Sodium bicarbonate for the prevention of contrast induced-acute kidney injury: a systematic review and meta-analysis
Brar SS, Hiremath S, Dangas G, Mehran R, Brar SK, Leon MB

CRD summary
This review assessed whether hydration with sodium bicarbonate helped prevent contrast-induced acute kidney injury (CI-AKI) and found no evidence of benefit within large randomised trials. The conclusion was based on a subgroup of included studies. The low quality of included studies, poor reporting of the review process and questions regarding the synthesis made the reliability of the conclusions unclear.

Authors' objectives
To assess the effectiveness of hydration with sodium bicarbonate for the prevention of contrast-induced acute kidney injury (CI-AKI).

Searching
The authors searched MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) for relevant articles published in any language from 1966 to 2008. Search terms were specified. Reference lists of included studies, systematic reviews, abstracts of selected scientific meetings and relevant websites were searched for relevant studies.

Study selection
Eligible studies used a randomised controlled design and compared periprocedural hydration with sodium bicarbonate and sodium chloride for the prevention of CI-AKI in adults (aged at least 18 years).

Most studies defined CI-AKI as creatinine increase of at least 25% within either 24 or 72 hours. Hydration protocols were variable. Most studies used low osmolar or iso-osmolar contrast types. Clinical settings included either mixed procedures or elective coronary interventions. Use of N-acetylcysteine varied substantially between studies; some studies did not permit use of this treatment and others provided doses of up to 1,200mg twice daily on the days pre- and post-procedure. The most common infusion protocol was administration of a fixed dilution of sodium bicarbonate or chloride at 3mL/kg/hour for one hour pre-procedure then 1mL/kg/hour for six hours post-procedure. Duration of hydration varied from one to 12 hours pre-procedure and four to 12 hours post-procedure. The mean age of participants ranged from 47 to 75 years. The proportion of males varied from 30% to 94%. The proportion of diabetic patients ranged from 24% to 57%.

Three reviewers identified studies for inclusion. Disagreements were resolved by consensus.

Assessment of study quality
Study quality was assessed using the Jadad scale of up to five points based on criteria of blinding, randomisation and withdrawals/drop-outs.

The number of reviewers involved at this stage of the review process was not reported.

Data extraction
Data were extracted to calculate risk ratios (RRs) with 95% CIs for the outcome of interest (development of CI-AKI).

The number of reviewers involved at this stage of the review process was not reported.

Methods of synthesis
Risk ratios with 95% CIs were pooled using a DerSimonian and Laird random-effects method. Statistical heterogeneity
was assessed using Q and I$^2$ statistics. Sensitivity analyses were used to assess the effect of study quality and clinical heterogeneity on outcomes using random-effects meta-regression. Meta-regression was also used to analyse effects of study size and publication status. Funnel plots were used to investigate publication bias.

**Results of the review**

Fourteen studies (n=2,320, sample size range 18 to 502) were included in the review (total sample size reported as 2,290 in parts of the review). One study received a Jadad score of 5 points, one study achieved 4 points and the others scored 3 points or fewer. No further study quality details were reported.

**CI-AKI**: The reviewers presented risk ratios from each study, but did not pool them overall, citing statistical heterogeneity (p=0.02, I$^2$=48%) as the reason. Statistical heterogeneity was largely related to study size. Within a subgroup of the 12 smallest trials (n=1,145), the authors found a pooled risk ratio that favoured bicarbonate over saline (RR 0.50, 95% CI 0.27 to 0.93) in a subgroup with substantial statistical heterogeneity (I$^2$=56%). Within a subgroup of the three largest trials (n=1,175), which had lower statistical heterogeneity I$^2$=0%), the pooled risk ratio was not statistically significant.

A range of other results related to changes in serum creatinine, effect of baseline risk and renal replacement therapy were reported. Sensitivity analyses indicated the results were not significantly affected by any single study. The authors interpreted a funnel plot as indicating some asymmetry and thus risk of publication bias.

**Authors’ conclusions**

Among the large randomised trials there was no evidence of benefit for hydration with sodium bicarbonate compared with sodium chloride for the prevention of CI-AKI. The benefit of sodium bicarbonate was limited to small trials of lower methodological quality.

**CRD commentary**

This review addressed a clear review question and used potentially reproducible study selection criteria. The search was thorough, had no date and language restrictions and included efforts to identify unpublished studies. Sufficient primary study details were provided, which increased the interpretation of generalisability of the results. A standard and appropriate tool was used to assess study quality. The number of reviewers who conducted the quality assessment and data extraction was not reported, so reviewer error and bias could not be ruled out. The quality of included studies was mixed. The proposed method of synthesis appeared appropriate, but the decision not to pool the main outcome due to moderate statistical heterogeneity was not explained fully.

The conclusion was based on a subgroup of trials of suboptimal quality and so may have been underpowered to detect differences between groups. As a result, readers should be careful not to interpret no evidence of benefit as evidence of no benefit. Given the low quality of included studies, poor reporting of the review process and questions regarding the synthesis, the reliability of the conclusions is unclear.

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

**Practice**: The authors stated that if sodium bicarbonate was effective, the treatment benefit was likely considerably smaller than that suggested by published positive trials.

**Research**: The authors stated that trials powered to detect an even larger difference in CI-AKI may be markedly underpowered and in search of a treatment benefit that was not likely to be clinically plausible; to detect a risk ratio of 0.85, a definitive trial with 90% power would require almost 10,000 patients. A large RCT was needed to look at concomitant use of N-acetylcysteine.

**Funding**

None stated.

**Bibliographic details**

PubMedID
19713291

DOI
10.2215/CJN.03120509

Original Paper URL
http://cjASN.asnjournals.org/content/4/10/1584.abstract

Other URL
http://ukpmc.ac.uk/abstract/MED/19713291

Indexing Status
Subject indexing assigned by NLM

MeSH
Acute Disease; Contrast Media /adverse effects; Creatinine /blood; Humans; Kidney /drug effects; Publication Bias; Randomized Controlled Trials as Topic; Renal Replacement Therapy; Risk; Sodium Bicarbonate /therapeutic use

AccessionNumber
12010000864

Date bibliographic record published
04/08/2010

Date abstract record published
16/03/2011

Record Status
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.