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ORIGINAL ARTICLE

Direct oral anticoagulants in oral surgery: a prospective cohort

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ABSTRACT

BACKGROUND: Quantitative assessment of bleeding in dental extractions is rarely reported in the literature. The assessment of bleeding might provide additional evidence to predict and minimize postoperative outcomes. The aim of this study was to evaluate the pattern of bleeding in individuals taking direct oral anticoagulants (DOACs) submitted to dental extractions.

METHODS: Intraoperative bleeding was evaluated by using total collected bleeding corrected by absorbance reading (dental bleeding score). To monitoring bleeding episodes from the day of surgery, this cohort was followed up until the seventh postoperative day.

RESULTS: Forty-five procedures were performed in three comparative groups, patients under DOACs, individuals taking vitamin K antagonists (VKAs) and without anticoagulant therapy. No bleeding events were observed in procedures carried out in individuals of the DOAC group. Additional hemostatic measures were required in two procedures in the VKA group and one in the non-anticoagulated group. The dental bleeding scores obtained for the DOAC and VKA groups were similar.

CONCLUSIONS: Our data suggest that the DOAC therapy did not result in increased bleeding outcomes in this sample.

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KEY WORDS: Anticoagulants; Oral surgical procedures; Tooth extraction; Postoperative hemorrhage.

Anticoagulant therapy has been widely used in the primary and secondary prevention of venous and arterial thromboembolic events.[1-5] Heparin was first introduced as an anticoagulant agent; however, one of the major drawbacks is the need for parenteral administration.[6] Warfarin has been the most popular oral anticoagulant drug used over the last 60 years, but it has limitations such as dietary and drug interactions, narrow therapeutic range, and the need for monitoring.[7] Therefore, in the last years, new anticoagulant agents have been introduced as alternatives to overcome the limitations of the conventional anticoagulant[8] improving safety and providing higher therapeutic value.[9]

The direct oral anticoagulants (DOACs) are novel targeted agents that present the advantages of more predictable pharmacokinetics and fewer drug interactions, which improves the quality of care and avoids a requirement for dosage adjustments and monitoring.[10] The DOACs comprise direct thrombin inhibitors that are represented

by dabigatran (Pradaxa®) and inhibitors of Xa factor, such as rivaroxaban (Xarelto®), apixaban (Eliquis®), edoxaban (Lixiana®) and betrixaban (Bevyxxa®).[11] The DOACs emerged as an alternative approach for the acute treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), for the prevention of stroke and systemic embolization in non-valvular atrial fibrillation (NVAF) and for venous thromboembolism (VTE) prophylaxis after orthopedic surgery.[12-16]

Limited evidence on the periprocedural management of DOAC therapy during dental extractions is available, and an optimal surgical protocol remains undefined.[17] Few clinical studies have evaluated bleeding outcomes in individuals under DOAC treatment during oral surgery[11, 17-21] and, there is no consensus and no defined clinical guidelines for this population thus far. The lack of evidence-based guidelines for patients on DOACs precludes assertive decisions of health providers about the safest way to perform tooth extractions in this group.[22]

The aim of this study was to evaluate the impact of DOAC therapy on bleeding outcomes, in individuals undergoing dental extractions, by means of a quantitative method to assess bleeding and hemorrhagic outcomes.

Materials and methods

Ethical guidelines

The study protocol was approved by the Institutional Ethics Committee of Universidade Federal de Minas Gerais (UFMG) (Protocol 48122215.4.0000.5149). The guidelines established in the Declaration of Helsinki (revised version/2002) for research involving humans were followed. The study also has the approval of the Department of Education and Research of the Hospital das Clínicas of the UFMG (HC/UFMG). Each participant signed a statement of informed consent to take part in the study. Anonymity was guaranteed to all participants.

