Peri-operative medication in patients with cardiovascular disease

In this article, Mohamed H. Rahman and Jane Beattie look at care of patients with cardiovascular disease who are to undergo a surgical procedure.

Conversely, sublingual nifedipine capsules should be used with caution for treating peri-operative hypertension because they have been associated with an increased risk of stroke. Similarly, potassium-sparing diuretics are usually omitted on the morning of surgery because tissue damage and reduced kidney perfusion in the peri-operative period may lead to hyperkalaemia. Alternatively, they may be substituted with a non-potassium-sparing diuretic during the peri-operative period.

Many other drugs, such as angiotensin-II receptor antagonists, have no clear evidence for discontinuation so they are usually continued with caution. Caution is also needed if new drug treatments are initiated, or patients become hypovolaemic in the peri-operative period.

Patients with CVD need their established drug treatments, pulse and blood pressure closely monitored peri-operatively. They are at increased risk of peri-operative myocardial infarction (MI), with an in-hospital mortality of about 30 per cent.

Digoxin

Omission of digoxin for a prolonged period can cause a recurrence of atrial fibrillation (AF), which is associated with a significant risk of thromboembolism, hypotension, tachycardia and myocardial ischaemia. Although therapy with digoxin must, therefore, be continued peri-operatively, a change to an intravenous (iv) or oral liquid preparation may be required if the patient is nil by mouth or tube fed post-operatively. There are differences in bioavailability (liquids being better absorbed than tablets), but dose alteration is not normally recommended due to the large variation in absorption between individuals. However, if treatment is given intravenously, later conversion to the oral route (eg, as the patient recovers gastrointestinal function) may require a 25 per cent dose increase.

It is advisable to measure serum digoxin levels at least 6–8 hours post dosage to ensure therapeutic levels are achieved. Peri-operative electrolyte changes, such as hypokalaemia, hypomagnesaemia or marked hyperkalaemia increase myocardial sensitivity to cardiac glycosides. Both surgical sequelae (eg, ileostomies and fistulae) and medicines (eg, diuretics, lithium and corticosteroids) can cause hypokalaemia.

Symptoms of digoxin toxicity can occur at the upper end of the normal therapeutic range. It should be noted that nausea and vomiting can be symptoms of digoxin toxicity but may be mistaken for nausea and vomiting relating to surgery.

In patients taking digoxin, the anaesthetist should use suxamethonium with caution because it can precipitate cardiac arrhythmias.

Diuretics

Thiazide and loop diuretics are usually continued peri-operatively. Chronic electrolyte imbalances, however, should be looked for and corrected before an operation, to reduce the risk of arrhythmias, particularly relating to hypokalaemia.

Hypovolaemia increases the risk of hypotension during anaesthesia, and is even more likely when pre-operative fluid intake has been restricted, or a patient has received purgative solutions (eg, before bowel surgery). It may be reasonable to withhold diuretics on the day of surgery to avoid patient discomfort (need to urinate) and volume depletion. It may also be unnecessary to continue diuretics during the nil-by-mouth period when iv fluids are being administered, but this decision should only be taken by a senior doctor. Inappropriate withdrawal may result in worsening symptoms of cardiac failure or advanced renal impairment, for which the diuretic was being taken.

The antihypertensive and diuretic effects of diuretics (especially loop) may be reduced by the concurrent administration of some non-steroidal anti-inflammatory drugs used peri-operatively. This combination need not be avoided, but the effects should be monitored closely and the diuretic dose adjusted if necessary.

Anti-arrythmic drugs

Amiodarone has been associated with reports of peri-operative atropine-resistant bradycardia, profound vasodilatation, low cardiac output and death. Even so, it is usually continued peri-operatively because discontinuation can result in the recurrence of rhythm abnormalities despite the drug’s long half-life (an average of 30 days according to the manufacturer).

