N-acetylcysteine in cardiovascular-surgery-associated renal failure: a meta-analysis
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CRD summary
This review found that N-acetylcysteine was not significantly more effective than placebo for preventing acute renal failure after cardiovascular surgery. The conclusions reflect the evidence presented and are likely to be reliable.

Authors' objectives
To determine the effectiveness of N-acetylcysteine for preventing acute renal failure after cardiovascular surgery.

Searching
The authors searched MEDLINE, EMBASE (both from inception to June 2008), the Cochrane Renal Health Library (Issue 4, 2007) and Google Scholar. Search terms were reported. No language restrictions were imposed. Reference lists of retrieved articles and reviews were searched for any additional studies.

Study selection
Randomised controlled trials (RCTs) comparing any dose or form of N-acetylcysteine with placebo were eligible for the review. Eligible participants were adults (aged over 18 years) undergoing cardiovascular surgical procedures. Trials had to report acute renal failure, acute renal failure requiring dialysis, mortality (primary outcomes) or other renal outcomes (listed).

Mean age of patients in included trials was 69 years. The majority were male (78%) and undergoing cardiac surgery. About half of the included trials involved patients with impaired renal function before the operation. In most included trials, N-acetylcysteine was administered intravenously during surgery and for 24 to 48 hours after surgery. Most trials used a cumulative dose of more than 150 mg/kg ('high dose' preparations) and two trials included co-interventions.

Two reviewers independently selected studies for the review.

Assessment of study quality
Validity was assessed using the Jadad scale, which considers randomisation, blinding and withdrawals/drop-outs. Trials scoring 0 to 2 out of 5 were considered low quality, those scoring 3 or 4 were considered moderate quality and those scoring 5 high quality.

It appeared that two reviewers independently assessed validity.

Data extraction
Two reviewers independently extracted data using a standardised form. Data on numbers of events and participants in each group were used to derive the odds ratio and 95% confidence interval for dichotomous outcomes. Group means and standard deviations were used to calculate weighted mean differences for continuous outcomes. Standard errors and interquartile ranges were converted to standard deviations.

Methods of synthesis
Studies were synthesised by meta-analysis using a random-effects (Mantel-Haenszel) model. Statistical heterogeneity was assessed using the $X^2$ and $I^2$ statistics, with $I^2 > 25\%$ taken to indicate significant heterogeneity. Possible sources of heterogeneity were explored. Subgroup analyses were performed to explore the effects of pre-existing renal insufficiency, type of surgery, and formulation and dose of N-acetylcysteine. Sensitivity analysis was performed by repeating the meta-analysis using a fixed-effect model and by restricting the analysis to high quality trials.

Results of the review
Twelve trials, with 1,324 participants, were included in the review. Eight trials were rated high quality, three moderate and one low.
**Primary outcomes:** There were no statistically significant differences between N-acetylcysteine and control groups for renal failure (odds ratio 0.89, 95% confidence interval (CI): 0.68 to 1.15), renal failure requiring dialysis (odds ratio 1.09, 95% CI: 0.57 to 2.09) or mortality (odds ratio 0.95, 95% CI: 0.53 to 1.71). There was no significant statistical heterogeneity for these outcomes. The effect of N-acetylcysteine on the primary outcomes remained non-significant in all the subgroup and sensitivity analyses.

**Secondary outcomes:** Treatment with N-acetylcysteine did not reduce length of hospital stay (weighted mean difference 0.34 days, 95% CI: -0.56 to 1.25) but there was significant statistical heterogeneity. Results for other secondary outcomes were reported.

**Authors’ conclusions**
N-acetylcysteine was not beneficial in the prevention of renal dysfunction after cardiovascular surgery.

**CRD commentary**
The review question and inclusion criteria were clear. The authors searched a range of relevant sources without language restrictions. Attempts to locate unpublished studies were not reported, so the review could be at risk of publication bias; risk of publication bias was not assessed. Validity was assessed using a standard scale and the results were used in the analysis. However, only summary scores were reported, so the assessment was not particularly informative for the reader. Appropriate methods were used to minimise reviewer errors and bias during the review process. Adequate details of included trials were presented. Trials were pooled by meta-analysis using appropriate methods and clinical heterogeneity was explored by subgroup analyses. The authors’ conclusions reflect the evidence presented and are likely to be reliable.

**Implications of the review for practice and research**
**Practice:** The authors stated that the routine use of N-acetylcysteine to prevent renal dysfunction after cardiovascular surgery should be avoided.

**Research:** The authors did not state any implications for research.

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