

ORIGINAL ARTICLE

The use of mannitol in cardiopulmonary bypass prime solution—Prospective randomized double-blind clinical trial

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Background: The optimal prime solution for the cardiopulmonary bypass (CPB) circuit in adult cardiac surgery has not yet been defined. Mannitol is widely used in the priming solution for CPB despite the fact that there is no clear consensus on the role of mannitol in cardiac surgery. The aim of this study was to investigate the effect of mannitol in the CPB prime solution.

Methods: This prospective, randomized, double-blind study included 40 patients with normal cardiac and renal functions, who underwent coronary artery bypass grafting. One group received a prime based on Ringer's acetate ($n = 20$), and the other a prime consisting of Ringer's acetate with 200 mL mannitol ($n = 20$). Changes in osmolality, acid-base status, electrolytes, and renal-related parameters were monitored.

Results: No significant differences were found in osmolality between the Ringer's acetate group and the mannitol group at any time. The mannitol group showed a pronounced decrease in sodium, from 138.7 ± 2.8 mmol/L at anaesthesia onset, to 133.9 ± 2.6 mmol/L after the start of CPB ($P < .001$). No differences were seen in the renal parameters between the groups, apart from a short-term effect of mannitol on perioperative urine production ($P = .003$).

Conclusion: We observed no effects on osmolality of a prime solution containing mannitol compared to Ringer's acetate-based prime in patients with normal cardiac and renal function. The use of mannitol in the prime resulted in a short-term, significant decrease in sodium level.

1 | INTRODUCTION

The vast majority of patients undergoing cardiac surgery require circulatory assistance in the form of cardiopulmonary bypass (CPB). Maintenance of the acid-base homeostasis and normal electrolyte levels is of great importance during CPB.¹ A CPB circuit prime influences several organ systems, such as the central nervous system and the renal system, as well as coagulation, osmolality, and electrolyte levels, all this can impact the outcome after cardiac surgery.¹⁻⁵ However, the choice of CPB prime is usually based on personal preferences and historical beliefs.⁶ Significant differences in CPB techniques and priming worldwide were reported in a recent survey,

although the reasons for such differences and their impact on clinical outcome remain uncertain.⁷ There are still no guidelines regarding the choice of CPB prime solutions in general, or how a CPB prime should be customized for the characteristics and conditions of a specific patient.

CPB prime solutions are normally based on crystalloid fluids, and often contain mannitol, a 6-carbon natural alditol.^{7,8} Mannitol acts as a volume expander, it has an osmotic diuretic effect and may influence various organ systems.⁹ It has been reported in some studies that the risk of postoperative acute kidney injury maybe reduced using mannitol,^{10,11} whereas other studies have shown the opposite, reporting harmful effects on the kidneys due to the induction

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of acute renal tubular injury.¹²⁻¹⁴ One study reported no effect on clinical outcomes after removing mannitol from the priming solution, and only economic benefits were identified.¹⁵ There is thus no clear consensus regarding the use of mannitol during cardiac surgery, and there are only a few studies that have been carried out on the effects of using mannitol in CPB prime solutions.¹⁶ We therefore designed a prospective, randomized, double-blind study to investigate the effects of mannitol when it is used in the CPB prime solution. According to a recent report by Malmqvist et al, measuring plasma osmolality is a more exact way to determine electrolyte balance than calculated osmolality during CPB and it should be included in studies when the effect of CPB prime solutions is evaluated.¹⁷ Plasma osmolality was therefore measured in our study with the freezing point depression method as it is an accurate technique for determining osmolality.¹⁸

The overall aim of this study was to investigate the perioperative effect of mannitol in the CPB prime solution compared with a prime based on Ringer's acetate following cardiac surgery in patients with normal preoperative cardiac and renal functions. We also investigated the short-time postoperative outcome including renal function.

