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Research Paper

Management of Epistaxis in Patients on Anti-Platelet and/ Or Anticoagulant Medication

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Abstract:
Objective: *To analyse necessity to withhold regular anticoagulant and/or antiplatelet medications to control epistaxis by introducing a modified protocol for management of such patients.*
Method: *One hundred and eighteen patients admitted with epistaxis were studied. First audit was a retrospective study to observe current practice. Second audit was carried out as a prospective study over the period of six months following modified treatment algorithm. These audits were compared on the basis of duration of hospital stay, need for surgical intervention, readmissions, re-bleed, drop in INR below target range.*
Results: *In this non-inferiority analysis the main interest is in the lower bound of the 90% confidence interval (CI) since we want to make sure the second audit approach is not much worse than the first audit approach.*
Conclusion: *The outcomes of the second audit were not significantly worse than first audit. As anti-platelet and anticoagulants were continued, we postulate that potential risks associated with stopping these medications (ie.risk of thrombo-embolism) were reduced without compromising epistaxis control.*
Keywords*: Anti-platelet and anticoagulant medication, Epistaxis, Thrombo-embolism.*

I. Introduction

Epistaxis is one of the commonest ENT emergencies.[1] Patients on anticoagulants or anti-platelet medication are more prone to frequent epistaxis.[2] With-holding these medications in order to control epistaxis could increase the risk of potential thrombo-embolism. We carried out 2 audit cycles to compare the effect of continued antiplatelet and/or anticoagulant medication, on management of epistaxis control.

II. Method

Two cycles of audit were carried out including patients admitted with epistaxis. The first cycle was a retrospective study from January 2014 till April 2014, and included 60 cases. The standard used for audit was 'no significant increase in re-bleeding or re-admission rate and no drop in INR below target level'. The data collected included the number of patients who were on antiplatelet and/or anticoagulant medications, whether the medication was stopped to control epistaxis, duration of hospital stay, readmissions due to recurrent epistaxis and change in INR. Data analysis revealed that it was not necessary to with-hold antiplatlet or anticoagulant medications to control epistaxis.

A new treatment algorithm was formulated by the Ear Nose and Throat(ENT) Department at Addenbrooke's Hospital considering the data from the first audit cycle, guidance from a Hematologist, guidelines from the British Society for Haematology and guidelines for perioperative management of antiplatelet and anticoagulant treatment.[6](Fig1).

As per this treatment algorithm, antiplatelet or anticoagulant medication was not discontinued unless INR was above 4, TED (anti-embolism stockings) stockings and LMWH (low molecular weight Heparin) were prescribed as per hospital guidelines. Early surgical intervention was carried out in patients with uncontrolled epistaxis. The Second audit cycle was a prospective study from October 2014 until March 2015, implementing the new treatment algorithm. A total of 58 cases were studied. Data from both audit cycles were compared on the basis of re-bleed, readmission, surgical intervention, duration of hospital stay and change in INR. (Fig.2,3).

