]

[1] Department of Ear Nose and Throat, Kırıkkale University, Faculty of Medicine, Kırıkkale, Turkey
[2] Department of Cardiology, Kırıkkale University, Faculty of Medicine, Kırıkkale, Turkey

ORCID of the author(s)

SK: https://orcid.org/0000-0003-3354-2212
HK: https://orcid.org/0000-0002-4462-7425

Corresponding Author
Süheyla Kandemir
Department of Ear Nose and Throat,
Kırıkkale University, Faculty of Medicine,
71450 Kırıkkale, Turkey
E-mail: dr.suheyla_bostan@hotmail.com

Ethics Committee Approval
The study was approved by the Ethics Committee of Kırıkkale University Faculty of Medicine, decision dated March 29, 2023 and numbered 2023.03.04.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

Financial Disclosure
The authors declared that this study has received no financial support.

Published
2024 October 10

Abstract

Background/Aim: There is a dearth of studies addressing the effects of next-generation anticoagulants on epistaxis. The aim of this investigation was to determine whether there are any differences between traditional and next-generation anticoagulants in the etiology of epistaxis.
Methods: This retrospective cohort study focused on a total of 7,110 individuals (3,278 females (46.1%) and 3,832 males (53.9%)) diagnosed with epistaxis between 2018 and 2022; the mean age of the patients was 37.7 years. Patient data (age, gender, outpatient and inpatient treatments, relevant laboratory parameters, and treatment evidence) were retrospectively reviewed from a hospital database. The severity of epistaxis was assessed based on treatment notes. Patients with hypertension and those undergoing antiaggregant therapy were excluded from the study. International Classification of Diseases (ICD) codes from the automated system were examined retrospectively. The data were used to establish three patient groups: the first group consisted of individuals taking next-generation oral anticoagulants, the second group consisted of individuals taking traditional oral anticoagulants, and the third group consisted of healthy controls.
Results: We found statistically significant differences among the groups in terms of age, the severity of epistaxis, the treatment modality, and laboratory findings (P<0.001); no statistically significant difference was found in terms of gender (P=0.954). Group 2 contained the largest number of hospitalized patients and patients with severe active nosebleeds.
Conclusion: Next-generation anticoagulants are more reliable than traditional anticoagulants in terms of the severity of epistaxis, the need for hospitalization, and laboratory results.

Keywords: epistaxis, anticoagulants, warfarin, rivaroxaban, dabigatran

How to cite: Kandemir S, Kandemir H. Comparison of traditional and next-generation oral anticoagulants in the etiology of epistaxis. J Surg Med. 2024;8(10):159-162.

Introduction

Epistaxis is a common otolaryngological problem that affects approximately 60% of the general population [1]. Medical treatment is required for about 6% of cases, and hospitalization is necessary for fewer than 0.2% of cases [2,3]. The majority of nosebleeds (90–95%) originate from the anterior region; the remaining cases derive from the posterior region [4]. While there are several risk factors for epistaxis, including allergic rhinitis, trauma, hypertension, anticoagulant use, bleeding disorders, seasonal factors, and sinonasal tumors, the most common cause (accounting for 38–40% of cases) is idiopathic (i.e., spontaneous bleeding without a clear trigger) [5-7]. Topical vasoconstrictors and nasal compression are usually effective at controlling most cases of epistaxis [8]. In severe cases, anterior or posterior nasal packing, electrical or medical cautery, or a balloon catheter may be used. In rare cases, surgical interventions such as embolization or endoscopic ligation may be necessary [9].

Patients with epistaxis who use anticoagulant drugs, particularly for associated cardiovascular diseases, often experience frequent nosebleeds due to their long-term treatment. The use of next-generation anticoagulants (NOAC) and traditional anticoagulants (COAC) is increasing in this patient population [8].

The aim of this study was to determine the demographic characteristics of patients with epistaxis, identify the risk factors for outpatient and inpatient treatment, assess the severity of epistaxis, systematically review laboratory parameters and treatment evidence, and compare the differences between NOAC and COAC.