2 | METHODS

2.1 | Study design

This single-center, prospective study was designed as a randomized double-blind, control trial. The study was approved by the ethics committee of southern Sweden (no. 2017/442), and was also reported to ClinicalTrials.org, id: NCT03302286. We recruited 40 adult patients who were scheduled for elective isolated coronary artery bypass grafting (CABG) at the Department of Cardiothoracic Surgery, Anesthesia and Intensive Care, Skane University Hospital, Lund, Sweden. The flowchart for the study is presented in Figure 1. All patients were informed orally and in

Editorial comment

In this prospective randomized double-blind study, the addition of mannitol to a priming solution for cardiopulmonary bypass (CPB) resulted in an increased diuresis and decrease in sodium concentration, but no changes in osmolality, acid-base status or other electrolytes. While the study is underpowered to detect differences in clinical outcomes such as acute kidney injury, it questions the routine use of mannitol for CPB priming solution.

writing prior to surgery by the authors, and written consent was obtained for study participation and publishing of the results. Data collection started in September 2017 and was completed by March 2018. Twenty patients were allocated to each arm using the sealed envelope system. Coding was performed by non-study staff and code key was revealed after the end of data collection. Randomization was performed by non-study clinical staff who prepared the study solution and gave this to the blinded perfusionist. The inclusion criteria were as follows: normal left ventricular function, defined as a left ventricular ejection fraction on preoperative echocardiogram of at least 50%, and normal renal function, defined as estimated glomerular filtration rate (eGFR) greater than 60 mL/min. Exclusion criteria were patient weight less than 50 kg, preoperative hematocrit less than 24% and previous history of cardiac surgery. In our study, the eGFR was the mean of the relative eGFR based on creatinine and the relative eGFR based on cystatin C. The revised Lund-Malmö equation¹⁹ was used to calculate eGFR based on creatinine and the CAPA equation²⁰ was used to calculate eGFR based on cystatin C.

The Ringer's acetate group (n = 20) received a priming solution of Ringer's acetate (Baxter Medical AB, Lund, Sweden) 1200 mL with 10 000 units heparin (Heparin Leo[®], Leo Pharma) and 80 mmol

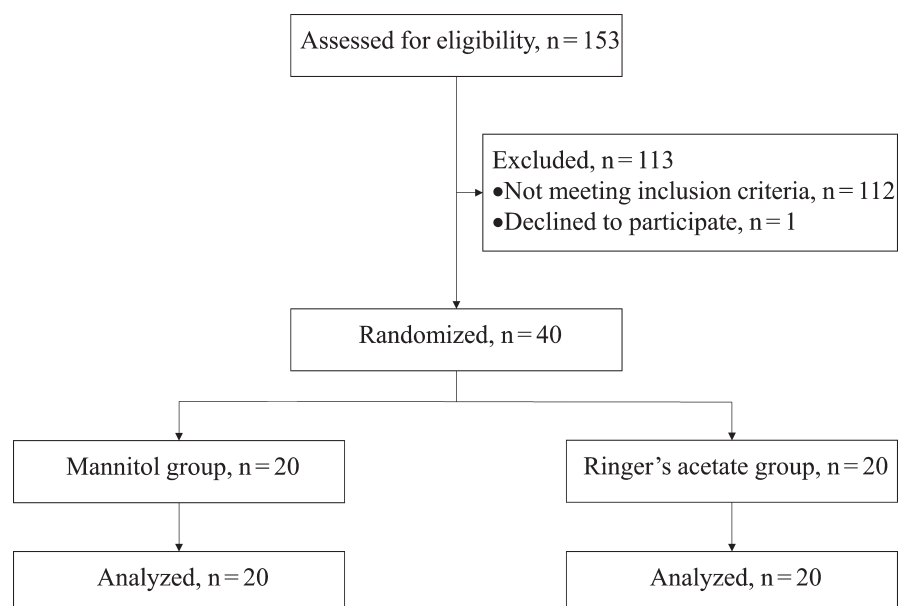


FIGURE 1 Flowchart of the study

sodium chloride (Fresenius Kabi AB). The mannitol group ($n = 20$) received a priming solution containing 1000 mL Ringer's acetate, 10 000 units heparin, and 80 mmol sodium chloride and 200 mL mannitol (Fresenius Kabi AB).

