

# Epistaxis in patients taking oral anticoagulant and antiplatelet medication: prospective cohort study

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## Abstract

**Objectives:** Epistaxis can be caused or exacerbated by anticoagulant and antiplatelet therapy. This prospective study assessed the prevalence of epistaxis in patients taking anticoagulant and antiplatelet medication, and monitored differences in patients' clinical courses.

**Method:** Prospective data were collected for consecutive patients referred with epistaxis from the emergency department over a seven-month period. Emergency department records were used to investigate prevalence and referral rates.

**Results:** Over the study period, 290 patients presented to the emergency department with epistaxis; this represented 0.9 per cent of all emergency attendances. Of these patients, 119 (39 per cent) were referred on to the ENT department, 62 per cent of whom were currently taking anticoagulant or antiplatelet medication. Patients taking anticoagulant and antiplatelet medication were a significantly older group (relative risk 1.50 (1.08–2.28),  $p = 0.01$ ) requiring longer in-patient stays (relative risk 2.50 (1.01–4.97),  $p = 0.01$ ) and more aggressive local haemostasis measures. Most patients taking warfarin had an international normalised ratio outside the appropriate range for their disease. Hypertension was not a factor in these patients' clinical course.

**Conclusion:** Increasingly, emergency and ENT departments are being presented with epistaxis in patients taking anticoagulant or antiplatelet medication. A better understanding of such medication and its effects may enable more effective management of these patients.

**Key words:** Epistaxis; Anticoagulants; Antiplatelets; Prevalence; Complications; Clinical Course

## Introduction

Epistaxis is a common ENT emergency which affects approximately 60 per cent of individuals at some time in their life.<sup>1</sup> Within this group, an estimated 6 per cent require emergency medical attention.<sup>1</sup> In the majority of cases, the cause of epistaxis is unknown.<sup>2</sup> Localised conditions within the nose and systemic factors have been identified. These systemic factors include oral anticoagulant medication (e.g. warfarin) and antiplatelet medication (e.g. aspirin and clopidogrel), which increase the risk of bleeding especially when used in combination.<sup>3</sup> Patients taking these medications form an important subgroup of epistaxis cases, as they are potentially more difficult to manage in the emergency department and have higher rates of co-morbidity (e.g. cardiovascular disease). Epistaxis resulting in major haemorrhage is life-threatening in all patients, but those taking anticoagulant and antiplatelet medication require special attention.<sup>4</sup>

The use of both warfarin and antiplatelet medication has increased markedly in the UK in recent years. The

most common use of warfarin is in the primary and secondary prevention of stroke in patients with atrial fibrillation.<sup>5</sup> Warfarin is also widely used for the treatment of arterial and venous thrombo-embolism, and in conjunction with prosthetic heart valves. Antiplatelet medication is widely used for various forms of cardiovascular disease, both in primary and secondary prevention.

For patients admitted to hospital with epistaxis, the goals of treatment include prompt resuscitation and haemorrhage control, a short hospital stay, and a low complication rate.<sup>6</sup> Treatment may take the form of local cauterisation or anterior and posterior nasal packing. If these initial measures fail and bleeding is severe, ongoing or life-threatening, arterial ligation or embolisation may be required.<sup>7</sup> In addition to these measures, patients taking anticoagulants may require blood products, coagulation factors or vitamin K to arrest bleeding.

There are many anecdotal beliefs regarding the common clinical problem of epistaxis and the potential

adverse influence of blood-thinning medication taken by an increasing population of elderly patients. However, no prospective studies have assessed the prevalence of epistaxis and the characteristics of patients requiring in-patient treatment. Furthermore, the clinical significance of concurrent warfarin and antiplatelet therapy has not been formally evaluated in these patients.

Our prospective study aimed to address these deficits. Our first aim was to establish the prevalence of epistaxis cases (both major and minor) presenting to a large district general hospital, and to assess the clinical course of such patients, in order to assess the admission rate and the clinical and demographic characteristics of this condition. Our second aim was to assess the proportion of patients taking oral anticoagulant and antiplatelet medication, and to analyse the impact of such medication on patients' length of hospital stay and any adjunctive treatment interventions required to control bleeding. By evaluating these findings, we hoped to highlight specific management issues and to provide clinical recommendations for the increasing population of patients taking oral anticoagulant and antiplatelet medication who present with significant epistaxis.

## Materials and methods

We collected prospective data for consecutive patients referred to the ENT department as an emergency with epistaxis, over a seven-month period between December 2007 and June 2008 at the Worcester Royal Hospital, UK. Data were recorded using a pre-designed pro forma. Information regarding the total number of attendances and subsequent admissions was collected from the emergency department attendance database. There were no exclusion criteria. We recorded patient characteristics, medication and in-patient management (including length of stay and interventions used to control epistaxis). Descriptive and comparative statistics were calculated and analysed using the Statistical Package for the Social Sciences for Windows version 10.0 software program. Non-parametric, normally distributed variables were compared using *t*-tests. Dichotomous variables were analysed in two by two tables using chi-square analysis.

