N-acetylcysteine for radiocontrast-induced nephropathy: potential role in the emergency department?

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CRD summary
This review assessed the efficacy and safety of N-acetylcysteine for the prevention of radiocontrast-induced nephropathy. The authors concluded that current evidence is insufficient to support the use of N-acetylcysteine in the emergency department. Although the review had several methodological limitations, this conclusion appears justified given the apparent lack of relevant studies in this setting.

Authors' objectives
To review the efficacy and safety of N-acetylcysteine (NAC) for the prevention of radiocontrast-induced nephropathy (RIN), and to discuss its role in the emergency department.

Searching
MEDLINE (from 1966 to December 2003) and EMBASE (from 1988 to December 2003) were searched for English language papers published in full; the search terms were reported. The reference lists of retrieved papers and review articles were checked for further studies.

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 that evaluated NAC for the prevention of RIN were eligible for inclusion. The comparators used in the included studies were placebo, fenoldopam or saline. In the included studies, NAC was administered either orally, twice daily, with dose ranging from 400 to 1,500 mg, or intravenously. In most studies NAC was first administered on the day prior to radiocontrast imaging, a regime not feasible for the emergency department.

Participants included in the review
Studies of participants requiring radiocontrast diagnostic imaging were eligible for inclusion. The participants in the included studies had chronic or stable renal insufficiency, or impaired renal function, and required imaging related to the management of these conditions.

Outcomes assessed in the review
Studies that reported RIN, using the definition specified by each study, were eligible for inclusion. Safety outcomes were also included in the review. Most of the included studies defined RIN as an increase in serum creatinine concentration of at least 44 mmol/L, or greater than 25% above baseline, at 48 hours after radiocontrast administration.

How were decisions on the relevance of primary studies made?
Two reviewers made decisions independently.

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

Data extraction
Two reviewers performed the data extraction independently. Data were extracted on the percentage of participants in
each group developing RIN and, where reported, the corresponding relative risk or odds ratio with 95% confidence intervals (CIs).

**Methods of synthesis**

*How were the studies combined?*

The studies were grouped into those demonstrating a benefit and those demonstrating no benefit of NAC, and each study was described in turn. Data on adverse events were reported separately.

*How were differences between studies investigated?*

The impact of differences between the studies, for example in the administration of NAC and radiocontrast agents, was investigated in the discussion.

**Results of the review**

Nine RCTs, involving 1,019 participants in total, were included.

Five RCTs found that NAC was associated with a significant reduction in the incidence of RIN. The percentage of participants developing RIN ranged from 2 to 8% in the NAC groups, and from 12 to 45% in the control groups. Only one study evaluated a regime appropriate to the emergency department.

Four RCTs found NAC did not have a significant effect on the incidence of RIN. The percentage of participants developing RIN ranged from 6.5 to 26.3% in the NAC groups, and from 6 to 22% in the control groups. Only one study evaluated a regime appropriate to the emergency department.

Adverse effects were reported by 4 RCTs. Two trials appear not to have found significant differences between the NAC and control groups. One trial reported adverse events, mostly gastrointestinal symptoms, in 16% of the NAC group. The only trial using intravenous NAC reported adverse events in 12.5% of the NAC group, leading to withdrawal from the trial in 3 cases.

**Authors' conclusions**

Current evidence did not support the use of NAC for urgent radiological investigation requiring contrast in the emergency department. Further research is needed.

**CRD commentary**

The review question was clear. The inclusion criteria were reasonably well defined, although they did allow the inclusion of intervention regimes unsuitable for the emergency department. Several relevant sources were searched for primary studies, but only papers published in English were eligible, suggesting that language and publication bias might exist. The study selection and data extraction processes were carried out by two reviewers independently to minimise the introduction of bias and errors into the review process. Since study quality was not assessed and no details relating to quality were provided, it was not possible to judge how similar or reliable the studies were.

The synthesis of the studies was very limited: they were simply divided into two groups and each study described individually. The authors did not explore reasons for any differences between the study findings, although study details were provided within the text of the review and these allowed some comparisons to be made. Despite these methodological limitations, the overall conclusion that there was insufficient evidence to support the use of NAC in the emergency room appears justified given the apparent lack of relevant studies in this setting.

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

Practice: The authors stated that the use of NAC for urgent radiologic investigations requiring contrast in the emergency department was not supported by current evidence.

Research: The authors stated that a well-designed prospective trial evaluating NAC just prior to radiocontrast
administration in high-risk emergency department patients is required to clarify the role of NAC in the emergency department.

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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.