

Masterclass in Clinical Practice

Implant Dentistry with

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Dental Implants and Anticoagulation therapy- a clinical dilemma

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Introduction

Dental implants have been widely used for replacement of missing teeth with an average success rate of around 95% at 10 years follow-up¹. However, in most clinical trials a rigorous inclusion criteria were set, meaning that only patients in physical status classification I or II of the American Society of Anaesthesiologists were included for investigation. In other words, this high success rate was achieved with implants placed in healthy subjects. It is of course doubtful whether similar success rates can be expected in medically compromised patients.

This Masterclass will deal with anticoagulation therapy in dental implant surgery patients.

Cardiovascular diseases: local anaesthesia, conscious sedation, and general anaesthesia

According to the WHO, cardiovascular diseases is the leading cause of death globally, responsible for an estimated 17.9 million deaths each year.²

Cardiovascular disease (CVD) include diseases of the heart, blood vessels, and circulation. The most common CVDs are hypertension, coronary artery disease (CAD), cerebrovascular disease, and peripheral vascular disease (aneurysms and peripheral arterial disease). Other CVDs include congenital heart disease, rheumatic heart disease, valvular heart disease, congestive heart failure, and cardiac arrhythmias.²

Although cardiovascular disease is not considered a contraindication for dental implant treatment and does not affect implant success, many patients with CVD might be taking anticoagulants, commonly known as "blood thinners". The dental implant surgeon should therefore have the knowledge of how to manage patients on anticoagulants.

Most dental implant surgery can be performed under local anaesthesia with or without sedation. Conscious sedation in the dental rooms is especially useful for treatment of patients with anxiety or a fear of dental treatment. Patients who require more extensive treatment and patients with complex medical histories may need to be treated under general anaesthesia for the additional lifesaving equipment that is available in hospitals. The decision of whether a patient with a history of cardiovascular disease is suitable for dental implant surgery under local anaesthesia, conscious sedation or general anaesthesia, should only be taken after consulting with the patient's medical physician (general medical practitioner, cardiologist, haematologist, specialist physician, anaesthesiologist).

Different anticoagulation therapies

Antiplatelet (AP) and anticoagulant (AC) medications are used in patients at risk of cardiovascular disease. AP drugs, e.g. acetylsalicylic acid (aspirin), dipyridamole and thienopyridines (clopidogrel, ticlopidine, and prasugrel), are most commonly used in patients suffering from ischemic cardiovascular diseases, cerebrovascular diseases and peripheral arterial disease.³ Due to a different mechanism of action of these drugs, they can be combined for so-called dual antiplatelet therapy (DAPT)⁴. DAPT usually involves a low



Figure 1: Clear subcutaneous bleeding on forearm due to self-medication of anticoagulant therapy

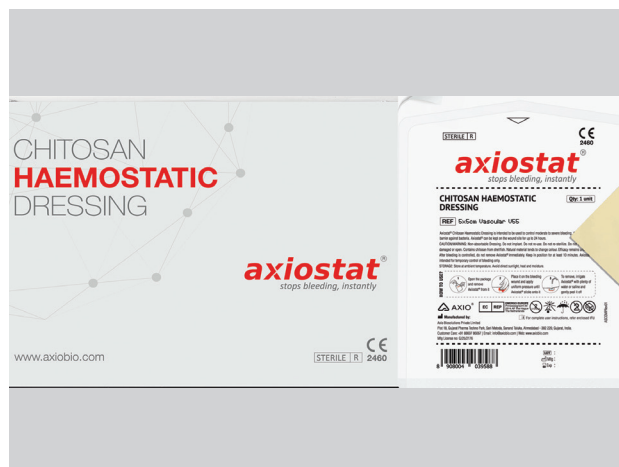


Figure 2: AxioStat® sponge which is available from online retail platforms.

dose of aspirin and clopidogrel, combined for prevention of thrombotic complications. Vitamin K antagonists (warfarin, acenocoumarol and phenprocoumon) are used in prevention and treatment of venous thromboembolism in patients with atrial fibrillation, mechanical prosthetic heart valves, deep vein thrombosis, or pulmonary embolism⁵. In the last decade, a new generation of anticoagulants, a direct thrombin inhibitor (dabigatran) and factor Xa inhibitors (rivaroxaban, apixaban, and edoxaban), were introduced into clinical practice. These drugs, called direct oral anticoagulants (DOACs), are used to prevent stroke or systemic embolism in patients with atrial fibrillation and for the prevention of thrombosis after elective hip and knee surgery⁶. Some of these DOAC's are safer than others regarding unwanted bleeding as a complication.⁷ Compared to traditional ACs, DOACs have pharmacokinetic advantages such as direct action, predictable anticoagulant response, wide therapeutic range, less interaction with drugs and food⁸ and have become more popular in recent years.

