DRUG INTERACTIONS BETWEEN ANTICOAGULANT THERAPY AND INVASIVE DENTAL PROCEDURES

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Abstract

The management of anticoagulated patients in dentistry presents a significant challenge, requiring a balance between hemorrhagic and thromboembolic risks. Anticoagulants, including vitamin K antagonists (VKAs), direct oral anticoagulants (DOACs), and low-molecular-weight heparins (LMWHs), increase bleeding risk during invasive dental procedures. Recent guidelines emphasize that maintaining anticoagulation with appropriate hemostatic measures is generally safer than treatment interruption, which may lead to thromboembolic complications. Preoperative assessment should consider the type of anticoagulant, the patient's medical status, and the procedure's risk level. VKAs require INR monitoring, while DOACs should be scheduled at their lowest plasma concentration. Advanced hemostatic agents (collagen, oxidized cellulose, tranexamic acid) and minimally invasive surgical techniques significantly reduce postoperative bleeding. Postoperative management includes patient education on bleeding control, avoiding NSAIDs, and close monitoring. Future research aims to develop predictable anticoagulants, advanced biomaterials, and AI-based risk assessment tools to improve patient safety. A multidisciplinary approach is essential for optimal care, ensuring successful dental treatment while minimizing complications. This review provides updated insights into best practices for managing anticoagulated patients in dentistry.

Keywords: Anticoagulants, bleeding risk, dental surgery, hemostasis, thromboembolism, patient management, multidisciplinary approach.

Introduction

Anticoagulant therapy is widely used for the prevention and treatment of thromboembolic conditions, such as atrial fibrillation, deep vein thrombosis, and pulmonary embolism. This includes coumarin anticoagulants (e.g., warfarin, acenocoumarol), direct oral anticoagulants (NOACs such as apixaban, rivaroxaban, dabigatran, edoxaban), and low molecular weight heparins (LMWH). Due to their mechanism of action, these drugs increase the risk of bleeding, which requires special attention in patients who require invasive dental interventions. The balance between hemorrhagic risk and prevention of thrombotic events is a major challenge in medical and dental practice [1-3].

Invasive dental procedures, such as tooth extractions, periodontal surgery, implant insertion, and other surgeries, can lead to significant bleeding, especially in patients undergoing anticoagulant treatment. In the past, a commonly used strategy was to temporarily stop anticoagulants before the procedure to reduce the risk of bleeding. However, recent studies show that discontinuation of treatment significantly increases the risk of thromboembolic events, which can have

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severe consequences, including strokes and heart attacks. Thus, the modern approach recommends the careful evaluation of each patient and the adaptation of the treatment according to the type of intervention and the individual risk [1-4].

One of the main factors to take into account is the type of anticoagulant used. Patients taking antivitamin K (VKA), such as warfarin or acenocoumarol, require monitoring of prothrombin time (INR). In the case of an INR between 2 and 3, most dental procedures can be performed without stopping treatment, applying appropriate hemostatic measures. If the INR exceeds 3, a reassessment is required before the intervention. In the case of patients treated with NOACs, the advantage is the lack of need for periodic coagulation monitoring, but each substance has a different half-life and a distinct elimination mechanism, which influences the perioperative therapeutic decision [2-5].

Heparins, especially low molecular weight heparins (e.g., enoxaparin, dalteparin), are commonly used in patients at high risk of thrombosis, especially in acute situations or in cases where VKAs or NOACs are not indicated. Because heparins act quickly and have a short half-life, their temporary discontinuation can be managed more easily than with other anticoagulants [3-6].

Another important aspect is the type of dental procedure. Interventions with low bleeding risk, such as scaling or dental fillings, can be performed without modifying anticoagulant therapy. In contrast, multiple extractions, extensive periodontal surgery, and implant insertion require a more cautious approach. For these cases, current guidelines suggest either maintaining anticoagulation with the application of appropriate hemostatic measures (sutures, topical hemostatic agents) or temporarily adjusting the treatment, depending on the specialist's recommendations [3-7].

Interdisciplinary communication between the dentist and the specialist who manages the patient's anticoagulation (cardiologist, hematologist, internist) is essential. This collaboration allows a correct assessment of the risk-benefit ratio and the adoption of the safest strategy for the patient. Patients must also be clearly informed about the risks and necessary measures before and after dental intervention [4-8].

