Use of isotonic sodium bicarbonate to prevent radiocontrast nephropathy in patients with mild pre-existing renal impairment: a meta-analysis

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CRD summary
The authors concluded that from limited data, isotonic sodium bicarbonate appeared to be safe and effective in reducing radiocontrast nephropathy in patients with mild pre-existing renal impairment. This was a generally well-conducted review. The authors' conclusions reflected the limited data and are likely to be reliable.

Authors' objectives
To evaluate the effectiveness of isotonic sodium bicarbonate in preventing radiocontrast nephropathy.

Searching
MEDLINE (1966 to April 2008), EMBASE (1990 to April 2008) and Cochrane Central Register of Controlled Trials (2007, issue 4) were searched. Search terms were reported. No language restrictions were applied. Websites of the International Network of Agencies of Health Technology Assessment and International Society of Technology Assessment in Health Care were searched. Reference lists of related editorials, reviews and original studies were screened.

Study selection
Randomised controlled trials (RCTs) that compared sodium bicarbonate with a placebo (no drug or 5% dextrose) or normal saline control in patients who underwent a radiocontrast-related procedure were eligible for inclusion. Studies that used the same co-intervention in both treatment arms were included. Studies could use any timing of the intervention and be conducted in any population.

The primary review outcome was the proportion of patients with an incremental rise in serum creatinine concentration greater than 25% above baseline or >0.050mg/dL (44 μmol/L). Secondary outcomes were acute renal failure requiring dialysis, mortality, urinary pH after administration of sodium bicarbonate and absolute change in serum creatinine concentration and creatinine clearance from baseline. Treatment-related adverse effects were also assessed.

All the studies were in adults. Patients in two studies underwent a variety of procedures that included vascular procedures and computed tomography; two studies were in patients who underwent diagnostic or therapeutic cardiac catheterisation. In three studies, the minimum baseline serum creatinine concentration ranged from 97 to 106 μmol/L; in one study baseline levels were above 176 μmol/L. Studies administered isotonic sodium bicarbonate treatment from one to six hours before the procedure to six hours after. Two studies used oral N-acetylcysteine (600mg or 1,200mg), started the day before the procedure in both treatment groups.

Two reviewers independently selected studies from full reports of identified studies. There were no disagreements.

Assessment of study quality
Two reviewers independently assessed allocation concealment, randomisation, blinding, intention-to-treat analysis and inclusion and exclusion criteria. There were no disagreements.

Data extraction
Means and standard deviations were extracted for continuous outcomes and event rates for dichotomous data. Relative risks were used for categorical data and mean differences used for continuous data. Means and standard deviations were estimated if required.

Two reviewers independently extracted data onto a standardised form. There were no disagreements.
Methods of synthesis
Pooled relative risks and weighted mean differences with 95% confidence intervals (CI) were calculated using a fixed-effect model. Heterogeneity was assessed using the \( \chi^2 \) and \( I^2 \) statistics; significant heterogeneity was indicated by \( I^2 \) greater than 40%. There were too few studies to use a funnel plot to assess publication bias.

Results of the review
Four RCTs were included (n=573). Sample size ranged from 59 to 219. In all studies, losses to follow-up were less than 10%. Two studies had adequate allocation concealment and none were blinded. Studies were judged to be at moderate risk of bias.

Isotonic sodium bicarbonate was associated with a statistically significant reduction in the risk of an incremental rise in serum creatinine concentration greater than 25% above the baseline (relative risk 0.22, 95% CI: 0.11 to 0.44, \( p<0.0001 \)). No significant heterogeneity was found (\( I^2=0\% \)).

Isotonic sodium bicarbonate was associated with a significant increase in urinary pH (weighted mean difference 0.98, 95% CI: 0.83 to 1.13, \( p<0.00001 \)) and a significant protective effect on the absolute change in serum creatinine concentration (weighted mean difference -9.4 \( \mu \)mol/L, 95% CI: -17.2 to -1.7, \( p=0.02 \)) and creatinine clearance from baseline (weighted mean difference 3.7 mL/minute, 95% CI: 0.55 to 6.80, \( p=0.02 \)). Significant heterogeneity was found for the absolute change in creatinine clearance (\( I^2=57\% \)), but not for the other outcomes.

There was no statistically significant difference between treatments in the incidence of acute renal failure requiring dialysis, but its incidence was low (1.4%).

There was no significant difference between isotonic sodium bicarbonate and control in mortality (one study, n=59) or changes in serum potassium (two studies). Only one treatment-related adverse effect was reported (a transient rise in blood pressure).

Authors’ conclusions
From limited data, isotonic sodium bicarbonate appeared to be safe and effective in reducing radiocontrast nephropathy in patients with mild pre-existing renal impairment.

CRD commentary
The review question was clearly stated. Inclusion criteria were defined for intervention, participants and study design and the primary review outcome was specified. Several relevant sources were searched and no language restrictions were applied, but no attempts were made to minimise publication bias. Methods were used to minimise reviewer errors and bias during the review process. Only RCTs were included, validity was assessed and results were reported. Appropriate methods were used for the meta-analyses and heterogeneity was assessed. Some limitations of the review were discussed. This was a generally well-conducted review and the authors’ conclusions reflected the limited data and are likely to be reliable.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that a large RCT was required to confirm the effects of isotonic sodium bicarbonate on relevant patient-centred outcomes and to assess its cost-effectiveness in patients with pre-existing renal impairment who underwent radiocontrast procedures.

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