PREVENTION OF ACUTE KIDNEY INJURY USING CEREBRAL OXIMETRY DURING CARDIOPULMONARY BYPASS IN CABG PATIENTS

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ABSTRACT

Objective: To determine the role of cerebral oximetry in addition to conventional monitors during cardiopulmonary bypass in coronary artery bypass grafting (CABG) patients for prevention of acute kidney injury.
Study Design: Randomized controlled trial.
Place and Duration of Study: Six months study at department of cardiac anesthesia, Armed Forces institute of Cardiology and National institute of heart diseases, Rawalpindi.
Methodology: We prospectively analyzed the collected data of 100 adult patients with normal.
Preoperative renal function who underwent isolated coronary artery bypass grafting (CABG) from June 2018 to Dec 2018. Patients were randomly allocated into two groups i.e., control group A (n=50) and test group B (n=50). Patients in group A were monitored for organ perfusion using standard tool i.e., MAP, SvO2, pump flow and lactate levels while patients in group B were monitored with near infrared spectroscopy (NIRS) in addition to standard monitoring. Kidney injury was assessed according to the Acute Kidney Injury Network criteria. Cerebral oximetery, hemoglobin and other important variables were measured every hour intra-operatively and for the first 24 hours postoperatively.
Results: AKI developed less in cerebral oximetery group as compare to control group i.e., 5 (10%) vs. 15 (30%). In this study, the rate of postoperative AKI development was high in patients with a low values of cerebral oximetry (SrcO2).
Conclusion: This randomized controlled trial showed that a lower cerebral oximetery is correlated well with AKI after CABG patients. Our study concludes that cerebral oximetry in addition to conventional perfusion monitoring may help to prevent AKI after cardiac surgery.

Keywords: Acute kidney injury, Cardiac surgery, Cerebraloximetry, Coronary artery bypass grafting, Near infrared spectroscopy.

INTRODUCTION

There has been increasingly importance on monitoring of oxygen delivery (DO2) during anesthesia but global delivery does not assess the sufficiency of DO2 and oxygen supply or demand at the tissue level, especially in brain[1].

Cerebral oximetry or near infra red spectroscopy (NIRS) is an intraoperative monitoring system, regional brain oxygen saturation is measured by it[2,3]. Neurological impairment associated with prolonged hospitalization, increased perioperative mortality or morbidity and high hospital cost during cardiopulmonary bypass may be prevented by Cerebral oximetry[4]. The multifactorial phenomenon of cerebral ischemia results from cerebral hypoperfusion and embolization that is further provoked during cardiopulmonary bypass (CPB) because of inflammatory responses, decrease oxygen delivery due to anemia and cardiac arrhythmias[4]. Cerebral oximetry provides continuous information regarding brain oxygenation and permits the use of brain as surrogate organ marking overall vital organ perfusion and injury[5-7].

The incidence of acute kidney injury is 1-40% after cardiac surgery and it is linked with increased mortality and morbidity that results in prolong hospital stay. The acknowledgedchief risk factors for AKI after cardiac surgery include old age, DM, pre existing renal disease, low ejection fraction, hypertension further provoked

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by intraoperative non pulsatile flow, systemic inflammatory response syndrome and renal hypoperfusion. Cerebral oximetry is real time measurement of regional cerebral oximetry. A significant predictor of impaired tissue perfusionis decrease in cerebral oximetry[8].

NIRS-based cerebral oximetry is a technology that is likely to contribute to the patient management. After the early evaluation with comparisons to same or similar biological parameters taken from other devices in laboratory and clinical situations, a new monitor must enlighten more a patient's clinical condition in order to improve outcome. In the past, studies of pulse oximetry and pulmonary artery catheters were in great difficulty to demonstrate the effect of monitoring of these parameters on changing outcomes[9,10].

The objective of this study was to test the hypothesis that cerebral oximetery is an indicator of organ perfusion during cardiopulmonary bypass and can be used as a predictor and also for prevention of postoperative acute kidney injury with timely interventions.

METHODOLOGY

Our study was a single centre randomized control study, conducted at department of cardiac anesthesia, Armed Forces Institute of Cardiology, Rawalpindi to study the prevention of acute kidney injury due to cardiopulmonary bypass with and without cerebral oximetry in CABG patients.