This paper is structured as a narrative review aiming to integrate recent data from the literature regarding interactions between anticoagulant therapy and invasive dental procedures. The novelty of this work lies in its interdisciplinary approach, combining pharmacological, clinical, and technological aspects. Notably, it highlights emerging concepts such as the use of biomimetic hemostatic materials and AI-based tools for bleeding risk assessment, which represent innovative directions with significant potential to enhance treatment individualization and procedural safety in anticoagulated dental patients.

Types of anticoagulants and their mechanisms of action

Anticoagulant therapy is used to prevent and treat thromboembolic disorders by inhibiting blood clotting mechanisms. There are three major classes of anticoagulants used in clinical practice: antivitamins K (VKAs), direct oral anticoagulants (NOACs), and heparins.

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Each class presents particularities regarding the mechanism of action, pharmacokinetics, and perioperative management in a dental context [5-10].

Antivitamin K (VKA)

Warfarin and acenocoumarol are the most widely used anticoagulants in this category. They work by inhibiting the enzyme epoxy reductase, blocking vitamin K regeneration, and reducing the synthesis of clotting factors II, VII, IX, and X, as well as anticoagulant proteins C and S [5-10].

An essential aspect of VKA therapy is prothrombin time (INR) monitoring, which should be between 2 and 3 for most therapeutic indications. Higher values significantly increase the risk of bleeding, while lower values increase the risk of thromboembolism. Because of this, before an invasive dental procedure, it is necessary to determine the INR to decide whether the treatment should be adjusted [6-11].

VKAs have a long half-life, which means that their effect persists for several days after discontinuation of administration. Therefore, complete discontinuation of therapy may require a period of bridging therapy (temporary substitution with low molecular weight heparins – LMWH). However, most modern guidelines suggest that patients with an INR ≤3 Can undergo invasive procedures without interruption of therapy, using appropriate hemostatic measures [6-11].

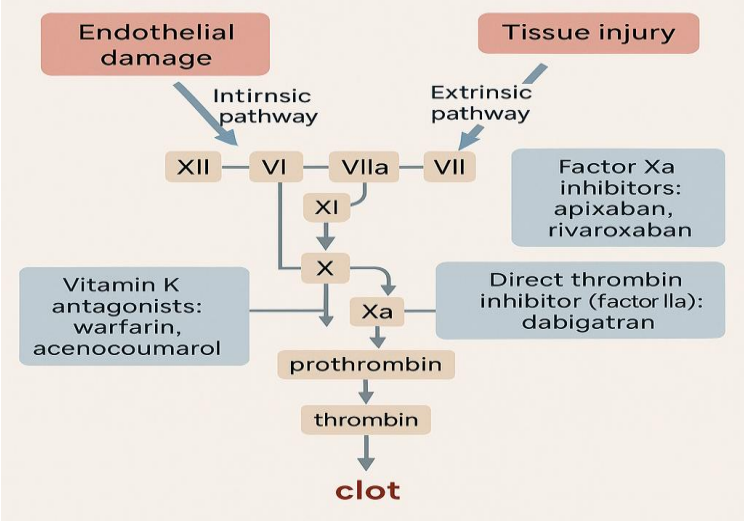

Figure 1. The process of blood coagulation [9-11].

Direct Oral Anticoagulant (NOACs)

This class includes dabigatran (direct thrombin inhibitor), apixaban, rivaroxaban, and edoxaban (direct factor Xa inhibitors). Unlike VKAs, NOACs offer the advantage of rapid action, predictable pharmacokinetics, and no need for frequent coagulation monitoring. Dabigatran directly inhibits thrombin (factor IIa), preventing the conversion of fibrinogen to fibrin. It has a half-life of about 12-17 hours and is predominantly eliminated renally. Apixaban, rivaroxaban, and edoxaban directly inhibit factor Xa, thereby blocking the formation of thrombin. Apixaban has the shortest window of action, which makes it easier to manage perioperatively. NOACs have a shorter half-life than VKA, which

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allows them to be interrupted 24-48 hours before dental procedures with high bleeding risk. In the case of minor interventions, it is usually not necessary to interrupt the treatment, but it is recommended to perform the intervention in the interval when the concentration of the drug is lowest (e.g., at the end of the dosing period) [9-12].

A disadvantage of NOACs is the lack of a usual test for monitoring, which makes it difficult to assess their effect on coagulation. Also, until recently, there were no specific antidotes widely available, but currently, idarucizumab is used for the reversal of dabigatran, and andexanet alfa is available to inhibit the effect of apixaban and rivaroxaban [9-14].

Table 1. Biochemical properties and role of clotting factors [14].