Participants

The sample consisted of individuals, who had been admitted to treatment at the Dental Service of the HC/UFMG, between January 2017 and January 2018. Patients enrolled in the study consisted of a group of individuals undergoing DOAC therapy (N.=11); a group of individuals under vitamin K antagonist (VKA) therapy with International Normalized Ratio (INR) values ≤3.5 (N.=15); and a group of non-anticoagulated individuals without coagulation disorders and who were not using an antithrombotic drug (N.=15). The criterion for recruitment of participants was a need for extraction of at least one erupted tooth. The following were excluded from the study: individuals with INR>3.5; individuals with any coagulation disorders not related to anticoagulant use (*i.e.*, hepatic diseases, thrombocytopenia); elderly individuals over the age of 80 years; and individuals presenting any tooth with acute inflammatory conditions (*i.e.*, periodontal or periapical abscess). Individuals who had undergone non-standard interventions and cases with incomplete follow up were excluded. A blood count test was requested for all participants. Individuals taking VKA were also subjected to INR tests. The tests were performed within three days prior to dental surgery.

Dental extraction

All procedures were carried out in the hospital outpatient clinic, early in the morning, under local anesthesia by qualified oral surgeons, trained and supervised by the principal investigator. For individuals under DOAC therapy, the dental extractions were performed without withdrawal of the daily dose, as long as possible after the last dose. When the medication had been taken in the morning, this dose was delayed until after the procedure, following the protocol proposed by Nathwani *et al.*[11] In the VKA group, the drug regimen was maintained. Blood pressure was measured previously and shortly after the surgical interventions. Local anesthesia was standardized for all patients and consisted of a regional block complemented with local infiltration of 2% lidocaine hydrochloride with epinephrine (Alphacaine 1:100,000; DFL Indústria e Comércio S.A, Rio de Janeiro, Brazil).

The surgical technique followed strictly preestablished parameters observed by the principal investigator. The surgical technique, including

the use of forceps and elevator, was carried out as atraumatic as possible. Hemostatic measures included wound closure with 3.0 nylon 14502 T sutures (Mononylon, Ethicon, Somerville, NJ, USA) and a piece of sterile gauze bitten by the participant for 20 minutes to compress the operated site. Twenty minutes later, the participants were examined to ensure that hemostasis was obtained, and the immediate postoperative bleeding outcome was evaluated. When increased levels of immediate postoperative or intraoperative bleeding were observed, additional hemostatic measures were performed, applying a 10 x 10 x 10-mm absorbable gelatin sponge (Hemospon, Technew, Rio de Janeiro, Brazil), tranexamic acid (Transamin, Nikkho, Rio de Janeiro, Brazil) and/or new sutures. Tranexamic acid paste (one 250-mg pill macerated and mixed with saline) was used to soak the gelatin sponge. The gelatin sponge was placed in the alveolar socket. An additional layer of the paste was applied on the wound after the sutures and covered with gauze under compression. For these individuals, local use of tranexamic acid mouthwash (one pill mixed in 100 mL of cold saline solution), four times a day, was recommended during the following seven postoperative days. The individuals received written postoperative instructions. Procedure time was measured with a stopwatch from the time of the first incision for the detachment of the gingiva until the complete suture was made.

Postoperative pain was managed with 500 mg of metamizole every six hours or 500 mg of acetaminophen every six hours for three days. Antibiotic prophylaxis was only used in individuals at risk of infective endocarditis as defined by the American Heart Association.[23]

Data collection

Information on participants' age and sex, history of bleeding in previous medical or dental procedures, and history of bleeding among family members (parents and/or siblings) were collected. Information on medical diagnosis, indication for oral anticoagulant therapy (OAT), type of OAT, INR (for VKA group) and platelet count was also obtained. The number of tooth extractions (one tooth, two or more teeth), type of teeth (single-rooted or multi-rooted teeth), the indication of surgical procedures (periodontal disease, dental caries or third molar) were recorded. Additional collected parameters were surgical procedure time, pain and number of gauzes used for hemostasis.

The outcome variables were as follows: the need for additional hemostatic measures (yes or no), immediate postoperative bleeding (yes or no), postoperative bleeding (yes or no), dental bleeding score, and wound healing (satisfactory, swelling/erythema or bone exposure). The postoperative bleeding events were recorded as well as the management of the bleeding (local hemostatic measures in outpatient care or hospital admission).