Other anti-arrythmic drugs should also be continued throughout the peri-operative period but not all are available as parenteral formulations and they may need to be substituted with an anti-arrythmic from a different class. Parenteral anti-arrythmics, especially substitutes, should be initiated under the advice of a cardiologist. Patients requiring parenteral anti-arrythmics need close cardiac and fluid balance monitoring.
Beta-adrenoceptor blocking drugs

There is good evidence to support perioperative continuation of beta-blockade. Within 12–72 hours of stopping beta-blockade, withdrawal effects can develop. These include nervousness, tachycardia, headache and nausea, exacerbation of myocardial ischaemia, myocardial infarction (MI), arrhythmias and sudden death. Symptoms depend on the nature and severity of the underlying CVD, the level of stress (due to increased sympathetic activity in the peri-operative period following withdrawal) and type of surgery. In addition, patients who normally take beta-blockers are more sensitive to sympathetic stimuli if their beta-blockers are withdrawn because an upregulated beta-adrenoceptor system is unmasked.

Increased catecholamine levels in the perioperative period play a major role in such cardiac complications. There are two theories explaining the protective effect conferred by beta-blockers:

- Beta-blockers antagonise the sympathetic effect of stress hormones (eg, catecholamines), which are secreted in large amounts during the peri-operative period, by reducing heart rate and blood pressure
- Beta-blockers control the ventricular rate if post-operative arrhythmias develop (fast AF is a risk factor for cardiovascular complications following surgery)

Some hospitals have clinical guidelines for administration of peri-operative beta-blockers, but this practice is not yet routine in the UK.

If a parenteral beta-blocker is required, care should be taken not to change to a parenteral non-selective agent (eg, propranolol) in patients who have been taking oral cardioselective beta-blockers (eg, metoprolol and bisoprolol) or beta-blockers with some intrinsic sympathomimetic effects (eg, celiprolol). This is particularly important for patients with asthma or ventricular failure, where a change of beta-blockade could result in bronchospasm and marked bradycardia.

Post-operatively, beta-blockers are usually continued at the pre-operative dose.

ACEIs

Evidence for withholding angiotensin-converting enzyme inhibitors (ACEIs) perioperatively is limited, so they are usually continued with caution. Clinical studies and case reports have described profound hypotension on induction of anaesthesia and reduced tolerance of hypovolaemia in patients taking ACEIs. There have also been reports that patients undergoing cardiopulmonary bypass surgery and receiving ACEIs show a significant reduction in vaspressor response to conventional vasoconstrictors. Therefore, in such patients and in those with uncomplicated cases of hypertension, some anaesthetists may require ACEIs to be withheld for 12 hours in the case of captopril or quinapril or 24 hours for longer-acting ACEIs (eg, enalapril, lisinopril and ramipril).

If the ACEI is withheld, fluid intake may need to be restricted and patients should be monitored for development of congestive cardiac failure, especially if ventricular function is impaired. Renal function should also be monitored closely. ACEIs are usually restarted immediately post-operatively and patients who are unable to tolerate oral drugs may be offered unlicensed enalapril injection.

Conversely, in a small study of patients with chronic heart failure, continuing ACEIs pre-operatively did not cause an increase in severity of hypotension at induction, and such evidence points towards continuation of ACEIs with caution.

Anticoagulant therapy

Although anesthesia and surgery are not contraindicated in patients taking anticoagulants, major surgery poses an increased risk of haemorrhagic complications. There is good evidence that surgery increases the risk of venous thromboembolisms (VTE) and so, for most patients (especially those at high-risk of thromboembolism), some form of anticoagulant therapy should continue for most of the peri-operative period.

Pre-operative management

The key principles of peri-operative anticoagulant management are summarised in Panel 1. Warfarin is usually discontinued three to four days before surgery to allow the international normalised ratio (INR) to fall below 1.5 — a level considered safe for most types of surgery to be performed. The British Committee for Standards in Haematology suggests that major surgical procedures can be carried out with INR of up to 2.5. Neurological or ocular procedures or surgery performed under epidural anaesthesia will require reversal of anticoagulation, to an INR of less than 1.3.