Oral surgery procedures in patients on anticoagulation therapy are challenging, as the balance between the risk of haemorrhage and thromboembolic incidents due to a drug interruption must be found. According to the available literature, dental implant surgery should be done without interruption of ACs, DOACs, or APs and with application of proper local haemostatic measures^{9, 10}. This includes haemostatic agents, such as bone wax, gelatine sponges, oxidized cellulose, and tranexamic acid to obtain a stable clot (see clinical tips below). Appropriate passive suturing is required to protect the clot and to ensure uneventful healing of the wound. These patients must be monitored after surgery to ensure that a stable clot is obtained and instructed regarding postoperative care (cold and soft diet, avoid smoking and no vigorous mouth rinsing).

It must be noted that a dental practitioner should not decide on anticoagulation therapy modifications without consulting the physician in charge of patient's treatment.

This is discussed in more detail below. Further studies are needed to give answers regarding the risk of bleeding when more extensive surgery such as bone grafting and sinus lift procedures are performed^{9, 11}. Apart from potential risk of bleeding, a recent study revealed that anticoagulation drugs may impede osseointegration and are associated with early implant failure. More research is required to investigate this.¹²

Who should decide to change the anticoagulation therapy ahead of surgery?

This decision lies with the medical practitioner who prescribed the anticoagulant. Under no circumstances may the dental practitioner change or stop a patient's anticoagulant therapy without consulting with the patient's treating medical physician.¹³ The risk of intra-operative and post-operative bleeding has to be weighed against the risk of changing a patient's anticoagulation therapy. It is further important to note that permission to change a patient's anticoagulant therapy and the recommended protocol, has to be obtained in writing. This will prevent any blame or unnecessary litigation in case there is a complication.

Changing anticoagulation therapy for oral surgery

A range of oral antiplatelet drugs is available for managing conditions associated with the cardio- and cerebrovascular systems, which can be used either as single antiplatelet therapy (SAPT) or as DAPT. The risks of thrombotic events due to altering or discontinuing the use of SAPT or DAPT outweigh the low risk of postoperative oral bleeding complications resulting from low bleeding risk dental procedures. Therefore, minor interventions such as simple dental extractions with limited wound size may be safely performed in patients receiving SAPT or DAPT.¹⁴ A systematic review of antiplatelet therapy and dental procedures found no clinically significant increased risk of postoperative bleeding complications from invasive dental procedures (tooth extractions, apicoectomy,

implant placement, torus removal, excisional biopsies, flap surgery, periodontal surgery) in patients on either SAPT or DAPT. The alteration or discontinuation of SAPT or DAPT is therefore not recommended for any dental procedures.¹¹

¹³ For high bleeding risk procedures, the use of local haemostatic measures is recommended (see clinical tips below).

Warfarin is the most widely used vitamin K antagonist. The risk of interrupting or reducing vitamin K antagonist (VKA) therapy outweigh the consequences of potential bleeding complications.

The interruption of VKA treatment before dental procedures is not recommended for low and high bleeding risk procedures if the INR of the patient is ≤ 3.5 24 hours before the planned intervention. If the INR is ≥ 3.5 , dose adjustment is required and the procedure should be delayed until the patient's INR has been reduced to less than 3.5.¹³ Some patients might require bridging anticoagulation. Bridging anticoagulation refers to giving a short-acting blood thinner, usually low-molecular-weight heparin given by subcutaneous injection around the time of the surgery, when warfarin is interrupted. This has to be done by the treating physician and not the dental surgeon so liaison with treating physician is essential in these cases.¹³

Several direct oral anticoagulants (DOACs) have been developed, which include the direct factor Xa inhibitors rivaroxaban (Xarelto), apixaban (Eliquis) and edoxaban (Lixiana), and the direct thrombin inhibitor dabigatran (Pradaxa). No specific evidence-based guideline recommendations are available for the management of dental patients receiving DOACs. Simple surgical interventions with a low bleeding risk such as dental extractions do not require the interruption of DOACs in patients with normal renal function. Where possible, it is recommended that the procedure is performed 12 or 24 hours after the last intake, depending on twice-daily or once-daily dosing. Interventions at peak plasma concentration should be avoided. Liaise with treating physician.¹⁵

INR to determine safe window in patients using anticoagulants

The Prothrombin time test serves to evaluate blood clotting and is calculated as an International Normalized Ratio (INR). In most cases, the therapeutic range of INR values is from 2.0 to 3.0. However, in patients with higher risk of thromboembolic events a range up to 3.5 is considered therapeutic.^{9, 13} In the context of dentistry, INR is used to observe the effects of oral ACs in patients that will undergo oral surgery procedures. As recommended, INR values are requested a few hours prior to surgery and if result is below 3.5, surgery can be performed. In cases with higher values,

the surgery should be postponed, and new testing requested after lowering the dosage. If INR value is out of therapeutic range, patient should be referred to physician to adjust the anticoagulation therapy scheme and drug dosages¹⁰.

