Sodium bicarbonate for prevention of contrast-induced acute kidney injury: a systematic review and meta-analysis

Hoste EA, De Waele JJ, Gevaert SA, Uchino S, Kellum JA

CRD summary
This review concluded that use of sodium bicarbonate in patients who underwent intravascular iodinated contrast-enhanced radiography procedures reduced the risk of contrast-induced acute kidney injury. This was a borderline effect and there was no benefit for other outcomes. The included studies had variable findings and were low quality. The authors' conclusions are appropriately cautious and likely to be reliable.

Authors' objectives
To evaluate the use of sodium bicarbonate for prevention of contrast-induced acute kidney injury (CI-AKI) in patients undergoing intravascular iodinated contrast-enhanced radiography procedures.

Searching
PubMed and Web of Science were searched from 1950 to 20 February 2009 for studies published in peer-reviewed journals. There were no language restrictions. Search terms were reported. Reference lists of retrieved articles and reviews and abstract books from 2006 to 2008 of the major nephrology and cardiology societies were searched.

Study selection
Prospective controlled studies where a treatment group received intravenous sodium bicarbonate for prevention of contrast nephropathy were eligible for inclusion, provided they administered intravenous or intra-arterial iodinated contrast (to ensure explicit reporting of contrast-induced nephropathy) and reported sufficient data to calculate the primary outcome. The primary outcome was CI-AKI defined as an increase in serum creatinine ≥25% or ≥0.5 mg/dL within 48 or 72 hours after the administration of contrast.

The included studies were of patients who underwent coronary procedures, emergency coronary procedures or a range of different contrast procedures. Patients varied between studies in terms of baseline kidney function and proportion with diabetes (3% to 98%). Mean age, where reported, ranged from 45 to 76 years, except for one paediatric study. Incidence of control group CI-AKI varied between studies. Where reported, low osmolar or iso-osmolar contrast agent was used; one study used a high osmolar contrast. The studies varied in volume of contrast agent administered and the route of administration. Sodium bicarbonate was given with or without N-acetylcysteine. Most of the included studies used the Merten protocol for sodium bicarbonate administration. Isotonic saline, with or without N-acetylcysteine, was used as the control in all studies except one that used isotonic saline plus acetazolamide (active comparator).

Studies were screened by three reviewers.

Assessment of study quality
Studies were assessed for several aspects of quality, which included adequacy of randomisation, allocation concealment, blinding, reporting of incomplete data and selective reporting.

Three reviewers undertook the quality assessment.

Data extraction
The number of events was extracted for outcomes of interest and the relative risk (RR) and 95% confidence interval (CI) was calculated. Where there were multiple intervention or control groups in a study, data were pooled into a single intervention or control arm.

Data were extracted by one reviewer and checked by a second.
Methods of synthesis
Studies were pooled in a meta-analysis using a fixed-effect model or, where there was statistical heterogeneity, a random-effects model. Heterogeneity was assessed using the I² statistic. Risk of publication bias was assessed by inspection of a funnel plot.

Results of the review
Eighteen prospective controlled trials (n=3,090) were included: nine full papers and nine published as an abstract only. The overall quality of the included studies was described as low: 33% reported allocation concealment and information on blinding was provided in 61% of trials; 73% of these did not use blinding.

There was a statistically significant reduction in incidence of CI-AKI with use of sodium bicarbonate compared to control (RR 0.66, 95% CI 0.45 to 0.95; 18 trials) in the overall analysis. When studies were subgrouped by the type of contrast procedure, there was a statistically significant benefit with sodium bicarbonate in the studies of coronary procedures only (RR 0.65, 95% CI 0.42 to 1.00; 10 trials) and emergency coronary procedures (RR 0.13, 95% CI 0.04 to 0.42; two trials), but not in the pooling of studies of coronary and non-coronary procedures (RR 0.68, 95% CI: 0.30 to 1.52; eight trials). There was moderate heterogeneity (>50%) in all the analyses except of acute coronary procedures. Other subgroup analyses based on a small number of studies are reported in the paper.

There was no statistically significant difference between sodium bicarbonate and control in the need for renal replacement therapy (11 trials) or in-hospital mortality (five trials).

Visual inspection of a funnel plot suggested publication bias when only data from full-papers were included, but not when all the included data (full papers and abstracts only) were considered.

Authors' conclusions
Use of sodium bicarbonate had a preventive effect on the risk of CI-AKI with borderline statistical significance. There was no benefit in need for renal replacement therapy or mortality. Given the low quality of the individual studies, the heterogeneity and possible publication bias, only a limited recommendation could be made in favour of use of sodium bicarbonate.

CRD commentary
The review had clearly stated inclusion criteria. The number of sources searched for studies was somewhat limited. There were no language restrictions and unpublished studies were sought, which reduced the risk of missing relevant studies. It appeared that appropriate methods were used to reduce error and bias in the review processes. The main analysis seemed appropriate, although some of the subgroup analyses were based on a small number of participants and there was unexplained heterogeneity in some analyses. This and the poor quality of the included studies were taken into consideration in the conclusions.

The authors' conclusions were appropriately cautious 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 large prospective trials were required to explore the effect of use of sodium bicarbonate on well-defined subgroups. These should include patients with different risk profiles who underwent coronary angiography and patients at risk for CI-AKI, which included patients in intensive care who underwent contrast enhanced computed tomography scans or interventional angiography procedures.

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