Fenoldopam reduces the need for renal replacement therapy and in-hospital death in cardiovascular surgery: a meta-analysis


CRD summary
The review investigated the efficacy of fenoldopam in preventing acute renal failure in patients undergoing cardiovascular surgery. The authors found that fenoldopam reduced the need for renal replacement therapy and reduced in-hospital death. Given problems with the review methodology and reporting, and the small size and low quality of the included studies, the results of the review may not be reliable.

Authors' objectives
To determine the efficacy of fenoldopam in the prevention of acute renal failure in patients undergoing cardiovascular surgery.

Searching
PubMed and Google Scholar were searched to November 2006. The PubMed search strategy is listed in the review. Conference proceedings from five relevant conferences (2002 to 2006) and bibliographies of identified articles were searched. International experts were contacted for additional studies. No language restriction was applied to the search.

Study selection
Clinical trials comparing fenoldopam to control, with outcome data on need for renal replacement therapy (RRT) or death, in patients undergoing cardiovascular surgery were eligible for inclusion. Both randomised and non-randomised designs were eligible, the latter were required to include adjustment for covariates. Crossover trials were not eligible for inclusion.

In the included studies, the dose of fenoldopam ranged from 0.03 to 0.3 μg/kg/min and treatment duration ranged from 2 to 72 hours. The control group was one of the following: placebo; dopamine with or without nitroprusside; furosemide followed by dobutamine; or standard treatment. In most of the included studies (all but three), the included patients had a high baseline risk of acute renal failure (ARF) based on high creatinine or other comorbidities. In all but two studies, fenoldopam was used to prevent ARF; the other two studies were of patients in early ARF and fenoldopam was used to prevent RRT.

Four reviewers independently selected the studies for the review. Discrepancies were resolved by consensus.

Assessment of study quality
Validity was assessed based on the Cochrane Collaboration risk of selection, performance, attrition and adjudication biases, and rated as low (A), moderate (B), high (C) or incompletely reported (D). Allocation concealment was also assessed and rated as adequate (A), unclear (B), inadequate (C) or not used (D). Two reviewers independently performed the validity assessment. Discrepancies were resolved by consensus.

Data extraction
Four reviewers independently extracted the data for the review. Discrepancies were resolved by consensus. Odds ratios (OR) and 95% confidence intervals (CI) for individual studies were calculated using Mantel-Haenszel methods.

Methods of synthesis
Fixed effect meta-analysis was used to compute pooled OR for dichotomous outcomes and weighted mean differences (WMD) for continuous outcomes.

Sensitivity analyses included: investigation of study population and baseline risk; withdrawal of each study one at a time; and a comparison of using random effects versus a fixed-effect model.
Statistical heterogeneity and inconsistency was measured using the Cochrane Q and $I^2$ tests. Inconsistency was defined based on $I^2$ values as low (25 per cent), moderate (50 per cent) or severe (75 per cent).

Publication bias was assessed using a funnel plot.

**Results of the review**

The quality of the included studies was generally moderate. Five studies (listed in the table; reported as four studies in text) reported adequate allocation concealment. Most of the studies had moderate to high risk of bias or did not report the trial in sufficient detail for the reviewers to assess this.

Thirteen studies (1,059 participants) were included in the review: nine studies (673 participants) were randomised controlled trials (RCTs) and four studies (386 participants) were case-matched or propensity-matched studies. All studies were small, ranging in size from 12 to 108 patients.

Fenoldopam was associated with a reduced risk of the need for RRT (seven studies, 869 participants), pooled OR 0.37 (95% CI 0.23, 0.59, $P<0.001$). There was no significant heterogeneity, $P=0.53$, $I^2 = 0\%$.

Fenoldopam was associated with a reduced risk of hospital death (seven studies, 770 participants), pooled OR 0.46 (95% CI 0.29, 0.75, $P=0.002$). There was no significant heterogeneity, $P=0.66$, $I^2 = 0\%$.

Fenoldopam was associated with a reduction in time on mechanical ventilation, WMD -0.93 hours (95% CI -1.57, -0.28, $P=0.005$), although there was significant statistical heterogeneity, $P=0.001$, $I^2 = 73\%$, and a shorter time in intensive care, WMD -0.93 days (95% CI -1.27, 0.58, $P<0.001$), although there was again a significant statistical heterogeneity, $P=0.003$, $I^2 = 67\%$. See CRD commentary for comment regarding this and other inconsistencies in the results.

Fenoldopam was associated with a higher rate of hypotensive episodes or use of vasopressin, pooled OR 1.94 (95% CI 1.19, 3.16, $P=0.008$). There was no significant heterogeneity, $P=0.76$, $I^2 = 0\%$.

Subgroup and sensitivity analyses, including restricting the analysis to only RCTs, did not substantially alter any of the results other than that fenoldopam was beneficial in patients undergoing cardiac surgery, but not those undergoing vascular surgery.

There was no evidence of publication bias.

**Authors’ conclusions**

Fenoldopam reduces the need for renal replacement therapy and reduces in-hospital mortality in patients undergoing cardiovascular surgery.

**CRD commentary**

The research question was clearly stated. The study design inclusion criteria for non-randomised studies was not clearly specified, which could have led to subjective decisions being made during the selection process. Although outcome inclusion criteria were stated, it appears from the results that these were not adhered to since three of the included studies did not contribute to the analyses of either of the primary outcomes.

The authors stated that PubMed was searched, but it was not clear if this included PreMEDLINE or not. The authors used Google Scholar without reporting the search terms used, so the search was not reproducible. Since these were the only computerised databases searched, relevant studies may have been missed. The lack of language restriction means that the results were not affected by language bias.

The authors made attempts to minimise errors and bias in the review process through the use of four reviewers to perform the selection and data extraction, and two to assess validity.

Meta-analysis was used appropriately to pool the studies.
There were errors in the reporting of the results: those reported in this abstract are those given in the text of the review, which were different to those given in the figures in the review. Also, the results given for time in the intensive care unit cannot be correct since the 95% CI and P value are not consistent with each other.

Given problems with the review methodology and reporting, as well as the reported small size and low quality of the included studies, the results of the review may not be reliable.

Implications of the review for practice and research
Practice: the authors did not state any implications for practice.

Research: a large multicentre RCT was needed to confirm the results of the review.

Funding
One author received funding from Cephalon to present the results of a study on the effects of fenoldopam in critically ill patients at meetings in Italy in 2006.

Bibliographic details

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Subject indexing assigned by NLM

MeSH
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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.