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[Intervention Review]

Alpha-2 adrenergic agonists for the prevention of cardiac complications among patients undergoing surgery

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ABSTRACT

Background

The surgical stress response plays an important role on the pathogenesis of perioperative cardiac complications. Alpha-2 adrenergic agonists attenuate this response and may thereby prevent cardiac complications.

Objectives

This review assessed the efficacy and safety of preoperative (within 24 hours), intraoperative, and postoperative (first 48 hours) α -2 adrenergic agonists for preventing mortality and cardiac complications after surgery performed under either general or neuraxial anaesthesia, or both.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2008, Issue 3), MEDLINE (1950 to August week 4 2008), EMBASE (1980 to week 36 2008), the Science Citation Index, and reference lists of articles.

Selection criteria

We included randomized controlled trials that compared α -2 adrenergic agonists (clonidine, dexmedetomidine, or mivazerol) against placebo or non- α -2 adrenergic agonists. Included studies had to report on mortality, myocardial infarction, myocardial ischaemia, or supraventricular tachyarrhythmia.

Data collection and analysis

Three authors independently assessed trial quality and extracted data. Two authors independently performed computer entry of abstracted data. We contacted study authors for additional information. Adverse event data were gathered from the trials.

Main results

We included 31 studies (4578 participants). Study quality was generally inadequate, with only six studies clearly reporting methods for blinding and allocation concealment. Overall, α -2 adrenergic agonists reduced mortality (relative risk (RR) 0.66; 95% CI 0.44 to 0.98; $P = 0.04$) and myocardial ischaemia (RR 0.68; 95% CI 0.57 to 0.81; $P < 0.0001$). However, their effects appeared to vary with the surgical procedure. The most encouraging data pertained to vascular surgery, where they reduced mortality (RR 0.47; 95% CI 0.25 to 0.90; $P = 0.02$), cardiac mortality (RR 0.36; 95% CI 0.16 to 0.79; $P = 0.01$), and myocardial infarction (RR 0.66; 95% CI 0.46 to 0.94; $P = 0.02$). With regard to adverse

effects, α -2 adrenergic agonists significantly increased perioperative hypotension (RR 1.32; 95% CI 1.07 to 1.62; $P = 0.009$) and bradycardia (RR 1.66; 95% CI 1.14 to 2.41; $P = 0.008$).

Authors' conclusions

Our study provides encouraging evidence that α -2 adrenergic agonists may reduce cardiac risk, especially during vascular surgery. Nonetheless, these data remain insufficient to make firm conclusions about their efficacy and safety. A large randomized trial of α -2 adrenergic agonists is therefore warranted. Additionally, future research must determine which specific α -2 adrenergic agonist should be used, and whether it is safe to combine them with other perioperative interventions (for example β -adrenergic blockade).

PLAIN LANGUAGE SUMMARY

Using alpha-2 adrenergic agonists to prevent heart complications after major surgery

Heart-related complications can lead to death and long hospital stays after surgery. These complications may occur, in part, because surgery stresses the heart. Alpha-2 adrenergic agonists are medicines that may prevent these complications by protecting the heart from the stress. In 31 studies that involved 4578 adult participants we found that alpha-2 adrenergic agonists may have some important benefits. During surgery on the major blood vessels (also called vascular surgery) they reduced the risk of dying or having a heart attack. When used during open-heart surgery they reduced the risk of poor blood flow to the heart. However, alpha-2 adrenergic agonists also had some important side-effects. Patients had a greater risk of having low blood pressures or low heart rates when given an alpha-2 adrenergic agonist. We concluded that although these results are encouraging more studies are needed. These studies should include more patients so that we can better determine whether alpha-2 adrenergic agonists can safely prevent heart-related complications. The studies should also determine whether one medicine (clonidine, dexmedetomidine, or mivazerol) is better than another, which specific patients would benefit from these medicines, and whether it is safe or beneficial to combine alpha-2 adrenergic agonists with other heart medicines.