2.2 | Surgical and anesthesia protocol

All patients underwent a routine CABG through a median sternotomy. General anesthesia was induced with midazolam, fentanyl, and propofol, whereas relaxation was achieved with rocuronium. Intravenous anesthesia was maintained by propofol and fentanyl throughout the operation. The target blood pressure during CPB was 40–80 mm Hg, norepinephrine was used when needed. A maximum of 1000 mL of Ringer's acetate could be given intravenously by the anesthetic team during the operation. Heparin was administered during CPB at a dose calculated to give an activated clotting time of 480 seconds or more.

2.3 | Cardiopulmonary circuit

The CPB setup was identical for all patients. The equipment used consisted of a Stöckert S5[®] heart-lung machine (Sorin Group Japan Co., Ltd), a CAPIOX FX25 advanced oxygenator with an integrated arterial filter, and a hard-shell venous reservoir with a volume of 4000 mL (both from Terumo Cardiovascular Group), and a Stöckert 3T heater-cooler unit and a CSC14 cardioplegia heat exchanger (both from LivaNova).

2.4 | Perfusion protocol

Standard, non-pulsatile perfusion was performed with a target cardiac index of 2.4 L/min/m². Normothermia, defined as a body

temperature above 36°C, was maintained during CPB. If required, patients could be given a maximum of 1000 mL additional Ringer's acetate during CPB. Myocardial protection was achieved with cold blood cardioplegia. Shed blood was collected in the venous reservoir. After weaning from CPB the blood remaining in the CPB-system was transferred to a cell saver (AutoLog[®] Autotransfusion System, Medtronic) and after processing it was transfused back to the patient according to local routine.

2.5 | Data collection

Preoperative blood samples were obtained from peripheral antecubital vein the day before surgery, and analyzed at the hospital's biomedical laboratory. Peri- and postoperative blood analysis was carried out according to Table 1. Osmolality was determined using the freezing point depression method using a Fiske 210 Micro-Osmometer (Advanced Instruments Inc). Electrolytes and pH were measured in whole blood using a blood analyzer (ABL800 FLEX, Radiometer Medical ApS). Data on peri- and postoperative fluid balance, diuresis and whether any diuretics were given, were retrieved from the patients' records.

2.6 | Statistical analysis

Based on a change of 10 mOsm/kg in the osmolality and a standard deviation of 11 mOsm/kg,²¹ a significance level of 5%, and a power of 80%, it was estimated that 20 patients would be required in each of the groups. Continuous variables were expressed as the mean \pm 1 standard deviation, and categorical variables as percentages. Student's *t* test or Mann–Whitney *U* test was used where appropriate for continuous

Time point	Sampling site	Parameters analyzed
T0. Day before surgery	Peripheral antecubital vein	Creatinine, urea, eGFR, cystatin C
T1. Before the onset of anesthesia	Arterial cannula	Plasma osmolality, Cl, blood gas
T2. Three minutes after the administration of the cardioplegia	Sample line CPB	Plasma osmolality, Cl, blood gas
T3. 30 min after start of CPB	Sample line CPB	Plasma osmolality, Cl, blood gas
T4. 60 min after start of CPB	Sample line CPB	Plasma osmolality, Cl, blood gas
T5. 15 min after termination of CPB	Sample line CPB	Plasma osmolality, Cl, blood gas
T6. 30 min after arrival at ICU	Arterial cannula	Plasma osmolality, Cl, blood gas, creatinine, urea, eGFR, cystatin C
T7. Day 1	Arterial cannula	Plasma osmolality, Cl, blood gas, creatinine, urea, eGFR, cystatin C
T8. Day 4	Central venous catheter	Plasma osmolality, Cl, blood gas, creatinine, urea, eGFR, cystatin C
T9. Three months after CABG	Peripheral antecubital vein	Na, K, Cl, creatinine, urea, eGFR, cystatin C