## Results and analysis

### Patient characteristics

During the seven-month study period, 33 396 patients attended the accident and emergency department of Worcester Royal Hospital, 290 of whom (0.9 per cent) had epistaxis as their primary clinical problem. Of this latter group, 119 patients (39 per cent) were referred to the ENT department for further assessment and treatment. Of the group requiring further specialist consultation, 24 (21 per cent) patients were taking oral anticoagulation therapy (i.e. warfarin) and 46 (41 per cent) were taking antiplatelet therapy (42

(37 per cent) were taking aspirin and four (3 per cent) clopidogrel). Three patients were taking both aspirin and warfarin, and one patient was taking both aspirin and clopidogrel. The remaining 43 (38 per cent) patients were not taking any form of anticoagulation or antiplatelet therapy (Figure 1).

The median age of patients referred to the ENT department with epistaxis was 72 years (range 22–97 years), with the majority (80 per cent) of patients being over the age of 60 years. Patients taking anticoagulants and/or antiplatelet medication (mean ages (ranges): 73 (52–93) and 77 (56–94) years, respectively) were significantly older than patients taking neither medication (whose mean age was 63 years; *t*-test,  $p < 0.001$ ). There were no significant differences between the ages of patients in the two groups the anticoagulant and antiplatelet patient groups (*t*-test,  $p = 0.15$ ). Furthermore, the proportion of patients taking anticoagulant and antiplatelet medication increased with age, and these patients were significantly more likely to be aged 70 years or more (relative risk 1.50; 95 per cent confidence interval (CI) 1.08–2.28;  $p = 0.01$ ), compared with patients taking neither type of medication (Figure 2).

### Warfarin cohort characteristics

Atrial fibrillation was the most common reason for anticoagulation, with deep venous thrombosis, heart valve replacement and arterial thrombosis being less common indications. Of those patients taking oral

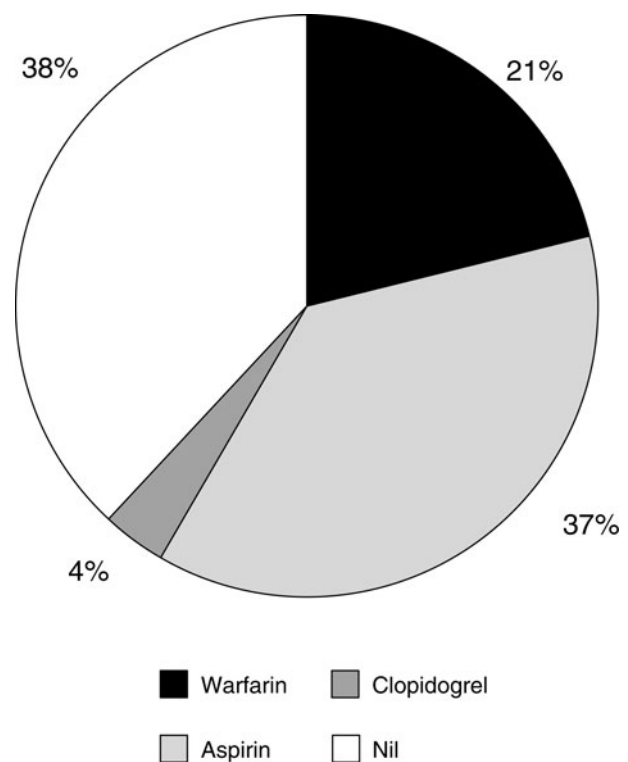


FIG. 1

Relative proportions of patients taking warfarin and antiplatelet medication, of those admitted to the ENT department with epistaxis.

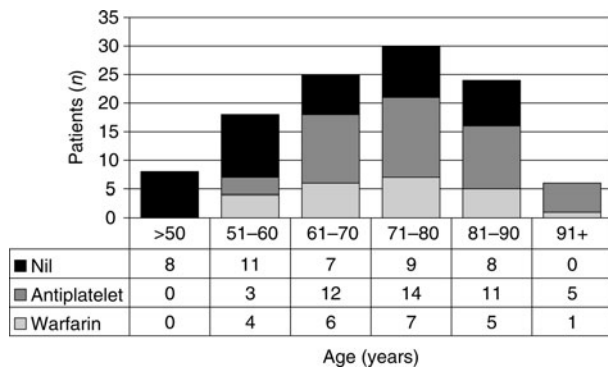


FIG. 2

Histogram and numerical data showing the increase in proportion of older patients taking warfarin or antiplatelet medication.

anticoagulation, 85 per cent ( $n = 18$ ) had an international normalised ratio (INR) outside their disease-specific range; 76 per cent ( $n = 16$ ) were over-warfarinised on admission.