Quantitative assessment of intraoperative bleeding: Dental Bleeding Score

The method proposed by Rocha *et al.* for the measurement of oral intraoperative bleeding was adopted and detailed below.[24]

Bleeding amount

The amount of intraoperative bleeding was quantified by means of the storage of the aspirated fluids during the surgical procedure in a portable vacuum pump (5005 BRS, Nevoni, São Paulo, Brazil). A standardized volume of 100 mL of saline solution was used for wound irrigation in all procedures. To avoid clot formation during aspiration, two mL of heparin sodium (5000 IU/mL) (Hepamax-S, Blausiegel, São Paulo, Brazil) was added to the final aspirated solution. Afterwards, the volume of the fluid was measured with a graduated cylinder. For each five mL of fluid, the sample was categorized from one to 10, from the lowest to the highest volume using the following score: samples with up to five mL were classified with score 1; samples with six to 10 mL were classified with score 2; samples with 11 to 15 mL were classified with score 3, and then successively until score 10; samples with more than 45 mL. The standardized values of saline solution and heparin were disregarded.

The absorbance of the aspirated fluid

A sample of the total aspirated fluids was collected and used to assess optical density (an indirect

measurement of red blood concentration) with a spectrophotometer at 537 nm (RA 50 clinical, Bayer, São Paulo, Brazil). With this analysis, control of the bias that salivary fluid might have had an influence over the total volume of aspirated fluid was feasible. The values of absorbance were also categorized in scores, from the lowest to the highest value as follows: absorbance up to 1.0 was classified as score 1; absorbance value of 1.1 to 2.0 was score 2; 2.1 to 3.0 was score 3 and 3.1 or more was considered as the maximum score of 4.

Bleeding score assessment

The scores of total aspirated fluid and absorbance were summed to achieve a final score of bleeding. The values varied from two to 14, for which lower scores indicated less intraoperative bleeding.

Postoperative bleeding

A clinical outcome characterized by a postoperative hemorrhagic event was defined as a marked hemorrhage that required one or more of the following outcomes: 1) telephone call to the dental service or to the principal investigator reporting concern of postoperative bleeding; 2) return to our or another outpatient facility due to postoperative bleeding; 3) need of hospitalization. With the aim of monitoring bleeding episodes from the day of surgery until one week after the dental extractions, the participants were instructed to use gauzes for local compression in case of bleeding and to record the number of gauzes used.

On the seventh postoperative day, participants returned for an appointment to remove the sutures and to evaluate the wound healing. Parameters such as the presence of local erythema/edema, bone exposure, and suppuration were also analyzed. During the appointment, the patients were surveyed regarding bleeding complications during the postoperative period and whether pain had occurred. The pain was measured by means of a numerical scale (NRS).[25] The scale ranged from 0 to 10. A score of 0 indicated no pain and a score of 10 indicated the highest perception of pain. Individuals who did not return for a follow-up visit were excluded from the analysis.

Data analysis

The analyses were carried out considering the number of procedures, rather than the number of individuals. Descriptive analyses regarding demographic, clinical and bleeding outcomes were performed using the Statistical Package for the Social Sciences (SPSS for Windows, version 23.0, Armonk, NY, USA). Results were reported with means, standard deviations (SD) and percentages.

Results

In this study, 45 surgical procedures were carried out in three groups. Following the application of the inclusion and exclusion criteria, fifteen dental extractions were performed in 11 individuals under DOAC therapy, fifteen procedures in 15 individuals under VKA therapy and fifteen in 15 non-anticoagulated individuals. One non-standard intervention was excluded from the analysis and 13 individuals using DOAC therapy were not included in the sample because they had not met the criterion for dental extraction.