TABLE 1 Time points and blood parameters analyzed

Abbreviations: CABG, coronary artery bypass grafting; Cl, chloride; CPB, cardiopulmonary bypass; eGFR, estimated glomerular filtration rate; ICU, intensive care unit.

variables. Categorical data were compared using the chi-squared test, or Fisher's exact test when the expected frequency was less than five. The paired-sample *t* test was used to compare changes in blood samples. A repeated-measurement, general linear model was used to test the main effect of prime solutions on osmolality, sodium, potassium, and chloride levels. Post hoc testing was performed using the Bonferroni correction. Criteria for post hoc testing were *P*-value < .05. Analysis of the residuals of the model was also performed to check for model adequacy regarding the assumptions of normality and heteroscedasticity. In cases where the residual assumptions were not met, variance stabilization transformation was performed. Statistical significance was defined as *P* < .05. Data analysis was performed using IBM SPSS Statistics, version 20.0.0 (Armonk, NY, USA).

3 | RESULTS

A total of 153 patients were screened. One patient declined to participate in the study and 112 patients did not meet inclusion criteria. In total 40 patients were randomized into either the Ringer's acetate group (*n* = 20) or the mannitol group (*n* = 20). All patients underwent CABG surgery due to coronary ischemic disease. The patients' baseline characteristics are given in Table 2. All patients had sinus rhythm preoperatively. There was no incidence of postoperative confusion or stroke. There was one reoperation in each group due to postoperative bleeding. The demographic

data did not differ significantly between the two groups except the postoperative length of stay at intensive care unit (Table 2). The 30-day survival was 100%.

3.1 | Osmolality and acid-base homeostasis

No significant differences in osmolality were found between the Ringer's acetate group and the mannitol group at any time (Supplementary figures). The mean osmolality for all 40 patients at T1 was 292.5 ± 5.2 mOsm/kg and rose significantly to 301.9 ± 4.1 mOsm/kg after starting CPB (T2) (*P* < .001). A significant decrease was seen in osmolality for all patients between T2 and day 4 (301.9 ± 4.1 mOsm/kg and 291.1 ± 5.9 mOsm/kg, respectively [*P* < .001]). There was no significant change in osmolality for all patients between the preoperative value at the onset of anesthesia and Day 4 (292.5 ± 5.2 mOsm/kg and 291.1 ± 5.9 mOsm/kg, respectively [*P* = .187]). No significant differences in lactate, pH, base excess, bicarbonate, and hemoglobin were found between the Ringer's acetate group and the mannitol group at any time (Supplementary figures).

3.2 | Sodium

The mean levels of sodium preoperatively did not differ between the Ringer's acetate group and the mannitol group (139.9 ± 1.8 mmol/L and 138.7 ± 2.8 mmol/L, respectively [*P* = .104]). There was, however, a significant difference in the mean sodium level between the

TABLE 2 Pre- and perioperative characteristics

	Ringer's acetate group (<i>n</i> = 20)	Mannitol group (<i>n</i> = 20)	<i>P</i> -value
Male gender	18 (90)	19 (95)	1.000
Age (y)	69 ± 8	64 ± 10	.133
BMI (kg/m ²)	27.1 ± 2.9	27.9 ± 4.3	.464
NYHA class I-II	20 (100)	20 (100)	
Logistic EuroSCORE I (%)	2.75 ± 1.68	2.2 ± 1.79	.324
Hemoglobin (g/L)	138.6 ± 7.3	138.9 ± 12.3	.795
Creatinine (μmol/L)	79.6 ± 12.1	74.6 ± 12.0	.196
CPB time (min)	64 ± 18.1	66 ± 19.7	.690
Cross clamp time (min)	42 ± 15	39 ± 10	.491
Hemofiltration during CPB	0	0	
Pre-/peroperative use of diuretics	0	0	
Peroperative blood transfusions	0	0	
CPB balance (mL)	1289 ± 274	1408 ± 568	.406
Total peroperative fluid balance (mL)	1888 ± 292	2067 ± 672	.282
ICU balance at postoperative day 1 (mL)	2469 ± 870	2764 ± 1267	.396
ICU length of stay (h)	22 ± 3	36 ± 25	.010
Postoperative AKI	1 (5)	4 (20)	.342

Note: Values are expressed as means ± 1 standard deviation or numerical values (%).

