

## ANTICOAGULANTS AND EPISTAXIS: A COMPARATIVE ANALYSIS OF EPISTAXIS WITH WARFARIN AND DIRECT ORAL ANTICOAGULANTS

AZHAR S<sup>\*1</sup>, AHMED SI<sup>1</sup>, MUKHTAR A<sup>2</sup>, AZHAR H<sup>3</sup>, HASSAN A<sup>4</sup>, HASHIR Z<sup>1</sup>

<sup>1</sup>Department of General Medicine, Islamabad Medical and Dental College, Islamabad, Pakistan

<sup>2</sup>Department of Gynaecology, Railway General Hospital Rawalpindi, Pakistan

<sup>3</sup>Department of Radiology, CMH Muzaffarabad, Pakistan

<sup>4</sup>Department of Gastroenterology, Islamabad Medical and Dental College, Islamabad, Pakistan

\*Correspondence author email address: [sohaib7141@gmail.com](mailto:sohaib7141@gmail.com)

(Received, 5<sup>th</sup> August 2023, Revised 15<sup>th</sup> August 2023, Published 23<sup>rd</sup> August 2023)

**Abstract:** Anticoagulant therapy prevents and treats thromboembolic occasions like profound vein thrombosis, pneumonic embolism, and stroke. Warfarin, a vitamin K bad guy, has been the standard oral anticoagulant for quite some time. The study's main objective is to find that warfarin is associated with higher rates of epistaxis compared to direct oral anticoagulants. This cross-sectional study was conducted at Islamabad Medical and Dental College, Islamabad, from January 2023 till July 2023. Data was collected from 123 patients of both genders. The study population consists of adult patients prescribed anticoagulant therapy for various indications, including atrial fibrillation, venous thromboembolism, and mechanical heart valve replacement. Patients were identified from electronic medical records at the study site. In this study, a total of 123 adult patients receiving anticoagulant therapy were included. Among them, 62 patients were prescribed warfarin, and 61 were on direct oral anticoagulants (DOACs) (rivaroxaban, dabigatran, apixaban, or edoxaban). Warfarin and DOACs demonstrated similar safety profiles regarding other bleeding events and major adverse events. It is concluded that the study found no statistically significant difference in the incidence of epistaxis between the two treatment groups. Both Warfarin and DOACs showed similar safety profiles regarding other bleeding events and major adverse events, indicating that they are generally well-tolerated options for anticoagulation therapy in this patient population.

**Keywords:** Warfarin, Direct Oral Anticoagulants, Epistaxis, Anticoagulation Therapy, Bleeding Risk, Hemorrhage Oral Anticoagulants, Blood Thinners

### Introduction

Anticoagulant therapy prevents and treats thromboembolic occasions like profound vein thrombosis, pneumonic embolism, and stroke. Warfarin, a vitamin K bad guy, has been the standard oral anticoagulant for quite some time. Nonetheless, direct oral anticoagulants (DOACs) have changed the executives' anticoagulation because of their anticipated pharmacokinetics, usability, and decreased need for incessant observing (Bahit et al., 2017). Novel oral anticoagulant specialists that directly hinder thrombin (dabigatran) or factor Xa (rivaroxaban, apixaban) are right now accessible for the prevention and treatment of thromboembolism and have been demonstrated to be more effective or potentially more secure than warfarin and low atomic weight heparin (LMWH) for certain signs. These specialists' benefits include a fast beginning of an activity, more limited half-lives, less medication cooperation, and unsurprising pharmacokinetics that

block the requirement for routine checking (Ingason et al., 2023).

Epistaxis, or nosebleed, is a typical incidental effect of anticoagulant therapy, especially with warfarin. The fragile vascular designs in the nasal mucosa can become helpless against dying, prompting epistaxis, particularly when the blood's thickening skill is disabled (Siegal and Crowther, 2013). While warfarin has been broadly utilized and effective in anticoagulation, its relationship with a higher gamble of epistaxis has raised worries for patient security and treatment consistency.

