Premedication and management of concomitant therapy

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Abstract

The management of a patient's co existing illnesses, including decisions about their normal medication is an important part of their perioperative care. Adequate pre-assessment, preparation and liaison with other healthcare professionals is essential to decrease patient morbidity and mortality and prevent unnecessary surgical delay or suboptimal management. A full medication history including prescribed, over-the-counter and complementary medications is required, along with decisions regarding which medications should be omitted, have dose alterations or formulation changes to account for *nil by mouth* status. Medications may need to be prescribed in addition to the patient's normal medications, for example thromboembolic prophylaxis. This article also summarizes current recommendations with regard to premedication and concomitant medication.

Keywords Fasting; perioperative; premedication; surgery

Introduction

Almost half of patients presenting for surgery in Western societies take regular medications. Many of these have important interactions and effects on the nature and conduct of both anaesthesia and surgery. Historically, there has been a lack of standard management of perioperative medication, reflecting in part systemic inefficiencies and individual variation in medical decision making. The changing nature in overall management of complex systems for hospital admission, surgical scheduling, and general perioperative care provides an incentive to standardize management of many elements of care, including medication. Examples include the increasing use of day of surgery admissions, day case surgery, and more complicated medication regimes (e.g. novel anti-coagulants, potent antihypertensives). The parallel development of preoperative assessment clinics provides the opportunity to provide a more structured and consistent approach to the management of medications in the perioperative period.

In general, patients are fasted prior to elective surgery to reduce the risks of intraoperative regurgitation and pulmonary aspiration. Usual recommended fasting times are 2 hours for clear fluids, and 6 hours for solids, or milky drinks etc. This may limit the ability of patients to take some medications, although most medications can be given within 6 hours without increased risk of aspiration.[1]

Another important consideration is an appreciation of the effective clinical duration of each medication, and the consequences of continuing or halting administration in the perioperative period. So, a long-acting drug with unwanted perioperative effects (e.g. clopidogrel) should be stopped for a longer period than a short-acting drug with similar effects (e.g. oral anticoagulants). Some medications (e.g. β-blockers, antipsychotics) may be best continued in a different preparation if a patient is unable to manage oral intake.

Specific drugs used preoperatively

Anxiolytics: due partly to improvements in anaesthetic induction agents, anxiolytics and sedative agents are less commonly required as routine 'pre-meds', although short-acting benzodiazepines (e.g. midazolam) may occasionally be prescribed by the anaesthetist for patients when reassurance alone does not allay their anxiety. This is more common in paediatric practice, or as part of a procedural sedation technique.

Prophylaxis against aspiration: fasting guidelines state that patients abstain for food for 6 hours prior and clear non-fizzy fluids for 2 hours prior to elective surgery to reduce the risk of aspiration of gastric contents and subsequent risk of pneumonitis. Patients who present for elective surgery are usually seen in the preoperative assessment clinic and those patients identified at high risk of aspiration are given prophylaxis to be taken the night before and the morning of surgery. Patients at increased risk are those who are pregnant, have a body mass index greater than 30, a history of symptomatic hiatus hernia or dyspepsia and those with diabetes mellitus. A combination of acid suppressants (e.g. ranitidine or lansoprazole) and a pro-kinetic agent (e.g. metoclopramide), is used.

Anti-sialogogues: anti-sialogogues (e.g. atropine, glycopyrrolate) are used to decrease oropharyngeal secretions and are sometimes prescribed by anaesthetists particularly if an awake fibre optic intubation is planned, or if anaesthesia or procedural sedation with ketamine is planned.

Analgesia: patients who are in pain should be encouraged to take their normal analgesia or be prescribed suitable analgesia prior to theatre. Oral analgesia can be taken with a small sip of water without compromising fasting. Preemptive analgesia is the administration of analgesia prior to the onset of the painful stimuli. There is some evidence that this decreases pain receptor activation and the production and activity of pain neurotransmitters. In addition to simple analgesia, gabapentin is sometimes prescribed preoperatively. Increasingly, preemptive analgesia is used as part of enhanced recovery programmes, although overall, the evidence for long-term benefit from preemptive analgesia is not compelling.[2]

Concomitant therapy

Cardiovascular medications: up to half of all patients presenting for surgery take medication, the largest group of which are for cardiovascular disease.

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Angiotensin-converting enzyme inhibitors (ACEI) and angiotensin II receptor blockers (AR2RB) – generally all cardiac medications should be continued up until and including the day or surgery. The exception of this is ACEI and AR2RB drugs. Due to the risk of profound hypotension intraoperatively (mediated through the renin–angiotensin system), many bodies recommend that these drugs be omitted on the day of surgery, and sometimes the day prior to surgery for longer acting agents, although for high-risk surgery, the possibility of worsening cardiac function due to cessation of ACEI or AR2RB should be considered on a case-by-case basis.[3]