After approval by the hospital ethical committee and informed consent, 100 consecutive patients were randomly divided into two group i.e. group A (non-cerebral oximetry) and group B (cerebral oximetry), 50 patients in each group. Patients were selected on the basis of random computer generation method. Consecutive non-probability sampling technique was used. Patients satisfying the inclusion criteria include, all patients with class American society of Anesthesiologist (ASA) I & II, III of both, age group of 18-60 years undergoing elective CABG . Patients excluded were, emergency cardiac surgeries, complicated surgeries, patients having history of neurological and psychiatric disorders, beating heart surgeries, aortic arch surgeries, patients requiring deep hypothermic cardiac arrest, patients with peripheral vascular disease, patients in chronic renal failure treated by hemodialysis or peritoneal dialysis, recent myocardial infarction (MI) history, multiple organ failure and surgical reopenings. All patients received standard induction with propofol 2 mg /kg, cisatracurium 0.15-0.2 microgram/kg, fentanyl 2-20 microgram/kg and maintainence with isoflurane MAC 1.2, cisatracurium 1-3 microgram/kg/hr, fentanyl 1-2 mcg/kg/hr during cardiopulmonary bypass. Patients in group A were monitored for organ perfusion using standard tool i.e., MAP, SvO2, pump flow and lactate levels while Patients in group B were monitored with near infrared spectroscopy (NIRS) in addition to standard monitoring. Use of flow/vasopressors was monitored by keeping values MAP >60, Svo2 >70, lactate <4 and NIRS >70.

We used an INVOS monitor (Somanetics Covidien, Medtronic, Minneapolis, MN, USA) to measure rScO2 intraoperatively and for 24 hours postoperatively. The INVOS sensors were placed on both the left and right forehead for rScO2 measurement after intubation. Induction and maintenance of general anesthesia with endotracheal intubation were standardized for all patients (fentanyl, midazolam, and desflurane in oxygen with air). The same surgical team performed all operations. After intubation, the rScO2 was continuously recorded every 2 minutes during cardiopulmonary bypass until the end of the operation. The rScO2 was then continuously recorded in the intensive care unit (ICU) for at least 24 hours postoperatively.

Postoperatively, the patients were followed in the ICU according to the protocols of our institution. Electrocardiography, systemic mean arterial pressure, central venous pressure, pulmonary artery and wedge pressures, cardiac output and index, arterial blood gases, chest tube output, and hourly urine output were monitored. Serum electrolytes were measured in conjunction with

arterial blood gas measurement. Fluid and electrolyte imbalances were corrected immediately with appropriate management. The serum creatinine, and serum electrolyte concentrations were measured daily in all patients until discharge from the hospital. Preoperative and postoperative Creatinine clearance and peak creatinine clearance were calculated according to the protocols of our institution.

Post-operatively patients from both groups were assessed for acute kiney injury by using Acute Kidney Injury Network criteria 11 as shown in table-I.

Patients were labeled to be having AKI according to AKIN criteria i.e., abrupt reduction in kidney functions (within 48 hrs) currently defined as absolute increase in serum creatinine of 0.3mg/dl or A percentage increase in serum creatinine of 50% or more (1.5 fold from baseline) and decrease urine output <0.5 ml/kg/hr for 6 hrs.

AKIN Criteria

Stage	Serum creatinine criteria	Urine output criteria
1	Increase to >26.5 micromol/L (0.3 mg/dl) OR increase of >150% to 200% (1.5 to 2 times)	<0.5 ml/kg/h for >6 h
2	Increase of >200% to 300% (>2x to 3x)	<0.5ml/kg/h for >12 h
3*	Increase of >300% (>3x) OR baseline concentration of >353.6 micromol/L (>4.0 mg/dL) inc-rease to >442 micro-mol/L (>0.5 mg/dL)	<0.3 mL/kg/ hr for >24 h OR anuria for >12h

*stage 3 also includes patients requiring renal replacement therapy independent of the stage.