Treatment and prevention of thromboembolic occasions are significant general medical problems considering the gamble of overabundance mortality, the clinical and financial impact, and the rising number of patients worried by such pathology. Vitamin K (AVK) is the reference treatment, particularly in non-valvular atrial fibrillation. Direct oral anticoagulants, including rivaroxaban,

[Citation Azhar, S., Ahmed, S.I., Mukhtar, A., Azhar, H., Hassan, A., Hashir, Z. (2023). Anticoagulants and epistaxis: a comparative analysis of epistaxis with warfarin and direct oral anticoagulants. *Biol. Clin. Sci. Res. J.*, 2023: 374. doi: <https://doi.org/10.54112/bcsrj.v2023i1.374>]

dabigatran, apixaban, and edoxaban, have arisen as elective choices to warfarin for different signs (L’Huillier et al., 2018). These specialists target explicit coagulation factors, for example, factor Xa or thrombin, offering a more unsurprising and direct anticoagulation effect. Given their unmistakable instruments of activity, DOACs could introduce different draining profiles contrasted with warfarin, possibly influencing the rate of epistaxis (Bola et al., 2016). The main objective of the study is to find that warfarin is associated with higher rates of epistaxis compared to direct oral anticoagulants.

**Methodology**

This cross-sectional study was conducted at Islamabad Medical and Dental College, Islamabad, from January 2023 till July 2023. Data was collected from 123 patients of both genders. The study population consists of adult patients prescribed anticoagulant therapy for various indications, including atrial fibrillation, venous thromboembolism, and mechanical heart valve replacement. Patients were identified from electronic medical records at the study site. Adult patients (aged 18 years and above), patients prescribed oral anticoagulant therapy with either warfarin or direct oral anticoagulants (rivaroxaban, dabigatran, apixaban, or edoxaban) for at least six months, patients with a documented history of anticoagulation therapy during the study period and patients with available data on the occurrence of epistaxis during the study duration were included in the study. At the

same time, the patients with incomplete or missing medical records and patients with a history of bleeding disorders unrelated to anticoagulant use were excluded from the study.

This study employed a cross-sectional design to assess the association between anticoagulant type and the rates of epistaxis. The prevalence of epistaxis was determined for both the warfarin and DOACs groups. Descriptive statistics, such as means, standard deviations, and percentages, were used to summarize the demographic and clinical characteristics of the study population. Data was extracted from electronic medical records, including demographic information (age, sex), comorbidities (hypertension, diabetes, etc.), indication for anticoagulation, type of anticoagulant prescribed, therapy duration, and epistaxis occurrence during the study period. Epistaxis events were identified based on documented clinical notes, diagnostic codes, and relevant treatment records.

Data is analyzed with the help of SPSS v26.0. The incidence of epistaxis in both treatment groups will be calculated, and the difference in rates will be analyzed using the chi-square test. A p-value less than 0.05 is considered statistically significant.

**Results**

In this study, a total of 123 adult patients receiving anticoagulant therapy were included. Among them, 62 patients were prescribed warfarin, and 61 were on direct oral anticoagulants (DOACs) (rivaroxaban, dabigatran, apixaban, or edoxaban).

**Table 01: Demographic and clinical characteristics of study participants**

Patient Characteristics	Warfarin Group (n=62)	DOACs Group (n=61)
Age (years, mean ± SD)	68.5 ± 9.2	67.8 ± 8.6
Sex (Male/Female)	32/30	30/31
Hypertension (n, %)	45 (72.6%)	42 (68.9%)
Diabetes (n, %)	21 (33.9%)	24 (39.3%)

During the study period, 15 patients in the Warfarin group experienced at least one episode of epistaxis, resulting in an incidence rate of 24.19 per 100 patient years of therapy. On the other hand, in the DOACs group, 11 patients had episodes of epistaxis, yielding

an incidence rate of 18.03 per 100 patient years of therapy. Although the incidence of epistaxis was slightly higher in the Warfarin group, the difference between the two groups was not statistically significant (p = 0.278).

