Clinical Communication

Evaluation of perioperative renal function in elderly patients with administration of hydroxyethyl starch (130/0.4) in below umbilicus orthopaedic surgery - Randomised controlled trial

INTRODUCTION

Colloids are a group of intravascular fluids which have gained popularity due to their tendency to stay in the intravascular compartment to a greater extent and for a longer duration compared to crystalloids.[1] The use of colloids in critically ill patients has been the subject of numerous researchers to determine how they affect renal parameters.

There is limited literature on the renal effects of perioperative use of 6% hydroxyethyl starch (HES) in elderly patients. Primary objective of this study was to evaluate the effect of 6% HES (130/0.4) on renal function in the elderly population as assessed by serum creatinine and blood urea levels.

METHODS

This was a triple-blinded randomised controlled trial conducted in a tertiary care institute conducted from 2017 June to 2021 July. The study was approved by the institutional ethics committee (EC/NIMS/1948/2017 dated 5th June 2017). Patients were enrolled after taking informed written consent. Patients aged more than 60 years, belonging to the American Society of Anesthesiologists (ASA) physical status I-III, undergoing below umbilicus orthopaedic procedures of 2–3 hours duration were included in the study. Patients with left ventricular ejection fraction less than 30%, renal insufficiency with oliguria or anuria or on renal replacement therapy, coagulation abnormalities, deranged liver function, known allergy to hydroxyethyl starch and dermatomal level of sensory block of more than T8 were excluded. A computer-generated randomisation table was prepared in blocks of 8 and the study population was divided into two groups at random (1:1) and given either crystalloids alone (group C) or hydroxyethyl starch in the HES (group H) as per randomisation. We used crystalloid and colloids self-sealing bags which are visually identical if the labels are concealed. The identity of fluids was concealed by the anaesthesia technician who was responsible for the allocation of groups according to randomisation, and the fluids were then handed over to the perioperative anaesthetist as per the sequence in the randomised table. Another anaesthesiologist who was involved in data collection but was not directly involved in the treatment of the participating patients measured and recorded the primary and secondary outcomes. Preoperative blood urea, creatinine and haemoglobin levels of the patients were assessed. A subarachnoid block was given to the patient in the sitting position. Lumbar puncture was done at L3-L4 with a 25-gauge Quincke spinal needle by midline approach. 10 mg of 0.5% bupivacaine heavy with 25 μg of fentanyl was given into the subarachnoid space. Positioning and surgery started after attaining block up to dermatomal level of T12. A fixed volume of 7.5 ml/kg of 6% HES (130/0.4) was coloaded as the first fluid to the patients who belonged to group H. The remaining fluid requirement was met with crystalloids as calculated. The patients who belonged to the group C received exclusively crystalloids. Fluid administration was done based on the 4:2:1 rule. A drop of mean arterial pressure (MAP) by more than 20% from baseline was managed initially by giving a intravenous (IV) fluid bolus of four ml/kg (crystalloid). Phenylephrine 1-2 μg/kg IV was administered if there was no response to fluid challenge. Patients with blood loss more than maximum allowable blood loss (MABL) received a blood transfusion. The requirement for blood transfusion and phenylephrine use was recorded. Blood urea and creatinine values were recorded at 24 hours, 48 hours, 72 hours after surgery and at discharge.

The sample size was calculated to be 531, taking the average incidence of acute kidney injury as 33% from a literature review by M. Vives R *et al.*,[2] with 95% confidence interval and 4% absolute precision. Assuming 20% drop out rates, the sample size was adjusted to 640 based on eight block randomisation technique. Statistical analysis was performed using version 21 of the Statistical Package for Social Sciences (SPSS Inc., Chicago). Paired t-test was used for comparison of baseline blood urea and creatinine with the parameters at different time points. T-test was used for mean arterial pressure and volume of fluid infused.

RESULTS

The study flow is summarised [Figure 1]. No significant intergroup differences were observed in the patient demographics, the duration of surgery and population distribution concerning comorbidities [Table 1].

In neither group did blood urea or serum creatinine levels rise above two times the baseline at any point in time [Table 2].

The intergroup comparison of the highest and least MAP showed a statistically significant difference, with significantly lower values in group C which did not receive HES [Table 3]. The proportion of patients experiencing an intraoperative decline in MAP of more than 20% from baseline at any point in time was considerably lower in group H (24) compared to roup C (56). The total volume of fluid required was also significantly lower in group H (623.4 ± 87.17) compared to group C (696.65 ± 168.902) ml.

