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Clinical Practice

Effects of intraoperative and early postoperative normal saline or Plasma-Lyte 148® on hyperkalaemia in deceased donor renal transplantation: a double-blind randomized trial

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Abstract

Background. Administration of saline in renal transplantation is associated with hyperchloraemic metabolic acidosis, but the effect of normal saline (NS) on the risk of hyperkalaemia or postoperative graft function is uncertain.
Methods. We compared NS with Plasma-Lyte 148® (PL) given during surgery and for 48 h after surgery in patients undergoing deceased donor renal transplantation. The primary outcome was hyperkalaemia within 48 h after surgery. Secondary outcomes were need for hyperkalaemia treatment, change in acid–base status, and graft function.
Results. Twenty-five subjects were randomized to NS and 24 to PL. The incidence of hyperkalaemia in the first 48 h after surgery was higher in the NS group; 20 patients (80%) *vs* 12 patients (50%) in the PL group (risk difference: 0.3; 95% confidence interval: 0.05, 0.55; $P=0.037$). The mean (SD) peak serum potassium was NS 6.1 (0.8) compared with PL 5.4 (0.9) mmol litre^{-1} ($P=0.009$). Sixteen participants (64%) in the NS group required treatment for hyperkalaemia compared with five (21%) in the PL group ($P=0.004$). Participants receiving NS were more acidaemic [pH 7.32 (0.06) *vs* 7.39 (0.05), $P=0.001$] and had higher serum chloride concentrations (107 *vs* 101 mmol litre^{-1}, $P<0.001$) at the end of surgery. No differences in the rate of delayed graft function were observed. Subjects receiving PL who did not require dialysis had a greater reduction in creatinine on day 2 ($P=0.04$).
Conclusions. Compared with PL, participants receiving NS had a greater incidence of hyperkalaemia and hyperchloraemia and were more acidaemic. These biochemical differences were not associated with adverse clinical outcomes.
Clinical trial registration. Australian New Zealand Clinical Trials Registry: ACTRN12612000023853.

Key words: acidosis; crystalloid solutions; delayed graft function; fluid therapy; hyperkalaemia; kidney transplantation; isotonic solutions; Plasma-lyte 148; sodium chloride

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Editor's key points

- Hyperkalaemia is a common and potentially severe complication of cadaveric kidney transplantation.
- Normal saline is commonly used as a potassium-free i.v. fluid therapy, but can cause hyperchloraemic acidosis and subsequent hyperkalaemia.
- In a randomized trial in deceased donor kidney transplant recipients, intraoperative and early postoperative use of normal saline was associated with more hyperkalaemia, hyperchloraeamia, and acidosis compared with a balanced i.v. fluid.

Hyperkalaemia is a common complication of kidney transplantation, occurring in 25–40% of recipients.[1–3] Although the outcomes of severe postoperative hyperkalaemia in kidney transplantation are not well studied, adverse consequences of hyperkalaemia in this setting include significant haemodynamic and neurological effects that result in respiratory paralysis or cardiac arrest if not treated urgently.[4 5] The aims of perioperative fluid administration in deceased donor renal transplantation include maintenance of adequate kidney transplant perfusion and the avoidance of electrolyte and acid–base disturbances, including hyperkalaemia.[6] Sodium chloride 0.9%, known as normal saline (NS), is potassium free and, partly for this reason, is the current standard of care for i.v. fluid therapy for kidney transplantation.[7]

Despite the preferential use of NS in renal transplantation, previous studies in live donor[2 8–11] and deceased donor renal transplant recipients[12] report that NS causes hyperchloraemic metabolic acidosis, which can increase the risk of hyperkalaemia. Significant geographical, institutional, and subspecialty variation persists regarding fluid therapy,[13] highlighting the uncertainty and paucity of evidence-based data surrounding the choice of best fluid in renal transplant recipients. Accordingly, we performed a double-blinded randomized trial comparing the effects of intraoperative and early postoperative NS or acetate-buffered crystalloid solution (Plasma-Lyte 148®; Baxter Healthcare, Toongabbie, NSW, Australia; PL) on hyperkalaemia, the need for hyperkalaemia treatment, acid–base status, and graft function in patients receiving a deceased donor renal transplant.

