Meta-Analysis of Sodium Bicarbonate Therapy for Prevention of Cardiac Surgery-Associated Acute Kidney Injury

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Objective: **The aim of this study was to determine whether or not perioperative administration of sodium bicarbonate had a preventive effect on cardiac surgery-associated acute kidney injury (CSA-AKI) as shown in randomized controlled trials.**

Design: **The authors conducted a systematic review and meta-analysis using MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), and KoreaMed.**

Setting: **The authors searched MEDLINE, EMBASE, CENTRAL, and KoreaMed without language and date restrictions. They used both MeSH and free-text terms to identify relevant studies. Electronic searches were undertaken on July 31, 2014.**

Participants: **Five randomized controlled studies included in this review.**

Measurements and Main Results: **There were no differences in the development of CSA-AKI among patients in the sodium bicarbonate group compared with those in the control group (5 trials, 1,092 patients; n = 233 of 547 in sodium bicarbonate (SB) group versus 225 of 545 in control group (SC); risk ratio (RR), 0.95; 95% confidence interval (CI), 0.74-1.22. Also, there were no statistical differences in in-hospital mortality (3 trials, 573 patients; n = 21 of 288 in SB versus 14 of 285 in SC; RR, 1.44; 95% CI, 0.76-2.72), need for renal replacement therapy (4 trials, 1,000 patients; n = 21 of 503 in SB versus 23 of 497 in SC; RR, 0.90; 95% CI, 0.50-1.60), length of stay in the intensive care unit (ICU) (hours) (4 trials, n = 969 patients, weighted men difference (WMD), 2.17; 95% CI, -1.15-5.49), and length of ventilation (hours) (4 trials, 969 patients; WMD, 0.34; 95% CI, −0.80-1.48).**

Conclusions: **Perioperative administration of sodium bicarbonate did not reduce the rate of CSA-AKI in randomized controlled trials. Therefore, use of perioperative administration of sodium bicarbonate for the prevention of CSA-AKI is questionable.**

KEY WORDS: acute kidney injury, cardiac surgery, sodium bicarbonate

CARDIAC SURGERY-ASSOCIATED acute kidney injury (CSA-AKI) is a common and serious postoperative complication following exposure to cardiopulmonary bypass (CPB). It has been reported to occur in 8.9% to 39% of cardiac surgery patients who undergo surgery with CPB.[1] This is related to increased mortality, morbidity, and hospital cost.[1] In addition, CSA-AKI is the second most common cause of acute kidney injury (AKI) in the intensive care unit (ICU).[2]

The pathogenetic features of CSA-AKI are complex and multifactorial. There are several intraoperative elements of CSA-AKI following CPB, including hypoperfusion, ischemia-reperfusion injury, decreased oxygen supply by hemodilution, activation of systemic inflammatory pathways, exogenous catecholamines, release of reactive oxygen species, and release of free hemoglobin and iron. These can reduce arterial oxygen content or impair renal oxygen delivery and contribute to AKI.[3] Small microemboli formed during CPB can damage renal capillaries directly.[4] Also, hemolysis and release of free hemoglobin may result in a variety of serious sequelae such as increased vascular resistance, altered coagulation activity, platelet dysfunction, and renal tubular injury.[1]

The exact mechanism of how sodium bicarbonate might be helpful to reduce AKI after CPB has not been revealed clearly, but there was a report that sodium bicarbonate reduces acidification of the urine and the renal medulla and, thus, decreases free radical production to protect the kidneys from injury.[5]

Therefore, in this meta-analysis, the authors' primary objective was to evaluate the effect of sodium bicarbonate in the prevention of CSA-AKI. Authors decided to include only randomized controlled trials (RCTs).

MATERIALS AND METHODS

This study was based on the Cochrane Review Methods. The authors report their findings according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.

Data and Literature Sources

The authors searched MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), and KoreaMed without language and date restrictions. They used both MeSH and free-text terms to identify relevant studies. Electronic searches were undertaken on July 31, 2014.

The following keywords were searched: "Sodium Bicarbonate," "Cardiac Surgical Procedures," or "Cardiopulmonary Bypass and Sodium Chloride". Search strategies were adapted for other databases based on the MEDLINE strategy (the authors present search terms in the Appendix). After the initial electronic search, they manually searched reference lists of identified studies to look for relevant studies their electronic searches might have missed. They also searched ClinicalTrials.gov to identify ongoing studies.

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Study Selection

Two reviewers (J.Y.K. and J.H.K.) independently screened titles and abstracts for eligible studies. If eligibility could not be determined, the authors screened the full text.

