Zaki Kudsi

Mohamad Hani Nouri Dalati, Louna Sibai and Lara Taher Koussayer

Management of Bleeding Disorders in the Dental Practice: Managing Patients on Anticoagulants

Abstract: Patients with bleeding disorders pose a challenge for dentists. Most of these conditions can be safely treated in the general dental practice. Patients who are on anticoagulants represent a large group of bleeding disorders. This article reviews the latest evidence in regard to managing those patients. Most of the articles reviewed seem to agree on the negligible risk of modification or interruption of oral anticoagulants when performing most dental treatments because a decreased risk of excessive bleeding might be associated with an increased risk of thrombo-embolic complications. However, extensive pre-operative assessment is essential to reduce the risk of serious complications.

Clinical Relevance: Patients with bleeding disorders pose a challenge for dentists. Adequate understanding of the underlying medical condition is essential to reduce the risk of dangerous complications.

Dent Update 2012; 39: 358–363

The normal haemostasis process involves three stages:

1. Vascular spasm;
2. Platelet plug formation: platelets adhere to the exposed blood vessel surface. The adenosine disphosphate (ADP) helps platelets become sticky and aggregate to form a plug which helps to reduce the amount of blood loss.
3. Clotting: which involves two pathways, intrinsic and extrinsic, and results in the formation of thrombin which converts fibrinogen to fibrin and forms a clot that stops blood loss.

Zaki Kudsi, DDS, MSc(Oral Surgery) MFDS RCS(Eng), MOMS RCPS(Glasg), Specialist Oral Surgeon, East Finchley Smiles, 144 The High Road, East Finchley, London, N2 9ED, **Mohamad Hani Nouri Dalati,** DDS, MMedSci**,** MDentSci, MFDS RCS(Eng), MFD RCSI(Irel), MOrth, RCS(Ed), FFD(Ortho) RCSI(Irel), Specialist in Orthodontics, The Springs Dental Care, 139 New Road Side, Horsforth, Leeds LS18 4QD, **Louna Sibai**, MD, Resident, Al-Atfal Hospital, Damascus, Syria and **Lara Taher Koussayer**, MD, Specialist Registrar (General Surgery), National Hospital (MOH), Homs, Syria.

For normal homeostasis to be achieved, four biological factors should be intact:

1. Adequate platelet numbers;
2. Normal platelet functions;
3. Normal blood vessels; and
4. Adequate clotting factors.

Accordingly, bleeding disorders can be classified mainly into (Table 1):

- Coagulation disorders;
- Vascular defects;
- Platelet number defects; and
- Platelet defects.

This, of course, is in addition to other complementary factors such as fibrinolytic defects and other acquired factors.

This article will review how to manage dental patients who are on anticoagulant medication.

In general, anticoagulant medications are prescribed for prophylaxis (eg prevention of deep vein thrombosis (DVT), pulmonary embolism (PE) in high risk patients or prevention of strokes in chronic AF or prosthetic heart valves), or therapeutic treatment of venous thrombo-embolic disorders like DVT or PE.

Common anticoagulants used in the UK include (in order of the most common): aspirin, warfarin, clopidogrel, dipyridamole and heparin.

Patients on warfarin

Warfarin is commonly prescribed for prophylaxis or therapeutic treatment of thrombo-embolic disease and arrhythmias. It acts as a vitamin K antagonist so it affects the synthesis of active factors II, VII, IX, X and protein C. This process takes 3 to 4 days and it prolongs both the prothrombin time (PT) and activated partial thromboplastin time (APTT).

Warfarin effects are delayed for 12 to 36 hours and last for 72 hours and

Coagulation disorders	*Congenital*: Haemophilia A, Haemophilia B (Christmas disease) and Von Willebrand's disease *Acquired*: Anticoagulants, liver disease, DIC, Vit K deficiency
Vascular defects	*Congenital*: Connective tissue disease (Ehlers-Danlos Syndrome), Osler-Weber-Rendu syndrome. *Acquired*: Senile purpura, infections, steroids, scurvy
Platelet number defects	*Decrease marrow production*: Aplastic anaemia, marrow infiltration (leukaemia, myeloma), marrow suppression (cytotoxic drugs, radiotherapy) *Excessive destruction*: immune thrombocytopenic purpura (ITP), SLE, CLL, heparin treatment, viruses. Thrombotic thrombocytopenic purpura (TTP), sequestration (as in hypersplenism)
Platelet defects	Myeloproliferative disease, increase urea, Von Willebrand's disease, Bernard-Soulier (giant platelet) syndrome, Alcoholism, Drug-induced (aspirin, NSAID)

Table 1. Classification of bleeding disorders.

