Acetylcysteine for prevention of contrast nephropathy: meta-analysis

CRD summary
This review evaluated acetylcysteine for the prevention of nephropathy in patients with chronic renal insufficiency who were receiving contrast agents for diagnostic or therapeutic purposes. It found that treatment with acetylcysteine significantly reduces the risk of nephropathy. The review methodology was sound, however, the potential for publication bias and the pooling of diverse results make the reliability of the results uncertain.

Authors' objectives
To determine whether prophylactic use of acetylcysteine reduces the incidence of contrast nephropathy in patients with renal insufficiency.

Searching
The authors searched BIOSIS RRM (Reports, Reviews, Meetings) (1989 onwards), MEDLINE (1966 onwards), Web of Science (1997 onwards), Current Contents Medizin and the Cochrane Library (1996 onwards) without any language restrictions; the search terms were reported. The reference lists of identified papers and published reviews, and proceedings of major nephrology and cardiology meetings, were also screened. Only published articles and abstracts were included.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies evaluating acetylcysteine were eligible for inclusion. The doses of acetylcysteine in the included studies ranged from 400 to 1,200 mg, and the total dose from 1,600 to 2,400 mg.

Participants included in the review
Eligible participants were patients with chronic renal insufficiency who were receiving contrast media intravenously or intra-arterially. The participants in the included studies were undergoing elective computed tomography (CT), coronary angiography with or without angioplasty, or cardiac catheterisation. The mean age of the participants ranged from 64 to 73 years, and 21 to 64% had diabetes.

Outcomes assessed in the review
The outcome measure was the development of contrast nephropathy, defined as an increase in serum creatinine of at least 44.2 micromol/L or 25% from baseline 48 hours after administration of contrast media. The outcomes reported in the included studies were a change in serum creatinine of at least 5 mg/L or 25% from baseline.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed studies for relevance. Any disagreements were resolved by discussion.

Assessment of study quality
Validity was assessed using the Jadad scale, which gives a score of 0 to 5 based on the reporting of randomisation, masking, and drop-outs and withdrawals. Two reviewers independently assessed the studies for validity. There was 100% agreement between them.

Data extraction
Two reviewers independently extracted the data from the primary studies. Any disagreements were resolved by discussion. Data on the occurrence of contrast nephropathy in each group were used to calculate the relative risk (RR) and its 95% confidence interval (CI).

**Methods of synthesis**

**How were the studies combined?**

The studies were combined using a random-effects meta-analysis. The authors evaluated the robustness of the analysis by also combining results using a fixed-effect meta-analysis. The risk of publication bias was assessed using a funnel plot.

**How were differences between studies investigated?**

Heterogeneity was assessed using the Q statistic, with P-values below 0.1 being considered significant. An additional meta-analysis, weighting studies by quality, was performed. A meta-regression was used to investigate the relationships of volume of radiocontrast media administered and degree of chronic renal insufficiency with risk of contrast nephropathy. The effect of excluding one study in which the participants had a potentially different risk profile from the others (elective CT rather than cardiovascular procedures) was investigated in a sensitivity analysis.

**Results of the review**

Seven RCTs (n=805) were included.

In terms of the quality of the studies, the Jadad scores ranged from 1 to 5 (median 3).

Four RCTs reported a significant reduction in the RR of the development of contrast neuropathy in the acetylcysteine group, while three reported no significant benefit. The pooled RR was 0.44 (95% CI: 0.22, 0.88) when using the random-effects model and 0.56 (95% CI: 0.37, 0.84) when using the fixed-effect model; both of these suggested a statistically significant benefit of acetylcysteine treatment. Significant statistical heterogeneity was present. The removal of the outlying trial did not greatly affect the results. The meta-regression indicated that neither volume of radiocontrast media administered nor degree of chronic renal insufficiency was associated with a relative risk of contrast nephropathy.

The funnel plot suggested possible publication bias, in particular an absence of small negative trials.

**Authors' conclusions**

Compared with hydration alone, acetylcysteine with hydration significantly reduced the risk of contrast nephropathy in patients with chronic renal insufficiency.

**CRD commentary**

This review addressed a clear question, and the inclusion and exclusion criteria were clear. The authors searched a range of sources for published material without any language restrictions, therefore the potential for language bias was reduced. However, the authors' assessment suggested that publication bias might be an issue. Appropriate methods were used to reduce the risk of bias and errors during the review process. A standard method (although not the most informative) was used to assess validity and the results were used in the analysis.

Relevant details of the included studies were tabulated. The studies were combined in a meta-analysis, but statistically significant heterogeneity between the studies was observed; this questions the appropriateness of combining the studies in this way. Some sources of heterogeneity were investigated using a sensitivity analysis and meta-regression without markedly affecting the results, therefore the source of the heterogeneity remains unclear. The review methodology used by the authors was sound and, overall, the authors' conclusions reflect the evidence presented. However, the potential for publication bias identified by the authors, the heterogeneity between studies, and the pooling of these heterogeneous results, make the reliability of the results uncertain.
Implications of the review for practice and research
Practice: The authors stated that the use of acetylcysteine for the prophylaxis of contrast nephropathy may be justified in view of its cheapness, ease of use and favourable adverse effect profile (not investigated in this review).

Research: The authors stated that trials to investigate the effects of acetylcysteine on the course of serum creatinine and on hard clinical end points are warranted.

Bibliographic details

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Other publications of related interest

This additional published commentary may also be of interest. Buller GK. Review: prophylactic acetylcysteine reduces contrast nephropathy in chronic renal insufficiency. ACP J Club 2004;140:41.

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Record Status
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.