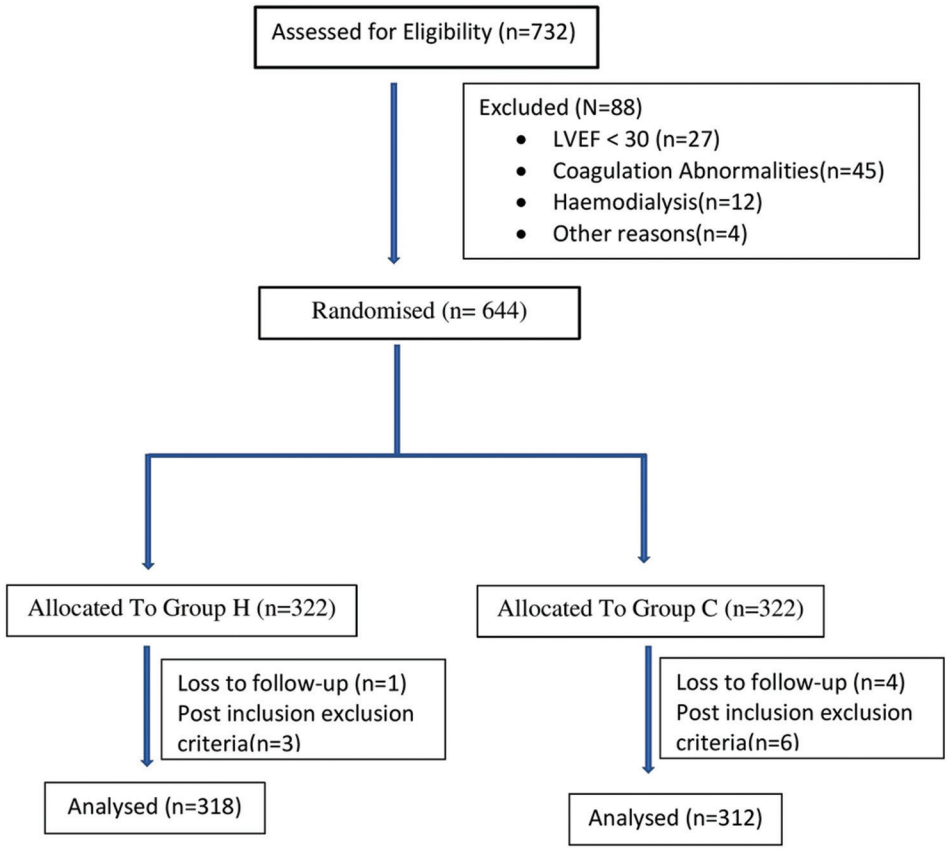

Figure 1: Consort flow diagram. LVEF: left ventricular ejection fraction,Group H: hydroxyethyl starch, group C: Crystalloid group

Table 1: Demographics with intergroup comparisons (described as median for age and absolute numbers for gender)

Demographic Data	HES (*n*-318) (Group H)	Crystalloids (*n*-312) (Group C)	*P*
Age: median (IQR)	68 (62-75)	65 (62-74)	
Gender: Male frequency (proportion)	147 (46.2%)	139 (44.5%)	0.316
Anaesthesia duration (minutes) (mean±SD)	116.97±21.51	116.36±21.86	0.26
Surgery {frequency} (proportion)			
Fracture femur	121 (38%)	124 (39.7%)	0.33
Fracture tibia	28 (8.8%)	25 (8%)	0.35
Total hip replacement	58 (18.2%)	46 (14.7%)	0.11
Total knee replacement	79 (24.8%)	95 (30.4%)	0.058
Others (ankle fracture, amputation, implant or screw removal)	32 (10%)	22 (7%)	0.088
Number of surgeries with tourniquet application (proportion)	139 (43.7%)	142 (45.5%)	0.32
Number of surgeries without tourniquet application (proportion)	179 (56.2%)	170 (54.4%)	0.324

HES: hydroxyethyl starch, SD: standard deviation, IQR: Interquartile range

In comparison to roup H (n = 16), more patients in the group C (n = 40) required IV phenylephrine to maintain target MAP. Both groups required similar amounts of blood transfusions [Table 3].

DISCUSSION

Our study has shown no increase in serum creatinine or blood urea above two times the baseline after intraoperative administration of HES in elderly patients. Haemodynamic parameters were better maintained with the administration of HES with less proportion of patients having a drop in MAP of more than 20% from baseline compared to only crystalloid administration. One of the factors most commonly associated with the development of postoperative acute kidney injury (AKI) are advanced age.[3] Majority of scoring systems have age as an independent risk factor in predicting either postoperative AKI or the requirement for the commencement of renal replacement therapy (RRT).[4]

Initial concerns about HES-induced renal side effects arose when osmosis nephrosis-like lesions were observed during routine kidney biopsies from renal transplant recipients.[5] The risk of renal injury is increased with an increase in molecular substitution due to delayed degradation. With reduced molecular weights and molar substitutions, products like tetrastarch (HES 130/0.4) have shorter half-lives and improved pharmacokinetics and pharmacodynamics.