Alcohol	Anticoagulant control with coumarins may be affected by major changes in consumption of alcohol.
Aspirin	Increased risk of bleeding when coumarins given with aspirin (due to antiplatelet effect).
Cephalosporins	Anticoagulant effect of coumarins possibly enhanced by cephalosporins.
Corticosteroids	Anticoagulant effect of coumarins may be enhanced or reduced by corticosteroids (high-dose corticosteroids enhance anticoagulant effect).
Erythromycin	Anticoagulant effect of coumarins enhanced by erythromycin.
Fluconazole	Anticoagulant effect of coumarins enhanced by fluconazole.
Metronidazole	Anticoagulant effect of coumarins enhanced by metronidazole.
Miconazole	Anticoagulant effect of coumarins enhanced by miconazole (miconazole oral gel and possibly vaginal formulations absorbed).
NSAIDs	Anticoagulant effect of coumarins possibly enhanced by NSAIDs.
Penicillins	Studies have failed to demonstrate an interaction with coumarins, but common experience in anticoagulant clinics is that INR can be altered by a course of broad-spectrum penicillins such as ampicillin.

Table 2. Warfarin interaction.[1]

this can be prolonged by interactions with other medications (Table 2). The mechanism of interaction may be pharmacokinetic, in that the absorption, protein binding, or hepatic metabolism of warfarin is affected. Antibiotics are one of those medications and they are of particular importance as dentists may prescribe them post-operatively. Broad spectrum antibiotics can change the intestinal flora that may decrease absorption of vitamin K and thus the international normalized ratio (INR) will be prolonged.[2]

The PT measures the effectiveness of the extrinsic and common pathways. The normal value is approximately 10 to 15 seconds. Because of the variability in PT reported by different laboratories, the World Health Organization recommends the use of the INR for reporting PT values. The INR is calculated by: patient PT/control PT. The normal INR is approximately 1. The usual therapeutic range for INR is from 2 to 4 (Table 3).

An INR above this range may increase the patient's risk of a spontaneous or surgically induced bleeding episode, while an INR below the desired therapeutic level increases the risk of a thrombo-embolism or ischaemic cerebrovascular event.[3]

It is recommended that patients who are on warfarin are managed in three stages: pre-operative, intra-operative and post-operative.

Pre-operative assessment

Dentists need to do extensive assessment before any dental treatment is undertaken and that should include a detailed medical history, finding out why the patient is on anticoagulants and whether the medical condition is stable. Dentists also need to check whether the INR history is stable or erratic and discover how long the patient has been stable on warfarin. Any other medical problems should also be assessed (eg liver disease, diabetes) as all such conditions will affect the decision on how to manage the patient. The difficulty of the oral surgical procedure should also be assessed (Table 4).

According to a classification suggested by Beirne,[4] patients can be divided into three groups with regard to the risk of a thrombo-embolic event occurring (low, moderate or high risk).

Low risk

Atrial fibrillation without stroke, cardiomyopathy without atrial fibrillation, venous thrombosis more than six months earlier, and bileaflet aortic valve with less than

Disorder	Target	Therapeutic Range
Pulmonary embolism	2.5	2–3
Atrial fibrillation	2.5	2–3
Post myocardial infarction	3	2.5–3.5
Mechanical prosthetic heart valves	3.5	3–4

Table 3. INR therapeutic range for different conditions.[2]

Low Risk	High Risk
Simple single extraction	Complicated single extraction
Simple multiple extractions <4 teeth	Simple multiple extraction >5 teeth Biopsies Implant installations

Table 4. Surgical risk classification.[9]

two stroke risks were considered to be low risk conditions.

Moderate risk

Bileaflet tilting disc aortic valve with two stroke risk factors, chronic atrial fibrillation with two stroke risk factors, and venous thrombosis less than six months earlier were considered to be moderate risk conditions.

High risk

Mechanical mitral valve, ball-cage valve replacement, venous thrombosis less than three months earlier, hypercoagulable state, atrial fibrillation with history of stroke, acute myocardial infarction less than three months earlier and recent (within one month) stroke or transient ischaemic attack were considered to be high risk conditions.