Materials and methods

Participants and study design

This retrospective cohort study was conducted between 2018 and 2022 at Kırıkkale Yüksek İhtisas hospital. Patients diagnosed with epistaxis were identified via the hospital's automated system. We retrospectively analyzed the patients' clinical information, as determined by their physicians using International Classification of Diseases (ICD) codes. The hospital's information technology personnel assisted in amassing the relevant data, which were transferred to an Excel spreadsheet using specific filters. The ICD code R04 (epistaxis) was required. In addition to code R04, diagnostic codes I48 (atrial fibrillation and flutter) and Z95.2 (heart valve prosthesis) were used to identify patients using NOAC and COAC. Patients diagnosed with R04+I10 (hypertension) were excluded from the study. We defined three patient groups: the first group consisted of NOAC users, the second group consisted of COAC users, and the third group consisted of healthy controls. Demographic characteristics (age, gender) and outpatient and inpatient treatments, laboratory parameters (if available), and evidence regarding treatment were recorded. Patients who received antiplatelet treatment (such as acetylsalicylic acid, clopidogrel, or ticlopidine) and patients whose files could not be accessed were excluded from the study.

Anticoagulant treatments

Anticoagulant therapy is used to prevent thromboembolic events. Warfarin, a classic anticoagulant derived from vitamin K, requires regular blood tests to monitor international normalized ratios (INRs). Low INR levels increase the risk of thromboembolic events, and high INR levels can cause bleeding. Warfarin also has many interactions with other drugs and food. Therefore, NOAC, including direct thrombin inhibitors (e.g., dabigatran etexilate) and direct factor Xa inhibitors (e.g., rivaroxaban and apixaban), have been developed in recent years. These agents are increasingly replacing warfarin because they do not require laboratory monitoring and have shown equivalent or superior efficacy in preventing systemic embolism or stroke in high-risk populations [10-12]. Laboratory parameters (especially INR) were obtained from the hospital's automated records system; patients without laboratory parameters were excluded from the study.

Epistaxis severity

Patients were classified into one of three groups based on the severity of their epistaxis:

1. No active bleeding or only occasional bleeding.
2. Active bleeding that stopped with an intervention in the outpatient clinic.
3. Severe active bleeding requiring hospitalization and cauterization in an operating room.

To determine these groups, the patients were first divided into inpatient and outpatient groups based on hospital data. The nasal mucosa of hospitalized patients was cauterized, and the operation code was scanned to determine the patients belonging to group 3. The outpatient procedure code for cauterization of the nasal mucosa was scanned to determine patients belonging to group 2. Patients in group 1 included individuals who were seen in the outpatient clinic but did not undergo any procedures.

The study was approved by the Kırıkkale University Faculty of Medicine Ethics Committee (decision dated March 29, 2023, number 2023.03.04). Given that this study was a retrospective file review, written informed consent was not obtained from the patients. All procedures were conducted in accordance with ethical guidelines and the principles of the Declaration of Helsinki.

Statistical analysis

SPSS version 25.0 (IBM Corp., Armonk, NY, USA) was used for the statistical analysis. Frequencies (number, percentage) were provided for categorical variables, while descriptive statistics (mean [standard deviation]) were given for numerical variables. The normality of the data was assessed using normal distribution parameters and the Shapiro-Wilk test. Nominal categorical variables were compared using the chi-squared test and Fisher's exact test. Non-parametric variables were analyzed using the Mann-Whitney U test and the Kruskal-Wallis test. A significance level of $P < 0.05$ was used.

Results

A retrospective search of Kırıkkale Yüksek İhtisas hospital database revealed 7,110 individuals with epistaxis. The mean age of the patients was 37.7 (24.3) years. Of those patients, 3,278 (46.1%) were female and 3,832 (53.9%) were male.

Group 1 consisted of 211 patients using NOAC (3.0% of the patient cohort), group 2 consisted of 303 patients using COAC (4.3% of the patient cohort), and group 3 (the control group) consisted of 6,596 patients not using anticoagulants (92.8% of the patient cohort).

Slightly more than half of the patients (4,473; 62.9%) did not have active bleeding when they were admitted to the hospital.

The mean age of those patients was 34.1 (23.1) years. On the other hand, 2,591 patients (36.4%) had active bleeding upon admission; the mean age of that cohort was 43.6 (24.9) years. Severe epistaxis was present in 46 patients upon admission (0.6%); that group had a mean age of 59.2 (28.2) years.

Nearly all of the patients (7,063; 99.3%) were treated as outpatients; 47 patients (0.7%) were treated as inpatients. The mean age of the outpatients was 37.6 (24.2) years; the mean age of the inpatients was 59.5 (28.0) years.

Laboratory parameters were not measured in 5,244 patients (73.8%); they were measured in 1,866 patients (26.2%). Among the patients for whom laboratory parameters were measured, 1,733 (24.4%) had values within the normal range; 133 (1.9%) had values outside the normal range.