The main clinical and demographic characteristics of the individuals enrolled in this study are reported in Table I. In the DOAC sample, six procedures were carried out in individuals taking apixaban (5 mg twice daily), five procedures were performed in individuals taking dabigatran (150 mg twice daily), and four procedures were carried out in individuals taking rivaroxaban (10 mg once daily). In the VKA group, all procedures were performed in individuals under warfarin (5 mg once daily) therapy, and the continuous variable INR was collected for this group in particular. The VKA and the non-anticoagulated individuals were matched to the DOAC group in relation to the individuals' age and sex as well as characteristics of the dental extraction.

Data on the number, type, and indication of extractions are summarized in Table II. Due to the standardized volume of 100 mL of saline solution stated in the method, extraction of impacted teeth were not included in the sample. The mean time of surgery was 43 minutes (interquartile range/IQR = 30-55). Individuals of the non-anticoagulated group complained more with

TABLE I.—*Clinical characteristics of individuals undergoing surgical procedures in study groups: Non-OAT (N.=15), DOAC (N.=15) and VKA (N.=15).*

Variables	Non-OAT	DOAC	VKA
Age (yrs)			
Mean (SD)	54.0 (11.0)	58.9 (11.1)	53.8 (10.1)
Min-max	30-66	35-70	34-72
Gender (%)			
Male	12 (80.0)	12 (80.0)	12 (80.0)
Female	3 (20.0)	3 (20.0)	3 (20.0)
Previous history of bleeding in a medical procedure			
No	11 (73.3)	15 (100.0)	14 (93.3)
Yes	04 (26.7)	00 (0.0)	01 (6.7)
Previous history of bleeding in a dental procedure			
No	15 (100.0)	13 (86.7)	13 (86.7)
Yes	0 (0.0)	2 (13.3)	2 (13.3)
Previous history of bleeding in family			
No	15 (100.0)	15 (100.0)	15 (100.0)
Yes	0 (0.0)	0 (0.0)	0 (0.0)
Platelet count			
Mean (SD)	246.5 (74.2)	273.2 (69.2)	230.7 (105.1)
Min-max	123-331	182-367	107-535
INR			
Mean (SD)	-	-	2.4 (0.4)
Min-max	-	-	1.8 - 3.41
Indication for OAT			
DVT	-	4	3
AF	-	7	5
MHV	-	-	4
PE	-	2	3
CIA	-	2	-
OAT prescribed			
Warfarin	-	-	15 (100)
Rivaroxaban	-	4 (26.7)	-
Dabigatran	-	5 (33.3)	-
Apixaban	-	6 (40.0)	-

DOAC: Direct oral anticoagulant; VKA: vitamin K antagonist; non-OAT: non- anticoagulated; yrs; years; SD: standard deviation; DVT: deep vein thrombosis; AF: atrial fibrillation; MHV: mechanical heart valve; PE: pulmonary embolus; CIA: cerebrovascular ischemic accident; INR: International Normalized Ratio; Min: minimum; Max: maximum.

respect to pain during the postoperative days, while the use of gauzes was higher among individuals undergoing DOAC therapy during the same period.

No occurrences of additional hemostatic measure, immediate postoperative bleeding or postoperative bleeding were observed in procedures carried out in individuals of the DOAC group (Table III). In the VKA group, two procedures required additional hemostatic measures. One episode of postoperative bleeding was observed and the participant returned to the outpatient facility. In the non-anticoagulated group, additional hemostatic measures were necessary for one procedure. All bleeding events were easily controlled with local measures and no individual included in the study had severe bleeding requiring hospitalization. Increased bleeding during the dental procedure was managed by applying tranexamic acid paste (one 250 mg pill macerated and mixed with saline) soaked in the gelatin sponge placed in the alveolar socket and digital compression with gauze soaked with tranexamic acid paste. For postoperative bleeding, surgical management of the wound was performed. The above-mentioned additional hemostatic measures, including topical hemostatic agents and new sutures were used to control bleeding.