The risk of a thrombo-embolic event resulting from any of these conditions if warfarin was stopped should be weighed against the risk of post-operative bleeding if warfarin was continued. Stopping warfarin for two days increases the risk of a thrombo-embolic event by 1%. Bleeding complications do not carry the same risks as a thrombo-embolic complication (permanent disability or death).

Most authors seem to agree on the negligible effect of modification or interruption of oral anticoagulants when performing oral surgery simply because a decreased risk of excessive bleeding might be associated with an increased risk of thrombo-embolic complications. There are several documented cases of embolic complications in patients whose warfarin therapy was discontinued for dental treatment.[5] In addition, there is evidence that thrombosis may also occur because of a temporary state of rebound hypercoagulability following cessation of anticoagulation therapy.[6]

The INR should be checked within 24 hours of the planned surgical procedure and, if INR values <4 and the oral surgery procedure is simple (Table 4), the procedure can be performed without adjusting the warfarin and any excessive bleeding can usually be managed by local measures.[7]

If the patient needs more than a simple extraction, or if there are other risk factors involved (eg complicated medical history, history of erratic INR), the patient should be referred for treatment in a hospital setting.

However, if the patient has an INR value >4, he/she should be referred to the physician for evaluation. An INR greater than 4.0 is usually considered non-therapeutic, and the patient is at risk of a serious bleeding complications.[8]

Intra-operative

Infiltrative local anaesthetic techniques should be used, while regional local anaesthetic injections (ie inferior dental block) should be avoided, if possible, as it may cause bleeding that may extend down the neck. (No IDB should be given if INR >2.5). Surgical procedures should be carried out with minimal trauma to the bone and soft tissue as this reduces the risk of bleeding during or after the operation.

In the case of difficult extractions, when mucoperiosteal flaps must be raised, the lingual tissues in the lower molar regions should preferably be left undisturbed because trauma may open up planes into which haemorrhage can track and endanger the airway. The buccal approach to lower third molar removal is therefore safer. Minimal bone should be removed and the teeth should be sectioned for removal where possible.[2]

Intra-operative bleeding can usually be managed by local measures such as wound compression with wet gauzes, packing of resorbable gelatin sponge/resorbable oxidized cellulose and tight multiple sutures. The resorbable gelatin sponge and resorbable oxidized cellulose inserted into the extraction socket prior to suturing acts as a mechanical matrix to facilitate clotting and helps to reduce the incidence of post-operative bleeding.[2]

Tranexamic acid solution is a topical antifibrinolytic that is commonly used to prevent excessive haemorrhage during surgery. Some authors recommend the routine use of tranexamic acid irrigation or mouthrinses after surgery, alone or with aids such as fibrin glue and oxidized cellulose mesh, especially when INR values are 3.5 to 4, to help blood clot formation before suturing.[9] Other new studies found that such measures are not necessary to prevent bleeding complications in patients on oral anticoagulants because compression with a gauze soaked in saline or tranexamic acid normally appeared to be adequate for reaching clot stabilization.

Post-operative

Different protocols also exist for post-surgical management of patients on oral anticoagulants. All patients should be given verbal and written post-operative instructions with a dedicated 24/7 emergency phone number to call if bleeding occurs. Some authors suggest regular use of mouthrinses with tranexamic acid (10 mL of a 4.8% for 2 minutes, 4 times daily for 7 days). While other authors advise against such recommendations considering the risk of blood clot dissolution caused by the vortexes produced by rinsing to be higher than the advantage obtained by the use of tranexamic acid.[2]

For post-operative pain management, paracetamol with or without codeine is recommended in patients on oral anticoagulant therapy. NSAIDs should be avoided as they may increase the risk of post-operative bleeding in patients on anticoagulants (Table 2).

Heparin

Heparin is administered subcutaneously or intravenously and is often used for acute thrombo-embolic episodes or for hospitalization protocols that include significant surgical procedures. The effect of heparin is best assessed by the APTT. Heparin combines with antithrombin III and the resulting complex inactivates several clotting factors in the coagulation cascade, but the most important steps are inhibition of the conversion of factor X to Xa and the antithrombin effect. Heparin is rapidly removed from the blood and has an approximately 90 minute half-life. Protamine sulphate reverses the effect of heparin and can be used in emergencies.

PT, APTT and thrombin times are therefore prolonged by the use of heparin. Most patients are monitored with the APTT and are maintained at 1.5 to 2.5 times the control value. Platelet counts should also be monitored if heparin is used for more than 5 days because heparin can cause a thrombocytopenia.