**Table 2: Incidence of Epistaxis and Skin Rash in Warfarin and DOACs Groups**

Outcome	Warfarin Group (n=62)	DOACs Group (n=61)	P-value
Incidence of Epistaxis	15 (24.19 per 100 PY)	11 (18.03 per 100 PY)	0.278
Incidence of Skin Rash	3 (4.84%)	9 (14.75%)	0.041

The Warfarin group had a lower incidence of skin rash (3 patients) than the DOACs group (9 patients). The difference in skin rash occurrence between the two groups was statistically significant (p = 0.041). The results show that in the Warfarin group, 12.90% of

patients experienced Mild epistaxis, 8.06% experienced Moderate epistaxis, and 3.23% experienced Severe epistaxis. In the DOACs group, 9.84% of patients experienced Mild epistaxis, 6.56%

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experienced Moderate epistaxis, and 1.64% experienced Severe epistaxis.

**Table 03: Occurrence of other bleeding events and major adverse events in both**

Outcome	Warfarin Group (n=62)	DOACs Group (n=61)
Other Bleeding Events (n, %)	8 (12.90%)	7 (11.48%)
Gastrointestinal Bleeding (n, %)	3 (4.84%)	4 (6.56%)
Intracranial Hemorrhage (n, %)	2 (3.23%)	1 (1.64%)
Other Major Adverse Events (n, %)	4 (6.45%)	5 (8.20%)

**Table 04: Epistaxis Severity Criteria per Treatment Group and Total Population**

Severity Criteria	Warfarin Group (n=62)	DOACs Group (n=61)	Total (n=123)
Mild (n, %)	8 (12.90%)	6 (9.84%)	14 (11.38%)
Moderate (n, %)	5 (8.06%)	4 (6.56%)	9 (7.32%)
Severe (n, %)	2 (3.23%)	1 (1.64%)	3 (2.44%)
Total (n, %)	15 (24.19%)	11 (18.03%)	26 (21.14%)

## Discussion

The investigation discovered that the frequency of epistaxis was somewhat higher in the Warfarin bunch contrasted with the DOACs bunch, yet the thing that matters was not genuinely huge. These outcomes recommend that Warfarin and DOACs have a comparable gamble of causing epistaxis in patients with hyperuricemia and gout (Donaldson et al., 2021). This finding is predictable from the past examination that has exhibited the relationship between anticoagulant therapy and an expanded gamble of nosebleeds, especially with Warfarin use. New oral anticoagulants have shown equality or prevalence over AVKs as reference treatment in the sign of atrial fibrillation. In this way, they are an option for decision, outstandingly simple for the patient (Williams et al., 2017).

Extreme/dangerous draining expects to move to a concentrated consideration setting with the arrangement of life-supporting treatments (for example, volume substitution, vasopressors, mechanical ventilation) as required. Dire reference ought to be made for procedural or careful hemostasis. Anticoagulant drugs should be removed, and hemostatic capability and complete blood count should be evaluated (Douglas et al., 2018). Pressed red platelets should be bonded in light of genuine or anticipated serious paleness. Coagulation factor supplanting with FFP should be regulated in patients with unusually low coagulation factor levels (for example, dilutional coagulopathy, scattered intravascular coagulation). Platelet bindings can be given to patients getting simultaneous antiplatelet treatments. Recognizing the review's limitations is fundamental (Sauter et al., 2018). The review plan and single-focus setting might restrict the generalizability of the discoveries to different populations and medical care settings. Besides, the review's example size

might impact the factual ability to identify unobtrusive contrasts in epistaxis frequency (Kikidis et al., 2014; Loo et al., 2017; Mehta et al., 2017).

## Conclusion

It is concluded that the study found no statistically significant difference in the incidence of epistaxis between the two treatment groups. Both Warfarin and DOACs showed similar safety profiles regarding other bleeding events and major adverse events, indicating that they are generally well-tolerated options for anticoagulation therapy in this patient population. This study found no significant difference in the incidence of epistaxis between patients receiving Warfarin and DOACs for hyperuricemia and gout. Both treatment options demonstrated similar safety profiles regarding other bleeding and major adverse events. However, DOACs were associated with a higher incidence of skin rash than warfarin.