Patients taking warfarin required a longer mean in-patient stay (4 days (range 1–15 days)), compared with the non-anticoagulated group (mean stay 2 days (range 1–10 days)). The median stay for all patients admitted to the ENT ward with epistaxis was 2 days. Patients taking warfarin were significantly more likely to require a median in-patient stay of more than 2 days (relative risk 2.50 (95 per cent confidence interval (CI) 1.01–4.97),  $p = 0.01$ ).

There was no significant association between blood pressure on admission and overall length of in-patient stay, for any of the study groups.

#### Clinical intervention and outcome

Of the 119 epistaxis cases referred to the ENT department, nine (8 per cent) stopped spontaneously and 22 (19 per cent) were controlled with silver nitrate cautery. The remaining 77 (68 per cent) patients required nasal packing; 68 (88 per cent) required anterior packing alone and nine (12 per cent) required posterior packing as definitive treatment. Of the patients requiring admission, five (4 per cent) required intervention in the operating theatre to control bleeding, with two (2 per cent) requiring sphenopalatine artery ligation. There were no significant links between blood pressure on admission and the type of intervention required to control bleeding.

The numbers in this study were insufficient to reach statistical significance (we found a relative risk of 2.23 (95 per cent confidence interval (CI) 0.83–6.44) for posterior packing or surgery in patients taking warfarin versus those not taking warfarin;  $p = 0.21$ ). However, an obvious trend was observed, with patients taking warfarin being less likely to resolve spontaneously and more likely to require more aggressive measures to control haemorrhage, compared with patients not taking anticoagulants (Figure 3). Seventeen per cent ( $n = 4$ ) of patients taking warfarin required posterior

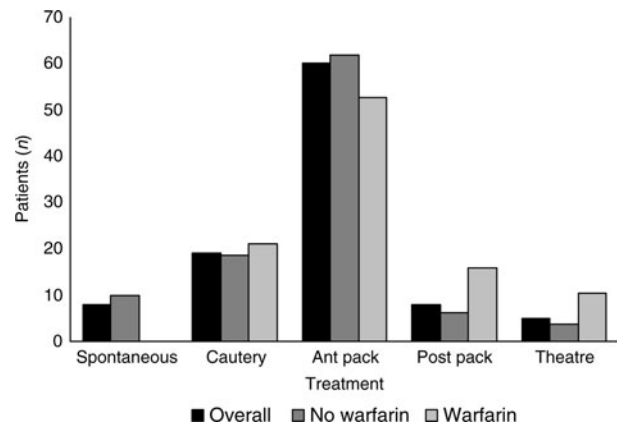


FIG. 3

Epistaxis treatment required to control bleeding in patients receiving or not receiving warfarin.

packing, compared with only 6 per cent ( $n = 5$ ) of non-anticoagulated patients. Furthermore, 8 per cent ( $n = 2$ ) of patients taking warfarin required haemorrhage control in the operating theatre, compared with only 3 per cent ( $n = 3$ ) in the non-anticoagulated group.

#### Discussion

Our prospective study revealed that 0.9 per cent of all accident and emergency department attendances were for epistaxis, and that approximately 40 per cent of such patients required in-patient admission for further treatment by the ENT surgeons.

Advances in medical care and improved socio-economic factors have improved life expectancy. The resultant, ever-ageing population is exposed to multiple therapeutic agents including anticoagulant and antiplatelet medication. Our study data is in keeping with these trends. The median age of our patients with epistaxis was 72 years overall, and higher still in the anticoagulant and antiplatelet groups; these ages are higher than those found in previously published series (which ranged from 55.8 to 70 years).<sup>7–10</sup> Furthermore, almost two-thirds of the patients needing referral to the ENT department were taking either anticoagulant or antiplatelet medication, with over one in five taking warfarin. These observations show a significant number of an increasingly elderly population, many taking warfarin, requiring in-patient epistaxis management in the ENT department. As the incidence of medical and social co-morbidity increases in the elderly population, resulting in growing numbers of patients requiring anticoagulation for medical problems, the significance of epistaxis (both clinical and financial) will increase for ENT and emergency departments.

