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Intraoperative Hemodilution and Its Effect on Postoperative Renal Function in Adult Cardiac Surgery Requiring Cardiopulmonary Bypass

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ABSTRACT

Background: Postoperative renal dysfunction after cardiac surgery is associated with morbidity and mortality. Many factors are responsible for renal dysfunction, including intraoperative hemodilution. In this study we have evaluated the effect of guided hemodilution on perioperative renal dysfunction.

Methods: All adult patients requiring cardiac surgery under cardiopulmonary bypass were included and their perioperative renal functions were evaluated in terms of blood urea nitrogen, creatinine and creatinine clearance. They were further divided into two groups with <30% (Group A) and > 30% (Group B) rise in creatinine/creatinine clearance to evaluate the effect of hemodilution on postoperative renal function.

Results: There was significant difference in preoperative and postoperative renal function between the groups. The preoperative creatinine and creatinine clearance in group A were 0.72±0.2 mg/dL and 97.2±56.5 ml/min respectively and in Group B were 1.1±0.3 mg/dL and 69.7±22.4 ml/min respectively. Postoperative creatinine and creatinine clearance in group A were 0.95±0.3 mg/dL and 78.4±37.7 ml/min respectively and in Group B were 1.35±0.6 mg/dL and 49.4±17.5 ml/min respectively. There were significantly lower mean arterial pressures in Group B (preoperative-72.1±8; postoperative- 71.2±11.4 mmHg) compared to Group A (preoperative- 77.8±10.7; postoperative-72.7±11.0 mmHg). There were significantly more use of packed cells in group B (Intraoperative- 141.2±75.5 ml; total- 297.3±175.4 ml) compared to Group A (intraoperative- 107.1±55.9 ml and total- 150.9±183.4 ml).

Conclusion: Optimal hemodilution during cardiopulmonary bypass do not have significant impact on postoperative renal function; however perioperative MAP and perioperative use of PCV are important factors responsible for postoperative rise in serum creatinine and creatinine clearanc.

Keywords: *cardiopulmonary bypass; hemodilution; renal dysfunction.*

INTRODUCTION

The development of cardiopulmonary bypass (CPB) and extracorporeal circulation have allowed surgeons to perform many complex cardiac surgeries.[1] Postoperative renal dysfunction after cardiac surgery under CPB ranges from 7-30%.[2,3,4] One to 3% of patients are reported to develop renal dysfunction requiring dialysis.[5,6]The current practice of hemodilution during CPB reduces the use of blood products. However, the optimal degree of hemodilution during CPB is still debatable. Studies have shown direct association between the severity of hemodilution and risk of renal dysfunction.[7,8] Earlier evidences, however, suggested that hemodilution allows renal protection.[9,10]Perioperative mean arterial pressure (MAP) has also been associated with postoperative renal dysfunction and hyperlactatemia. Patients with low MAP require longer intensive care and complications like renal dysfunction.[11,12] The present study aims to observe the intraoperative hemodilution and its effect on renal function using the changes in renal biochemical indices such as blood urea nitrogen, Serum Creatinine, and Creatinine clearance.

METHOD

The study was conducted at tertiary level hospital in adult patients undergoing cardiac surgery under CPB from January 2019 to December 2021 after ethical approval from institute research committee. All patients aged 18-60 years with serum creatinine less than 1.2 mg/dl were included in the study. Patients with preoperative renal failure, with serum creatinine more than 1.2 mg/dl, patients with a history of preoperative dialysis, patients with the use of contrast within three days, patients with a history of ICU admission due to acute heart failure, patients undergoing cardiac surgery without CPB,