This study thereby showed that HES does not cause significant renal injury when used in the intraoperative period in the elderly population.

Hideki Miyao *et al*.[6] have conducted a retrospective multicentre cohort study that concluded that 6% HES 130/0.4 did not increase postoperative AKI incidence or severity. It was associated with a lower incidence of renal replacement therapy when used for surgical patients.

Lee *et al*.[7] studied the immediate and delayed renal effects of intraoperative HES in patients undergoing nephrectomy and reported that HES group did not differ significantly from the non-HES group.

The present study results have shown better haemodynamic stability with the group H compared to the group C. Hypotension and hypovolaemia have been included in classical risk factors for postoperative AKI in the elderly,[8] emphasising the need to maintain strict euvolaemia and haemodynamic stability in the intraoperative period. In elderly patients who are more likely to become dehydrated, intravenous isotonic hydration is recommended to prevent prerenal azotaemia.[9]

Total volume infused carries clinical significance especially in patients in whom fluid overload can be deleterious such as cardiac failure or preexisting renal failure.

Table 2: Intergroup comparison of blood urea and serum creatinine in the perioperative period

	HES (Group H) Mean±SD	Crystalloid (Group C) Mean±SD	*P*
Blood Urea			
Baseline	29.68±10.12	31.04±10.9	0.079
At 24 h	27.67±9.89	29.98±12.8	0.096
At 48 h	29.23±10.61	29.23±11.07	0.998
At 72 h	33.67±18.28	36.63±20.61	0.717
At discharge	29.67±10.28	33.67±12.28	0.565
Serum Creatinine			
Baseline	0.88±0.20	0.91±0.30	0.405
At 24 h	0.89±0.21	0.94±0.11	0.082
At 48 h	0.88±0.19	0.94±0.23	0.09
At 72 h	0.92±0.18	0.91±0.14	0.12
At discharge	0.9±0.16	0.92±0.18	0.18

h: hours, SD: standard deviation

Table 3: Intergroup comparison of intraoperative hemodynamic parameters

Hemodynamic Parameters	HES (Group H)	Crystalloids (Group C)	*P*
HR baseline median (IQR)	70 (64-78)	72 (65-78)	0.708
MAP baseline median (IQR)	90 (84-96)	88 (86-97)	0.237
Number of patients with intraoperative MAP <65 mm Hg (proportion of population of the group)	24 (7.5%)	56 (17.9%)	0.001
MAP least in mm of Hg (mean)	74.6	64	0.001
MAP highest in mm of Hg (mean)	97.3	89.3	0.001
Volume of fluid infused in millilitre (mean±SD)	623.4±87.1	696.6±168.9	0.002
Urine output 1st 24 h (mean±SD)	1368.07±223	1339±194.2	0.462
Number of patients requiring phenylephrine (proportion)	16 (5.03%)	40 (12.8%)	0.001
Number of patients requiring blood transfusion (proportion)	42 (13.2%)	52 (16.66%)	0.899

HES: hydroxyethyl starch, HR: heart rate, MAP : mean arterial pressure, SD: standard deviation, IQR: interquartile range

AKI has been strongly associated with perioperative red blood cell transfusions.[10] This study focused on the effect of HES use on blood transfusion requirements. The blood transfusion requirement was comparable in both the groups which might be due to the minimal blood loss associated with tourniquet use in all the below-knee procedures and knee arthroplasty. However, the vasoactive agent (phenylephrine) requirement was significantly low in the group H of our study population owing to the stable haemodynamics compared to the group C.

A limitation of the study was the assessment of renal function using simple laboratory parameters, such as blood urea and serum creatinine. GFR and advanced markers such as Neutrophil gelatinase-associated lipocalin (NGAL) would provide more accurate results of renal function. However, we have chosen the parameters due to their easy availability in our institute and a better cost–benefit ratio.

CONCLUSION

The administration of a fixed volume of 6% HES (130/0.4) to elderly below umbilicus orthopaedic surgeries showed no adverse effects on perioperative renal function and provided good haemodynamic stability compared with crystalloids.

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Nil.

Conflicts of interest
There are no conflicts of interest.

A. Chaitanya Pratyusha, CH. Rama Krishna Prasad[1], Metta Rajasekhar[2], Gopinath Ranganathan

Department of Anaesthesiology, ESIC Medical College and Hospital, Hyderabad, Telangana, [1]Department of Anaesthesiology, All India Institute of Medical Sciences, Bibinagar, Telangana, [2]Department of Anaesthesiology, All India Institute of Medical Sciences, Mangalagiri, Andhra Pradesh, India

Address for correspondence:
Dr. CH. Rama Krishna Prasad,
Flat 301, Sri Sai Enclave, Naveen Nagar Colony, Banjara Hills Road Number 1, Hyderabad, Telangana, India.
E-mail: ram19chikkala@gmail.com

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