Regarding the dental bleeding score, values observed in the non-anticoagulated group (8.6±3.4), DOAC (7.5±2.8) and VKA (7.9±2.8) individuals were quite similar. A tendency of unsatisfactory

TABLE II.—*Clinical characteristics of procedures for tooth extraction performed in groups: non-anticoagulated (N.=15), DOAC (N.=15) and VKA (N.=15).*

Variables	Non-OAT	DOAC	VKA
Tooth extraction			
1 tooth	6 (40.0)	5 (33.3)	5 (33.3)
2 or more teeth	9 (60.0)	10 (66.6)	10 (66.6)
Teeth			
1 root	3 (20.0)	4 (26.7)	1 (6.7)
More than 1 root	12 (80.0)	11 (73.3)	14 (93.3)
Indication			
Periodontal disease	4 (26.7)	3 (20)	4 (26.7)
Decay	11 (73.3)	11 (73.3)	11 (73.3)
Third molar	-	1 (6.7)	-
Procedure time (minutes)			
Mean (SD)	43.3 (13.5)	46.6 (10.8)	40.3 (15.4)
Min-max	20-65	30-60	20-60
Pain			
Mean (SD)	4.0 (3.4)	2.53 (2.9)	0.9 (1.3)
Min-max	0-10	0-9	0-4
Gauzes			
Mean (SD)	0.6 (1.4)	3.4 (4.8)	2.6 (2.4)
Min-max	0-5	0-10	0-5

VKA: Vitamin K Antagonist; DOAC: direct oral anticoagulant; Non-OAT: non-anticoagulated; SD: standard deviation; Min: minimum; Max: maximum.

TABLE III.—*Clinic and quantitative assessment of bleeding and outcomes in study groups: non-anticoagulated (N.=15), DOAC (N.=15) and VKA (N.=15).*

Variables	Non-OAT	DOAC	VKA
Additional hemostatic measures			
No	14 (93.3)	15 (100.0)	13 (86.7)
Yes	1 (6.7)	0 (0.0)	2 (13.3)
Immediate postoperative bleeding			
No	15 (100.0)	15 (100.0)	15 (100.0)
Yes	0 (0.0)	0 (0.0)	0 (0.0)
Postoperative bleeding			
No	15 (100.0)	15 (100.0)	14 (93.3)
Yes	0 (0.0)	0 (0.0)	1 (6.7)
Bleeding score			
Mean (SD)	8.6 (3.4)	7.5 (2.8)	7.9 (2.8)
Min - Max	4-14	3-13	3-13
Wound healing			
Satisfactory	11 (73.3)	7 (46.7)	10 (66.7)
Swelling/erythema	4 (26.7)	8 (53.3)	5 (33.3)

VKA: Vitamin K antagonist; DOAC: direct oral anticoagulant; non-OAT: non- anticoagulated; SD: standard deviation; Min: minimum; Max: maximum.

wound healing was observed among individuals undergoing DOAC therapy (Table III). Data of procedures performed in individuals under DOAC therapy are summarized in Table IV.

Discussion

Few studies have investigated the surgical dental management of individuals under DOAC therapy.[11, 17-21] Individuals enrolled in this study showed a low incidence of bleeding complications following dental extractions of erupted teeth. Bleeding episodes were not observed amongst the individuals taking DOACs, following a non-cessation protocol. The data regarding bleeding outcomes observed in individuals under DOAC therapy were similar to those obtained by analyses of the VKA and non-anticoagulated groups.

TABLE IV.—*Baseline characteristics of DOAC individuals on whom the procedures were performed (N.=15).*

Case	Gender	Age	DOAC	Indication for OAT	Bleeding history	Platelet count	Number of teeth extracted	Dental bleeding score	Bleeding complication
1	M	59	D	AF	No	182	2	13	No
2	M	68	D	CIA	Yes	244	3	12	No
3	M	68	D	CIA	Yes	244	2	7	No
4	M	60	D	PE	No	183	2	6	No
5	M	70	R	DVT	No	261	1	3	No
6	F	49	R	DVT	No	205	1	6	No
7	M	60	D	PE	No	183	2	4	No
8	M	66	R	DVT	No	280	1	9	No
9	M	66	A	AF	No	339	3	5	No
10	M	66	A	AF	No	339	3	8	No
11	M	66	A	AF	No	339	3	7	No
12	M	66	A	AF	No	339	2	6	No
13	F	35	A	AF	No	367	1	10	No
14	M	42	R	AF	No	363	1	7	No
15	F	43	A	DVT	No	231	3	10	No

M: Male; F: female; D: dabigatran; R: rivaroxaban; A: apixaban; DVT: deep vein thrombosis; AF: atrial fibrillation; PE: pulmonary embolus; CIA: cerebrovascular ischemic accident.

