BJA

British Journal of Anaesthesia, 115 (5): 736–42 (2015)

doi: 10.1093/bja/aev346
Clinical Practice

Effects of acute plasma volume expansion on renal perfusion, filtration, and oxygenation after cardiac surgery: a randomized study on crystalloid *vs* colloid

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Abstract

Background: In the present randomized study, we evaluated the differential effects of a colloid and a crystalloid fluid on renal oxygen delivery (RD_{O_2}), glomerular filtration (GFR), renal oxygen consumption ($R\dot{V}O_2$), and the renal oxygen supply–demand relationship (i.e. renal oxygenation) after cardiac surgery with cardiopulmonary bypass.

Methods: Thirty patients with normal preoperative renal function, undergoing uncomplicated cardiac surgery, were studied in the intensive care unit in the early postoperative period. Patients were randomized to receive a bolus dose of either a crystalloid (Ringers-acetate® 20 ml kg^{-1}, *n*=15) or a colloid solution (Venofundin® 10 ml kg^{-1}, *n*=15). Systemic haemodynamics were measured via a pulmonary artery catheter. Renal blood flow and GFR were measured by the renal vein retrograde thermodilution technique and by renal extraction of ^{51}Cr-EDTA (=filtration fraction). Arterial and renal vein blood samples were obtained for measurements of renal oxygen delivery (RD_{O_2}) and $R\dot{V}O_2$. Renal oxygenation was estimated from the renal oxygen extraction.

Results: Despite an increase in cardiac index and renal blood flow with both fluids, neither of the fluids improved RD_{O_2}, because they both induced haemodilution. The GFR increased in the crystalloid (28%) but not in the colloid group. The crystalloid increased the filtration fraction (24%) and renal oxygen extraction (23%), indicating that the increase in GFR, the major determinant of $R\dot{V}O_2$, was not matched by a proportional increase in RD_{O_2}.

Conclusions: Neither the colloid nor the crystalloid improved RD_{O_2} when used for postoperative plasma volume expansion. The crystalloid-induced increase in GFR was associated with impaired renal oxygenation, which was not seen with the colloid.

Clinical trial registration: NCT01729364.

Key words: colloids; crystalloids; glomerular filtration rate; plasma volume expansion; postoperative treatment; renal blood flow; renal oxygen consumption and oxygenation

Acute kidney injury (AKI) after cardiac surgery with cardiopulmonary bypass continues to be a significant cause for morbidity and mortality. Depending on the complexity of the procedure, the incidence of postoperative AKI, defined as an increase of serum creatinine by >50%, ranges between 15 and 30%.[1–4] Dialysis-dependent AKI, occurring in 2–5% of cardiac surgery patients,

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Accepted: August 31, 2015

Editor's key points

- Acute kidney injury is one major postoperative complication after cardiac surgery with cardiopulmonary bypass, and it is not known whether or not there are differences in renal oxygen delivery between plasma volume expansion with crystalloid and colloid.
- In a randomized design, effects on renal oxygen delivery and other renal factors were compared between plasma volume expansion with crystalloid and colloid.
- Neither colloid nor crystalloid improved renal oxygen delivery, but crystalloid, but not colloid, increased the GFR with impaired renal oxygenation.

carries a mortality between 50 and 80% and is associated with high hospital costs.[5–7] Furthermore, increasing evidence suggests that a minor elevation in serum creatinine after cardiac surgery is an independent risk factor for increased mortality and for prolonged stay in the intensive care unit and in hospital.[6 8 9]

The pathogenesis of cardiac surgery-associated AKI involves a variety of pathways.[10] Impaired renal oxygen delivery (RD_{O_2}), causing ischaemic tubular cell injury, has been considered to be one of the main mechanisms underlying postcardiac surgery AKI.[11] A decreased oxygen delivery may be caused by haemodilution-induced anaemia and intraoperative hypotension together with low postoperative cardiac output, in turn caused by heart failure or hypovolaemia.[3 12–14] The renal medulla, particularly the outer portion, is on the verge of hypoxia even in normal conditions. This is caused by the high utilization of oxygen of the medullary thick ascending limb and a relative medullary hypoperfusion, when compared with the cortex. The outer portion of the renal medulla is therefore particularly sensitive to impaired RD_{O_2}.[15]

I.V. fluids, such as colloids or crystalloids, are commonly used for treatment of postoperative hypovolaemia after cardiac or other major surgery, to prevent or ameliorate early AKI.[16] However, even though i.v. fluids may increase cardiac output and renal blood flow (RBF), they will also decrease arterial oxygen content by haemodilution, with potentially no or minor beneficial net effects on RD_{O_2}. Indeed, recent animal studies have shown that colloids or crystalloids do not increase RD_{O_2} despite increases in cardiac output and that crystalloids, in contrast to colloids, may impair regional renal microvascular oxygenation.[17 18]