Statistical analysis revealed a significant difference between the groups in terms of age, severity of epistaxis, treatment modality, and laboratory findings (P<0.001). However, no statistically significant difference was found in terms of gender (P=0.954) (Table 1). Severe active epistaxis was most common in group 2 (41.3% of patients), and patients with active bleeding upon admission more commonly belonged to group 2 rather than group 1 (Table 2). Inpatients were most frequently in group 2 (Table 3).

Table 1: Patient demographic and clinical features

Parameter	Group 1 (NOAC) (n=211)	Group 2 (COAC) (n=303)	Group 3 (Control) (n=6596)	*P*-value
Age, years, Mean (SD)	77.9 (5.3)	79.2 (7.1)	34.5 (22.2)	<0.001
Gender, female/male, n	99/112	138/165	3041/3555	0.954
Epistaxis severity, no active bleeding/there is active bleeding/active bleeding is severe, n	151/49/11	177/107/19	4145/2435/16	<0.001
Laboratory parameter, not checked/normal/ abnormal, n	154/38/19	188/93/22	4902/1602/92	<0.001
Treatment, outpatient/inpatient, n	200/11	283/20	7063/47	<0.001

Bold values indicate statistical significance. NOAC: New generation oral anticoagulant, COAC: Classical oral anticoagulant

Table 2: Epistaxis severity in groups

Epistaxis severity		Group 1 (NOAC)	Group 2 (COAC)	Group 3 (Control)	Total
No active bleeding	Count	151	177	4145	4473
	% within	3.4%	4.0%	92.7%	62.91%
There is active bleeding	Count	49	107	2435	2591
	% within	1.9%	4.1%	94.0%	36.44%
Active bleeding is severe	Count	11	19	16	46
	% within	23.9%	41.3%	34.8%	0.64%
Total	Count	211	303	6596	7110
	% within	3.0%	4.3%	92.8%	100.0%

NOAC: New generation oral anticoagulant, COAC: Classical oral anticoagulant

Table 3: Treatment in groups

Treatment		Group 1 (NOAC)	Group 2 (COAC)	Group 3 (Control)	Total
Outpatient	Count	200	283	6580	7063
	% within	2.8%	4.0%	93.2%	99.3%
Inpatient	Count	11	20	16	47
	% within	23.4%	42.6%	34.0%	0.66%
Total	Count	211	303	6596	7110
	% within	3.0%	4.3%	92.8%	100.0%

NOAC: New generation oral anticoagulant, COAC: Classical oral anticoagulant

Discussion

Epistaxis is a common emergency in otolaryngology that accounts for approximately 0.5% of total emergency admissions and 25–30% of ENT emergencies [13,14]. The condition can range from minor bleeding that can be stopped with simple interventions to life-threatening bleeding [15]. Previous studies have shown that epistaxis is more common in men than in women [16]. Our study found a similar distribution, with 53.9% of cases occurring in men and 46.1% occurring in women.

As life expectancy increases, the prevalence of chronic diseases, including prothrombotic conditions, also increases. There is a consequent uptick in the usage of antithrombotic drugs, particularly among older individuals [17,18]. The use of anticoagulants has been identified as a risk factor for epistaxis in numerous studies [19,20]. New oral anticoagulants, such as factor Xa inhibitors (e.g., rivaroxaban, apixaban) and direct thrombin inhibitors (e.g., dabigatran), have gained popularity due to their shorter half-lives and ease of discontinuation [21,22]. The introduction of a next generation of oral anticoagulants over the past decade has significantly increased awareness of the complexity of managing nosebleeds in antithrombotic therapy settings. In our study, patients had a history of using next-generation anticoagulants such as direct-factor Xa inhibitors (rivaroxaban and apixaban) and thrombin inhibitors (dabigatran). They also used warfarin as a classical anticoagulant. Up to 17% of all predicted epistaxis cases in the general population involve anticoagulant use [23,24]. In our study, we observed the use of both NOAC and COAC, with an overall rate of anticoagulant use of 7.2%.