The present study evaluated bleeding during dental extractions by means of a quantitative method, using the total collected bleeding corrected by absorbance reading – *the dental bleeding score*. The assessment of the dental bleeding score was, in general, similar among the three groups, with a slight increase among the individuals in the non-anticoagulated group. Currently, there has been no standardized methodology for the measurement of quantitative bleeding in dental practice. In the present study, the protocol proposed by Rocha *et al.* was adopted for the measurement of oral intraoperative bleeding that otherwise might be considered unfeasible due to salivary interference. The combination of the optical density of the sample with the total amount of aspirated fluid made the estimation attainable.[24]

The evaluation of intraoperative bleeding was performed by Miclotti *et al.*,[17] in their case-control study. The assessment was estimated by a scale, in which 1 was no bleeding and 5 was continued bleeding despite standard measures. The method suggested by Miclotti *et al.* differs from the current one since our method allowed us to objectively assess bleeding during dental extraction. The authors did not observe a significant difference in intraoperative bleeding between individuals taking DOAC (N.=26) and matched controls (N.=26). In the same study, seven individuals of the DOAC group presented delayed postoperative bleeding episodes. This outcome was not observed in the control group. It is important to emphasize that individuals with bleeding were significantly older than individuals without bleeding.[17] In the present study, elderly individuals (>80 years old) were excluded from the sample with the intent to mitigate likely bias.[1]

Findings in the literature are heterogeneous regarding the postoperative outcomes of dental procedures. Mauvipirez *et al.*,[19] found no statistical difference in the number of bleeding complications between individuals under DOAC therapy and individuals under VKA therapy. Similarly, in another comparative clinical study, only one individual undergoing DOAC therapy and two individuals undergoing VKA therapy presented postoperative bleeding, and no statistically significant difference was observed between the groups.[21] In a study comparing individuals under DOAC therapy and under bridging anticoagulation (warfarin replaced by low-molecular-weight heparin), the authors reported no complications among individuals in the DOAC group and 15% of bleeding incidence in the bridging group.[26]

Similar to our findings, no bleeding episode was described among DOAC individuals in a retrospective cohort study of Miller & Miller.[18] Interestingly, the authors reported a variability in DOAC discontinuance and in the duration of dis-

continuance advocated by the practitioners. Bensi *et al.*[20] pointed out in their systematic review that the included articles followed different protocols in the management of individuals taking DOACs: 46.1% of the providers did not discontinue the therapy, while 53.9% changed the anticoagulant administration. In the present study, the surgery was performed as long as possible after the last dose. When the medication had been taken in the morning, the intake was postponed until after the procedure, following the protocol proposed by Nathwani *et al.*[11]

DOAC-related postoperative bleeding episodes have also been described in the literature. In a case series, one of the five individuals developed significant postoperative bleeding after multiple extractions, which ceased after dabigatran withdraw.[27] In a cohort of 111 procedures performed in individuals under DOAC therapy, a 13.5% incidence of postoperative complications was observed. In this study, the authors discontinued DOAC doses before and/or after the procedure and they concluded that the drug discontinuation or continuation had not been a factor affecting bleeding outcomes.[28] Similarly, other authors demonstrated that the time between the last DOAC dose and the extraction in patients with or without bleeding was not significantly different.[17]