Abbreviations: AKI, acute kidney injury; BMI, body mass index; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; ICU, intensive care unit; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction.

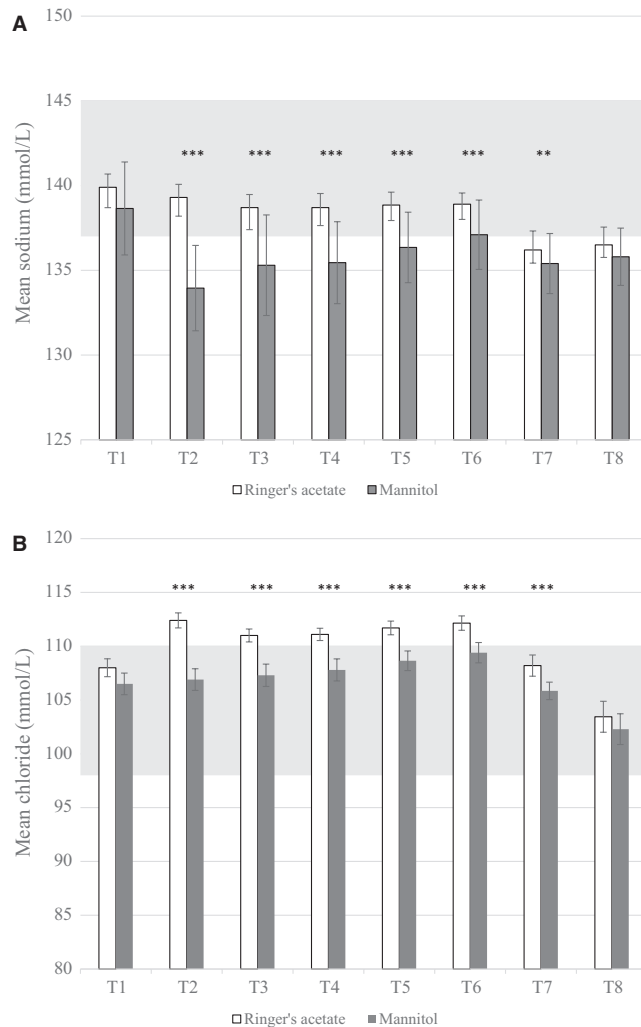


FIGURE 2 Changes in sodium (A) and chloride (B) measured before the onset of anesthesia (T1), 3 min after cardioplegia (T2), 30 min after start of CPB (T3), 60 min after start of CPB start (T4), 15 min after termination of CPB (T5), 30 min after arrival at the ICU (T6), on Day 1 (T7), and on Day 4 (T8). *** $P < .001$, ** $P < .01$. The band of pale gray indicates normal range. The error bars present 95% confidence intervals

two groups from T2 through T6, as can be seen from Figure 2A. The mannitol group showed a pronounced decrease in sodium, from 138.7 ± 2.8 mmol/L at T1 to 133.9 ± 2.6 mmol/L after starting CPB (T2) ($P < .001$). The sodium level did not vary in the Ringer's acetate group between T1 and T2 (139.9 ± 1.8 mmol/L and 139.3 ± 1.8 mmol/L, respectively [$P = .094$]). The sodium level in the mannitol group increased significantly, from 133.9 ± 2.6 mmol/L at T2 to 137.1 ± 2.1 mmol/L at T6 ($P < .001$). No significant change in sodium was seen in the Ringer's acetate group between T2 and T6 (139.3 ± 1.8 mmol/L and 138.9 ± 1.6 mmol/L, respectively [$P = .276$]).