β-blockers – several studies have shown that β-**blockers** reduce perioperative ischaemia in those with underlying cardiac disease. β-blockers reduce myocardial oxygen demand, increase myocardial oxygen delivery, prevent arrhythmia and protect against plaque rupture. There is credible evidence that abruptly stopping β-blocker treatment in those on chronic β-blockers is harmful, and wide agreement exists that such patients should have therapy continued, even if by a different route in nil by mouth cases. Perhaps the most influential recent study has been the POISE trial.[4] Although the trial structure has been criticized, it demonstrated an overall increased mortality from the use of perioperative β-blockade in at-risk patients, principally from excess strokes, despite a cardioprotective effect. The result of this is that some authorities (American Heart Association, American College of Cardiology) recommend only that those already on β-blockers should continue them perioperatively. Other bodies (e.g. European Society of Cardiology) recommend in addition that patients with coronary artery disease, especially with inducible ischaemia on exercise testing, and patients undergoing high-risk surgery should also receive β-blockade. All recommend that treatment should be started early (30 days or more preoperatively) and titrated to effect (heart rate and blood pressure control). This is unlikely to be achievable for many patients presenting for surgery in the era of mandated short waiting lists and rapid referral pathways. A working knowledge of one's own institutional policies is required to manage individual patients.

Statins may prevent vascular events through mechanisms including reduced inflammation and plaque stabilization. There is evidence that statins may be cardioprotective, and current recommendations are that chronic treatment should continue, while patients having vascular surgery should have statins started 7–10 days preoperatively.

Anti-platelet drugs – aspirin is an irreversible inhibitor of platelet cyclo-oxygenase. A large proportion of perioperative acute coronary syndromes has been attributed to abrupt cessation of aspirin, so as a general rule, this should be continued. For patients undergoing surgery where perioperative haemorrhage may be catastrophic, for example neurosurgery, vitreo-retinal or prostatic surgery, aspirin should be stopped 7 days preoperatively.

Clopidogrel is a platelet P2Y12 receptor blocker. It is often administered following the insertion of coronary stents as part of dual anti-platelet therapy. There are two types of coronary stents; bare metal and drug eluting. Bare metal stents require clopidogrel for a minimum of 12 months and drug-eluting stents for a minimum of 6 weeks to try to reduce the risk of re-stenosis. Elective surgery should be postponed whenever possible until the minimum duration of therapy is completed. If clopidogrel must be stopped due to the risk of perioperative bleeding then seeking advice from a cardiologist is recommended. If clopidogrel is stopped and the patient is at high risk of intra-stent thrombosis or re-stenosis 'bridging therapy' with alterative agents is used. These include the heparins but also infusions of short-acting glycoprotein (GP) IIb/IIIa inhibitors. This is a rapidly changing area of cardiology and perioperative practice, and up-to-date information should be sought for these often complex patients.

Dipyridamole is an agent with anti-platelet and vasodilator properties used for patients following transient ischaemic attacks (TIAs) and strokes. There are no data on the safety of dipyridamole perioperatively and as with all drugs affecting haemostasis, there is balance between an increased risk of bleeding and ischaemic events.

Non-steroidal anti-inflammatory drugs (NSAIDs) – they are reversible inhibitors of cyclo-oxygenase which have anti-platelet effects due to reduced concentration of thromboxane A2. In patients at high risk of bleeding they should be stopped. Due to their potential for nephrotoxicity, they should be avoided in patients with evidence of renal impairment and dehydration especially if co-administered with other nephrotoxic drugs including ACEI, diuretics, gentamicin and intravenous contrast agents. NSAIDs also may cause gastric mucosal ulceration, and are perhaps best avoided after major surgery when significant fluid shifts and splanchnic hypoperfusion may occur.

Anti-coagulants

Many patients take anti-coagulants for a range of medical problems from cardiovascular disease to stroke prophylaxis. Continuing these medications is associated with an increased risk of perioperative bleeding but cessation may increase the risk of thromboembolism. The risk–benefit of stopping these agents is dependent on the individual patient and the surgical procedure.

Warfarin is usually stopped 4–5 days preoperatively with a target international normalized ratio of less than 1.5 on the day of surgery. It may be continued during minor procedures with a low risk of bleeding (e.g. dental or superficial skin surgery). Patients taking warfarin for atrial fibrillation are at relatively low risk for thrombosis and do not require 'bridging therapy'. Those with prosthetic heart valves, recent or recurrent thrombosis are at higher risk and bridging therapy with therapeutic low-molecular-weight heparin (LMWH) is often used perioperatively until warfarin can be recommenced. In the first month following the signature thromboembolic event, the chances of further thromboembolic events are much higher, so if possible elective surgery should be postponed until after this time. If surgery is urgent, vitamin K, prothrombin complex concentrates and fresh frozen plasma can be used.

Due to the risk of rebound hypercoagulability following cessation of anticoagulation perioperative thromboembolism prophylaxis with unfractionated heparin or LMWH should be considered.

Dabigatran and rivaroxaban are novel oral anti-coagulants increasingly encountered in perioperative practice. Dabigatran is an oral direct thrombin inhibitor, and rivaroxaban a direct factor Xa inhibitor. Initially licensed for venous thrombosis prevention, both are now also available for stroke prevention in atrial fibrillation. Unlike warfarin, both drugs provide simple dosing without monitoring requirements but neither has an