To our knowledge, the effects of i.v. fluids on RD_{O_2} and renal oxygenation have not been studied in postoperative patients after major surgery. Furthermore, perioperative data on the differential effects of crystalloids *vs* colloids with respect to RBF, RD_{O_2}, glomerular filtration rate (GFR), renal oxygen consumption ($R\dot{V}O_2$), and renal oxygenation, defined as the renal oxygen supply–demand relationship, are lacking. We therefore performed a randomized study to evaluate the differential renal effects of bolus doses of a crystalloid and a colloid. In the present study, we tested the null hypothesis that there is no difference between a crystalloid and a colloid with respect to changes in RD_{O_2} and renal oxygenation after major surgery.

Methods

Patients

The study protocol was approved by the Gothenburg Regional Ethics Committee (www.epn.se). Written informed consent was obtained from each patient before the operation. The study was registered in ClinicalTrials.gov, identifier: NCT01729364. The inclusion criteria were as follows: (i) age >18 yr; (ii) elective coronary artery bypass surgery with cardiopulmonary bypass; (iii) preoperative normal serum creatinine; (iv) left ventricular ejection ≥40%; and (v) attainment of target levels of central venous pressure (5–10 mm Hg), mean arterial pressure (MAP; >70 mm Hg), and mixed venous oxygen saturation (Sv_{O_2}; >60%) before randomization, according to our local clinical treatment protocol. The exclusion criteria were as follows: (i) combined cardiac surgery procedures; (ii) excessive postoperative bleeding (>100 ml h^{-1}); (iii) intra- or postoperative need for inotropic or vasoactive support or diuretics (furosemide, mannitol); or (iv) hypotension because of arrhythmias.

Premedication consisted of oxazepam (10 mg) and oxycodone (10 mg). Anaesthesia was induced by fentanyl (5–10 μg kg^{-1}) and propofol (1–1.5 mg kg^{-1}). Before and after cardiopulmonary bypass, anaesthesia was maintained with sevoflurane (0.5–2.5%) in a 50% O_2–air mixture. During cardiopulmonary bypass, anaesthesia was maintained with an i.v. infusion of propofol (2–4 mg kg^{-1} h^{-1}). The pump was primed with acetated Ringer's solution (1300 ml) without mannitol. Normothermic, non-pulsatile cardiopulmonary bypass was performed at a flow of 2.4 litres min^{-1} m^{-2} and a target haematocrit of 20–25%. In the intensive care unit, the patients were sedated with propofol (1.5–3.6 mg kg^{-1} h^{-1}) and morphine (0.5–1 mg h^{-1}) and mechanically ventilated.

Systemic haemodynamics

Arterial blood pressure was measured continuously via a radial or femoral artery catheter. A pulmonary artery thermodilution catheter (Baxter Healthcare Corporation, Irvine, CA, USA) was used for measurements of central venous pressure, pulmonary artery and wedge pressures and cardiac output. Bolus measurements of thermodilution cardiac output were performed in triplicate and indexed to the body surface area for cardiac index (CI). Systemic vascular resistance index, pulmonary vascular resistance index, and stroke volume index (SVI) were calculated according to standard formulae.

Measurements of renal variables

An 8 Fr catheter (Webster laboratories, Baldwin Park, CA, USA) was introduced into the left or right renal vein, via the right femoral vein under fluoroscopic guidance. The catheter was placed in the central portion of the renal vein, with the position being confirmed by venography using ultra-low doses of iohexol, 5–15 mg I kg^{-1} (Omnipaque 300 mg I ml^{-1}; GE Healthcare, Stockholm, Sweden). Renal blood flow was measured in duplicate by the continuous retrograde thermodilution technique.[19–22] At the end of each urine collection period, the bladder was rinsed with 100 ml of sterile water. After the collection of blood and urine blanks, an i.v. priming dose of chromium ethylenediaminetetraacetic acid (^{51}Cr-EDTA; GE Healthcare, Amersham, UK) was given, followed by an infusion at a constant rate, individualized to body surface area and preoperative serum creatinine. Serum ^{51}Cr-EDTA activity from arterial and renal vein blood was measured using a well counter (Wizard 3', 1480, Automatic gamma counter; Perkin Elma LAS, Turkuu, Finland).

Experimental procedure

The experimental procedure was performed 4–6 h after the end of cardiopulmonary bypass when the patients had a stable body