Also of concern was our observation that more than three-quarters of epistaxis patients taking warfarin were over-anticoagulated at the time of presentation. Although access to anticoagulation clinics has improved, facilitating effective local monitoring of patients taking warfarin, evidence from large-scale monitoring of such

clinics suggests that only 50 per cent of patients will be within their target anticoagulation range at any one time.<sup>11</sup> Furthermore, home testing kits are increasingly being used to measure INR, thus increasing patients' reliance on self-monitoring (with its attendant compliance risks). Warfarin therapy is also significantly influenced by concurrent medication, new medication, alcohol ingestion, hepatic disease and acute illness, all of which are more common in elderly populations.<sup>12</sup> Patients' bleeding risk has been shown to increase exponentially with rising INR, and to be related to the time spent with a raised INR level.<sup>13</sup> These points considered, it is perhaps predictable that we found such a high rate of over-anticoagulation in our actively bleeding cohort. This provides further indirect evidence that over-warfarinisation is an important contributory risk factor for epistaxis severe enough to require hospital care.

In our study, those patients admitted with epistaxis who were taking warfarin were less likely to cease bleeding spontaneously with conservative measures, or to be controlled with simple haemostasis measures, and were thus more likely to require more aggressive measures such as posterior nasal packing and surgical intervention, compared with non-anticoagulated patients. Approximately one in 12 warfarinised patients required intervention in the operating theatre to control bleeding, compared with only one in 38 non-anticoagulated patients. This may be expected, given that the former patients' clotting capability was abnormal, thus requiring more robust anti-haemorrhagic measures. In addition, our observation may be further explained by the fact that the majority of our warfarinised patients were over-anticoagulated at the time of admission with epistaxis. Although previous studies have demonstrated no difference in treatment requirements in their warfarinised patient groups, these studies predominantly included patients with satisfactory therapeutic INR values.<sup>14</sup>

In our study, the median hospital stay for epistaxis treatment was two days. Patients taking warfarin had longer in-patient stays, on average double the duration of the non-anticoagulated group. There are (at least) several possible explanations for this. Firstly, as we have shown, patients taking warfarin are more likely to be resistant to simple haemostasis measures and to need greater intervention, consequently requiring extended admissions. Secondly, these patients are more elderly and thus more likely to have other medical problems that may become complicated by a new hospital admission, thus precluding early discharge. A third possibility is that patients may need extended monitoring or 'bridging therapy' with low molecular weight heparin while their INR reaches therapeutic levels prior to discharge. A fourth explanation is that a poor understanding of warfarin therapy on the part of the ENT team, together with suboptimal monitoring for specific and often complex medical problems, may lead to inadequate INR management, delaying rapid resolution and discharge. For this reason, the systematic, early involvement of a haematologist and cardiologist may be beneficial.

Given these multiple possible underlying factors, we believe that better understanding of these issues could lead to more efficient discharge in this patient group, and may contribute to reducing the complications associated with an extended hospital stay. Indeed, well established multidisciplinary care programmes have been shown to significantly reduce the duration of stay of warfarinised patients admitted to hospital. Furthermore, acknowledgement of these issues and establishment of better INR monitoring facilities in the community may decrease the incidence of significant epistaxis in warfarinised patients.

#### *Limitations and recommendations*

There are very limited prospective data available on the clinical course of patients taking anticoagulant and antiplatelet medication who are admitted to hospital with epistaxis. Our study demonstrates some of the differences and challenges faced by the clinician when managing epistaxis patients taking such medication, compared with patients not taking such medication. In summary, the former group are more elderly, with medical problems requiring anticoagulant or antiplatelet treatment (together with other co-morbidities), and as a result of their constitution and their frequently observed over-warfarinisation they require more invasive interventions and extended in-patient hospital stays. Although our study was limited by low patient numbers, our findings raise many important points relevant to clinical practice modifications and further research. A greater understanding of this vulnerable patient group, and greater expertise and confidence in managing the underlying medical aspects of epistaxis, would be beneficial in what may become an increasingly common complication.

- **There is little information regarding the clinical course of patients with epistaxis complicated by medical therapy**
- **Patients taking anticoagulant and antiplatelet medication constitute an increasingly large subgroup of in-patient admissions with epistaxis**
- **They are a significantly older group requiring longer in-patient stays and possibly more aggressive haemostasis measures**
- **Discharge delays may lead to higher in-patient morbidity, especially within this group**
- **Awareness of these issues, and collaboration with other specialties, may facilitate more efficient in-patient management and discharge of such patients**

Based on our observations, we recommend co-operation with haematologists and cardiologists to develop guidance for safe and effective in-patient management, and to facilitate earlier discharge, for

patients taking anticoagulant or antiplatelet medication who are admitted with epistaxis. To this end, we are presently developing a multidisciplinary treatment algorithm and care pathway which will facilitate optimal care delivery for newly admitted patients whose admission is complicated by their anticoagulation therapy.

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Mr J Smith takes responsibility for the integrity of the content of the paper

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