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Fig.1: Treatment algorithm

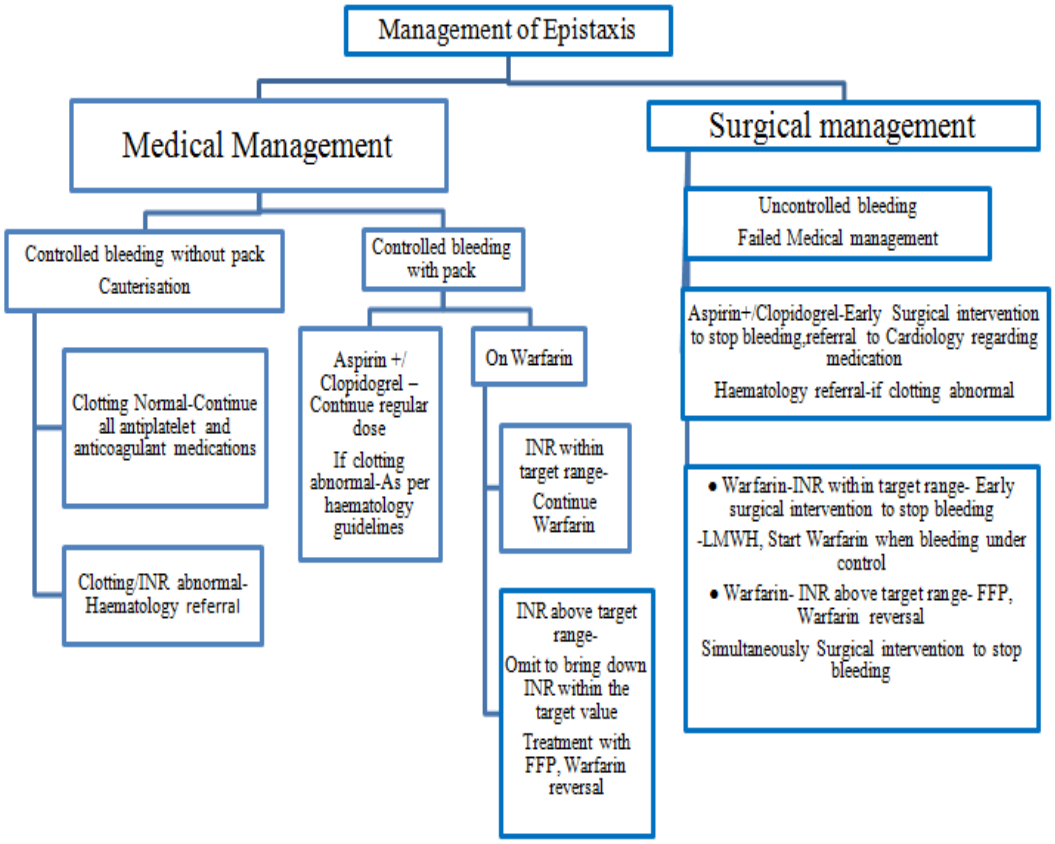


Fig.2- Distribution of patients as per their history of medication and presentation

