Review: Evidence of benefit for perioperative β-blockers in noncardiac surgery is unreliable

Devereaux PJ, Beattie WS, Choi PT, et al. **How strong is the evidence for the use of perioperative β blockers in non-cardiac surgery? Systematic review and meta-analysis of randomised controlled trials.** BMJ. 2005;331:313-21.

Clinical impact ratings: GIM/FP/GP ★★★★☆☆☆ Hospitalists ★★★★★★☆ Cardiology ★★★★★★☆

QUESTION

In patients having noncardiac surgery, do β-blockers reduce cardiovascular events?

METHODS

Data sources: MEDLINE (1966 to 2002), EMBASE/Excerpta Medica (1980 to 2002), and SciSearch (April 2003); hand-searching 7 anesthesia journals (1985 to 2002); consulting experts; and scanning reference lists and "see related articles" in PubMed.

Study selection and assessment: Studies were selected if they were randomized controlled trials (RCTs) that assessed β-blockers in patients having noncardiac surgery. RCTs were excluded if there was no control group that received placebo or usual care or if no relevant events occurred in the treatment and control groups. Study quality was assessed (e.g., allocation concealment, stopping early for unexpected large treatment effects, and blinding).

Outcomes: Main outcomes included perioperative (i.e., within 30 d of surgery), all-cause, and cardiovascular mortality; nonfatal myocardial infarction (MI); nonfatal cardiac arrest; nonfatal stroke; hypotension needing treatment; and bradycardia needing treatment.

MAIN RESULTS

22 RCTS (n = 2437) met the selection criteria. Perioperative β-blocker treatment ranged from brief intravenous β-blocker therapy just before surgery to 30-day postoperative β-blocker use. Perioperative β-blockers did not reduce any individual outcome and increased bradycardia and hypotension that required treatment (Table). The number of patients included in the meta-analysis was substantially suboptimal for reliably detecting a treatment effect for β-blockers.

CONCLUSIONS

In patients having noncardiac surgery, the evidence supporting the use of perioperative β-blockers is limited and too unreliable to allow definitive conclusions. β-blockers increase perioperative bradycardia and hypotension requiring treatment.

Source of funding: Not stated.

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Perioperative β-blockers vs placebo or usual care (control) for noncardiac surgery at 30 days*

Outcomes	Number of trials (n)	Weighted event rates		RRR (95% CI)	NNT (CI)
		β-blockers	Control		
All-cause death	4 (907)	2.4%	4.2%	44% (–131 to 86)	NS
CV death	4 (907)	1.2%	2.9%	60% (–15 to 86)	NS
Nonfatal MI	6 (853)	3.4%	9.0%	62% (–29 to 89)	NS
Nonfatal cardiac arrest	2 (299)	1.6%	3.3%	50% (–129 to 89)	NS
				RRI (CI)	NNH (CI)
CHF	5 (861)	5.4%	3.4%	54% (–17 to 187)	NS
Nonfatal stroke	1 (200)	4.0%	1.0%	308% (–54 to 3487)	NS
Hypotension needing treatment	10 (1712)	26%	20%	27% (4 to 56)	19 (9 to 24)
Bradycardia needing treatment	9 (1196)	12%	5.4%	127% (53 to 236)	15 (8 to 35)

*CHF = congestive heart failure; CV = cardiovascular; MI = myocardial infarction; NS = not significant. Other abbreviations defined in Glossary; weighted event rates, NNT, NNH, and CI calculated from data in article using a random-effects model.

COMMENTARY

Lee and colleagues have shown that about 1.4% of patients having noncardiac surgery will experience an adverse cardiovascular event (1). Experts have recommended β-blockers for at-risk patients to minimize the risk for perioperative cardiac events. These opinions have been largely influenced by the RCT by Poldermans and colleagues, which showed a highly significant reduction in adverse events among high-risk patients having vascular surgery (2). However, several trials of perioperative β-blockers failed to show any significant benefit. This well executed meta-analysis by Devereaux and colleagues emphasizes that the evidence does not support routine use of β-blockers to prevent adverse cardiac events in surgical patients. Of the included trials, only the RCT by Poldermans and colleagues showed a clinically and statistically significant reduction in adverse events. A recent observational study by Lindenauer and colleagues suggests that β-blockers may be protective in patients at high risk for adverse events, neutral in intermediate-risk patients, and possibly harmful in low-risk patients (3). Another RCT reported recently in abstract form by Juul and colleagues randomized 921 surgical, diabetic patients to a β-blocker or placebo (4). No benefit was seen for perioperative β-blockers. In this trial, 61% of patients were at intermediate to high risk for adverse events.

The heterogeneity of patient characteristics and β-blocker interventions in the meta-analysis by Devereaux and colleagues emphasizes the need for a large RCT in patients who have been stratified for cardiac risk and type of surgery. We also need to know whether differences exist among β-blockers and the optimal dose, timing, and duration of use.

Based on available evidence, clinicians should be cautious in the use of β-blockers to prevent adverse cardiac events in surgical patients. Patients should be stratified using a validated risk assessment tool, such as the Revised Cardiac Risk Index (1). In our practice, we will continue to use β-blockers in high-risk patients and to withhold them in low-risk patients. Patients at intermediate risk might benefit from further risk stratification with noninvasive cardiac stress testing before choosing to use β-blockers.

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