3.3 | Potassium

No significant differences in potassium were found between the Ringer's acetate group and the mannitol group at any time (Supplementary figures). There was a significant increase in the

potassium levels in the Ringer's acetate group between T1 and T2 (4.0 ± 0.2 mmol/L and 4.9 ± 0.4 mmol/L, respectively [$P < .001$]) and in the mannitol group (3.9 ± 0.3 mmol/L and 4.8 ± 0.4 mmol/L, respectively [$P < .001$]).

3.4 | Chloride

A significant difference was seen in the mean chloride levels between the groups from T2 through T7 as can be seen from Figure 2B. The Ringer's acetate group showed an increase in chloride between T1 and T2 (108.0 ± 1.9 mmol/L and 112.4 ± 1.6 mmol/L, respectively [$P < .001$]), whereas no significant difference was seen between T1 and T2 in the mannitol group (106.5 ± 2.4 mmol/L and 106.9 ± 2.4 mmol/L, respectively [$P = .273$]).

3.5 | Renal function and fluid balance

The values describing the renal function are presented in Table 3, no clinically significant differences were found between the Ringer's acetate group and the mannitol group at any time. The mean eGFR at baseline was lower in the Ringer's acetate group than in the mannitol group (75.2 ± 9.1 mL/min/1.73 m² and 80.8 ± 7.7 mL/min/1.73 m², respectively [$P = .043$]), although both values were within the normal range. The incidence of postoperative acute kidney injury, determined according to the RIFLE classification based on the eGFR changes, was investigated. Acute kidney injury of low grade was found in one patient (5%) in the Ringer's acetate group and in four patients (20%) in the mannitol group ($P = .342$).

The mean urinary output perioperatively was 231 ± 118 mL in the Ringer's acetate group and 354 ± 128 mL in the mannitol group ($P = .003$). Comparison of the postoperative diuresis, measured until the morning of Day 1, showed no significant difference in urine output; the mean value being 1932 ± 698 mL in the Ringer's acetate group and 2068 ± 948 mL in the mannitol group, $P = .609$ (Figure 3).

4 | DISCUSSION

The results of this study showed that the use of mannitol in CPB priming solution during a routine CABG did not affect osmolality, acid-base homeostasis, and renal function compared with priming based on Ringer's acetate, whereas sodium and chloride levels were significantly lower in the mannitol group than in the Ringer's acetate group.

Changes in plasma osmolality during cardiac surgery have been poorly investigated. The use of hyperosmolar CPB prime has been reported to result in a dramatic elevation of the plasma osmolality,¹⁷ which may have negative effects on the central nervous system.²² No studies on the impact of mannitol on plasma osmolality following CPB could be found in the literature. An increased osmolality in relation to mannitol dose has been reported by Manninen et al in neurosurgical settings.²³ We observed no effect of mannitol on osmolality, compared to a Ringer's-acetate-based prime in this study. We found