Factor	Plasma (mg/dL)	Half-life (h)	Main Function
XI	0.4–0.6	45–80	Activates FIX (intrinsic pathway)
XII	1.5–4.5	50–70	Initiates the intrinsic pathway
Prekallikrein	1.5–4.5	36	Precursor of kallikrein
HMW Kininogens	8–9	144–156	Cofactor for FXI, FXII, and prekallikrein
II (Prothrombin)	10–12	60–72	Inactive form of thrombin
VII	0.05–0.06	3–6	Initiates the extrinsic pathway with tissue factor
IX	0.4–0.5	18–25	Activates FX (intrinsic pathway)
X	0.7–1.2	24–40	Activates prothrombin with TF
Protein C	0.39–0.59	8–14	Inhibits coagulation in the activated form
Protein S	2.5	40–60	Cofactor for Protein C
Protein Z	0.22	–	Enhances FXa inhibition via ZPI
V	0.4–1.4	12–36	Cofactor in prothrombinase complex
VIII	0.5–1	8–12	Cofactor in the intrinsic tenase complex
Thrombomodulin	–	–	Modulates thrombin function
Tissue Factor (TF)	–	–	Triggers the extrinsic pathway with FVIIa
Fibrinogen	200–400	90	Precursor of fibrin
XIII	1–2	168–288	Stabilizes fibrin clot
Antithrombin III	15–20	68	Inhibits thrombin, FXa, FIXa, FXIa, FXIIa
Heparin Cofactor II	6.1–8.2	60	Heparin-dependent thrombin inhibitor
Protein C Inhibitor	0.5	23.4	Inhibits activated PC, thrombin, kallikrein, FXIa
Z Protein Inhibitor	0.1–0.16	–	Inhibits FXa and FXIa with Protein Z
TF Pathway Inhibitor	0.006	1–2	Blocks TF/FVIIa and FXa complexes

Heparins

Heparins are used especially for inpatients or those requiring bridging therapy on VKA discontinuation. They are classified into two main types: unfractionated heparin (UFH) and low molecular weight heparins (LMWH). Unfractionated heparin (UFH) works by binding to and activating antithrombin III, inhibiting factors IIa and Xa. It has a short half-life and requires constant monitoring (activated clotting time – aPTT). Low

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molecular weight heparins (LMWHs), such as enoxaparin and dalteparin, work primarily by inhibiting factor Xa and have a longer half-life. They do not require regular monitoring and are frequently used on an outpatient basis [9-15].

In the dental context, patients under LMWH may require a temporary adjustment of treatment depending on the type and risk of the procedure. Unlike VKAs and NOACs, heparins have the antidote (protamine sulfate), which makes them easier to manage in case of severe bleeding [10-15].

The management of patients undergoing anticoagulant therapy in dentistry requires a clear classification of invasive procedures according to hemorrhagic risk. Dental interventions range from minimally invasive maneuvers, with a reduced risk of bleeding, to complex surgical procedures, where hemorrhage can become a major complication. In this context, the risk must be assessed individually, taking into account both the specifics of the intervention and the patient's profile [9-16].

Invasive dental procedures and hemorrhagic risk

Table 2. Categorize dental procedures based on hemorrhagic risk in patients undergoing anticoagulant therapy

Type of procedure	Examples	Anticoagulant management	Hemostatic measures	Patient risk
Low hemorrhagic risk procedures	Supragingival scaling, simple fillings, non-incisional endodontic treatments, and impressions	No need to stop anticoagulants	Local compression if needed	Minimal, manageable with standard measures
Moderate hemorrhagic risk procedures	Single tooth extractions, periodontal curettage, apicoectomy	Maintain anticoagulants, schedule the procedure when the NOACs' effect is lowest	Sutures, hemostatic agents (collagen, tranexamic acid), and local pressure	Moderate, requires additional precautions
High hemorrhagic risk procedures	Multiple extractions, extensive periodontal surgery, implant placement, sinus lift, and bone grafting	Interdisciplinary collaboration, possible anticoagulant therapy adjustment	Aggressive hemostasis, use of advanced hemostatic agents, and close postoperative monitoring	High requirements require careful management and supervision.

Table 2 categorizes dental procedures based on hemorrhagic risk in patients undergoing anticoagulant therapy. It provides examples of procedures, anticoagulant management strategies, necessary hemostatic measures, and patient risk levels. Low-risk procedures generally do not require therapy adjustments, while moderate and high-risk interventions may need specialized management. Proper coordination between dental and medical professionals ensures patient safety by balancing the risk of bleeding with the need for thrombosis prevention [9-16].

