Effect of dopexamine infusion on mortality following major surgery: individual patient data meta-regression analysis of published clinical trials

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CRD summary
This review concluded that low-dose (up to 1μg/kg/min) dopexamine was associated with reductions in 28-day mortality and hospital stay and that further trials were required to confirm this finding. The conclusion reflected the evidence of the review and may be reliable, however, an inappropriate validity assessment was employed as an inclusion criterion and this may necessitate some caution.

Authors' objectives
To determine whether peri-operative low-dose dopexamine infusion (up to 1μg/kg/min) is associated with reduced mortality and duration of hospital stay following major surgery.

Searching
MEDLINE, EMBASE, CINAHL and The Cochrane Library were searched without language restrictions up to July 2006. Search terms were reported. An internet search using Google Scholar was conducted, issues from seven relevant journals were handsearched for the previous 20 years and references of identified articles and relevant reviews were checked. Only studies published in peer reviewed journals were eligible for inclusion.

Study selection
Randomised controlled trials (RCTs) of dopexamine infusion in patients undergoing major abdominal, vascular or urologic surgery, which reported mortality and length of hospital stay were eligible for inclusion.

In the included studies the median patient age was 68 years (range 18 to 91), approximately two thirds of patients were males and approximately one eighth had emergency surgery.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Studies were assessed for validity using the Jadad scale, which awards up to 5 points based on the following criteria: randomisation, blinding and treatment of withdrawals and dropouts. Studies which scored fewer than 3 points were excluded from the review. The authors did not state how many reviewers performed the validity assessment.

Data extraction
Authors and sponsors were contacted for individual patients data (IPD) on age, treatment, duration of postoperative hospital stay and mortality.

Methods of synthesis
Studies were combined in IPD meta-analyses using both intention-to-treat (ITT) and per protocol data. Pooled odds ratios (ORs) with 95% confidence intervals (CIs) for 28 day mortality were calculated using a multilevel logistic regression model to look at the effects of dose. Patients were categorised as control, low-dose dopexamine (up to 1 μg/kg/min) or high-dose dopexamine (over 1 μg/kg/min). The model was adjusted for age, gender, centre, fluid volume and urgency of procedure. The statistical significance of interactions between variables was assessed. Hospital stay was analysed using a Cox proportional hazards model. Hazard ratios (HRs) were estimated for low- and high-dose dopexamine groups compared with control. This model was stratified by study to allow for differences between studies. A subgroup analysis comparing patients having elective versus emergency surgery was also performed.

Results of the review
Five RCTs (N = 833) were included in the review.
The ITT analysis found that, after adjustment for other variables including age and fluid volume, there was no statistically significant difference in 28-day mortality between patients treated with dopexamine and control (OR 0.78, 95% CI: 0.31, 1.99). Analysis of the effect of dopexamine dose found that patients treated with low doses (up to 1 μg/kg/min) had statistically significantly lower 28-day mortality than controls (OR 0.50, 95% CI: 0.29, 0.88, p = 0.016), but that there was no significant difference between high dose dopexamine and control groups.

Dopexamine was associated with a statistically significantly shorter hospital stay than control treatments (HR 0.85, 95% CI: 0.73, 0.91, p = 0.03). The duration was significantly shorter for low dose dopexamine (HR 0.75, 95% CI: 0.64, 0.88, p = 0.0005). There was no significant difference for high doses compared to control.

The per protocol analyses did not produce significantly different results. Results of subgroup analysis were also reported.

**Authors' conclusions**

There was an overall reduction in hospital stay, but not in 28-day mortality in the dopexamine-treated patients. However, at doses up to 1μg/kg/min both mortality and hospital stay were reduced; further clinical trials were needed to confirm this finding.

**CRD commentary**

The review question and inclusion criteria were clear. The authors searched a number of relevant databases and other sources without language restrictions. The decision to limit the review to published, peer-reviewed studies may have led to the introduction of publication bias as well as the exclusion of some relevant studies, but this was not likely to have been a major issue with an IPD analysis. The authors did not report using methods designed to reduce reviewer bias and error at any stage of the review process. The decision to use a conventional summary assessment of validity, and to employ this as an additional inclusion criterion was unusual for an IPD meta-analysis. In addition to being uninformative it was inappropriate in that it may have led to the exclusion of poorly reported studies that an examination of trial data would have revealed to be methodologically sound. No checking of raw data was reported. The methods of the meta-analysis appear to have been appropriate, although some aspects were not fully reported, and the authors' conclusions reflect the results of the review. The conclusions may be reliable, but the inappropriate use of a validity assessment as an inclusion criterion should be borne in mind.

**Implications of the review for practice and research**

Practice: The authors did not state any implications for practice.

Research: The authors stated that further adequately powered clinical trials were required to establish the efficacy of low-dose dopexamine in patients undergoing major surgery.

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