As stated before, if INR values are up to 3.5, dental implants should be performed without interruption of oral ACs, with local haemostatic measures applied (see clinical tips below). However, it is important to note that this cannot be applied to DOACs, as INR is not relevant in DOAC.

Supplements and over-the-counter drugs (OTCD) with anticoagulation properties.

Supplements and OTCD's have become extremely popular over the past few years. This is probably due to the availability of a vast array of supplements in supermarket type pharmacies, aggressive advertising, and the information overload on the internet of claimed benefits. In the US spending on supplementary medications passed the \$200 billion mark more than ten years ago.¹⁶ Dare one say that many benefits are based on at the very best anecdotal information with no evidence? The problem with these drugs is the fact that we have no regulations from the statutory bodies controlling prescription drugs. Warfarin may be affected by supplements and may cause serious or life-threatening bleeding after surgery.

- In a recent systematic review,¹⁷ it was shown that warfarin metabolism may be affected by various foodstuffs and supplements, with the potential of life-threatening bleeding episodes. Cranberry juice is one which has even had fatalities attributed to it in a warfarin user. This is through the inhibitory effect on Cytochrome P450 system in liver with Camomile tea and St. John's wort also playing a similar role.¹⁷ Other food and supplements may cause an erratic INR by increasing Vit K uptake, such as sushi, green tea and spinach which contain high levels of Vit K. Excessive intake of these foods may therefore lead to less anticoagulation effect. Smoking inhibits the effect of warfarin, so people who recently stopped smoking may need to lower warfarin intake, but regular INR testing should control this.¹⁷
- Omega-3 is a controversial supplement for possible anticoagulation properties. Flaxseed, one of the omega-3 substances, has been shown to have blood thinning properties. It is advisable to stop flaxseed supplements 2 weeks before surgery.¹⁸
- Curcumin may also potentiate the effect of warfarin and likewise should be discontinued before surgery.¹⁷

Patients should make a full disclosure of any supplements or change in diet before any dental surgery and INR testing should be done just before surgery if they are on warfarin.

This must be incorporated in medical questionnaires in every practice, as most patients will not volunteer such information if not prompted.

The fact remains that OTCD's have side effects like prescribed pharmaceutical drugs, may interfere with prescription drugs, and may modify their actions.^{17, 18, 19, 20}

Conclusion

Patients on AC therapy should declare all supplements to the treating physician and any changes that may have been introduced between consultations. Often patients will self-medicate and develop tell-tale danger signs of thin blood such as subcutaneous bleeding without realising the danger. As clinicians we should always examine the arms/legs for these signs. Figure 1 shows a lady who presented on day of extractions with a clear sign of subcutaneous bleeding from high levels of anticoagulant self-medication.

As dentists we often use antibiotics, and metronidazole has been a stalwart with amoxicillin in treating dental infections. Metronidazole may potentiate warfarin dramatically and should never be prescribed in these patients.²¹ Should you experience a bleeding complication after dental surgery, tranexamic acid may be used as a mouth rinse and chitosan as a wound dressing. Chitosan is a battlefield development for stopping serious arterial bleeds.²² It has found its way into a dressing suitable for external use in oral bleeds and the authors have used this to good effect in stopping bleeding complications in dental surgery.

Clinical Tip 1

Axiostat® (Figure 2) is readily available in South Africa through various online ordering platforms and has been shown to stop bleeding effectively. It is applied externally to the bleeding site and may be left in place for 24 hours before removing with a simple water rinse.²³ It also has antibacterial properties which may benefit wound healing. It can be put in place by simple finger pressure, suturing over the sponge or by using a vacuum suck down mouth guard to keep it in contact with wound more securely.

Clinical Tip 2

Using tranexamic acid (Cyklokapron®) as an oral rinse instead of oral tablets is a safe way of obtaining control over problematic bleeding. It is done by using 10ml of a 5% tranexamic acid, 2 minutes / 4 times a day, for 7-10 days.²⁴ Gentle but thorough rinsing is advised before expelling. To mix a 500mg tablet is dissolved in 10ml water for a few minutes. The solution will contain unsolved particles and it must be used as is.

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