Vitamin K can be used to reverse the anticoagulant effect if there is insufficient time to allow the INR to fall to a desired level, but it should be noted that this can interfere with the effect of warfarin for many days. In an emergency, administration of clotting factors or fresh frozen plasma (under haematologist advice) may be warranted.

As the INR falls, intravenous unfractionated heparin (UH), or low molecular weight heparin (LMWH) is started. The dose used depends on the risk of thromboembolism. All patients considered as high-risk for VTE must be considered for a “treatment” dose of UH (eg, 15,000 units injected subcutaneously, twice daily) or a LMWH (eg, dalteparin 200units/kg sc once daily) as temporary replacement for oral anticoagulant therapy. High-risk patients are those with:

Panel 1: Principles of peri-operative anticoagulant therapy management

- Discontinue oral anticoagulant
- Start unfractionated heparin or low molecular weight heparin (LMWH) just before surgery
- Restart unfractionated heparin or LMWH after surgery
- Restart oral anticoagulant
- Discontinue heparin when INR returns to within the desired range
Multiple risk factors, such as diabetes and hypertension, should be considered for patients with multiple risk factors, such as diabetes or AF without history of embolism but would not usually receive “treatment” doses of anticoagulants. They should suffice.

If treatment doses of anticoagulants are being considered for regional anaesthesia. Spinal or epidural anaesthesia is, therefore, contraindicated in patients concurrently receiving treatment doses of anticoagulants.

However, in patients receiving prophylactic doses, regional anaesthesia can be established provided sufficient time has elapsed between drug administration and establishing the neural blockade. This is six hours for UH and 12 hours for LMWHs. By this time the anti-Xa effect should have decreased to a level safe for surgery and anaesthesia to proceed.

Regional anaesthesia and anticoagulation

Although it is not absolutely contraindicated, extreme caution is needed when patients receiving anticoagulants are being consulted for regional anaesthesia. Spinal or epidural neural blockade is controversial, because of the risk of causing an epidural or subdural haematoma which can lead to permanent neurological damage. The risk of bleeding is increased at the time of needle or removal before the first dose of UH or LMWH is restarted. Using a regimen that allows a brief, but controlled, interruption to anticoagulation should protect from the risks of thromboembolic incidents with no major increase in haemorrhage or hospital stay.

Low-dose aspirin

Aspirin induces an irreversible inactivation of platelet cyclooxygenase, which lasts the lifetime of the platelet (seven to 10 days on average). There is no absolute consensus about whether or not low dose aspirin should be continued perioperatively. The risk of haemorrhage versus the risk of predisposing the patient to a thromboembolic complication, such as a coronary event, transient ischaemic attack or stroke must be considered. Reports of MI following cessation of aspirin before coronary artery bypass graft surgery, prompt the suggestion that aspirin should not be stopped.

It is uncommon for serious complications to occur in patients taking aspirin in the perioperative period, although surgical blood loss is increased. It is sensible to withdraw aspirin in patients whose risks of post-operative bleeding are high. Patients undergoing transfemoral prostatectomy have been found to have significantly increased peri-operative bleeding if aspirin is continued and so, for these patients, aspirin is usually discontinued seven to 10 days preoperatively. Other examples include patients for retinal, major orthopaedic or intracranial surgery. Patients undergoing minor surgery do not need to stop aspirin.

Patients taking aspirin may also be at an increased risk of haematoma formation with spinal or epidural anaesthesia. The clinical significance of this is of considerable debate and there are reports showing the safety of regional anaesthesia in patients receiving aspirin or non-steroidal anti-inflammatory drugs, although some anaesthetics consultants may wish to avoid this practice.

If stopped, aspirin is usually restarted when diet returns to normal. Following transurethral prostatectomy aspirin is sometimes withheld for one week.

Dipyridamole

The manufacturer recommends that discontinuation of dipyridamole 24 hours preoperatively is sufficient to reverse its effect. Dipyridamole is generally restarted in the immediate post-operative period.

References and further reading