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ANTICOAGULANTS AND DENTAL SURGERY- A REVIEW

Mohamed Yasser Kharma, Salah Sakka, Ghassan Aus, Basel Tarakji, Mohammad Zakaria Nassani

ABSTRACT

A dental patient under anticoagulant medication is a challenge for the dentists, as anti-coagulant therapy produces an increased risk of bleeding and cessation of therapy increases the risk of thromboembolism. This paper gives a brief review of dental management of patients using anticoagulants.

Keywords: Anticoagulant therapy: Dentists; Surgery

Many dental professionals are unaware of their patients' coagulation status, and still discontinue antiplatelet therapy. Also hematologists, oral surgeons, and maxillofacial surgeons routinely interrupted anticoagulation therapy for tooth extractions. The risks of bleeding with dental extraction in individuals not receiving oral anticoagulants is approximately 1%.^{1,2} Dental patients who are taking oral anticoagulants are at increased risk of significant prolonged bleeding following dental extractions/surgery (defined as bleeding for more than 12 hours post-operatively which cannot be controlled by local measures alone).³

Discontinuation of anticoagulant therapy carries significant risks of morbidity, sometimes with a fatal outcome, from thromboembolic complications.⁴ One of the most frequently cited studies regarding thromboembolic risks in dentistry is Wahl's literature review in which 5/493 patients who stopped anticoagulants for a dental procedure had serious embolic complications, including 4 deaths.⁵ This report has been criticized because the patients had stopped anticoagulation for longer than usually recommended and the relationship to coagulation status was unclear.⁶ Therefore it is considered that, in the majority of clinical situations, the risks of discontinuing oral anticoagulant therapy outweigh the minimal benefits of reduced post-operative bleeding.

Dental management of these patients is based on good operative technique, use of local measures to minimize bleeding and the avoidance whenever possible, of changes to the patient's anticoagulant regime. The following medical problems may affect coagulation and clotting such as liver impairment and/or alcoholism, renal failure, thrombocytopenia, haemophilia or other disorder of haemostasis and current course of cytotoxic medication.³ Patients with any of these conditions, who also take anticoagulants, should be discussed with a Senior Dentist before undertaking a procedure which carries a significant risk of bleeding.¹

Many dental procedures do not involve a significant risk of bleeding and therefore no special measures are required when treating patients who take an oral anticoagulant drug. These procedures are simple restorative treatment, supragingival scaling, local anaesthesia by buccal infiltration, intraligamentary or mental block and impressions, orthodontic treatment and other prosthetics procedures.⁷ Invasive procedures which carry a risk of significant bleeding and for which the dentist needs to consider the management of the patient in

relation to their anticoagulant therapy are Local anesthesia by inferior alveolar or other regional nerve blocks or lingual or floor of mouth infiltrations, Subgingival scaling and Root Surface Instrumentation (RSI), Crown and bridge preparations, Extractions, Minor oral surgery, Periodontal surgery, Biopsies, Incision and drainage of swellings, Endodontics procedures (root canals).⁷⁻⁹

The effect of anticoagulant drugs is measured by the International Normalized Ratio (INR). Since 1983 The World Health Organization recommends the use of the international normalized ratio (INR) for reporting PT values (Table 1).^{10,11} The INR is calculated from the ratio of the patient's PT and control PT, raised to the power of the international sensitivity index value (ISI). $INR = (patient\ PT / mean\ normal\ PT)^{ISI}$.

The normal coagulation profile is an INR of 1.0. The INR must be measured prior to dental procedure, ideally should be done within 24h before the procedure.¹⁰ Although some suggest 3 days prior to the procedure if the INR stable or to allow time for corrective measures if the INR is too high.¹¹ Scientific literature has advocated that minor dental surgical procedure can safely be carried with the INR within the therapeutic range (2.0-4.0) when local hemostatic measures are used for control bleeding^{6,9,12} and uncomplicated extraction may be planned to remove 2-3 teeth at a time.¹³ However, patients who have an INR greater than 4.0 should not undergo any form of surgical procedure.

INR values as low as 1.3-2.0 may be effective prophylaxis for deep vein thrombosis, but 2.0-3.0 is the target for most indication, including atrial fibrillation. Higher values such as 2.5-3.5 are required for patients at greater risk, such as those with mechanical mitral valves.¹⁴ Antithrombotic drugs include those that inhibit platelet aggregation (Antiplatelet drugs), Inhibit formation of fibrin strand (Anticoagulants), and dissolve existing clots (Fibrinolytics). The main antiplatelet drugs used are illustrated in the table 2.

