Systematic review: sodium bicarbonate treatment regimens for the prevention of contrast-induced nephropathy

CRD summary
This generally well-conducted review concluded that the effectiveness of sodium bicarbonate treatment to prevent contrast-induced nephropathy in high-risk patients remained uncertain. Given the paucity of good quality data, this cautious conclusion and the recommendations for practice and research seem appropriate.

Authors’ objectives
To determine the effect of sodium bicarbonate on the risk for contrast-induced nephropathy.

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials were searched without language restrictions from 1950 to December 2008; search terms were reported. ClinicalTrials.gov, conference proceedings and bibliographies of relevant trials and reviews were searched.

Study selection
Completed randomised controlled trials (RCTs) that assessed intravenous sodium bicarbonate as a preventative strategy for contrast-induced nephropathy (25% increase from baseline serum creatinine or absolute increase of 44μmol/L two to five days after radiocontrast administration) in adults (over 18 years) were eligible for inclusion. Kidney function was not an inclusion criteria. Most studies used 154mEq/L (milliequivalents/L) sodium bicarbonate compared to 154mEq/L sodium chloride, with similar hydration protocols. Most studies were in patients with impaired renal function. Contrast was being used for cardiac catheterisation, computed tomography or other arteriography.

Where reported: mean age of participants ranged from 48 to 75 years; the proportion of male participants ranged from 59% to 84%; baseline creatinine levels ranged from 71μmol/L to 177μmol/L; mean volume of contrast used ranged from 65mL to 285mL; and the proportion of patients with diabetes ranged from 24% to 58%.

It was unclear how many reviewers performed the study selection.

Assessment of study quality
Quality was assessed by two independent reviewers for randomisation, allocation concealment, blinding, similarity at baseline, eligibility criteria, completeness of follow-up and the use of an intention-to-treat analysis. The Jadad scale was also used (maximum score 5). Disagreements were resolved by a third reviewer.

Data extraction
The number of patients who developed contrast-induced nephropathy, required dialysis, died and developed heart failure was extracted. Relative risks (RR) with 95% confidence intervals (CI) were calculated for each study. Authors/investigators were contacted for data. Data were extracted by two independent reviewers; disagreements were resolved by a third reviewer.

Methods of synthesis
Pooled risk ratios and 95% CIs were calculated using a random-effects model. Where an arm had no events, a continuity factor (reciprocal of the size of opposite treatment group) was added to each cell. Heterogeneity was assessed using the I² statistic. The impact of study quality, sample size and numbers of events were investigated using traditional meta-analyses; study quality was further investigated with univariate meta-regression. Analyses were stratified according to publication status. Sensitivity analyses using continuity correction constants of varying sizes were conducted. Publication bias was assessed using funnel plots and the Egger test.

Results of the review
Twenty three studies met the inclusion criteria: nine published and 14 unpublished (n=3,563, range 18 to 502). Reported study quality criteria in published studies was poor: only four reported allocation concealment; six reported blinding of patients; three reported blinding of outcome assessors; and two reported blinding of care providers. One study scored 5 on the Jadad scale, one scored 4, three scored 3, three scored 1 and one scored 0. There seemed to be no assessment of the quality of unpublished studies. Publication bias was observed (p=0.009).

The overall incidence of contrast-induced nephropathy ranged from 3.4% to 20.3% across the studies. When all studies were combined, sodium bicarbonate significantly reduced the risk of contrast-induced nephropathy (RR 0.62, 95% CI 0.45 to 0.86) compared to saline-based control regimens. When published and unpublished studies were combined separately, a significant reduction in the risk of contrast-induced nephropathy was observed in the published studies (RR 0.43, 95% CI 0.25 to 0.75), but not unpublished studies (RR 0.78, 95% CI 0.52 to 1.17). Statistically significant heterogeneity was observed for all analyses. The addition of N-acetylcysteine seemed to have no impact on the effectiveness of sodium bicarbonate. The administration of sodium bicarbonate had no significant impact on the requirement for dialysis, mortality or the incidence of heart failure.

Meta-regression showed increased estimates of effect for studies published prior to 2008, those with few events and participants, where contrast-induced nephropathy was measured within 48 hours of an event and where study quality was poor. Neither baseline renal function nor proportion of patients with diabetes contributed to the observed heterogeneity.

**Authors’ conclusions**
The effectiveness of sodium bicarbonate treatment to prevent contrast-induced nephropathy in high-risk patients remained uncertain.

**CRD commentary**
The authors addressed a clear review question with defined inclusion criteria. Several relevant sources were searched for both published and unpublished studies in any language, which reduced the potential for language and publication biases. Searching, data extraction and quality assessment were conducted in duplicate, but it was unclear whether this also applied to study selection. Quality was assessed using appropriate criteria, but only published studies were assessed. Measures of effect were greater in published studies and publication bias was demonstrated. Therefore, the quality of the unpublished studies was uncertain. All but two of the studies were in patients with impaired renal function; the applicability of the results to those with normal renal function was uncertain. This was a generally well-conducted review. Given the paucity of good-quality data, the cautious conclusions drawn by the authors seem appropriate, as do the recommendations for practice and research.

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

**Practice:** The authors stated that the discrepancy between published and unpublished studies was sufficiently large to merit caution when considering the use of sodium bicarbonate to prevent contrast-induced nephropathy; based on data at the time of the review, routine administration was premature.

**Research:** The authors stated that a large, well-designed, multicentre RCT was required to establish whether use of sodium bicarbonate was effective at preventing contrast-induced nephropathy. Future studies needed to assess clinical outcomes, rather than just surrogate outcomes such as changes in creatinine levels.

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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.