Large medical trials, such as the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY),[14] EINSTEIN-Extension[13] and ARISTOTLE[15] have investigated several outcomes among individuals under DOAC therapy, including bleeding complications. However, detailed information on dental procedures has been unavailable. The RE-LY study consisted of an evaluation of 7637 procedures, comparing outcomes regarding the intraoperative use of dabigatran with warfarin. This trial has demonstrated that both drugs are associated with similar rates of bleeding.[14] The Continued Treatment Study EINSTEIN-Extension was a double-blind study, in which the authors included 602 patients in the rivaroxaban group and 594 in the placebo group. Four individuals in the rivaroxaban group had major bleeding (0.7%), *versus* none in the placebo group.[13] Data from the ARISTOTLE Trial, have shown that individuals taking apixaban, may be subjected to low-risk procedures without OAT discontinuance.[15]

For the safe management of individuals under DOAC therapy, caution must be exercised in some critical situations. Impaired renal function, comorbidities, multiple tooth extractions, and poor oral hygiene may negatively influence bleeding outcomes.[21, 22] In addition, despite the favorable bleeding profiles of DOACs, the occurrence of major bleeding may, sometimes, be of difficult management, due to the lack of prompt access to techniques for controlling and reversing drug activity.[29] Idarucizumab is the only reversal agent approved by the United States Food and Drug Administration (FDA). Other hemostatic factors that have been studied as potential nonspecific DOAC reversal agents are prothrombin complex concentrates (PCCs), activated PCCs (aPCCs), recombinant activated factor VII, and fresh-frozen plasma (FFP).[30] Laboratory measurement of the anticoagulant effect of DOACs can be necessary in cases of hemorrhage. The monitoring may be accomplished in its best with specialized assays that are expensive and routinely unavailable.[31]

In the context of antithrombotic therapy, the impact of antiplatelet agents on dental bleeding is also widely explored in the literature. Although a typical past approach was to suspend the therapy, the current evidence shows that dental surgery in patients under antiplatelet therapy might be carried out without altering the drug regimen.[32] It is because the risk of bleeding is low and the interruption of therapy exposes patients to an increased risk for thromboembolic events, which can result in major disability or death.[32, 33]

Clinicians should also be attentive to the evaluation of clotting disorders related to some systemic diseases. In patients with end-stage chronic liver disease, for example, the coagulopathy often results from an impairment of liver function reducing the production of clotting factors II, V, VII, IX, X, and XI.[34] Furthermore, conditions involving severe thrombocytopenia (platelet count $<50{,}000/mm^3$) significantly increase the risk of bleeding and require platelet transfusions.[35] In hereditary coagulopathies, for instance, hemophilias and Von Willebrand's disease (VWD), a genetic defect determines a functional deficiency of the coagulation factor VIII in hemophilia type

A, factor IX in hemophilia B and Willebrand factor in VWD.[36] In these cases, for surgical treatment, it is recommended to request hematological advice to establish the severity of hemophilia, the presence of inhibitor VIII, and the dosage and type of replacement therapy.[37]

Limitations of the study

In the present study, the DOAC sample was composed of individuals who had undergone 15 procedures for dental extraction performed under rivaroxaban prophylactic dosage; dabigatran and apixaban in therapeutic form. The small sample depicts issues regarding DOAC implementation in Brazil. DOACs are costly[38] precluding free supply by the national health system. Individuals who have access to expensive treatments with DOAC present higher socioeconomic levels, access to private health services and improved oral health. Twenty-five individuals under DOAC therapy had been evaluated in this study; however, 13 did not meet the dental extraction criterion and were excluded. The strict exclusion criteria justify the small sample in this group, which is the major limitation of this study. It is clear that more research is needed to develop evidence-based guidelines for the dental management of individuals on DOAC therapy. Furthermore, trials with larger sample sizes should be performed to confirm our results.

Conclusions

Our data suggest that bleeding risk during and after dental extractions in individuals under DOAC therapy is low and bleeding complications could be easily managed in the outpatient setting by using local hemostatic measures. Further studies are warranted to develop evidence-based guidelines for the safest clinical strategy in the management of patients on DOACs. Moreover, the proposed method of bleeding assessment may be a useful parameter to be tested in different at-risk populations.

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