The most common antiplatelet drugs are acetylsalicylic acid known as aspirin (ASA), clopidogrel and dipyridamole. ASA is still the most non-steroidal anti-inflammatory drugs (NSAID) commonly prescribed for the prevention of myocardial infarction and ischemic stroke,¹⁵ its maximum antiplatelet effect is achieved within 1 hour following an initial dose of 325 mg, baby aspirin (81 mg) is the most conventional dose prescribed for coronary diseases.¹⁶ Most of the available data on

antiplatelet agents in dental procedures comes from studies of tooth extractions where ASA was being taken (2 controlled trials and one observational study, total exposed to ASA =89 at doses ranging from 75-325 mg/d). ASA did not significantly increase "excessive bleeding"(blood loss of > 30 to 50 mL) or in intra- and post-operative bleeding complications.¹⁶⁻¹⁸

The antiplatelet activity of clopidogrel is greater than that of ASA in the prevention of myocardial infarction and peripheral arterial insufficiency, but it is very expensive, so it is used only selectively in patients resistant to treatment with ASA. There is also growing evidence that antiplatelet agents such as ASA and clopidogrel can be safely continued.⁷ Data on clopidogrel or clopidogrel+ASA is limited. Dipyridamole is ineffective as antiplatelet drug when used alone (its antiplatelet activity is less than ASA), but its combination with aspirin (Aggrenox) is effective in the secondary prevention of ischemic stroke.⁶ Ticagrelor has antiplatelet influence but these advantages are tempered by its side effects such as dyspnea, bradyarrhythmia and elevated serum creatinine.¹⁹ The goal of anticoagulant therapy is to prevent clot formation, these agents act directly on specific activated factors (table 3).

Warfarin (Coumadin, Coumarin) is the most anticoagulant used acts in the liver competing with vitamin K to inhibit the synthesis of factors VII, IX, X, and II (prothrombin). Following warfarin administration the peak effect is realized within 72 hours. If warfarin therapy is stopped, it would take about four days for INR to reach 1.5 and with this INR any surgery can be safely performed.^{10,13} Heparin is a parenteral anticoagulant, which is often used for acute thromboembolic episodes or for hospitalization protocols that includes surgical procedures. Heparin is administered subcutaneously or intravenously to prevent deep venous thrombosis and pulmonary emboli.¹⁰ It acts on activated factors IX to XII and platelet, also it has an immediate effect on blood clotting for only 4-6 hours.

Heparin is available as standard or unfractionated heparin or low-molecular weight (LMW) heparin. The anticoagulants effects of standard or unfractionated heparin has an immediate effect on blood clotting, which is usually lost within less than 6 hours of stopping heparin.¹⁰ LMWH such as enoxaparin (Lovenox) and dalteparin (Frabmin) are effective as heparin but are more selective in inhibiting factors (table 3), these an-

ticoagulants require less dosing but these advantages offset their cost, which is 10-20 times that for heparin. For minor surgical procedures there is no evidence of increased risk for postoperative hemorrhage in patients taking warfarin and having a therapeutic INR <3.5 with respecting a rigid preoperative instruction.^{20,21} For patient requiring extensive surgery at significant risk for thromboembolic events, consideration should be given to the use of "bridge therapy: replacing anticoagulants with LMWH" in consultation with the physician.¹⁵

On the other hand, most of dental surgical procedure require postoperative medication such as antibiotherapy and using of NSAIDs. Anticoagulants therapy presents a contraindication to use of NSAIDs for postoperative pain and inflammation, this is true for all anticoagulants. The major concern with NSAIDs is their risk for producing erosion and ulceration of gastric mucosa that may bleed more profusely in patients who are anticoagulated.¹⁵ This is a rarely consideration with low-dose aspirin, but is significant with analgesic and anti-inflammatory doses of aspirin or other NSAIDs.²² For patients stably anticoagulated on warfarin (INR 2-4) and who are prescribed a single dose of antibiotics as prophylaxis against endocarditis, there is no necessity to alter their anticoagulant regimen.²³ There is any indication for routinely prescribing antibiotics for patients who take oral anticoagulants. Where antibiotics are required, it should be noted that many antibiotics interact with coumarin and ideally the INR should be rechecked four days after starting a course of antibiotics.²⁴ Antibiotics prescribed commonly in dentistry include amoxicillin, ampicillin, clindamycin and azithromycin (table 4).

