To beta-block or not?

Perioperative beta-blockers are used in patients with established or more than two risk factors for coronary artery disease to improve myocardial oxygen-demand relationship and attenuate the stress response to surgery. Historical trials showing improved outcomes have been questioned and the benefits are less clear. Should beta-blockers be given or not?

Arguments for beta-blockade

The Multicenter Study of Perioperative Ischaemia (Managano et al, 1996) trial, in which atenolol was given pre-induction of anaesthesia, found a reduction in perioperative cardiac ischaemic events and mortality at 2 years in the atenolol group. However, this was not an intention-to-treat analysis and the study has been criticized for including patients who were on beta-blockers preoperatively and then abruptly stopping them if randomized to the placebo arm (Cole and Francis, 2014).

Arguments against beta-blockade

The POISE Study Group et al (2008) reported a large randomized controlled trial of 8351 patients with risk factors for coronary artery disease. Of these, 4174 received metoprolol (controlled release) 2–4 hours before surgery and for 30 days after.

The primary end point was a composite outcome of cardiovascular death, non-fatal myocardial infarction or non-fatal cardiac arrest. This was lower in the metoprolol group, accounted for by a reduction in myocardial infarction. However, the metoprolol group had statistically significant increases in episodes of hypotension, stroke and overall mortality at 30 days.

Dr Shamir Karmali *is Anaesthetic Trainee in the Central School of Anaesthesia,* **Dr Ravin Mistry** *is Anaesthetic Registrar and Research Fellow in Perioperative Medicine in the Department of Anaesthesia, and* **Dr David Walker** *is Consultant Anaesthetist and Intensivist in the Department of Anaesthesia and Intensive Care, University College London Hospital NHS Trust, London NW1 2BU*

Correspondence to: Dr S Karmali (shamir.karmali@nhs.net)

The observed increased risk of stroke was partly attributed to more hypotensive episodes in the metoprolol group. Critics blamed this on a non-titrated high dose of metoprolol given too soon before surgery, although this is a usual clinical starting dose (Cole and Francis, 2014).

The DECREASE studies (Poldermans et al, 1999) formed the bedrock of evidence that American College of Cardiology/American Heart Association (ACC/AHA) and European Society of Cardiology (ESC) guidelines were based on. These studies found exciting but improbable results with a 91% reduction in death and myocardial infarction and a number needed to treat of 3.2. However, in 2014 the DECREASE studies (excluding DECREASE I which had insufficient data) were discredited (Erasmus Medical Centre, 2014) for falsification of study protocol and lack of patient data to support the study's results and conclusions.

Bouri et al's (2014) meta-analysis of 10 529 patients (excluding the DECREASE trials) found that newly started beta-blockers reduce cardiac events perioperatively, but increase stroke and all-cause mortality at 30 days. However, the conclusions have been criticized, as smaller studies' findings may be eclipsed by the large POISE trial.

A systematic review by Wijeysundera et al (2014) on behalf of the ACC/AHA assessed the effects of perioperative beta-blockade when the DECREASE trials were included or excluded. They compared pooled outcome measures of remaining studies to the POISE trial to see if any treatment effect had been overshadowed by the POISE results in previous meta-analyses. When the DECREASE studies are included, pooled findings suggest reduced rates of all-cause mortality and cardiovascular death, but when DECREASE studies are excluded, pooled results are qualitatively similar to POISE, broadly supporting the conclusions of POISE and other meta-analyses.

Current guidance

The ESC and ACC/AHA both endorse continuation of beta-blockers in patients taking them preoperatively (1b). In 2014 they revised grades of recommendation for initiating beta-blockers in patients with risk factors or established coronary artery disease from 1a to 11b (ESC) and 1b to 11b (ACC/AHA). These have been criticized for not going far enough given the evidence and for advocating their use in 'high risk' patients, who suffered the greatest harm in the POISE trial (Cole and Francis, 2014).

Conclusions

Until well-conducted randomized controlled trials show which patients will benefit from perioperative beta-blockade and how best to introduce it, a cautious case-by-case approach is warranted when considering starting beta-blockers before surgery. **BJHM**

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Anaesthetic and critical care dilemmas are coordinated by Dr Matthew Henley, Specialist Registrar in Anaesthetics, Royal Free Hospital, London and Dr Ramanathan Kasivisvanathan, Speciality Registrar in Anaesthetics, University College Hospitals London, London