Vol. 14, No. 1, January - March 2022

COMPARISON OF BLEEDING RISKS WITH NEW ORAL ANTICOAGULANTS VERSUS ACENOCUMAROLUM – part 2

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ABSTRACT

Aim of the study

Oral anticoagulants have been used to prevent first or recurrent stroke, especially among patients with arterial fibrillation and y atherosclerotic disease. Despite the widespread use in dental patients, safety of anticoagulants are controversial. The uncertainty is due to the lack of definitive clinical data. In the present review, we have attempted to compare the relationship between the risk factors and postoperative hemorrhage after tooth extraction among patients with recent stroke receiving acenocumarolum versus new oral anticoagulants users.

Material and methods This is a retrospective study of all patients exposed to oral anticoagulants who required tooth extraction treated in Clinic of Oral and Maxillofacial Surgery, Carol Davila University Bucharest - Hospital of Oral and Maxillofacial Surgery from 2019 to 2020. Clinical and operative records of all patients were retrieved and reviewed from the hospital's medical records. All data were analyzed using Stata/IC 16 software (StataCorp). Ethical approval from the local institutional ethics comitee was obtained for this study.

Results In our study, there were no significant differences between continuous oral anticoagulation use prescribd for antecedents of stroke and bleeding rate (32.14% vs. 20.92%, $p > 0,05$). Additionally, post-extraction bleeding was statistically significant associated with the type of anticoagulant used among concomitant diabetes patients.

Conclusions

In patients with prior cerebrovascular accident, concomitant use of new oral anticoagulants was associated with increased risk of postoperative bleeding. Concomitant diabetes contribute to the risk of bleeding.

Keywords: Bleeding rate. Acenocumarolum. New oral anticoagulants

INTRODUCTION

The prevalence of stroke continues to increase because of improved survival of patients already with atrial fibrillation or with comorbidities which are likely to lead to atrial fibrillation, as diabetes. Post-extractiobal bleeding is a common side effect of anticoagulant use; however, the majority of bleeding events can be managed conservatively in dental office.

New oral anticoagulant agents that directly inhibit thrombin (dabigatran) or factor Xa (rivaroxaban, apixaban) are currently available for the prevention and treatment of stroke. However, there are no antidotes to reverse their anticoagulant effect. In this work, we hypothesized that outcomes among

patients with atrial fibrillation would be influenced by the specific type of anticoagulant prescribed.

MATERIAL AND METHODS

We included all patients exposed to oral anticoagulants who underwent am elective tooth extraction in the Clinic of Oral and Maxillofacial Surgery, Carol Davila University Bucharest - Hospital of Oral and Maxillofacial Surgery between 2019 and 2020. Medical comorbidities were identified by examining secondary diagnosis codes from admission. We excluded from the study cohort patients with valve replacements and patients who were prescribed both acenocumarolum and new oral anticoagulants within 30 days.

Patients were further classified based on their anticoagulation regimen as acenocumarolum users or new oral anticoagulants (dabigatran, apixaban or rivaroxaban) users. All patients needed to have at least one tooth extracted according to an oral examination and panoramic radiography.

Postoperative hemorrhage was defined as oozing after the use of gauze pressure. Patients were instructed to visit our Clinic if postoperative hemorrhage occurred at a later date. The follow-up period was 3 days postoperatively.

The study was approved by the Committee of the Ethics of the Hospital of Oral and Maxillofacial Surgery, Bucharest. Informed consent was obtained from each patient.

Categorical data were summarized as percentages, and differences between comparison groups were tested with the chi-square test. All propensity-weighted analyses accounted for the following covariates: age, sex and history of diabetes. Statistical significance was defined by a 2-sided $p \leq 0.05$. Analyses were performed with Stata/IC 16 software (StataCorp).

RESULTS AND DISCUSSIONS

A total of 181 patients exposed to oral anticoagulants underwent tooth extraction during the study period, with a mean age of 70.82 years (+/- 9.74). 85 cases (46,96%) were females and 96 cases (53.04%) were males. Although the prevalence was higher among patients with a history of stroke, there were no significant associations between the presence of postextractional hemorrhage and the presence of stroke (Table 1).

Table 1 – Postoperative hemorrhage among patients with a history of stroke

Stroke history	Hemorrhage following extractions	
	Yes	No
Yes	121 (79.08%)	32 (20.92%)
No	19 (67.86%)	9 (32.14%)

In these individuals, post-extraction bleeding was not affected by the type of anticoagulant used (Table 2).