Some studies have reported that anticoagulant use is both an etiological factor for epistaxis and something that increases its recurrence rate [25]. However, other studies have found no increased risk in patients using new oral anticoagulants compared with the general population [20]. Additionally, hospital stays have been found to be shorter for patients receiving NOAC therapy compared with patients receiving vitamin K-derived anticoagulation therapy [26]. In another study, Sauter et al. [27] showed that NOAC recipients actually had lower hospitalization rates. There is evidence suggesting that the risk of bleeding events, including epistaxis, is significantly lower in patients using NOAC compared with COAC [28,29]. While Send et al. [30] found similar bleeding severity and results with NOAC compared with COAC, Gökdoğan et al. [29] noted that it was more difficult to control bleeding in patients taking NOAC. Other studies have reported a lower rate of hospitalization in patients taking NOAC compared with patients taking COAC [26,27]. Yaniv et al. [31] determined that next-generation oral anticoagulants are safer than older anticoagulant/antiplatelet drugs in terms of severity of bleeding, the need for hospitalization and length of hospital stay. Our study found that severe active nosebleeds and inpatient treatment were most common in the group of patients using COAC.

Routine coagulation studies are not necessary for all patients presenting with epistaxis; the exception is children and individuals using warfarin [32-34]. However, patients using warfarin and patients whose nosebleeds do not respond to local treatment should have their INR levels checked [35,36]. In our study, laboratory parameters were evaluated in only 26.2% of patients, and the majority of these patients had normal values.

Overall, our study provides valuable insights into the characteristics and management of epistaxis. However, follow-on research is necessary to explore the specific effects of different anticoagulant therapies on the severity and outcomes of epistaxis.

Limitations

This study has several limitations. Firstly, the data collection was retrospective and only based on what was recorded in the hospital's automated system. Secondly, the data were collected from a single institution, which limits the generalizability of the findings. Thirdly, although the number of patients included in the study was sufficient, the control group constituted a significant portion of the study population. Therefore, future prospective studies should be conducted to validate our results.

Conclusion

Our findings indicate that NOAC are more reliable than COAC in terms of the severity of epistaxis, the need for hospitalization, and laboratory results. These results suggest that patients using NOAC have a lower hospitalization rate and can be managed with a more conservative approach.