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Dental procedures must be approached according to the hemorrhagic risk, and therapeutic decisions must balance the prevention of bleeding with the avoidance of thromboembolic complications. Most procedures can be performed without stopping anticoagulants, but with the use of appropriate hemostatic measures. Close communication between the dentist and the specialist managing the patient's anticoagulation is essential for the safety and success of the treatment [9-16].

Management of patients under anticoagulant therapy in dentistry

The management of patients under anticoagulant therapy in dentistry is essential for the prevention of hemorrhagic and thromboembolic complications. The right approach begins with a careful evaluation of the patient, taking into account the type and dose of anticoagulant, medical history, comorbidities, and thromboembolic risk. Patients treated with antivitamin K, such as warfarin or acenocoumarol, require INR monitoring 24-48 hours before the procedure. Values between 2 and 3 allow for most interventions without interruption of treatment, while an INR above 3 requires dose adjustment or consultation with the treating physician. In the case of direct oral anticoagulants, such as rivaroxaban, apixaban, dabigatran, or edoxaban, there is no need for INR monitoring, but interventions should be timed to coincide with the decrease in the plasma concentration of the drug, ideally at the end of the dosing interval. Patients treated with low molecular weight heparins require adjustment of the timing of administration to reduce the risk of intraoperative bleeding [10-17].

Discontinuation of anticoagulants is not recommended for procedures with low bleeding risk, such as supragingival scaling, fillings, or endodontic treatments without incisions, as the risk of bleeding is minimal and easy to control. For single tooth extractions, periodontal curettage or apical resection, anticoagulant therapy is maintained, but it is recommended to perform the intervention at the moment of minimum anticoagulant activity, i.e., at least 12-24 hours after the last dose of NOACs. In the case of multiple extractions, extensive periodontal surgery, implant insertion, or complex procedures such as sinus lift and bone grafts, interdisciplinary collaboration is required to adjust therapy, especially if the patient has a high INR or is on dual antithrombotic therapy. Discontinuation of anticoagulants should be avoided as much as possible to prevent thromboembolic events, and in cases where it is necessary, low molecular weight heparin replacement therapy should be instituted [11-18].

Controlling bleeding during and after the dental procedure is essential for therapeutic success and patient safety. Applying prolonged local pressure immediately after the intervention, for 10-15 minutes, is a simple and effective method to stop bleeding. The use of absorbable sutures helps stabilize the blood clot and prevent postoperative bleeding. Local hemostatic agents, such as collagen, absorbable gelatin, cellulose oxide, and tranexamic acid, can be used to facilitate hemostasis, especially in patients at high risk of bleeding. It is also recommended to avoid unnecessary trauma to soft tissues and

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to use minimally invasive techniques to reduce the risk of hemorrhagic complications [12-18].

Patients should be instructed to follow certain measures to prevent postoperative bleeding. It is essential to avoid excessive rinsing of the mouth during the first 24 hours, as this can dislodge the blood clot and prolong bleeding. Also, hard, hot, or spicy foods should be avoided in the first days after the intervention, to prevent irritation of the surgical wound. Applying cold compresses to the cheek can help reduce inflammation and the risk of bleeding. Patients should be advised to use safe analgesics, such as paracetamol, avoiding non-steroidal anti-inflammatory drugs, which can increase the risk of bleeding. The resumption of anticoagulants should be done according to the indications of the specialist, and the patient should be monitored for signs of prolonged bleeding. If the hemorrhage persists or intensifies, medical re-evaluation and the application of additional measures, such as reapplication of hemostatic agents or additional sutures [9,12-19], are necessary.

Recent studies highlight that the management of anticoagulated patients in dentistry must not only balance hemorrhagic and thromboembolic risks but also integrate advances in biomaterials and clinical strategies, as reflected in current research on ceramic orthodontic devices, post-extraction complications, tonsillolith management, bioresorbable scaffolds, dentin sensitivity, and biocompatibility of pre-implant biomaterials [20–25].

The optimal management of anticoagulated patients in dentistry requires a balanced strategy between preventing bleeding and avoiding thromboembolic complications. Correct preoperative evaluation, careful adjustment of anticoagulant therapy when necessary, and the use of effective hemostatic measures are essential for the success of treatment. Interdisciplinary collaboration between the dentist, the specialist who manages the anticoagulation, and the patient is essential for personalizing the therapeutic approach and reducing the associated risks. In recent years, studies have shown that maintaining anticoagulation in most dental procedures, combined with effective bleeding control techniques, is a safer strategy than discontinuing treatment, which can expose the patient to severe thromboembolic events. Therefore, the modern approach of the anticoagulated patient is based on adapting the treatment according to each case, minimizing the risks and ensuring a favorable prognosis both from a dental and systemic point of view [26-30].