RESULTS

In total, all 100 adult patients were evaluated in this study. The patient's demographics and operative data are shown in table-II. Post-operative AKI occurred in total 20 (20%) patients i.e. 15 (30%) in group A and 5 (10%) in group B. Patient population was 35 (70%) male and 15 (30%) females in group A while it was 30 (60%) males and 20 (40%) in group B. There was no significant difference in gender distribution and history of smoking in both groups as shown in table-II. However, patients in group A had more mean age and pre-operative hypertension. The incidence of diabetes mellitus was found to be more in group B. Comorbids are found significant in both groups. The preoperative mean serum creatinine concentration was almost same in both groups (p=0.12). Statistical analysis showed that lower cerebral oximetry levels were associated with a higher incidence of postoperative AKI (95% confidence interval; p=0.001) as shown in table-I.

Table-I: Patient demographics and comorbids in both groups.

Variables	Group A (n=50)	Group B (n=50)	*p*-value
Age	57.8 ± 8.5	50.6 ± 6.8	0.001
Gender			
Males	35 (70%)	30 (60%)	1.00
Females	15 (30%)	20 (40%)	
Hypertension	38 (76%)	28 (56%)	0.03
Diabetes millitus	15 (30%)	36 (72%)	0.001
Base line Crea-tinine levels	1.01 ± 0.14	1.0 ± 0.12	0.29

According to AKIN criteria, all patients of AKI of both groups are shown in table-II. The mean ICU stay was 35.63 ± 10.74 hours in patients without AKI; however, it was 115.83 ± 25.70 hrs in patients who developed AKI (p<0.001).

In this study, 5(10%) is the rate of post-operative AKI development which is high in patients with a low rSO2. AKI developed post-operatively in 20 patients, 15 (30%) in control group and 5 (10%) in cerebral oximetery group. Additionally, the rate ofpostoperative AKI development was highin patients with a low rSO2 values.

DISCUSSION

Brain and kidney injury are shockingcomplications after cardiac surgery. Kidney injury is linked with in-hospital mortality. The cerebral blood flow is autoregulated to assure the metabolic needs of the brain tissue. The renal blood flow is autoregulated to control bodilytoxins and

fluid balance and to protect the glomerular structure[12]. Despite these brainand renal autoregulation mechanisms, brain and renal tissue may be damaging during CABG. Monitoring of brain tissue oxygenation is recommended during CABG. Among the methods available for such monitoring, we used NIRS in the presentstudy. NIRS is a non-invasive technique that allows for measurement of the oxygenation state of hemoglobin and mitochondrial cytochromes[13]. The oxygenation status of cytochromes along the electron transportchain appears to present the best estimateof cellular oxygenation. The technology forsuch measurement has been included into instrumentsable to measure theblood oxygen saturation in the brain[14].

Table-II: Clinical characteristics of patients who develop AKI in both groups.

Variables	Group A (n=15)	GroupB (n=5)	*p*-value
Baseline serum Creatinine	1.01 ± 0.15	0.85 ± 0.12	0.001
LVEF %	59.6 ± 2.9	58.0 ± 4.4	0.011
Baseline Creatinine clearance	98.0 ± 3.4	100 ± 1.0	0.149
Baseline Mean arterial pressure (MAP) mean value	75.1 ± 15.9	74.4 ± 5.7	0.83
Baseline lactate levels	1.1 ± 1.7	2.1 ± 0.13	0.404
Baseline haemoglobin (Hb)	13.6 ± 3.1	14.7 ± 0.8	0.01
Baseline SVO2	69.8 ± 13.8	67.1 ± 13.9	0.36
Pump flow	5.6 ± 0.3	5.3 ± 0.2	0.96
Mean lactate levels	2.5 ± 1.45	2.5 ± 1.14	0.618
On pump mixed venous	67.3 ± 8.5	71.6 ± 10.6	0.198
Post-op serum Creatinine	2.3 ± 1.3	2.2 ± 0.4	0.012
Post-op Creatinine clearance (CrCl)	55.6 ± 8.1	56.0 ± 10.2	0.784
Post-op MAP	99.6 ± 3.1	96.6 ± 3.1	0.451
Post-op mixed venous	70.9 ± 8.5	65.4 ± 0.8	0.04
Post-op lactate levels	3.9 ± 0.25	4.0 ± 0.02	0.04