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patients with congenital heart diseases and patients with uncontrolled diabetes mellitus were excluded. After approval of the institutional ethical committee, pretested and structured data sheets were used to collect demographic details, clinical history of systemic illness, preoperative (baseline), intraoperative and postoperative-hematocrit (HCT), blood urea nitrogen (BUN), serum creatinine, creatinine clearance, blood lactate levels and blood sugar levels. The baseline hematocrit, blood lactate levels, and blood sugar levels were noted down before induction of anaesthesia and initiation of surgery. The intraoperative trends in hematocrit, blood lactate, and sugar levels were observed during the conduct of CPB and after the termination of CPB. Post-operative hematocrit, blood lactate, mean arterial pressure and sugar levels were observed till 48 hours. Patients were investigated after 96 hours (4^{th} post-operative day) of surgery for levels of BUN, serum creatinine, and creatinine clearance. Preoperative renal biochemical markers were compared with their postoperative values. Based on the fourth postoperative days' serum creatinine level, the patients were divided into two groups (Group A and B) for analytic and comparison purposes. Group A consisted of patients whose postoperative serum creatinine showed a lower, equal, or incremental (not exceeding >30%) value compared to the baseline. Group B consisted of those patients who experienced > 30 % increment in postoperative serum creatinine value compared to the baseline. The cut-off of a 30% increment was taken concerning the definition of postoperative renal injury (dysfunction) used in most of the reference articles used as a guide to the study.[4] The creatinine clearance was calculated by Cockcroft-Gault formula.The data were entered and analysed by using Microsoft Excel version 2010. Descriptive analysis was done to summarize continuous variable by using mean and standard deviation. Frequency and proportion were calculated to describe the categorical variables. The intergroup comparison of explanatory variables was done and analysed with "t- test". P value <0.05 was considered as significant.

RESULTS

A total of 160 patients were included in the study; 111 (69.4%) were male and 49 (30.6%) were female. There were 109 (68.1%) patients in Group A and 51 (31.9%) patients in Group B. There was no statistically significant difference between the groups in terms of age, body surface area (BSA) and baseline hematocrit level. However there was significant difference in baseline MAP, creatinine and creatinine clearance level. Although absolute values of creatinine were within normal range in both the groups (Table 1).

Table 1. Baseline comparison of Group A (n=109) and Group B (n=51).

Variables	Group A (Mean ±SD)	Group B (Mean±SD)	p- value (t-score)
Age (years)	53.1±13.4	54.1±12.5	0.65 (-0.4607)
Body surface area (m^2)	1.6±0.3	1.6±0.1	1 (0)
Hb (gm/dL)	13.5±1.8	13.2±1.6	0.291 (1.0612)
HCT	41.4±4.0	39.9±4.7	0.05 (1.969)
BUN (mg/dl)	26.5±10.3	28.9±11	0.19(-1.312)
Serum Creatinine (mg/dL)	0.72±0.2	1.1±0.3	<0.05(-8.23)
Creatinine clearance (ml/min)	97.2±56.5	69.7±22.4	<0.05(4.3965)
MAP (mmHg)	77.8±10.7	72.1±8	<0.05(3.754)

As shown in Table 2, there was statistically significant difference between the groups considering the PCV used during surgery and MAP. Whereas there was no statistically significant difference between the groups in the flow rate, duration of CPB, extent of hypothermia and hematocrit maintained during surgery (p-value>0.05).

As shown in Table 3, there was statistically significant difference between the groups considering the MAP at baseline, pre-CPB and after 36 hours of surgery (p<0.05). However, the MAP was not significantly different during conduct of CPB (P=0.23).The mean arterial pressure baseline in group A was 77.8±10.7 mmHg as compared to 72.1± 8.0 mmHg and was statistically significant (p<0.05). The MAP before cardiopulmonary bypass (Pre-CPB) in group A was 75.5± 12.5 mmHg as compared to 69.6±16.3 mmHg and was statistically significant (p<0.05). The Mean arterial pressure 36 hours after surgery in group A was

79.4±9.1 mmHg as compared to 74.6±11.7 mmHg and was statistically significant ($p<0.05$).