Table 2 – Postoperative hemorrhage depending on the type of anticoagulant drug used

Stroke history	Hemorrhage following extractions	
	Yes	No
New oral anticoagulants	13 (65%)	7 (35%)
Acenocumarolum	6 (75%)	2 (25%)

The acenocumarolum users group consisted of 50 patients - mean age of 68.5 years (+/- 9.45). Of these, 29 cases (58%) were females and 21 cases (42%) were males.
The new oral anticoagulants users group consisted of 131 patients - mean age of 71.71 years (+/- 9.75). Of these, 56 cases (42.75%) were females and 75 cases (57.25%) were males.
There was a significant difference between new oral anticoagulant users and acenocumarolul users regarding the overall bleeding rate (26.72% vs 12%, p = 0.03, chi-square test).
No significant differences were observed between the ages or genders of the patients in whom postoperative hemorrhage had occurred.
Many investigators reported on postoperative hemorrhage after tooth extraction in patients receiving anticoagulants [4-6]. The risk of bleeding is dominated by medical comorbidities and medications that affect hemostasis [7].
The most common indication in both groups was atrial fibrillation - 132 (72,93%) patients; of these, 36 (72%) patients received acenocumarolum and 96 (73.28%) received new oral anticoagulants.The atrial fibrillation was not associated with an increased risk of overall bleeding events in none of the two groups.
Congestive cardiac failure was reported in 74 (40.88%) patients. Of these, 23 (46%) patients received acenocumarolum and 51 (38.93%) received new oral anticoagulants. The rate of postoperative hemorrhage in the patients with congestive cardiac failure who received anticoagulants was significantly higher (32.43% vs 15.89%, p=0,009, chi-square test) (Table 1).

Table 1 – Postoperative hemorrhage in congestive cardiac failure patients

Congestive cardiac failure	Hemorrhage following extractions	
	Yes	No
Yes	90 (84.11%)	17 (15.89%)
No	50 (67.57%)	24 (32.43%)

New oral anticoagulants administration and concomitant congestive cardiac failure were

found to be significant factors related to postoperative hemorrhage (37.25% vs 20%, p=0,03, chi-square test).
There were no significant differences between valvulopathies and postoperative hemorrhage (23.33% vs 22.52%, p≥ 0.05).

Although conclusive associations cannot be made given the small sample size, the hypertension was found to be a significant predictor of postoperative hemorrhage (26.43% vs 9.76%, p = 0.032, Fisher's exact test) (Table 2).

Table 2 – Postoperative hemorrhage in valvulopathies patients

Hypertension	Hemorrhage following extractions	
	Yes	No
Yes	37 (90.24%)	4 (9.76%)
No	103 (73.57%)	37 (26.43%)

We recognize that this study has a number of limitations. Thus, the sample size of each cohort was limited to the eligible patients who presented to our Clinic and provided informed consent, sample size calculations were not performed. In addition, the number of patients was relatively small, particularly for those on acenocumarolum. Also, given that this study was not randomized, results may have been affected by residual confounding.

CONCLUSIONS

In this study, we present one of the largest Asian cohort on pediatric airway FB. Airway FB can be easily missed or delayed in diagnosis. Non-otorhinolaryngologists should have a high index of suspicion but yet understand that airway FB can be present for a long time without causing significant symptoms. In an Asian population, walnut, and sunflower/pumpkin seeds feature more prominently compared to Western populations. Sunflower seed FBs tend to present earlier as they are found intact in the trachea. Rigid bronchoscopy is the most common technique used to remove such FBs and pulmonary-related complications post-operatively, though rare, are the most common adverse outcomes. Preventive strategies targeting the appropriate age group and this type of FB may be useful in an Asian population.

Among patients who underwent tooth extraction, patients with preoperative atrial fibrillation who were treated with new oral anticoagulation had higher bleeding rates when compared with acenocumarolum users. In addition, we found that patients with valvulopathies who were treated with new oral antiacoagulants or acenocumarolum had similar bleeding outcomes after elective teeth extraction. Further investigations are needed to understand the mechanisms underlying the postoperative bleeding risk associated with common comorbidities in oral anticoagulants users.

Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgment
In this article, all authors have an equal contribution as the first author.

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