As with peripheral tissues, low regional (frontal) cortical oxygenation (rScO2) levels grant an indication of a mismatch between cerebral perfusion or oxygen delivery, and regional oxygen requirements. Cerebral oximetery has been shown to correlate well with jugular venous bulb saturation, which is the standard for estimating global cerebral saturation[15]. The typical range of rScO2 is 55–80% and absolute rScO2 values <50% or a 20% drop from individual rScO2 baseline is commonly considered as intervention trigger. The incidence of these findings in patients undergoing coronary artery bypass grafting (CABG) is as high as 42%[16]. These findings are similar to our study results in a way that incidence in our study is found to be 15 (30%) in control group and 5 (10%) in cerebral oximetery group.

Table-III: Characteristics of cerebral oximetry patients who did and did not develop AKI (n=50).

Variables	AKI (n=5)	Non AKI (n=45)	*p*-value
Baseline cerebral oximetry rScO2 (Right)	52.6 ± 13.4	60.0 ± 2.9	0.282
Baseline cerebral oximetry rScO2 (Left)	57.0 ± 4.5	58.6 ± 4.6	0.453
Intra-op cerebral oximetry rScO2 (Right)	70.5 ± 9.5	68.5 ± 8.6	0.600
Intra-op cerebral oximetry rScO2 (Left)	68.0 ± 3.6	68.1 ± 5.5	0.95
On pump cerebral oximetry rScO2 (Right)	64.0 ± 4.0	63.7 ± 2.4	0.784
On pump cerebral oximetry rScO2 (Left)	63.2 ± 1.5	65.4 ± 3.9	0.232
Post-op cerebral oximetry rScO2 (Right)	51.4 ± 1.3	60.2 ± 2.2	0.001
Post-op cerebral oximetry rScO2 (Left)	54.6 ± 0.89	65.5 ± 4.1	0.001

According to Yao *et al*. a rSO2 <45% or a 25% drop from individual baseline values are measured as critical threshold for adverse neurological outcome. For example, a study involving 100 cardiac surgical patients showed that significantly more impairment in postoperative cognitive function developed in those patients with either a rScO2 below 35% or with rScO2-values below 40% for more than 10 min[17]. No such postoperative cognitive impairment func-tion has been observed in our study results.

Fischer *et al*. suggested in another study that patients undergoing aortic arch surgery who spent more than 30 min under the absolute rScO2 threshold of 60% had an extended hospital stay of 4 days leading to substantial additional costs[18]. Although our patient population was of CABG procedure; still this finding is in accordance with our study results. The mean ICU stay of our study was 35.63 ± 10.74 hours in patients without AKI; however, it was 115.83 ± 25.70 hours in patients who developed AKI (p<0.001).

Steppan *et al*. Expalined that brain tissue oxygenation may be reflected by renal tissue oxygenation. In the present study, the incidence of AKI was higher than expected in patients with low rScO2. We determined that the rate of AKI development was higher in patients with low rScO2 and hemoglobin levels[19]. This finding is also in accordance with our study results as shown in table-II.

Another study by Sgouralis *et al*. also supported our results which showed that rScO2 was low in patients with low hemoglobin concentrations. A low hemoglobin concentration decreases the tissue oxygen transport capacity and rScO2. Decreased oxygen transport capacity to the tissue also increases the incidence of AKI 20.

CONCLUSION

NIRS offers non-invasive online monitoring of tissue oxygenation in a wide range of clinical scenarios. A common application is to measure cerebral oxygenation (rScO2), e.g. during cardiac surgery. In conclusion, monitoring of the rScO2 and hemoglobin concentration during CABG can be beneficial in terms of estimating peri-operative and postoperative complications. The risk of peri-operative AKI development in patients with a low SvO2 and hemoglobin concentration should be considered. Although there is no direct evidence for such a correlation, our study showed that the incidence of AKI was higher in patients with low levels of rScO2. Therefore, nephrotoxic drugs should beavoided and renal protective measures must be taken. Optimum average blood pressure and hemoglobin levels may have to be reached for this purpose.

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CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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