Table 2. Comparison of flow rate, duration of CPB, extent of hypothermia, PCV used and HCT level during surgery between Group A (n=109) and Group B (n=51).

Variables	Group A (Mean±SD)	Group B (Mean±SD)	p-value (t-score)
Duration of CPB (minutes)	95.3±26.2	97.2±24.1	0.65 (-0.4518)
Flow rate on CPB (Litres/min)	3.8±0.5	3.7±0.4	0.18 (1.357)
Extent of hypothermia (°C)	33.3±3.0	33.9±2.2	0.16 (-1.4243)
PCV ml used during surgery	107.1±55.9	141.2±75.5	<0.05 (-2.8775)
HCT during surgery (%)	26.8±3.1	26.8±2.9	1 (0)

Table 3. Comparison of MAP- Baseline, Pre-CPB, during CPB, in ICU and after 36 hour between Group A (n=109) and Group B (n=51).

MAP (mmHg)	Group A (Mean±SD)	Group B (Mean±SD)	p-value (t-score)
Baseline	77.8±10.7	72.1±8.0	<0.05 (3.754)
Pre-CPB	75.5±12.5	69.6±16.3	<0.05 (2.289)
During CPB	69.2±11.3	67.0±10.5	0.23 (1.205)
ICU stay	72.7±11.0	71.2±11.4	0.43 (0.7842)
After 36 Hrs	79.4±9.1	74.6±11.7	<0.05 (2.5865)

As shown in Table 4, there was statistically significant difference between the groups considering postoperative BUN, serum creatinine, creatinine clearance and total PCV used ($p<0.05$). The postoperative serum creatinine in group A was 0.95± 0.3 mg/dL as compared to 1.35 ± 0.6 mg/dL and was statistically significant ($p<0.05$). The postoperative creatinine clearance in group A was 78.4± 37.7 ml/min as compared to 49.3 ± 17.5 ml/min and was statistically significant ($p<0.05$).Whereas, there was no statistically significant difference total stay in ICU (p=1).

DISCUSSION

Both groups were comparable in terms of age and BSA. The mean age and BSA in group A was 53.1±13.4 years and1.61 ± 0.28 m^2 respectively and in group B was 54.08 ±13.56 years1.62 ± 0.15 m^2respectively. The average baseline serum creatinine and creatinine

Table 4. Comparison of postoperative BUN, serum creatinine, creatinine clearance, total pcv used, and total stay in ICU.

Variables	Group A Mean ± SD	Group B Mean ± SD	p-value (t-score)
Postoperative BUN (mg/dL)	39.1±18.0	51.5±29.2	<0.05 (-2.7944)
Postoperative serum creatinine (mg/dL)	0.95±0.3	1.35±0.6	<0.05 (-4.505)
Postoperative creatinine clearance (ml/min)	78.4±37.7	49.4±17.5	<0.05 (6.645)
Total PCV used (ml)	150.9±183.4	297.3±175.4	<0.05 (-4.848)
Total say in ICU (days)	4.2±0.5	4.2±0.4	1 (0)

