BJA

British Journal of Anaesthesia, 117 (4): 450–7 (2016)

doi: 10.1093/bja/aew256
Cardiovascular

Sodium bicarbonate does not prevent postoperative acute kidney injury after off-pump coronary revascularization: a double-blinded randomized controlled trial

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Abstract

Background: Acute kidney injury (AKI) is a common morbidity after off-pump coronary revascularization. We investigated whether perioperative administration of sodium bicarbonate, which might reduce renal injury by alleviating oxidative stress in renal tubules, prevents postoperative AKI in off-pump coronary revascularization patients having renal risk factors.

Methods: Patients (n=162) having at least one of the following AKI risk factors were enrolled: (i) age >70 yr; (ii) diabetes mellitus; (iii) chronic renal disease; (iv) congestive heart failure or left ventricular ejection fraction <35%; and (v) reoperation or emergency. Patients were evenly randomized to receive either sodium bicarbonate (0.5 mmol kg^{-1} for 1 h upon induction of anaesthesia followed by 0.15 mmol kg^{-1} h^{-1} for 23 h) or 0.9% saline. Acute kidney injury within 48 h after surgery was assessed using the Acute Kidney Injury Network criteria.

Results: The incidences of AKI were 21 and 26% in the bicarbonate and control groups, respectively (P=0.458). Serially measured serum creatinine concentrations and perioperative fluid balance were also comparable between the groups. The length of postoperative hospitalization and incidence of morbidity end points were similar between the groups, whereas significantly more patients in the bicarbonate group required prolonged mechanical ventilation (>24 h) relative to the control group (20 *vs* 6, P=0.003).

Conclusions: Perioperative sodium bicarbonate administration did not decrease the incidence of AKI after off-pump coronary revascularization in high-risk patients and might even be associated with a need for prolonged ventilatory care.

Clinical trial registration: NCT01840241.

Key words: acute kidney injury; cardiac surgery; coronary artery bypass; off-pump; sodium bicarbonate

Accepted: May 26, 2016

Editors' key points

- Previous studies show that sodium bicarbonate administration might protect the kidneys.
- The authors thus performed a randomized controlled trial among patients undergoing off-pump coronary revascularization.
- Included patients had one or more risk factors for acute kidney injury.
- Sodium bicarbonate use did not reduce the incidence of kidney injury.

Acute kidney injury (AKI) is a frequent complication of cardiac surgery that adversely affects prognosis.[1 2] Unfortunately, there are no established treatments for AKI, and research is focused mainly on the prevention of AKI.

The pathogenesis of cardiac surgery-induced AKI is complex, and apart from the patient's risk factors, it has been predominantly attributed to cardiopulmonary bypass (CPB)-induced systemic inflammation, ischaemia–reperfusion injury, haemolysis, and microembolism.[3] Nonetheless, despite the avoidance of CPB, the incidence of postoperative AKI is not reduced in off-pump coronary bypass surgery (OPCAB) relative to on-pump surgeries.[4] Off-pump coronary bypass surgery involves inevitable periods of heart displacement and regional myocardial ischaemia–reperfusion injury causing haemodynamic deterioration,[5] thereby exposing the kidney to oxidative stress.

Sodium bicarbonate infusion has a renoprotective effect by reducing oxidative stress in renal tubular cells.[6–8] The proposed mechanisms include attenuation of free radical generation, direct peroxynitrite scavenging, and urinary alkalinization.[7 9] In conjunction, a pilot study in cardiac surgical patients undergoing CPB showed renoprotective effects of sodium bicarbonate infusion.[10] In order to attenuate contrast-induced AKI, in which oxidative stress also plays a major role as in AKI after OPCAB, the recent guideline by the Acute Kidney Injury Work Group and Canadian Association of Radiologists recommends i.v. bicarbonate infusion.[11] In contrast, several trials have reported that i.v. bicarbonate infusion failed to prevent AKI after cardiac surgery[12] or contrast-induced AKI in high-risk patients.[13]

So far, evidence regarding the renoprotective effect of sodium bicarbonate seems inconsistent, depending on the clinical scenario. Nonetheless, despite a high prevalence of AKI after OPCAB, renoprotective efficacy of sodium bicarbonate in OPCAB has not previously been addressed.

In this double-blind randomized controlled trial, we investigated whether perioperative i.v. sodium bicarbonate administration reduces the occurrence of postoperative AKI in OPCAB patients having renal risk factors.

