Hydration with sodium bicarbonate for the prevention of contrast-induced nephropathy: a meta-analysis of randomized controlled trials

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CRD summary
The review concluded that evidence from this systematic review favoured hydration with sodium bicarbonate (as compared with sodium chloride) for prevention of contrast nephropathy. The review was generally well conducted, but the poor quality of some of the included trials limits the reliability of the authors’ conclusions.

Authors’ objectives
To evaluate the benefit of sodium bicarbonate-based hydration for the prevention of contrast-induced nephropathy.

Searching
MEDLINE was searched from 1950 to October 2008 for articles published in English. Search terms were reported. Cochrane Central Register of Controlled Trials (CENTRAL) was also searched. Abstracts from seven scientific meetings were searched manually between 2005 and 2008. An update search of MEDLINE was conducted in May 2009. A further update search was conducted in July 2009.

Study selection
Randomised controlled trials (RCTs) of adult patients randomised to receive a bicarbonate-containing intravenous solution versus an alternate solution were eligible for inclusion. Trials had to report the incidence of contrast-induced nephropathy based on serum creatinine criterion and had to use a uniform contrast agent (unless randomisation was stratified according to type of contrast). Abstracts were included. Trials permitted cointerventions if both arms were administered similarly. Trials were excluded if they used differing rates of infusion, significantly different osmolarity and if they used prophylactic agents that were administered in a non-standardised or non-stratified manner.

The included trials compared sodium bicarbonate with sodium chloride in seven countries (China, USA, South Korea, Japan, Turkey and Germany were included). Trials generally used a non-ionic low osmolar contrast agent. Most patients underwent cardiac angiography. Contrast-induced nephropathy was defined by either relative increase in serum creatinine (≥25%) or absolute increase in serum creatinine (≥0.05mg/dL).

Two authors independently performed study selection. Disagreements were resolved by discussion.

Assessment of study quality
Two reviewers independently assessed trial quality using the Jadad scale and Delphi criteria. Quality items such as blinding, randomisation, intention-to-treat, similarity of baseline groups, withdrawals and allocation concealment were assessed. The Jadad scale was used to give a quantitative estimate of quality: trials were scored from 1 (poor quality) to a maximum of 5 (high quality). Disagreements between reviewers were resolved by discussion.

Data extraction
Two reviewers extracted data on contrast-induced nephropathy using a pre-defined sheet and used these data to calculate odds ratios (OR) and 95% confidence intervals (CI). Trial authors were contacted for missing data.

Methods of synthesis
Fixed-effect meta-analysis was undertaken to obtain pooled odds ratios and 95% CIs. Statistical heterogeneity was assessed using I² and Woolf’s test. Subgroup analysis excluded studies that allowed N-acetylcysteine co-therapy. Sensitivity analysis was undertaken using random-effects meta-analysis. Publication bias was assessed with funnel plots and Macaskill’s test.

Results of the review
Ten RCTs were included in the review (n=1,090 patients), five of which were abstracts. Trial sample sizes ranged from...
18 to 323 patients. Trial quality was variable: five trials (mostly abstracts) scored 1, one trial (abstract) scored 2, three trials scored 3 and one trial scored 5.

Compared with sodium chloride, there was a statistically significantly lower rate of contrast-induced nephropathy with sodium bicarbonate (OR 0.57, 95% CI 0.38 to 0.85, I²=39%; 10 RCTs).

Subgroup analysis excluded four trials that included N-acetylcysteine co-therapy and resulted in a greater effect size with sodium bicarbonate compared with sodium chloride (OR 0.33, 95% CI 0.17 to 0.62, I²=52%; six RCTs).

There was no evidence of publication bias. Sensitivity analysis with the random-effects model did not alter the results significantly.

**Authors' conclusions**
Evidence from this systematic review favoured hydration with sodium bicarbonate (as compared with sodium chloride) for prevention of contrast nephropathy.

**CRD commentary**
Inclusion criteria for the review were broadly defined. Several relevant data sources were searched. There was potential for language bias, as only English-language articles were included. Publication bias was assessed and was not detected in either analysis. Attempts were made to reduce reviewer error and bias throughout the review process. Quality assessment based on standard criteria indicated the variable quality of the included data (acknowledged by the authors). Appropriate methods were used to pool the results and statistical heterogeneity was assessed, which appeared appropriate.

The review was generally well conducted, but the poor quality of some of the included trials limits the reliability of the authors' conclusions.

**Implications of the review for practice and research**
**Practice:** The authors stated that, notwithstanding the review limitations, the results suggested that peri-contrast hydration with sodium bicarbonate was preferable to sodium chloride unless additional data were forthcoming and refuted this view.

**Research:** The authors stated that future trials should assess the impact on clinical outcomes rather than solely laboratory-based outcomes.

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