Sodium bicarbonate therapy for prevention of contrast-induced nephropathy: a systematic review and meta-analysis

Navaneethan SD, Singh S, Appasamy S, Wing RE, Sehgal AR

CRD summary
This review assessed whether hydration with sodium bicarbonate reduced the risk of contrast-induced nephropathy in comparison to hydration with normal saline. The authors concluded that use of sodium bicarbonate reduced contrast-induced nephropathy, but found no evidence for a reduction in mortality or need for dialysis. The review was well conducted and the authors’ conclusions reliably reflect the evidence presented.

Authors' objectives
To determine whether intravenous hydration with sodium bicarbonate is superior to hydration with normal saline for the prevention of contrast-induced nephropathy.

Searching
MEDLINE and EMBASE were searched from inception to January 2008. Abstracts presented at annual meetings between 2004 and 2007 of American Society of Nephrology, National Kidney Foundation, European Renal Association, American College of Cardiology, Transcatheter Cardiovascular Therapeutics, American Heart Association and Radiology Society of America were searched. Reference lists of included studies were examined for additional papers. Search terms were provided. No language restrictions were applied.

Study selection
Randomised controlled trials (RCTs) that reported on contrast-induced nephropathy following hydration with sodium bicarbonate versus hydration with normal saline in adults who underwent any form of contrast procedure (elective or emergent) were eligible for inclusion. N-acetylcysteine could be given as a cointervention so long as it was administered similarly in both study arms. Trials of patients with and without pre-existing kidney disease were eligible. Treatment protocols varied considerably in terms of dose, duration and timing of the hydration intervention. Contrast procedures used non-ionic contrast with iso-osmolarity or low osmolarity. Most trials were reported to include participants with underlying decreased kidney function undergoing coronary angiography. Trials variously compared sodium bicarbonate to sodium chloride and/or normal saline.

The primary outcome measure was development of contrast-induced nephropathy (defined as either >25% or >0.5mg/dL increase in serum creatinine level from baseline within 96 hours of contrast administration). The actual time period from contrast administration ranged from 48 hours to 96 hours. Secondary outcome measures were: need for renal replacement therapy; in-hospital mortality; length of hospital stay; worsening of pre-existing congestive heart failure or the development of pulmonary edema; and change in serum bicarbonate levels at the end of the study period.

Two reviewers independently screened all abstracts and subsequently all full-text articles for inclusion in the review.

Assessment of study quality
Study quality was assessed using the Jadad scale of randomisation, blinding and withdrawals and dropouts.

Study quality was assessed by two reviewers.

Data extraction
Odds ratios (OR) and 95% confidence intervals (CIs) were estimated for dichotomous data and weighted mean differences (WMDs) and 95% CIs were estimated for continuous data.

Study authors were contacted for clarification of data, where necessary.
Data extraction was performed by two reviewers independently. Any disagreements were referred to a third reviewer.

**Methods of synthesis**
A meta-analysis was performed to pool odds ratios and weighted mean differences, with 95% CIs, using the DerSimonian and Laird random-effects model. If one arm contained a zero cell value, a continuity correction of 0.5 was added.

Heterogeneity was assessed using $\chi^2$ (Cochran’s $Q$) and $I^2$ test. $I^2$ values greater than 25%, 50% and 75% were considered to provide evidence of low, moderate and high levels of statistical heterogeneity. Where $I^2$ was greater than 50%, sensitivity analyses were planned to examine the effects of fixed-effect or random-effects methods of meta-analyses and the effect of excluding each study one at a time. Subgroup analyses were carried out based on the severity of kidney disease at baseline (defined as glomerular filtration rate less than or greater than 60mL/min/1.73m$^2$), emergency versus elective contrast procedures and journal versus abstract publication status.

**Results of the review**
Twelve RCTs (n=1,854) were included. Trial quality was considered to be low to moderate: six RCTs scored 1 or 2 points on the Jadad scale and six scored 3 or 4 points. Quality was generally higher for the six trials published in full compared to the six that were available only as conference proceedings, with better descriptions of the randomisation method and of withdrawals and drop-outs in the full publications. Both groups of studies scored poorly on items relating to blinding.

A significant reduction in risk of contrast-induced nephropathy was found (12 RCTs, n=1,652) from sodium bicarbonate-based hydration regimens compared to control regimens (OR 0.46, 95% CI 0.26 to 0.82); moderate levels of heterogeneity were identified ($I^2=55.9\%$). The seven trials that compared sodium bicarbonate alone to normal saline alone produced a similar result (OR 0.39, 95% CI 0.20 to 0.77). A non-significant result was obtained when N-acetylcysteine was added to both arms (eight RCTs).

No statistically significant differences in need for renal replacement therapy, in-hospital mortality and congestive heart failure or pulmonary oedema were identified. There were insufficient data to analyse any impact on length of hospital stay.

Sensitivity analyses identified similar effects on risk of contrast-induced nephropathy from use of a fixed-effect model and when individual studies were excluded from the analyses. Analyses restricted to studies of patients who underwent elective or emergency contrast procedures and those restricted to patients with pre-existing renal disease showed results similar to the overall pooled result. Analyses by publication status found significant decreases in the risk of contrast-induced nephropathy found in published trials (OR 0.26, 95% CI 0.10 to 0.64), but considerably smaller and non-significant reductions from studies published as conference proceedings only (OR 0.85, 95% CI 0.46 to 1.57).

**Authors’ conclusions**
The authors concluded that sodium bicarbonate-based hydration reduced the incidence of contrast-induced nephropathy in comparison to normal saline; there was no evidence of benefit in terms of mortality or need for dialysis.

**CRD commentary**
The aim and inclusion criteria for this review were clear and appropriate. Two major medical databases were searched without language restrictions and a thorough attempt to identify grey literature was made, which reduced risks of language and publication biases. All stages of the review were carried out in duplicate to reduce risks of reviewer bias. A well-recognised quality assessment tool for RCTs (Jadad scale) was used to evaluate trials. Reasonably comprehensive study details were provided; these included details of how trials rated on individual quality criteria. More information on patient characteristics would have been useful to enable an assessment of the generalisability of results. The results of the quality assessment were used only to make a general comment on the overall quality of the trials; this was likely to have been influenced by the fact that half of the included RCTs were available only in abstract
form. The amount of design-related information that can be included in abstract is limited and quality assessment is likely to reflect these limitations in reporting, rather than the true quality of the trials themselves. The statistical synthesis of included studies was appropriate, as were the methods used. Sensitivity analyses were conducted, including attention to potential publication bias.

Overall, the review was carried out to a good standard and the authors’ conclusions are reliably based on the data presented.

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

**Practice**: The authors did not state any implications for practice

**Research**: The authors stated that adequately powered trials that measured patient-oriented outcomes in participants with and without kidney disease and who underwent a range of contrast-enhanced procedures were needed.

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