clearance were higher in group B compared to Group A, although it was statistically significant. The baseline and pre-CPB MAP was significantly lower in group B as compared to group A. This probably signifies that patients in group B are prone to have renal dysfunction and explain the significant rise in post-operative serum creatinine and creatinine clearance values in this group. Furthermore, maintain the hematocrit values within the acceptable range, the amount of PCV used in Group B was significantly higher compared to Group A. This probably explains that intraoperative usage of PCV is associated with a significant rise in post-operative renal biochemical parameters. These findings support the fact that the perioperative mean arterial pressures (MAP) and usage of blood in the perioperative period are factors related postoperative rise in creatinine, BUN, and creatinine clearance. This may be an indicator of subsequent postoperative renal dysfunction. None of the patients in the study required dialysis support in our study. To maintain the adequate HCT during CPB in order to maintain adequate organ perfusion and oxygen delivery to the tissues, institutional protocols accept addition of PCV on CPB whenever the hematocrit on CPB drops below 24%.This correction required significantly higher usage of PCV in group B as compared to group A. The mean packed cell volume used during CPB in group A was 107.1±55.9ml as compared to 141.2±75.5 ml in Group B. This suggests that the usage of blood on CPB is associated with a significant rise in serum creatinine, BUN, and creatinine clearance in the postoperative period. Similarly, the total packed cell volume (PCV) used in group B was significantly higher compared to group A. Group A required significantly lesser PCV unit (150.9±183.4 ml) transfusions to maintain haemoglobin within accepted ranges as compared to Group B (197.3±275.4 ml). The MAP in Group B was significantly lower in preoperative (72.1±8.0 mmHg) and postoperative period (74.6±11.7 mmHg) compared to Group A (77.8±10.7 and79.4±9.1 mmHg) which can be a reason for deranged renal function in Group B in comparison to Group A. Studies have shown that even short durations of an intraoperative MAP less than 55 mmHg are associated with AKI and myocardial injury.[11] In a study to determine the risk factors of renal dysfunction after cardiac surgery under cardiopulmonary bypass, postoperative renal dysfunction occurred in 17.2% patients. Thirty- seven patients (5.7%) had a moderate increase (30-50%), 11.5% patients had a >50% increase in serum creatinine level and 3.2% required dialysis. Postoperative renal dysfunction was more frequent in patients with preoperative renal impairment (19.4% versus 11.4%; P<0.001). These results are matching to the results of our study as there was a statistically significant difference in baseline serum creatinine in both groups.[13] In a study by Habib et al the increased hemodilution severity during CPB was associated with worse perioperative organ dysfunction and greater short and intermediate term morbidity/mortality.[14]. In our study, as per the institutional protocols, the nadir hematocrit on CPB was maintained above 24%. None of our cases from either group required dialysis. These findings may be due to rather U-shaped relationship than linear between the degree of hemodilution during CPB and post–cardiac surgery renal dysfunction. Hematocrit concentrations at the trough of the curve would confer the lowest risk of renal dysfunction, with the risk increasing as the hematocrit deviates from this optimal concentration in either direction. In a similar prospective study to assess the effect of hemodilution, 1.5% patients had acute renal failure necessitating dialysis support. There was an independent, nonlinear relationship between nadir hematocrit concentration during cardiopulmonary bypass and acute renal failure necessitating dialysis support. Moderate hemodilution (nadir hematocrit concentration, 21%-25%) was associated with the lowest risk of acute renal failure necessitating dialysis support; the risk increased as nadir hematocrit concentration deviated from this range in either direction. Compared with moderate hemodilution, the adjusted odds ratio for acute renal failure necessitating dialysis support with severe hemodilution (nadir hematocrit concentration 21%) was 2.34 and for mild hemodilution (nadir hematocrit concentration =25%) it was 1.88. Our study stresses the fact that if the on-pump hematocrit is maintained between 23–25 % (moderate range), the risk of perioperative renal dialysis and replacement therapy is minimum. However, administration of PCV to maintain HCT on-pump above 25% may lead to renal dysfunction in the postoperative period.[7]

CONCLUSION

From this study we conclude that perioperative MAP and perioperative use of PCV are important factors responsible for postoperative rise in serum creatinine and creatinine clearance which are the markers of perioperative renal dysfunction. Similarly, optimal hematocrit and hemodilution during cardiopulmonary bypass do not have significant impact on postoperative renal function.

Limitations: The effect of clinical characteristics like pre-operative left ventricular function, previous myocardial infarction, and heart failure was not considered during the analysis and deriving the results. The study was restricted to the adult population; no inclusion was made to study the causes of renal dysfunction in paediatric cardiac surgery. Similarly, our study did not include type of surgery and its relation to renal dysfunction.

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