Inclusion criteria for studies were as follows: Studies were randomized controlled trials for prevention of CSA-AKI; conducted during cardiac surgery the intervention was perioperative infusion with sodium bicarbonate versus sodium chloride. Final inclusion of studies was based on the agreement of both reviewers.

Data Collection

From eligible randomized controlled trials, 2 reviewers independently collected information on study characteristics using a predesigned data extraction form. Any discrepancy unresolved by discussion was put under the review of a third author.

The following variables were extracted from studies: AKI, mortality, need for renal replacement therapy, length of ventilation, length of stay in the ICU, and length of stay in the hospital. Dichotomous data (AKI, mortality, need for renal replacement therapy) were analyzed using the risk ratio (RR) measure and its 95% confidence interval (CI), and continuous variables (length of ventilation, length of stay in the ICU, length of stay in the hospital) were analyzed using the weighted mean difference and its 95% CI.

Assessment of Methodologic Quality

The authors used the Cochrane Collaboration's tool (sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, other sources of bias) to assess the risk of bias of randomized controlled trials. Two blinded reviewers independently assessed the risk of bias for each study. Disagreements were resolved by discussion between the reviewers.

The authors did not assess publication bias because of the low statistical power when the number of included studies was fewer than 10.

Statistical Analysis

The primary outcome of the authors' review was the difference in the presence of CSA-AKI between patients treated with sodium bicarbonate and those treated with sodium chloride. Secondary outcomes were mortality, the length of stay in the ICU, length of stay in the hospital, length of time on artificial ventilation, and whether or not postoperative renal replacement therapy was required. The presence of AKI, mortality, and postoperative renal replacement therapy were

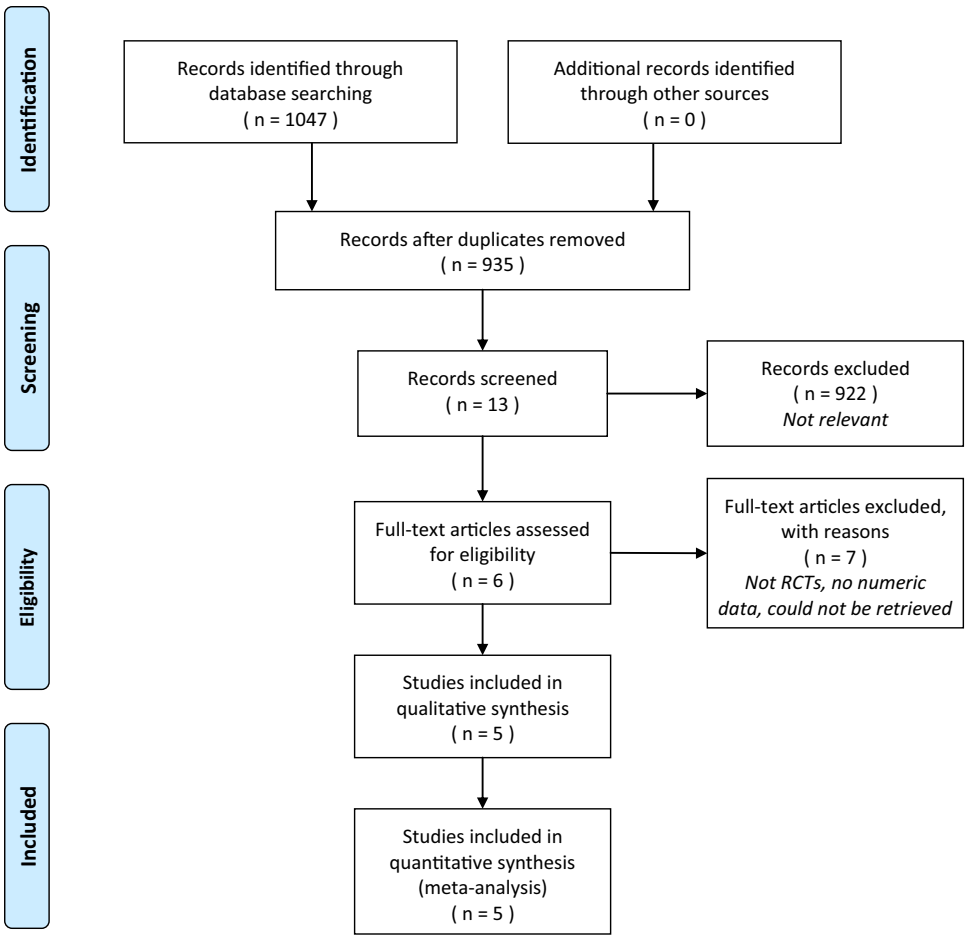

Fig 1. Study flowchart.