Methods

The Austin Health Research and Ethics Committee approved this study (HREC no. H2011/04526). The trial was prospectively registered with the Australian New Zealand Clinical Trials Registry (ACTRN12612000023853). Between September 2012 and April 2015, the trial was conducted at Austin Hospital, a university teaching hospital in Melbourne with expertise in renal transplantation. Inclusion criteria included adult patients (age $\geq$18 yr) undergoing deceased donor renal transplantation. Exclusion criteria included preoperative hyperkalaemia $>$6.0 mmol litre^{-1} that was not corrected before transplantation, pregnancy, chronic liver disease (liver function tests $>$1.5 times normal value), known allergic reaction to study solutions, and patients undergoing multi-organ transplantation. All participants provided written informed consent.

A statistician generated a computerised randomization sequence of 50 allocation codes, 25 for each group. Independent research staff sealed the allocation codes into sequentially-numbered opaque envelopes. The sequence was decoded after data analysis. Study participants, anaesthetists, surgeons, nephrologists and all perioperative clinicians and renal nursing staff caring for patients were blinded to the trial fluid intervention. Baxter Healthcare (Toongabbie, NSW, Australia) provided either NS or PL as 1000 ml identical blinded carrier solution containers. The PL contained sodium (140 mmol litre^{-1}), potassium (5 mmol litre^{-1}), magnesium (3 mmol litre^{-1}), chloride (98 mmol litre^{-1}), acetate (27 mmol litre^{-1}), and gluconate (23 mmol litre^{-1}). The NS contained sodium (154 mmol litre^{-1}) and chloride (154 mmol litre^{-1}).

Before surgery, all subjects were fasted for a minimum of 2 h for clear fluids and 6 h for solids. Immediately upon arrival in the operating room, subjects were randomized. After preoxygenation, general anaesthesia was induced using propofol (1–3 mg kg^{-1} i.v.), fentanyl (1–3 μg kg^{-1} i.v.), and cisatracurium (0.15–0.2 mg kg^{-1} i.v.). Anaesthesia was maintained with sevoflurane or desflurane in a 50:50 oxygen–air mixture, maintaining a bispectral index of 40–60. Additional doses of fentanyl and cisatracurium were administered as appropriate.

All participants were prescribed a minimum of 2000 ml trial fluid during surgery, in accordance with Victorian Kidney Transplant Collaborative Renal Transplant Protocol. There was no standardized hourly rate, and the timing of fluid administration was at the discretion of the anaesthetist. Additional trial fluid boluses were permitted, with the rate, timing, and number of boluses individualized and based on estimates of surgical blood loss. Electrocardiography, pulse oximetry, capnography, blood pressure, urine output, and core body temperature were monitored. Use of invasive arterial blood pressure monitoring was at the discretion of the anaesthetist. Measurement of central venous pressure (CVP) was not used for the assessment of volume responsiveness because of the very poor relationship between CVP and blood volume and the inability of CVP or change in CVP to predict haemodynamic response to a fluid challenge. Other advanced haemodynamic monitoring devices were not used. Mean arterial pressure was maintained within 20% of the baseline preoperative value and supported with vasoactive therapy where appropriate. Open-label fluids (dextrose 5%, colloids, or blood products) were used at the discretion of the anaesthetist. Blood was transfused for haemoglobin $<$80 g litre^{-1}, or $<$90 g litre^{-1} when further bleeding was anticipated. During surgery, the patient's temperature was kept constant at 36 °C with a forced air-warming device, and arterial partial pressure of CO_2 was maintained at 35–40 mm Hg. Frusemide (125 mg i.v.) was administered 5 min before reperfusion according to standard institutional practice.

After surgery, all subjects received a maintenance infusion of trial fluid, with a starting rate of the previous hour's urine output plus 30 ml. The trial fluid was continued as the designated crystalloid fluid for the first 48 h after surgery. The treating medical staff could alter the rate of trial fluid administration as clinically required or cease the infusion if crystalloid therapy was no longer needed. Other open-label fluids or blood products could be given if required in the opinion of the treating doctor. Any additional fluid boluses of trial crystalloid solution could be administered to any patient if volume supplementation was required. After 48 h the study fluid ceased, and the rate and type of any further fluid was at the discretion of the treating clinician. Immunosuppression was according to the local standard of care, with a regimen of tacrolimus (0.15 mg kg^{-1} in divided doses initially and then adjusted to achieve a therapeutic trough tacrolimus concentration of 5–10 ng ml^{-1}), mycophenolate