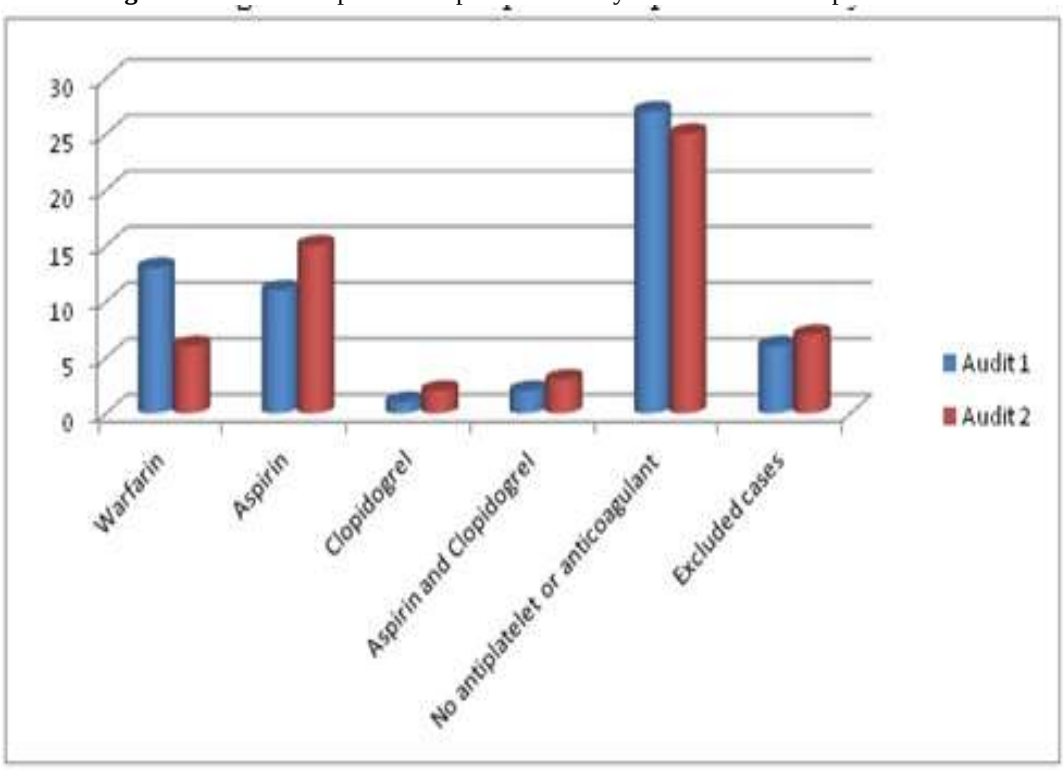
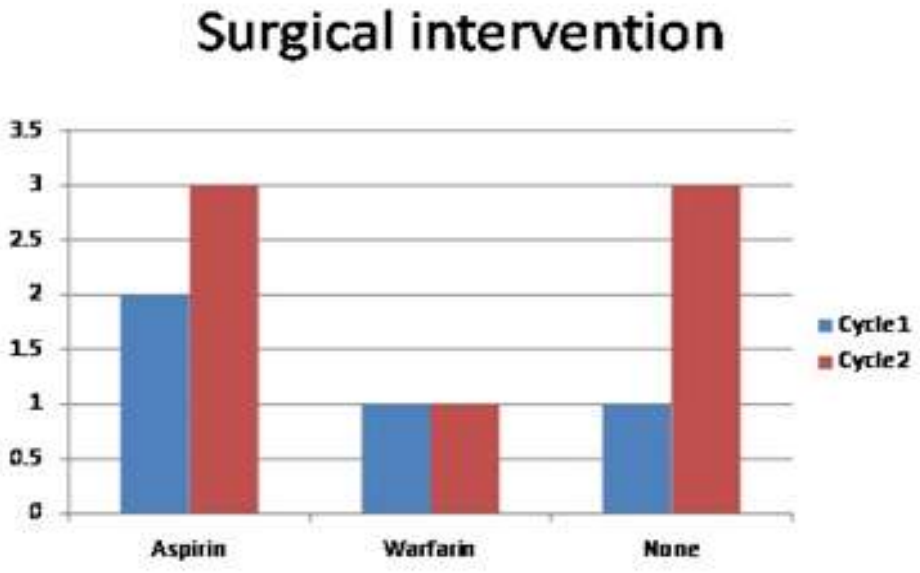


Fig. 3: Comparison of number of cases required surgical intervention:



III. Results

Six patients from the first audit have been excluded from the analysis. Two paediatric patients were excluded, further two were patients with traumatic epistaxis, one of these patients had factor 'VIII Deficiency' and another was an orthopaedic patient on Heparin. None of the patients removed had a readmission, re-bleed, surgery or a drop in INR. Both trauma cases were on Warfarin. One of the patients who was transferred from another hospital so had medication (Warfarin) withdrawn and was also given Vitamin K and Bariplex, has been excluded from second audit cycle and the analyses below. They had a significant drop in INR to 1.1. A further six patients have been excluded from second audit; three of them were paediatric patients, one of which had a re-bleed; two patients were post-operative nasal surgery, one of them had a readmission and a re-bleed and surgical intervention who was on aspirin; another was on therapeutic heparin for pulmonary embolism.

IV. Demographics

In the first audit cycle 24/54 (44.4%) were females and in the second audit cycle 19/51 (37.3%) were females. The mean age in the first and second audit cycle was 69.5 with standard deviation of 15.6 and 66.8 with standard deviation of 17.0 respectively. Including only those that were on medication, female population was 14/27 (51.9%) and 7/26 (26.9%) in first and second audit cycle respectively. The mean age in the first audit was 75.6 (standard deviation was 10.3) and in the second audit was 76.0 (standard deviation was 9.9). Length of stay: One of the Patients from the second audit was excluded from this analysis because the length of stay was due to being unsteady on their feet. Interquartile range (IQR) is the 25% percentile value to the 75% percentile value in the same way that the median is the 50% percentile value (once the values are put into order).Including only those on medication, the median length of stay in the first audit (N=27) was 2 days (IQR 2-4, Range 1-9) and the median length of stay in the second audit (N=26) was 2 days (IQR 1-3.5, Range 1-27). Including those not on medication as well as those on medication, the median length of stay in the first audit (N=54) was 2 days (IQR 2-3 Range 1-9) and the median length of stay in the second audit (N=50) was 2 days (IQR 1-3, Range 1-27).