The complications associated with dental procedures in patients on anticoagulant therapy are mainly prolonged bleeding and thromboembolic risk, and their management requires a balanced approach. Excessive bleeding is the most common complication, occurring either immediately postoperatively or a few hours or days after the intervention. This can be influenced by the type of anticoagulant used, the patient's clotting level, and the surgical technique applied. Patients treated with VKA (warfarin, acenocoumarol) have a higher risk of bleeding if the INR exceeds 3, and those on NOACs have a variable bleeding risk depending on the timing of the last dose [26-29].

To prevent and manage prolonged bleeding, it is essential to apply rigorous hemostatic measures, including the use of

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sutures, prolonged local compression, and hemostatic agents such as absorbable collagen, cellulose oxide, and tranexamic acid. Patients should be instructed to avoid excessive rinsing, strenuous physical exertion, and hard or hot foods within the first 24-48 hours postoperatively. If bleeding persists, reapplication of hemostatic agents, resuturing, or even medication to reduce fibrinolysis may be used. In severe cases, it is necessary to consult a specialist to assess the need for systemic intervention, such as administration of antidotes for NOACs or adjustment of anticoagulant therapy [26-29].

On the other hand, discontinuation of anticoagulant therapy exposes the patient to an increased risk of thromboembolic events, especially in those with a history of stroke, atrial fibrillation, or deep vein thrombosis. The risk increases proportionally to the duration of treatment interruption and the severity of the underlying disease. Patients at high risk of thromboembolic events often require bridging therapy with low molecular weight heparins if discontinuation of VKA is necessary, but for most patients, maintaining treatment with the application of local bleeding control measures is a safer strategy [24,26-30].

Complications associated with anticoagulants in dentistry are manageable through careful planning and the use of the right hemostatic techniques. The bleeding risk must be balanced with the thromboembolic risk, and the approach must be personalized according to the patient's characteristics. Interdisciplinary collaboration between the dentist, cardiologist, or hematologist is essential for safe and effective treatment [26-31].

Conclusions

The management of patients under anticoagulant therapy in dentistry remains a challenge, requiring the balancing of hemorrhagic and thromboembolic risk. Recent studies demonstrate that, in most cases, maintaining anticoagulation with the application of effective hemostatic measures is safer than discontinuing treatment, which can expose the patient to severe complications. Current guidelines recommend individualizing the therapeutic strategy, taking into account the type of anticoagulant, the nature of the procedure, and the patient's medical status.

In patients treated with VKA (warfarin, acenocoumarol), maintaining an INR ≤3 Allows most invasive procedures to be performed without interruption of treatment. Patients receiving NOACs (rivaroxaban, apixaban, dabigatran, edoxaban) require adjustment of the timing of administration to reduce the risk of bleeding. Still, without prolonged discontinuation, and patients on low molecular weight heparins (LMWHs) should be carefully managed according to the pharmacokinetics of the drug. The interruption of anticoagulants should be reserved only for cases with a major bleeding risk, and in such situations, it is essential to consult the treating specialist.

The development of advanced topical hemostatic agents, such as resorbable collagen, cellulose oxide, local tranexamic acid, and fibrin gels, has revolutionized bleeding control in oral surgery, allowing moderate- and high-risk procedures to be performed without

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significant changes in anticoagulant therapy.

An important aspect in the management of these patients is postoperative monitoring and patient education. Patients should be clearly informed about measures to prevent postoperative bleeding, avoid local trauma, and use safe analgesics such as paracetamol instead of non-steroidal anti-inflammatory drugs that can worsen bleeding.

From the perspective of future research, an area of interest is the development of anticoagulants with more predictable action and effective antidotes, which would facilitate perioperative management. Also, new technologies, such as smart hemostatic biomaterials and the use of artificial intelligence to assess individual bleeding risks, can significantly improve the safety and efficiency of treatment.

It is essential to provide practical recommendations for dental practitioners, including the optimal timing between anticoagulant administration and dental procedures, as well as standardized hemostatic strategies. Moreover, differentiating clinical scenarios in which anticoagulant therapy can be safely continued from those requiring temporary adjustment would enhance both the safety and efficacy of dental interventions.

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