TABLE 3 Renal parameters

Variable/Time	Ringer's acetate group (n = 20)	Mannitol group (n = 20)	P-value
Creatinine ($\mu\text{mol/L}$)			
T0	79.6 \pm 12.1	74.6 \pm 12.0	.196
T6	79.2 \pm 15.2	76.1 \pm 11.2	.472
T7	76.4 \pm 14.7	72.5 \pm 15.0	.412
T8	84.6 \pm 14.8	83.0 \pm 18.7	.766
T9	78.9 \pm 12.9	78.5 \pm 17.1	.934
Cystatin C (mg/L)			
T0	0.97 \pm 0.13	0.91 \pm 0.13	.174
T6	0.87 \pm 0.14	0.82 \pm 0.13	.285
T7	0.85 \pm 0.14	0.79 \pm 0.13	.170
T8	1.09 \pm 0.16	1.03 \pm 0.17	.301
T9	1.12 \pm 0.17	1.06 \pm 0.20	.379
eGFR (mL/min/1.73 m ²)			
T0	75.2 \pm 9.1	80.8 \pm 7.7	.043
T6	79.2 \pm 10.5	83.9 \pm 6.8	.099
T7	80.5 \pm 10.0	85.4 \pm 8.8	.108
T8	68.4 \pm 10.2	73.6 \pm 12.5	.164
T9	70.6 \pm 10.8	74.6 \pm 12.6	.288
Urea (mmol/L)			
T0	5.7 \pm 1.6	5.1 \pm 1.2	.216
T6	4.9 \pm 1.2	4.2 \pm 0.9	.034
T7	4.5 \pm 1.4	3.8 \pm 0.9	.067
T8	6.4 \pm 2.2	6.4 \pm 1.8	.975
T9	5.9 \pm 1.4	5.7 \pm 1.3	.551

Note: Values are expressed as mean \pm 1 standard deviation.

Times: T0 = day before surgery, T6 = 30 minutes after Intensive Care Unit arrival, T7 = Day 1, T8 = Day 4, T9 = Three months after surgery.

Abbreviation: eGFR, estimated glomerular filtration rate.

that the use of mannitol in the CPB prime did not affect changes in osmolality in CABG patients with normal cardiac and renal function. However, the osmolality increased significantly during CPB in all the patients, but only to a level slightly above the normal range, and it remained slightly elevated throughout surgery. This finding is in line with the previous study by Malmqvist et al.¹⁷ The much less pronounced increase in osmolality in our study, compared to that reported by Malmqvist et al, may be due to differences in the prime solutions. In addition, the high potassium content of the cardioplegia solution and substitutional treatment with electrolytes pre- and postoperatively in our study may have contributed to the increase in osmolality. The changes in plasma osmolality are, however, short-term and the osmolality had returned to pre-intervention levels by day four postoperatively.

The role of mannitol in the kidney is controversial. Renal dysfunction is a serious complication after cardiac surgery, causing increased mortality and morbidity.²⁴ Therefore, every attempt should be made to preserve renal function during CPB. It has been found

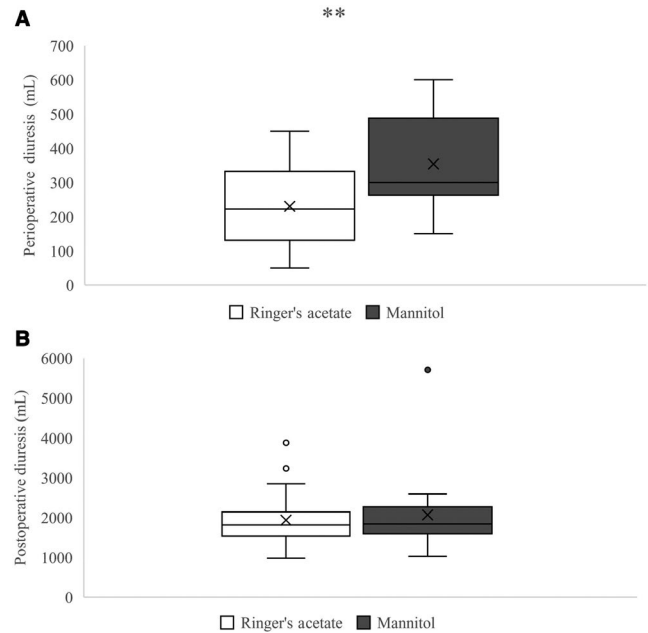


FIGURE 3 Perioperative (A) and postoperative (B) diuresis in the Ringer's acetate group and the mannitol group. The boundary of the boxes indicates the 25th and 75th percentiles, whiskers indicate the 10th and 90th percentiles. The line inside the box indicates the median value. The cross inside the box indicates the mean value. The three data points shown in the postoperative diagram are outliers. ** $P < .01$