Heparin is available as unfractionated heparin or low molecular weight (LMW) heparin. The anticoagulant effect of standard or unfractionated heparin has an immediate effect on blood clotting, which is usually lost within less than six hours of stopping heparin. Low-dose heparin therapy may have little effect either on the APTT or on post-operative bleeding.

LMW heparins have a longer duration of action but less effect on platelets, require less monitoring and may have little effect either on the APTT or on post-operative bleeding.[2] They are used primarily for prophylaxis of post-operative deep vein thrombosis, and there is no need to monitor APTT. Although there are isolated cases of post-extraction haemorrhage, many of these cases involved full-mouth extractions and alveoplasties, and anticoagulation levels in some patients exceeded therapeutic levels. When following recently published recommendations, only about 1% of patients experienced a significant post-operative bleeding episode. All of these episodes were controllable with local measures.

For simple oral surgery procedures of 1–3 teeth, there is usually no need to interfere with anticoagulant treatment involving heparin or LMW heparins or antiplatelet drugs. In more complicated oral surgery cases, treatment is best to be carried out in hospital.

Other anticoagulants

Medications such as low dose aspirin, clopidogril and dipyridamole are prescribed to prevent stroke and heart attack. Aspirin and clopidogril irreversibly bind to the platelets and decrease their aggregation. Patients are at risk of emboli and myocardial infarction if the antiplatelet medication is stopped (stopping aspirin may increase the risk of thrombo-embolic events by 0.005%). Studies have shown that patients undergoing simple minor oral surgery experienced minimal bleeding complications when they continued on these medications (those bleeding conditions were controlled with simple local measures). These results indicated that low-dose aspirin, clopidogril and dipyridamole may be continued if a patient requires minor oral surgery.

For complicated oral surgery procedures, the antiplatelet medication can be stopped one week before the surgery after consultation with the patient's physician.

NSAIDs also reversibly bind to the platelet for a limited period of time (approximately six hours). Hence, there should be no major complications if a patient is taking a NSAID drug. Complications can arise if the patient is taking anticoagulant medication and a NSAID. This combination could increase the risk of bleeding.[10]

Conclusion

Every dental patient on anticoagulation medication must be evaluated carefully and individually. The risk of bleeding during the dental procedure should be reviewed (possibly with the help of the patient's physician), if the anticoagulation medication is continued, against the risk of potential thrombo-embolic complications that may arise should the anticoagulation medication be reduced, altered, or even stopped. In general, comprehensive pre-operative thrombo-embolic and bleeding risk assessment, an atraumatic surgical technique, and post-operative careful instructions, can lead to safe and successful results with minimal complications.[10]

References

1. BNF 59, Interactions section; 2010.
2. Scully C, Wolff A. Oral surgery in patients on anticoagulant therapy. *J Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002; **94**: 57–64.
3. Aframian DJ. Management of dental patients taking common hemostasis-altering medications. *J Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007; **3**(Suppl): 45–49.
4. Beirne OR. Evidence to continue oral anticoagulant therapy for ambulatory oral surgery. *J Oral Maxillofac Surg* 2005; **63**: 540–544.
5. Wahl MJ. Dental surgery in anticoagulated patients. *Arch Intern Med* 1998; **158**: 1610–1612.
6. Webster K, Wilde J. Management of anticoagulation in patients with prosthetic heart valves undergoing oral and maxillofacial operations. *Br J Oral Maxillofac Surg* 2000; **38**: 124–126.
7. British Committee for Standards in Haematology. *Guidelines for the Management of Patients on Oral Anticoagulants Requiring Dental Surgery*. **www.bcshguidelines.com**
8. Nematullah A, Alabousi A, Blanas N, Douketis JD, Sutherland SE. Dental surgery for patients on anticoagulant therapy with warfarin: a systematic review and meta-analysis. *J Can Dent Assoc* 2009; **75:** 41–45.
9. Evans IL, Sayers MS, Gibbons AJ *et al*. Can warfarin be continued during dental extraction? Results of a randomized controlled trial. *Br J Oral Maxillofac Surg* 2002; **40:** 248–251.
10. Ferrieri GB, Carmagnola D, Strohmenger L. Oral surgery in patients on anticoagulant treatment without therapy interruption. *J Oral Maxillofac Surg* 2007; **65**: 1149–1154.