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## Short Communication

## Direct Oral Anticoagulants in the Scenario of Oral Surgery: Safety Aspects in a Single Center Experience -

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## ABSTRACT

Direct oral anticoagulants have been introduced as an alternative to Vitamin K antagonists. Therefore, it is important to consider the risks and benefits related to the cessation or not of direct oral anticoagulants in oral surgeries. This short communication intends to describe our experience of 15 exodontia procedures in 10 patients with atrial fibrillation on continued use of direct oral anticoagulants (rivaroxaban, dabigatran or apixaban), following a standardized protocol that recommends not to interrupt the drug. Only one procedure resulted in a minor bleeding. We suggest that discontinuation of anticoagulants is not necessary before oral surgeries with low bleeding risk.

**Keywords:** Anticoagulants; Hemorrhage; Tooth extraction; Oral surgery; Dentistry

## INTRODUCTION

Direct Oral Anticoagulants (DOACs) were formulated by the drug industry as an alternative for Vitamin K antagonists (VKAs) because their advantages [1,2]. Our initial experience reflects the current availability of three DOAC medications: dabigatran (Pradaxa<sup>®</sup>, a direct thrombin inhibitor), and two direct factor Xa inhibitors, rivaroxaban (Xarelto<sup>®</sup>) and apixaban (Eliquis<sup>®</sup>) [5-8]. Although relatively new in the market, these drugs are prescribed widely in cardiology centers and have become a reality and a challenge for dental healthcare. It is essential to be aware that the discontinuation of the anticoagulant increases the risk of thromboembolic events, which may cause permanent sequels and even death. On the other hand, intraoral bleeding is easily controllable [1-7]. Regarding VKAs, there are well-established protocols developed for dental surgical procedures. However, there is still no consensus over DOACs [4,7], nor there are reports on well-established protocols on how to safely manage these patients in a real-world scenario. This short communication intends to describe our initial experience of 15 simple exodontia procedures in ten patients with nonvalvular atrial fibrillation, on continued use of one of the available direct oral anticoagulants (rivaroxaban, dabigatran or apixaban), following a standardized surgical protocol that recommends not to interrupt the drug.

## METHODS

This short communication is part of a prospective study approved by the Ethics Committee of the Heart Institute (InCor), Sao Paulo University School of Medicine (approval number SDC 4468/16/134), registered at Clinical Trials (NCT03181386), which is in progress. The study is being performed according to the declaration of Helsinki guidelines.

A literature search for clinical essays and case reports in the Pubmed and Scielo databases led to the proposition of a dental surgical protocol elaborated by the Dentistry and Arrhythmia team of InCor. The protocol includes the non-cessation of DOACs in simple dental extractions, and the addition of methods to increase safety of the surgery.

Based on the pharmacokinetic and pharmacodynamic profiles of DOACs [8], the lower level concentration of the drug in the blood was established as the shorter hemorrhage risk interval, which is for rivaroxaban, about 12 to 15 hours after the last ingestion; and for dabigatran and apixaban, about 6 to 9 hours after the last ingestion [8]. Local hemostatic measures must be associated: intra-alveolar filling with 250 mg of tranexamic acid, dissolved in 0.9% normal saline solution; suturing and compressing the surgery site by patient biting of gauze soaked with liquid tranexamic acid, for proper hemostasis.

## RESULTS

Fifteen exodontia procedures (22 teeth), all considered of low bleeding risk, were performed without drug cessation in accordance to the established protocol, in ten patients with nonvalvular AF, three on dabigatran, four on rivaroxaban, and three on apixaban. Dental extractions were divided in surgery sessions according to the teeth localization on the dental arch (Table 1).

Only one of the patients, in use of apixaban and who required an odontosection, osteotomy and mucoperiosteal incision, presented with complication in the first 24 hours (deranged blood clot) easily controlled (Table 1). Surgical cleansing of the alveolus and local hemostatic measures, the same as those performed for the surgery, were done. The patient remained without any more bleeding or other complications. The remainder of the patients did not show any recent or late postoperative bleeding.

## DISCUSSION

In recent studies the authors universally indicate not to withdraw the anticoagulant in procedures with low risk of bleeding (simple dental extractions, periodontal scaling, unitary implants, soft tissue biopsies  $\leq 1$  cm) [1,3,4]. In cases where there is a high risk of significant bleeding it is recommended to discontinue the medication for 24 to 48 hours before the procedure, depending on the patient's renal function, and to reintroduce it at least 24 hours after the surgery [2-4].

The protocol proposed by this study group was based on two points inherent in DOACs, their bleeding rates and predictable pharmacodynamics. Firstly, this new class of drugs presents bleeding rates similar to those of warfarin. Therefore, a satisfactory hemostasis can be expected, and if the patient presents with postoperative bleeding, this could be controllable with local hemostatic measures [1,4,7].

Secondly, DOACs present predictable pharmacokinetics and pharmacodynamics, by which their anticoagulation effect is in proportion to the plasma concentrations of the drug. Maximal concentration is achieved in about two hours. The elimination of these drugs is bi-exponential, a large quantity is metabolized in the first moment, thus generating a significant fall of its half-life plasma concentration [5,6,8]. This led to our notion that the surgical procedure should be performed in about 6 to 9 hours after the last ingestion of dabigatran and apixaban, and in 12 to 15 hours of rivaroxaban, which is time enough for the formation of an organized and stable blood clot until the peak of action of the next dose.

The initial results of our study demonstrate that this dental management protocol in patients on continuous use of DOACs is feasible and is secure, since the trough and peak levels of action of



**Table 1:** Summary of the case series: medications used by patients, time of DOAC ingestion and of dental surgery, number of sessions and teeth extracted, and the presence or not of postoperative bleeding.

Patient	DOAC and dose	Preoperative time of ingestion	Time of exodontia	Postoperative time of ingestion	Teeth extracted	Post-op Bleeding
1	Dabigatran 150 mg (2x/dia)	8:00 AM	4:15 PM	8:00 PM	31 e 32	No
			4:20 PM		33 e 34	
			4:15 PM		41 e 44	
			5:00 PM		21 e 23	
2	Dabigatran 110 mg (2x/dia)	11:00 AM	5:45 PM	11:00 PM	17	No
			6:00 PM		27	
3	Dabigatran 110 mg (2x/dia)	8:00 AM	4:00 PM	8:00 PM	33 e 43	No
4	Rivaroxaban 20 mg (1x/dia)	12:00 AM	1:00 PM	12:00 AM	38	No
			1:00 PM		37	
5	Rivaroxaban 20 mg (1x/dia)	9:00 PM	10:20 AM	9:00 PM	45	No
6	Rivaroxaban 20 mg (1x/dia)	8:00 PM	10:15 AM	8:00 PM	36	No
7	Rivaroxaban 20 mg (1x/dia)	8:00 PM	10:20 AM	8:00 PM	31, 41 e 42	No
8	Apixaban 5 mg (2x/dia)	10:00 AM	5:20 PM	10:00 PM	36	No
9	Apixaban 5 mg (2x/dia)	8:00 AM	4:15 PM	8:00 PM	16	Yes
10	Apixaban 5 mg (2x/dia)	9:00 AM	5:50 PM	9:00 om	25	No

\*It was necessary to perform mucoperiosteal incision and osteotomy for extraction

these drugs are respected. These encouraging initial results should be extended to a larger number of patients and should be reproduced by other centers of excellence in research.

## CONCLUSION

The continued use of the direct oral anticoagulant drugs was safe in oral surgeries with low bleeding risk, once the surgeon is aware of the drug's pharmacology, complications, how to avoid them, as well as what should be done in the case of complications.

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