42. Anticoagulation and Surgery

Many patients are receiving anticoagulant therapy because they are at risk of thromboembolism due to atrial fibrillation, previous thrombosis or because they have mechanical heart valves. Most of them will be receiving the coumarin drug warfarin which works by blocking the formation of prothrombin and clotting factors 2, 7, 9 and 10. It prevents the metabolism of vitamin K to its active form for synthesis of these factors. Warfarin binds strongly to plasma proteins so it has a long half-life of about 36 hours which means the full anticoagulant effects take some time to be reached and continue for several days after the medication is stopped.

The degree of anticoagulation is measured with the prothrombin test and is expressed as the INR (International Normalized Ratio) which is the ratio of the prothrombin time divided by a laboratory control. An INR of 1 would be normal, i.e. no anticoagulation, and 2 would mean the blood would take twice as long to clot. Patients have their warfarin doses adjusted to achieve the INR appropriate to the problem they have which might lead to thromboembolism. This will be between 2 and 3 for patients at risk due to atrial fibrillation, a previous deep vein thrombosis or pulmonary embolism or transient ischemic events or strokes. A higher ratio of between 3 and 4 is appropriate for those who are at risk because of heart valve disorders including mechanical heart valves or a recent myocardial infarct.

It has been shown that patients who are anticoagulated within these therapeutic ranges of INR 2-4 are likely to have some additional risk of bleeding over those who are not anticoagulated if they have minor oral surgery including dental extractions. However when they do bleed this is nearly always susceptible to being stopped by simple local measures such as packing, suturing and tranexamic acid used locally. Stopping the anticoagulation places them at increased risk of rebound thrombosis so it is generally recommended that no adjustment is appropriate if the patient's INR is within the therapeutic range (INR <4).

Patients who take warfarin will have an anticoagulant card with all their blood results on it. If they have a stable result they should not need to come to hospital for dental extractions. However some patients will have confounding factors which put them at additional risk such as an unstable and variable INR, additional disease processes which might affect their coagulation such as liver disease, renal failure, other coagulopathy or history of alcohol abuse. Some patients may be taking additional medication which may potentiate warfarin such as anti-hypertensives, antifungals, carbamazepine, steroids, phenytoin, aspirin, and antibiotics such as erythromycin and metronidazole. In these situations treatment in hospital will give the patient greater confidence that should excess bleeding occur measures will be quickly available to help.

In all cases oral wounds should be packed with oxidized cellulose gauze and sutured with absorbable sutures. If bleeding persists locally applied tranexamic acid will be helpful. In the very unusual situation where an anticoagulated patient continues to bleed after local measures have been applied help from a haematologist should be requested. Warfarin can be reversed with intravenous vitamin K or with fresh frozen plasma. Reversal with vitamin K is slower and has the disadvantage that there may be later resistance to warfarin. Reversal with fresh frozen plasma is immediate and does not have this problem.

Occasionally a patient on warfarin may present as an emergency with facial injuries. In this case the haematologist should be involved as the patient will probably need the anticoagulation reversing if there is persistent bleeding. If the patient does not appear to be actively bleeding or it has stopped it would be prudent to inform the haematologist of the patient's existence in case a problem develops.

Sometimes an anticoagulated patient will need more extensive surgery. This is most likely to be an elderly patient who needs cancer ablation which may involve a neck dissection where post-operative haemorrhage is potentially dangerous. Here the warfarin should be reduced over 4 or 5 days before, until the INR is about 1.5. In this case the increased risk of thromboembolism will have to be accepted. In patients where the risk is highest, such as those with a recent thromboembolic event, the anticoagulation can be replaced by 'bridging therapy' with sub-cutaneous injections of low molecular weight heparin (enoxaparin). Low molecular weight heparin has a half-life of only a few hours and its effect can be reversed with protamine. In a very few cases it will be

necessary for the patient to receive intra-venous heparin with the dose being adjusted monitored by APPT testing.

It has been suggested that patients taking anticoagulants should not receive inferior dental nerve blocks because of the risk of serious bleeding into the medial pterygoid muscle. There has been no scientific proof that this is the case and we have never seen a case where this has been a problem.

Recently newer anticoagulant drugs sometimes termed 'target specific' or 'novel' anticoagulants have been developed which have certain advantages over warfarin for long term anticoagulation. Dabigatran etixilate is a direct thrombin inhibitor and rivaroxaban, apixaban and edoxaban are factor 10a inhibitors. These drugs have much shorter half-lives than warfarin so they have a more rapid onset of action after oral ingestion and a much quicker offset, provided the patient does not have renal failure. They have a lower risk of unwanted bleeding, few drug interactions, much reduced variability of effect between individuals, and do not require anticoagulant monitoring; indeed there is no reliable test to do so. On the negative side there is no effective way of reversing their effect other than by stopping the medication. However idarucizumab, a newer drug which is a humanised antibody fragment, has been recently developed which binds to dabigatran and neutralises its anticoagulant effect and can therefore be used in an emergency situation.

It was only in 2012 that dabigatran received approval from the National Institute of Clinical Excellence for thrombo-prophylaxis for stroke and patients with atrial fibrillation (not accompanied by valve disease). It is therefore too soon for a definitive experience to have been established on how patients taking these drugs should be managed during surgery. However it would appear that patients requiring dental extraction and minor oral surgery do not suffer any major problems if these drugs are continued as normal. It is recommended that ideally the surgery should be carried out 12 hours after the last dose, wounds should be sutured and that the patient should rinse with 5% tranexamic acid for a few days after the surgery.

At present drugs for the reversal of these anticoagulants are only in development, apart from dabigatran, so it would be prudent that patients who need more major surgery should have them temporarily discontinued and re-started afterwards. Obviously this management should be supervised in hospital by a specialist haematologist.

Although not anticoagulants we would like to mention antiplatelet medication with Aspirin, clopidogrel and dipyridamole. These drugs are used to prevent platelet adhesion and prevent unwanted vascular events such as acute coronary thrombosis, stroke and transient ischemic attacks. For minor oral surgery such as surgical dental extraction the risk of bleeding which cannot be controlled by local measures is very low so surgery should proceed without stopping the medication.

However for more major surgery each case should be considered on its own merit; there is little in the way of clinical trials to help firm guidelines to be formulated. If medication is to be ceased it will need to be done several days in advance as the drugs have half-lives of several days. The decision should be made by the senior surgeon in discussion with the haematologist as in some cases this may be potentially dangerous. Some patients who have had 'drug eluting stents' fitted to prevent coronary artery occlusion are at serious risk of thrombosis if their combined Aspirin and clopidogrel therapy is stopped. In such cases the cardiologist should be involved in the decision with the Consultant surgeon. You should never make the decision to stop medication yourself.

Key Points

- For MOS for patients on Warfarin check INR is stable
- Proceed if below 4, pack wound with oxidised cellulose gauze and suture
- Patients on 'novel anticoagulants' proceed as normal and pack and suture as above
- Patients on clopidogrel, aspirin or dipyridamole proceed as normal for MOS
- For more major surgery involve haematologist.
- Never stop medication on your own volition