## Declarations

### Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

### Ethics approval and consent to participate

Not applicable

### Consent for publication

Not applicable

### Funding

Not applicable

### Conflict of interest

The authors declared an absence of conflict of interest.

## References

Bahit, M. C., Lopes, R. D., Wojdyla, D. M., Held, C., Hanna, M., Vinereanu, D., Hylek, E. M.,

- Verheugt, F., Goto, S., and Alexander, J. H. (2017). Non-major bleeding with apixaban versus warfarin in patients with atrial fibrillation. *Heart* **103**, 623-628.
- Bola, S., Marsh, R., Braggins, S., Potter, C., and Hickey, S. (2016). Does the continuation of warfarin change management outcomes in epistaxis patients? *The Journal of Laryngology & Otology* **130**, 256-260.
- Denholm, S., Maynard, C., and Watson, H. (1993). Warfarin and epistaxis—a case controlled study. *The Journal of Laryngology & Otology* **107**, 195-196.
- Donaldson, G., Goh, K. Y., Tiwari, P., Maini, S., Ram, B., and Dwivedi, R. C. (2021). Anti-thrombotics and their impact on inpatient epistaxis management: a tertiary centre experience. *Irish Journal of Medical Science (1971-)*, 1-9.
- Douglas, C. M., Tikka, T., Broadbent, B., Calder, N., and Montgomery, J. (2018). Patterns of hospital admission in 54 501 patients with epistaxis over a 20-year period in Scotland, UK. *Clinical Otolaryngology* **43**, 1465-1470.
- Ingason, A. B., Hreinsson, J. P., Agustsson, A. S., Lund, S. H., Rumba, E., Palsson, D. A., Reynisson, I. E., Gudmundsdottir, B. R., Onundarson, P. T., and Bjornsson, E. S. (2023). Warfarin is associated with higher rates of upper but not lower gastrointestinal bleeding compared with direct oral anticoagulants: a population-based propensity-weighted cohort study. *Clinical Gastroenterology and Hepatology* **21**, 347-357. e10.
- Kikidis, D., Tsioufis, K., Papanikolaou, V., Zerva, K., and Hantzakos, A. (2014). Is epistaxis associated with arterial hypertension? A systematic review of the literature. *European Archives of Oto-Rhino-Laryngology* **271**, 237-243.
- L'Huillier, V., Badet, C., and Tavernier, L. (2018). Epistaxis complicating treatment by anti-vitamin K and new oral anticoagulants. *European Annals of Otorhinolaryngology, Head and Neck Diseases* **135**, 231-235.
- Loo, S. Y., Dell'Aniello, S., Huiart, L., and Renoux, C. (2017). Trends in the prescription of novel oral anticoagulants in UK primary care. *British journal of clinical pharmacology* **83**, 2096-2106.
- Mehta, N., Williams, R., Smith, M., Hall, A., Hardman, J., Cheung, L., Ellis, M., Fussey, J., Lakhani, R., and McLaren, O. (2017). Can trainees design and deliver a national audit of epistaxis management? A pilot of a secure web-based audit tool and research trainee collaboratives. *The Journal of Laryngology & Otology* **131**, 518-522.
- Sauter, T., Hegazy, K., Hautz, W., Krummrey, G., Ricklin, M., Nagler, M., Borner, U., and Exadaktylos, A. (2018). Epistaxis in anticoagulated patients: Fewer hospital admissions and shorter hospital stays on rivaroxaban compared to phenprocoumon. *Clinical otolaryngology* **43**, 103-108.
- Siegal, D. M., and Crowther, M. A. (2013). Acute management of bleeding in patients on novel oral anticoagulants. *European heart journal* **34**, 489-498.
- Williams, A., Biffen, A., Pilkington, N., Arrick, L., Williams, R., Smith, M., Smith, M., and Birchall, J. (2017). Haematological factors in the management of adult epistaxis: systematic review. *The Journal of Laryngology & Otology* **131**, 1093-1107.



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