Methods

The present study was registered at clinicaltrials.gov (NCT01840241) after approval by the institutional review board. All participants gave written informed consent before their surgeries. Patient flow is reported using the Consolidated Standards of Reporting Trials (CONSORT) recommendation. Patients undergoing elective OPCAB were included when they had one or more of the following risk factors: (i) advanced age (>70 yr); (ii) diabetes mellitus; (iii) congestive heart failure, defined as New York Heart Association class ≥III or low left ventricular ejection fraction (<35%); (iv) pre-existing chronic renal disease (estimated glomerular filtration rate using modification of diet in renal disease formula 30–89 ml min^{-1} 1.73 m^{-2}); or (v) reoperation or emergency. Patients were excluded for the following reasons: (i) pre-existing acute renal failure; history of renal replacement therapy, or both; (ii) steroid therapy (>10 mg day^{-1} prednisone or equivalent); (iii) pre-existing hypernatremia, alkalosis, or severe pulmonary oedema; or (iv) pre-existing anaemia (haemoglobin <10 mg dl^{-1}).

Between April 2013 and September 2015, 162 patients were evenly randomized to the sodium bicarbonate or the control group by a computer-generated randomization list using a permuted two-block strategy. Concealment of group allocation to attending physicians, intensivists, nurses, patients, and investigators was ensured by using non-transparent envelopes. Envelopes were opened on the morning of surgery by an anaesthetic nurse who was not involved in the patient's care, who would prepare 154 mequiv l^{-1} of sodium bicarbonate in H_2O or 0.9% sodium chloride according to the group allocation.

Intervention and study protocol

After the insertion of a pulmonary artery catheter, patients in the sodium bicarbonate group received an i.v. dose of 0.5 mmol kg^{-1} for 1 h followed by continuous infusion of 0.15 mmol kg^{-1} h^{-1} during 23 h. Patients in the control group received the same volume of 0.9% sodium chloride instead.

Standard monitoring during surgery included an arterial catheter, a Swan–Ganz catheter (Swan-Ganz CCombo CCO/SvO_2; Edwards Lifesciences, Irvine, CA, USA), and transoesophageal echocardiography. Anaesthesia was induced with midazolam i.v., sufentanil i.v., and rocuronium i.v. and maintained with inhalation of sevoflurane and continuous infusion of sufentanil and vecuronium. Grading of aortic atherosclerosis (Katz) was done using transoesophageal echocardiography.[14] Proximal anastomosis at the ascending aorta was carried out without side-clamping using the Heartstring Proximal Seal System (Guidant, Indianapolis, IN, USA) after visual confirmation by epiaortic ultrasonography.

During surgery, patients received balanced crystalloid (Plasma solution A 1000 inj; CJ, Seoul, Korea) at 6 ml kg^{-1} h^{-1}, and balanced synthetic colloid (Volulyte; Fresenius Kabi, Bad Homburg, Germany) was infused to replace estimated blood loss at a maximal dose of 1000 ml. Intraoperative blood loss was estimated by the amount of collected blood through a cell-saving device, which was infused into the patient before leaving the operating room. Target mean arterial pressure (MAP) was >70 mm Hg, which was achieved by norepinephrine infusion and a 5–10° Trendelenburg position during grafting. Subsequently, vasopressin was added if the target MAP could not be achieved, in a stepwise additive fashion. Milrinone (0.5 μg kg^{-1} min^{-1}) was infused when there was a persistent decrease in mixed venous oxygen saturation (Sv_{O_2} <60% for more than 10 min) or newly developed severe (grade ≥3) mitral regurgitation. Allogeneic packed erythrocytes (pRBCs) were transfused when the haematocrit was decreased to <25% throughout the study period.

After surgery, all participants were managed in the intensive care unit (ICU) by the institutional standardized protocols, which are as follows. In brief, crystalloid solution at 2–3 ml kg^{-1} h^{-1} was infused for maintenance. Blood loss (amount of chest tube drainage) was replaced either with colloid solution (<20 ml kg^{-1} day^{-1}) or with pRBCs depending on the haematocrit targeted at ≥25%. If the cardiac index declined below 2.0 litre min^{-1} m^{-2}, 200 ml of crystalloid was challenged. Milrinone (0.3–0.7 μg kg^{-1} min^{-1}) was used when the cardiac index was <2.0 litre min^{-1} m^{-2} for longer than 30 min despite adequate heart rate, haematocrit, and preload. Any MAP <70 mm Hg was treated with norepinephrine infusion. If the target MAP could not be reached with