that mannitol increases renal blood flow, which may have a positive effect on renal function in a postoperative acute kidney injury following cardiac surgery.^{10,25} On the other hand, there is a body of evidence indicating increased apoptosis of endothelial cells as a result of mannitol, and that it is harmful in acute kidney injury.²⁶⁻²⁸ Carcoana et al have revealed the complex relationship between dopamine and mannitol in patients undergoing CPB, reporting that this combination increased the microglobulin excretion rate, which is a sensitive marker of proximal renal tubular dysfunction.²⁹ When comparing mannitol and Hartmann's solution in CPB prime, Yallop et al found no difference in creatinine, fluid balance or diuresis.¹⁶ We found no differences in renal parameters or fluid balance between the groups in this study. All patients had normal preoperative renal function, and no patient received any diuretic pre- or perioperatively. Interestingly, we found no difference in urine output between the groups postoperatively, but a significant increase in urine output in the mannitol group perioperatively, indicating that mannitol has a short-term effect on urine output. In concordance with the study by Yallop et al we found no clear benefit of using mannitol in CPB prime in patients with normal renal function.

A dose-related decrease in sodium following the administration of mannitol has been reported previously by Manninen et al.²³ Our results confirmed these findings, showing that the mannitol group had a significantly lower level of sodium following CABG. Apart from the plasma sodium dilution effect, mannitol causes inhibition of sodium reabsorption in renal tubules,³⁰ which may contribute to the development of hyponatremia during CPB. It has been shown

that hyponatremia is a potentially dangerous condition associated with the risk of brain edema.³¹⁻³³ Another serious condition, central pontine myelinolysis, may occur when hyponatremia is treated rapidly.^{34,35} Minimizing the risk of hyponatremia may benefit the outcome after cardiac surgery,³³ and preventing hyponatremia during CPB is most important. Prime solution without mannitol may facilitate the achievement of this goal.

Findings concerning the relation between mannitol and potassium are limited and inconsistent. Several studies have reported a significant increase in serum potassium levels when using mannitol, although these were in noncardiac surgery settings.^{36,37} We found no significant differences in potassium levels over time between the two groups. However, an increase in potassium was observed in both groups after starting CPB, as a result of cardioplegia during CPB and the ensuing substitutional treatment during the intensive care stay. The effect of mannitol on potassium levels in the cardiac surgery setting is still uncertain and requires further investigation.

Few studies have been carried out to investigating the effect of mannitol on chlorides. Manninen et al found a decrease in serum chlorides when using mannitol in neurosurgical patients.²³ In our study, the Ringer's acetate group showed a significant increase in chloride levels during CPB, compared to the mannitol group. An additional amount of Ringer's acetate, given instead of mannitol in CPB prime, may have contributed to this variation. The clinical importance of this finding remains unclear, especially bearing in mind the identical plasma osmolality in the two groups.

4.1 | Limitations

The application of our results is limited to one particular type of cardiac surgery (CABG) and to patients with normal preoperative renal function. In addition, all the patients had received a maximum of 1000 mL Ringer's acetate as part of the perioperative anesthetic fluid therapy, and there is an unknown variation in the amount of Ringer's acetate administered to the patients, which may have had an effect on the levels of electrolytes. The main strength of our study is its design, as the randomized clinical trial allowed the investigation of the impact of mannitol as part of CPB prime, following CABG. The other strength is the use of the freezing point depression method to determine plasma osmolality.

5 | CONCLUSIONS

This prospective, randomized, double-blind study revealed no effect of mannitol on osmolality, compared to a CPB prime solution based on Ringer's acetate, in patients with normal cardiac and renal functions. The use of mannitol in prime resulted in a short-term, but significant, decrease in sodium. A significant increase in osmolality was seen in all patients during CABG, which cannot be attributed to mannitol, but is interpreted as the consequence of CPB. We, therefore, conclude that the role of mannitol in cardiac surgery requires further investigation.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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