

Beta blockers in the perioperative period

The cardiovascular effects of beta blockers are widespread, so their use in the perioperative period ought to be beneficial, although this is not clear cut. This article discusses the evidence for and against the use of beta blockers perioperatively and gives guidance for best practice.

Cardiac complications in the perioperative period are a major concern, particularly with an ageing population who increasingly present with cardiovascular comorbidities. Surgery and general anaesthesia trigger a series of neuroendocrine, hormonal and cardiovascular responses, which together are labelled the physiological stress response. This results in an increase in cardiac output, retention of fluid and mobilisation of energy substrates, which may have conferred an evolutionary benefit in the past but can be deleterious in the comorbid surgical patient. In particular, the tachycardia, arrhythmias and haemodynamic instability associated with the stress response can lead to a mismatch between oxygen supply and demand to the vital organs, leading to morbidity and mortality.

Interest in the role of beta blockade in the perioperative period to reduce the risk of cardiovascular complications has a logical basis. Beta blockers decrease heart rate and contractility, thereby reducing myocardial oxygen demand. They increase diastole and the time for coronary perfusion and reduce arrhythmias, so their use in the perioperative period ought to be beneficial. They also have an established place in the management of heart failure, one of the most significant risk factors for perioperative mortality. Furthermore, many risk stratification systems contain components which are potentially influenced by beta-blocker therapy. Lee's revised cardiac risk index, for example, includes three cardiovascular comorbidities (congestive heart failure, cardiac ischaemia and cerebrovascular events), which together predict an 11% chance of a major perioperative cardiac event.

A randomised controlled trial published in the *New England Journal of Medicine* in 1996 first highlighted the potential benefits of perioperative beta blockade (Mangano et al, 1996). In this study, atenolol was found to reduce mortality compared with placebo for patients undergoing non-cardiac surgery. This was closely followed by the DECREASE-1 trial (Poldermans et al, 1999), which showed similar mortality benefits from perioperative bisoprolol. However, as perioperative beta blockade subsequently became an accepted part of clinical practice, further moderate-sized randomised controlled trials failed to produce the same results.

A turning point came with the publication of POISE-1 (Devereaux et al, 2008). This was the first randomised controlled trial adequately powered to investigate the safety of perioperative beta blockade. It found that while the incidence of non-fatal myocardial infarction fell, there was an increase in non-fatal stroke, bradycardia, hypotension and death in patients started on metoprolol within the 24 hours before undergoing non-cardiac surgery. Criticisms of this trial have focused on its use of high doses of long-acting metoprolol. However, subsequent randomised controlled trials using alternative shorter acting agents have also produced similar adverse findings. In addition, accusations of scientific misconduct have largely discredited the findings of the DECREASE trials, the only recent major studies to have found mortality benefits.

Best practice

So where does this leave us with regards to current best practice? A Cochrane review in 2014 concluded that in non-cardiac surgery there is low to moderate level evidence that perioperative beta blockade increases all-cause mortality and stroke (Blessberger et al, 2014). However, it did emphasise the established role of beta blockers before cardiac

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surgery. Here, perioperative beta blockade reduces arrhythmias and is pivotal to optimising the patient, although its influence on stroke risk and other complications in this setting is poorly understood.

Guidelines have been produced by the American Heart Association on perioperative cardiovascular evaluation and management of patients undergoing non-cardiac surgery, which were updated in 2014 (Fleisher et al, 2014). They recommend continuing beta blockers throughout the perioperative period in any patients already taking them, while considering initiation of therapy in specific at-risk groups:

- Those at high or intermediate risk of cardiac ischaemia
- Those presenting with three or more components of the revised cardiac risk index.

If beta blockers are to be started, therapy should begin well in advance of surgery and be carefully titrated, with initiation on the day of surgery considered potentially harmful.

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