To summarize the management of anticoagulants patient undergoing dental procedure the following guidelines are important : The risk of significant bleeding in patients on oral anticoagulants and with a stable INR in the therapeutic range 2-4 (i.e. <4) is very small and the risk of thrombosis may be increased in patients in whom oral anticoagulants are temporarily discontinued. Oral anticoagulants should not be discontinued in the majority of patients requiring out-patient dental surgery including dental extraction. According to Scully and Wolff¹⁰ oral procedures must be done at the beginning of the day because this allow more time for hemostasis before night-fall, and early in the week to avoid problems at the weekend.

HbA1c	PT	Thrombotest	INR
Normal Level	<1.3	>70%	1
Therapeutic Range	2-4.5	5-20%	2.5
Levels at which minor Oral procedures can be carried out*	<2.5	>15%	<3.5

Table 1. Oral anticoagulant therapy and oral surgery²⁵

PT - Prothrombin Time, INR-International Normalized ratio, * uncomplicated forceps extraction 1 to 3 tooth

Aspirin	Prasugrel (Effient)
Dipyridamole (Persantin, Persantin Retard)	Aspirin / Dipyridamole combination
Clopidogrel (Plavix)	Ticagrelor (Brilinta)

Table 2. Antiplatelet Drugs

Oral Anticoagulant	
Warfarin (Coumadin-Coumarin)	Inhibits "synthesis "of multiple factors
Dabigatran (Pradaxa)	Inhibits "Activity "of (IIa)
Rivaroxaban (Xarelto)-Apixaban (Eliquis)	Inhibits "Activity "of (Xa)
Parenteral Anticoagulants	
Heparin	Inhibits "Activity "of multiple factors
LMWH : Enoxaparin(Lovenox) Dalteparin (fragmin)	Inhibits "Activity "of IIa and Xa
Bivalirudin (Angiomax)	Inhibits "Activity "of (IIa)
Fondaparinux (Arixtra)	Inhibits "Activity "of (Xa)

Table 3. Oral Anticoagulants & Parenteral Anticoagulants

Amoxicillin	Methicillin sodium	Rifampicin
Ampicillin and derivatives	Penicillin G	Sulphonamides
Azithromycin	Cephalosporins	Trimethoprim

Table 4. Antibiotics that may be used in patients for dental surgery that can impair anticoagulants drugs function

Local anesthesia containing a vasoconstrictor should be administered by infiltration or intraligamentary injection wherever practical.^{10,26} Extractions should be restricted to a maximum of three teeth per visit with only a single tooth being extracted at the first visit, when possible, to assess the amount of bleeding. Surgery should be carried out with minimal trauma to both bone and soft tissue.¹⁰ In case of difficult extractions, when mucoperiosteal flap must be raised, the lingual tissues in the lower molar region should preferably be left undisturbed because trauma may open up planes into which hemorrhage can track and endanger the airway.²³ Meticulous curettage of the extraction site is essential to avoid excessive bleeding related to local infection. Socket should be gently packed with an absorbable haemostatic dressing such as : oxidized regenerated cellulose (Surgicel); resorbable gelatin sponge; collagen or fibrin glues and carefully sutured. Resorbable sutures are preferable as they attract less plaque.¹⁰ If not resorbable suture are used they should be removed after 4-7 days. Following closure, atraumatic pressure should be applied to the socket using a gauze pad for 15 to 30 min.⁶

Scully and Cawson²⁷ also developed the following list of instruction containing avoid rinsing the mouth for 24h; not to suck hard or disturb the socket with tongue or any foreign object; to avoid hot liquids and hard food for the rest of the day; to avoid chewing on the affected side until that a stable clot has formed. A special care should be taken to watch for hematoma formation, which may manifest itself with swelling, dysphagia. Many patients can be managed after surgery with antifibrinolytic agents given topically as a mouthwash during the first 7 to 10 days. The best known agent is tranexamic acid.²⁸ For post-operative pain control, paracetamol is the safest painkiller. If paracetamol alone is not sufficient to manage pain, the patient should consult their doctor for advice on pain relief. Appropriate telephone contact details should be issued to the patient, in writing, and the patient should know how to obtain advice and/or help both in and out of hours, if bleeding

occurs. When performing dental surgery in patients receiving anticoagulants, clinicians must weigh the risk of bleeding complications in continuous anticoagulation vs that of thromboembolic complications with anticoagulation interruption.

In conclusion, local hemostatic measures are almost sufficient for dental surgery in patient on anticoagulants drugs with no long term complications. We would encourage dentists and other clinicians to consider individual patient characteristics in deciding on the best management course.

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