V. Analysis

The following analysis has been done as a 'non-inferiority analysis' since the interest is not in which approach is superior but to make sure that the second audit outcomes are not worse than the first audit outcomes. In the analysis that follow, the difference is in terms of the first audit outcome proportion minus the second audit outcome proportion so a positive difference means the second audit approach is better (since it has a lower proportion with the outcome than the first audit) and a negative difference means the first audit approach is better. In this non-inferiority analysis the main interest is in the lower bound of the 90% confidence interval (CI) since we want to make sure the second audit approach is not much worse than the first audit approach. A proportion that represents non-inferiority needs to be determined either clinically or statistically. The difference that is acceptable clinically would be determined by how much worse the second audit outcome can be before

being considered problematic. For readmission and drop in INR, non-inferiority of the second audit method compared to the first audit method is established at the 5% significance level. Although the re-bleed rate was very similar in the first and second audit, non-inferiority cannot be established due to the lower limit being -18.6%. This is likely to be a result of the relatively small sample size. The surgery rate appears to be higher in the second audit meaning that non-inferiority could not be established.

Non-inferiority of the second audit method compared to the first audit method is established at the 5% significance level for readmission and drop in INR but it is not established for re-bleed or surgery. Rebleed rate and surgery were not significantly better, but not worse than first audit cycle. (Tables 1 and 2 and Fig.4).

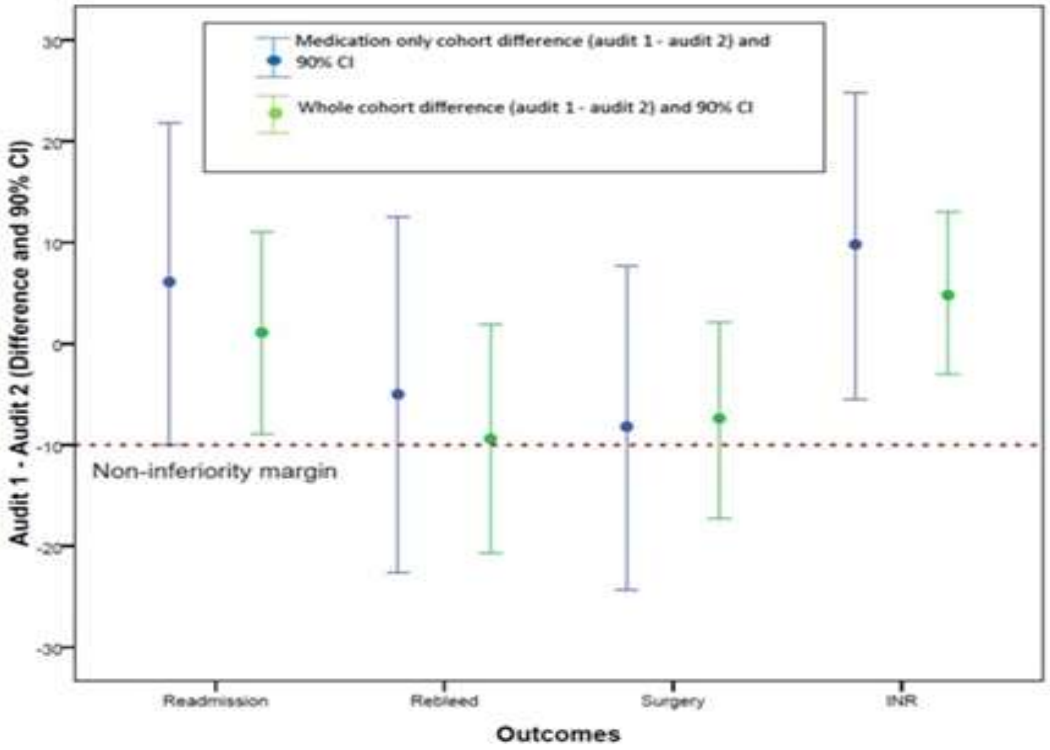
Table 1 : Analysis of the whole cohort:

Outcome	Audit 1 (N=54) Exclusions: 6	Audit 2 (N=51) Exclusions: 7	Difference (Audit 1 - 2)	90% CI
Readmission	7 (13.0%)	5 (9.8%)	3.2%	*-7.5%*, 13.7%
Re-bleed	7 (13.0%)	9 (17.6%)	-4.7%	*-16.5%*, 7.0%
Surgical intervention	4 (7.4%)	7 (13.7%)	-6.3%	*-16.9%*, 3.8%
Drop in INR	5 (9.3%)	2 (3.9%)	5.3%	*-3.3%*, 14.3%

Table 2: Analysis only including those on medication:

Outcome	Audit 1 (N=27)	Audit 2 (N=26)	Difference (Audit 1 - 2)	90% CI
Readmission	5 (18.5%)	3 (11.5%)	7.0%	*-9.8%*, 23.4%
Re-bleed	5 (18.5%)	5 (19.2%)	-0.7%	*-18.6%*, 17.0%
Surgical intervention	3 (11.1%)	4 (15.4%)	-4.3%	*-20.5%*, 11.7%
Drop in INR	5 (18.5%)	2 (7.7%)	10.8%	*-5.2%*, 26.6%

Fig.4 Outcome of audits:



VI. Discussion

Epistaxis is one of the commonest ENT emergencies. The causes of epistaxis include hypertension, trauma, tumour, HHT (Hereditary Haemorrhagic Telangiectasia), bleeding disorders, idiopathic. Spontaneous epistaxis with unknown etiology is more prevalent. The Common areas of bleeding are anterior nasal septum in the region called Little's area, which is supplied by Kisselback's plexus. The two primary anatomic sites of posterior epistaxis include posterior lateral nasal wall and posterior nasal septum.[3]

Patients on anti-platelet and/or anticoagulant medication are at high risk of spontaneous epistaxis. These medications are prescribed as a standard treatment for prevention of thrombo-embolism, including

transient ischeamic attack(TIA), cardiovascular attack(CVA), deep vein thrombosis(DVT), pulmonary embolism(PE).[4] There are standard guidelines for perioperative modification of medication for patients on antiplatelet and/or anticoagulant medications; but there are no guidelines for these patients presenting with epistaxis. As per the analysis of our audits we have proposed an algorithm to manage epistaxis in patients on antiplatelet and/or anticoagulant medications.

As per our observation, even though these patients are at high risk, most of them do not have deranged clotting or INR above the therapeutic range; when they present with epistaxis. With-holding anti-platelets or anticoagulants increases the potential risk of thrombo-embolism in these patients.[4] It is difficult to quantify the risk as it depends on multiple factors like severity of the disease, duration since thrombo-embolic episode, other contributing co-morbidities. Patients with ischaemic heart disease are generally treated with antiplatelet therapy. The British Cardiovascular Intervention Society recommends dual antiplatelet therapy for 1 year for drug-eluting stents.[5] All stents require a minimum of 1 month combination of dual anti-platelet therapy. In one study which examined factors associated with stent thrombosis, discontinuation of therapy was associated with a hazard ratio of 161:1.[6]

Does discontinuation of antiplatelets and/or anticoagulants actually help to control epistaxis: Routine investigation of INR and/or clotting screen revealed 3 patients from first audit cycle with INR of 3.4, 3.9 and 3.1. Patients on Aspirin and Clopidogrel did not have abnormal clotting screen in both audit cycles. In second audit cycle there were 2 patients with INR 3.5, 4.0. One patient was seen in emergency department with history of epistaxis and INR of 4.2; but did not have active bleeding, it had stopped without any intervention. It is obvious that there are factors other than abnormal clotting which contribute to epistaxis.