References

1. Cohen O, Shoffel-Havakuk H, Warman M, Tzelnick S, Haimovich Y, Kohlberg GD, et al. Early and Late Recurrent Epistaxis Admissions: Patterns of Incidence and Risk Factors. Otolaryngol Head Neck Surg. 2017;157:424-31.
2. Krulewitz NA, Fix ML. Epistaxis. Emerg Med Clin North Am. 2019;37:29-39.
3. Neshewat J, Wasserman A, Alexandris-Souphis C, Haymart B, Feldeisen D, Kong X, et al. Reduction in epistaxis and emergency department visits in patients taking warfarin after implementation of an education program. Thromb Res. 2021;199:119-22.
4. Douglas R, Wormald PJ. Update on epistaxis. Curr Opin Otolaryngol Head Neck Surg. 2007;15:180-3.
5. Sowerby LJ, DeSerres JJ, Rudmik L, Wright ED. Role of season, temperature and humidity on the incidence of epistaxis in Alberta, Canada. J Otolaryngol Head Neck Surg. 2014;43:10.
6. Tunkel DE, Anne S, Payne SC, Ishman SL, Rosenfeld RM, Abramson PJ, et al. Clinical Practice Guideline: Nosebleed (Epistaxis). Otolaryngol Head Neck Surg. 2020;162:1-38.
7. Chaaban MR, Zhang D, Resto V, Goodwin JS. Demographic, seasonal, and geographic differences in emergency department visits for epistaxis. Otolaryngol Head Neck Surg. 2017;156:81-6.
8. Purkey MR, Seeskin Z, Chandra R. Seasonal variation and predictors of epistaxis. Laryngoscope. 2014;124:2028–33.
9. Riviello RJ. Otolaryngologic procedures. In: Clinical Procedures in Emergency Medicine, 4th, Roberts JR, Hedges JR (Eds), WB Saunders, Philadelphia, 2004; p.1300
10. Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011;365:883–91.
11. Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med. 2009;361:1139–51.
12. Granger CB, Alexander JH, McMurray JJ, Lopes RD, Hylek EM, Hanna M, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365:981–92.
13. Pallin DJ, Chng YM, McKay MP, Emond JA, Pelletier AJ, Camargo CA Jr. Epidemiology of epistaxis in US emergency departments, 1992 to 2001. Ann Emerg Med. 2005;46:77-81.
14. Viehweg TL, Roberson JB, Hudson JW. Epistaxis: diagnosis and treatment. J Oral Maxillofac Surg. 2006;64:511-8.
15. Seidel DU, Sesterhenn AM, Kostev K. Seasonal Variation of Epistaxis in Germany. J Craniofac Surg. 2018;29:365-7.
16. Huang CL, Shu CH. Epistaxis: a review of hospitalized patients. Zonghua Yi Xue Za Zhi (Taipei). 2002;65:74-8.
17. Bermüller C, Bender M, Brögger C, Petereit F, Schulz M. Epistaxis and anticoagulation - a medical and economic challenge? Laryngorhinootologie. 2014;93:249-55.
18. Andreotti F, Rocca B, Husted S, Ajjan RA, ten Berg J, Cattaneo M, et al. Antithrombotic therapy in the elderly: expert position paper of the European Society of Cardiology Working Group on Thrombosis. Eur Heart J. 2015;36:3238–49.
19. Ho JPK, Bari N, Riffat F. Management of epistaxis in patients on novel oral anticoagulation therapy. J Laryngol Otol. 2020;134:316-22.
20. Buchberger AMS, Baumann A, Johnson F, Peters N, Piontek G, Storck K, et al. The role of oral anticoagulants in epistaxis. Eur Arch Otorhinolaryngol. 2018;275:2035-43.
21. Raghavan N, Frost CE, Yu Z, He K, Zhang H, Humphreys WG, et al. Apixaban metabolism and pharmacokinetics after oral administration to humans. Drug Metab Dispos. 2009;37:74–81.
22. Weitz JI, Eikelboom JW, Samama MM. New antithrombotic drugs: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidencebased clinical practice guidelines. Chest. 2012;141:120–51.
23. Suzuki S, Otsuka T, Sagara K, Semba H, Kano H, Matsuno S, et al. Nine-year trend of anticoagulation use, thromboembolic events, and major bleeding in patients with non-valvular atrial fibrillation- shinken database analysis. Circ J. 2016;80:639–49.
24. Rubboli A, Becattini C, Verheugt FW. Incidence, clinical impact and risk of bleeding during oral anticoagulation therapy. World J Cardiol. 2011:3:351–8.
25. Gomes P, Salvador P, Lombo C, Caselhos S, Fonseca R. Role of age and anticoagulants in recurrent idiopathic epistaxis. Acta Otorrinolaringol Esp. 2020;71:160-5.
26. L'Huillier V, Badet C, Tavernier L. Epistaxis complicating treatment by anti-vitamin K and new oral anticoagulants. Eur Ann Otorhinolaryngol Head Neck Dis 2018;135:231–5.
27. Sauter TC, Hegazy K, Hautz WE, Krummrey G, Ricklin ME, Nagler M, et al. Epistaxis in anticoagulated patients: fewer hospital admissions and shorter hospital stays on rivaroxaban compared to phenprocoumon. Clin Otolaryngol. 2018;43:103–8.
28. Kittelson JM, Steg PG, Halperin JL, Goldenberg NA, Schulman S, Spyropoulos AC, et al. Bivariate evaluation of thromboembolism and bleeding in clinical trials of anticoagulants in patients with atrial fibrillation. Thromb Haemost. 2016;116:544–53.
29. Gökdogan O, Akyildiz I, Sayin BY, Okutucu S, Tanalp AC, Arslan N. The rate of epistaxis incidence in new generation anticoagulants and perioperative approach in otorhinolaryngological practices. J Craniofac Surg. 2017;28:178–82.
30. Send T, Bertlich M, Horlbeck F, Schafigh D, Freytag S, Eichhorn KW, et al. Management and outcome of epistaxis under direct oral anticoagulants: a comparison with warfarin. Int Forum Allergy Rhinol. 2019;9:120–4.
31. Yaniv D, Zavdy O, Sapir E, Levi L, Soudry E. The impact of traditional anticoagulants, novel antikoagulants and antiplatelets on epistaxis. Laryngoscope. 2021;131:1946-51.
32. Spielmann P, Barnes M, White P. Controversies in the specialist management of adult epistaxis: an evidence-based review. Clin Otolaryngol. 2012;37:382–9.
33. Sandoval C, Dong S, Visintainer P, Ozkaynak MF, Jayabose S. Clinical and laboratory features of 178 children with recurrent epistaxis. J Pediatr Hematol Oncol. 2002;24:47–9.
34. Thaha M, Nilssen E, Holland S, Love G, White PS. Routine coagulation screening in the management of emergency admission for epistaxis – is it necessary? J Laryngol Otol. 2000;114:38–40.
35. Béquignon E, Teissier N, Gauthier A, Brugel L, De Kermadec H, Coste A, et al. Emergency department care of childhood epistaxis. Emerg Med J. 2017;34:543–8.
36. Horton JD, Bushwick B. Warfarin therapy: evolving strategies in anticoagulation. Am Fam Physician. 1999;59:635–46.