Update: prevention of contrast-induced nephropathy in the emergency department

Sinert R, Doty CI

CRD summary
This review concluded that theophylline, bicarbonate, and ascorbic acid are appropriate to an emergency department setting and decreased the risk of contrast-induced nephropathy. Doubts over how outcomes were interpreted, coupled with methodological limitations, means the authors' conclusions should be interpreted with caution.

Authors' objectives
To assess effectiveness of therapies (emergency department setting) to prevent contrast-induced nephropathy.

This review was an update of a review conducted in 2007 and this abstract encompassed details and results from both papers (see Other Publications of Related Interest).

Searching
MEDLINE, EMBASE and The Cochrane Library were searched from inception to April 2008; search terms were reported. Bibliographies of eligible articles and reviews were screened.

Study selection
Randomised controlled trials (RCTs) of interventions to prevent contrast-induced nephropathy in patients (aged over 18 years) who received radiocontrast agents and had baseline renal insufficiency were eligible for inclusion. Interventions had to be initiated up to two hours before contrast administration. Studies of both venous and arterial injection were eligible. Studies of agents not readily available in most emergency departments or of agents that required intensive monitoring were excluded.

Interventions used in included studies were N-acetylcysteine (varying doses), theophylline (200mg), bicarbonate and ascorbic acid. Types of contrast agent used varied; non-ionic low osmolality agents were the most common. All comparator groups received saline hydration (doses varied). Studies recruited patients using varying baseline creatinine levels as an inclusion criterion. Most studies defined contrast-induced nephropathy as a 25% increase in serum creatinine.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
Study quality was assessed using the following criteria: randomisation; allocation concealment; use of intention-to-treat analysis; baseline comparability; blinding; use of cointerventions; and losses to follow-up.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Relative risks and numbers needed to treat with 95% confidence intervals were extracted.

The authors stated neither how data were extracted for the review nor how many reviewers performed data extraction.

Methods of synthesis
A narrative synthesis was presented, along with tables and a forest plot (without pooling). Differences between studies were discussed in the text.
Results of the review

2007 paper:

Seven RCTs were included in the original review (n=789). All trials stated they were randomised, but only three detailed methods used for adequate randomisation and allocation concealment. Three of the seven trials excluded or limited use of concomitant treatments. Blinding of patients and physicians was adequate in all except one study. Only two trials achieved complete follow-up at 48 hours.

Five studies reported a statistically significant decrease in nephropathy with the intervention (two studies of theophylline and one each of N-acetylcysteine, bicarbonate and ascorbic acid) and two found no significant difference (both N-acetylcysteine). The confidence intervals of the relative risks overlapped, which suggested that there was no single superior treatment. However, the ascorbic acid study reported a significant difference only after re-analysing data using the least stringent outcome measure (25% increase in creatinine). Numbers needed to treat, where reported, ranged from 6.4 to 9.1.

Two studies found no complications resulting from treatment with N-acetylcysteine. One study reported that 14.6% of patients experienced transitory allergic reactions. One study reported a small increase in pulse (>15 beats/minute) with theophylline. The bicarbonate study found an increase in blood pressure after fluid infusion in both treatment groups. The ascorbic acid trial did not present results for complications.

2009 update:

Two further RCTs were found (n=202). Both had adequate allocation concealment, but only one used blinding. A new study on bicarbonate reported benefit similar to the bicarbonate trial in the 2007 review, but a new study of ascorbic acid found no significant difference in effectiveness between the groups.

Authors’ conclusions

Theophylline, bicarbonate and ascorbic acid were appropriate to an emergency department setting and decreased the risk of contrast-induced nephropathy; evidence for effectiveness for N-acetylcysteine was less certain.

CRD commentary

The review addressed a clear question and was supported by use of appropriate inclusion criteria. Attempts to identify relevant studies were undertaken by searching electronic databases and checking references, but it appeared that no steps were taken to minimise risk of language and publication biases, so relevant studies may have been missed. The authors did not report using methods that could minimise risk of reviewer error and bias (such as independent duplicate study selection and data extraction).

Study quality was adequately assessed and the results were used to inform interpretation of the review findings. Sufficient study details were provided and an appropriate narrative synthesis of the data was undertaken, with heterogeneity issues discussed. However, the number of events in most studies was low, which increased the possibility of chance results.

Although the authors discussed the issue of whether an increase in serum creatinine was an appropriate surrogate for clinically important outcomes of contrast-induced nephropathy, they did not reflect this in their conclusions. The conclusions appeared somewhat over-optimistic in reflecting the evidence. This, coupled with some methodological limitations of both the review and the included studies, means the authors’ conclusions should be interpreted with caution.

Implications of the review for practice and research

Practice: The authors stated that the best way to prevent nephropathy in at-risk patients was to avoid contrast administration; if contrast was unavoidable then adequate volume resuscitation was not controversial. In the update review, the authors stated that bicarbonate may represent a relatively low-risk prophylactic agent, but that withholding or limiting the volume of intravenous contrast, selecting a less nephrotoxic contrast agent and appropriate levels of hydration should also be considered.
Research: The authors stated a need for research that compared complications from contrast-induced nephropathy in a diverse group of cardiac patients to an equally varied group of emergency department patients.

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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.