N-Acetylcysteine and contrast-induced nephropathy: a meta-analysis of 13 randomized trials
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CRD summary
The review evaluated the effects of N-acetylcysteine in the prevention of contrast-induced nephropathy. The review identified relevant published and unpublished data, and concluded reliably that the current available data did not justify changes in clinical practice and public policy.

Authors' objectives
To evaluate the effects of N-acetylcysteine (NAC) in the prevention of contrast-induced nephropathy (CIN).

Searching
The reviewers searched MEDLINE (1966 to November 2003), the Cochrane Controlled Trial Register (issue 2, 2003), ACP Journal Club, and proceedings of meetings of the American Heart Association, American College of Cardiology, European Society of Cardiology, American Society of Nephrology and International Society of Nephrology (1998 to the end of 2003); the search terms were reported. In addition, the reference lists of major cardiology and nephrology textbooks, UptoDate and published reviews of CIN were screened. No language restrictions were applied. Authors were contacted for additional information on the trials.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials were eligible for inclusion in the review. All included studies were placebo controlled.

Specific interventions included in the review
Studies on NAC in conjunction with coronary angiography for patients receiving intravenous fluids and low osmolarity non-ionic contrast media were eligible for inclusion. The included studies varied in the NAC dose given before and after contrast exposure, the method of intake (oral or intravenous), and the time NAC was introduced before and tapered after the procedure. The intravenous fluid regimen was most commonly 0.45% saline, 1 mL per kg, 12 hours before and 12 hours after contrast.

Participants included in the review
Studies of patients with impaired renal function with a creatinine level over 1.2 mg/dL were eligible for inclusion. The proportion of diabetic patients in the included studies ranged from 36 to 63%, and the mean baseline serum creatinine level ranged from 1.2 to 2.8 mg/dL.

Outcomes assessed in the review
The primary outcome was CIN, defined as an increase in creatinine level of either at least 0.5 mg/dL or more than 25% from baseline to 48 hours after contrast administration. The secondary outcome was the occurrence of acute renal failure requiring dialysis. The review also reported the baseline and mean 48-hour serum creatinine level for the intervention and control groups and the mean contrast volume.

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

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Two reviewers extracted the data. The relative risk (RR) of developing CIN was calculated for each study, as was the absolute risk difference and corresponding 95% confidence interval (CI).

Methods of synthesis
How were the studies combined?
Pooled estimates and their CIs were computed using a random-effects model.

How were differences between studies investigated?
Statistical heterogeneity was assessed using chi-squared and the I-squared statistic. Several subgroup and sensitivity analyses were performed.

Results of the review
Thirteen trials (n=1,892) were included in the review.

Thirteen trials showed a pooled RR of 0.68 (95% CI: 0.46, 1.01). The pooled result showed statistically significant heterogeneity (P=0.006). The absolute risk difference ranged from -0.37 to 0.04 in the individual trials. Of the 13 patients requiring dialysis, 4 belonged to the treatment group and 7 to the control group (2 were unclear).

Authors’ conclusions
The available data concerning the use of NAC before coronary angiography, to prevent CIN in patients with impaired renal function, is neither conclusive nor provides proof beyond a reasonable doubt to influence clinical practice and public policy.

CRD commentary
The review stated a clear question and inclusion criteria. The search emphasised the identification of unpublished relevant studies on the topic. Some measures were taken to reduce errors and bias in the review process. The validity of the included studies was not assessed, so the quality of the studies on which the review is based remains unclear. The presentation of individual study details was thorough. Sources of heterogeneity were followed up. The conclusions are reliable.

Implications of the review for practice and research
Practice: The authors stated explicitly that the results of the review do not indicate changes in clinical practice and public policy.

Research: The authors stated that more data from large randomised trials investigating clinical outcomes, rather than biochemical parameters, are needed.

Bibliographic details

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Other publications of related interest
Birck R, Krzossok S, Markowetz F, Schnulle P, van der Woude FJ, Braun C. Acetylcysteine for prevention of contrast

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