Antiplatelet and anticoagulant medication: Most platelet inhibitors bind irreversibly to their target molecules in platelets and only newly synthesized platelets are able to restore platelet function in vivo. Therefore, most platelet inhibitors cause impaired haemostasis for nearly 7 days because this is the time needed to synthesize new platelets for a complete platelet turnover. Acetylsalicylic acid (ASA) is an exception, where only 3 days are required for cessation.[4] With-holding these medications would not necessarily help to control the bleeding immediately. Discontinuation of antiplatelets in absence of abnormal clotting would increase the risk of thrombo-embolism, rather stopping epistaxis.

Warfarin is a coumarin derivative, widely used oral vitamin K antagonist. Half life of warfarin is over 40 hours, with a prolonged dose-dependent terminal phase of elimination with detectable warfarin levels 120 hours after a single dose.[6] Discontinuation of warfarin is only advisable if the INR is greater than 4. The therapeutic range of INR for these patients is on an average is 2.5-3. Reversal of Warfarin by vitamin K leads to drop in INR significantly below therapeutic range. In audit cycle 1 all of the three patients' INR was dropped to ~1, exposing them to higher risk of thrombo-embolism.

Newer oral anticoagulants(NOAC) like direct thrombin inhibitors (dabigatran etexilate), direct factor Xa inhibitors (rivaroxaban, apixaban, edoxaban) have been developed in an attempt to overcome some of the limitations of conventional anticoagulant therapy. Incidence of major bleeding and clinically relevant non-major (CRNM) bleeding was comparable between NOAC and conventional anticoagulant therapy.[7] There is no established antidote or procedure for their reversal. If there is uncontrolled epistaxis with abnormal clotting, potential options are: prothrombin complex concentrate, recombinant factor VIIa, activated charcoal if <2-3 hours of administration; [8] though the treatment or alteration in NOAC needs to be as per haematologist's and/or cardiologist's advice.

Abnormal coagulation: In the second audit cycle, child with Von Willibrand disease needed transfusion to stop bleeding. Another child with pancytopenia needed bone marrow transplant despite multiple surgical interventions, to control epistaxis. A lady with recent pulmonary embolism (PE) needed therapeutic heparin. If clotting is abnormal in patients on antiplatelet medication with uncontrolled bleeding, they would need treatment with platelet transfusion. INR above 4 would need reversal with vit K/vit K and FFP; but always along with therapeutic/prophylactic LMWH as per haematologist's advice.

Epistaxis is a spontaneous bleeding. Although the sight of large amounts of blood can be alarming and may warrant medical attention, nosebleeds are rarely fatal.[9] 60% of the adult population suffers from epistaxis.[10,11] Most episodes are self-limiting.[12] The important factors to control epistaxis are: meticulous thorough examination, suction cleaning of nostrils, cauterisation of active bleeder, packing the nose appropriately to stop active bleeding and if required early surgical intervention.

The limitations of our study include, small cohort, practice couldnot be strictly standardised but influenced by subjective variation. We suggest need for regional or national audits following this standard algorithm for treatment of epistaxis, which would provide plenty of data for further analysis.

VII. Conclusion

- Epistaxis is one of the commonest ENT symptoms, mainly idiopathic.

- The patients on antiplatelet and/or anticoagulants are at high risk of frequent episodes of epistaxis. Whilst treating these patients, we have to weigh the risk of bleeding against the risk of thrombo-embolism.
- The proposed treatment algorithm to treat epistaxis patients who are on antiplatelets and/or anticoagulants was successful.
- Hospital stay/ surgical intervention/ readmissions does not vary significantly if the antiplatelet and/or anticoagulant medications are continued in patients of epistaxis who are on antiplatelet and/or anticoagulant medications.
- If INR or clotting screen is abnormal then only, we should consider any alteration in these medications.
- Epistaxis can be successfully treated by thorough examination of nose and early surgical intervention.

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