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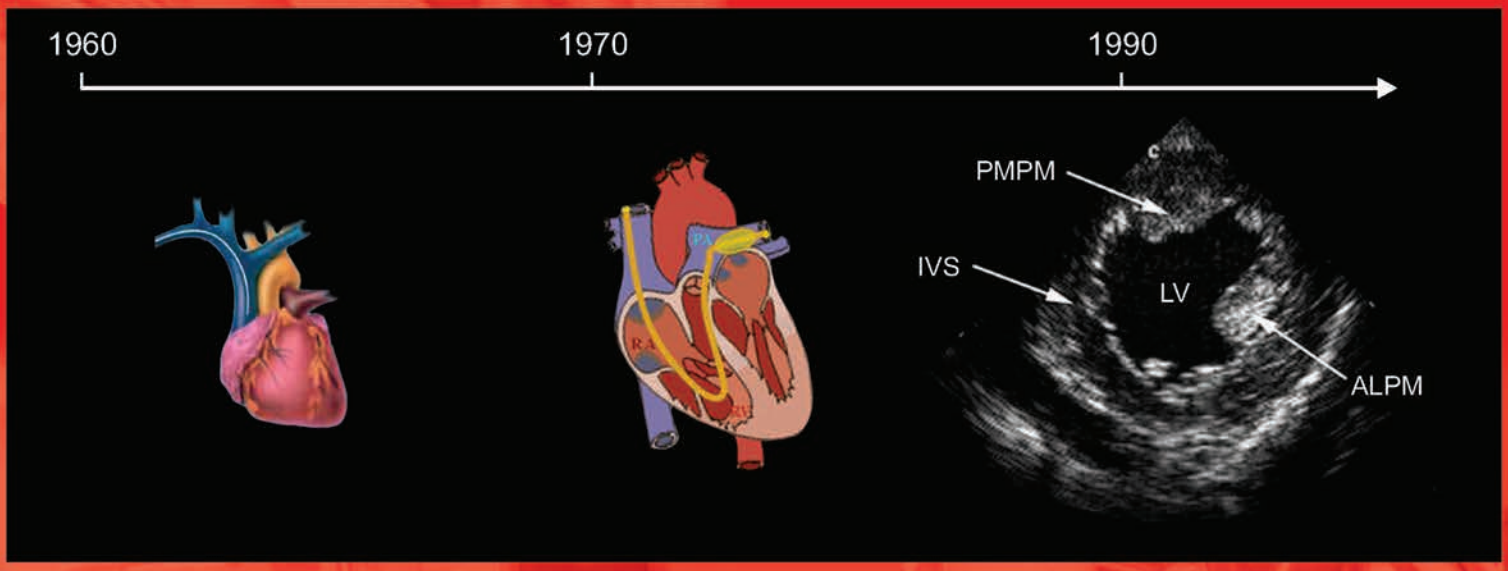

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Original Article

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Impact of monitoring cerebral oxygen saturation on the outcome of patients undergoing open heart surgery

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ABSTRACT

Aims and Objectives: We studied the usefulness of regional cerebral oxygen saturation (rSO_2) monitoring during cardiopulmonary bypass (CPB) and evaluated effects of cerebral oxygen desaturation on the postoperative neurological outcome. **Materials and Methods:** 100 patients were randomly allocated to either control or intervention group. In the control group rSO_2 was recorded continuously, but the attending anesthesiologist was blinded. In the intervention group specific interventions were initiated in case of cerebral desaturation. Neurocognitive testing was done using a simplified antisaccadic eye movement test (ASEM) and mini-mental state examination (MMSE). Data was analyzed using Chi-square test, and unpaired *t*-test. **Results:** In both the groups rSO_2 declined during CPB. The decrease in rSO_2 was significant ($P < 0.001$) in the control group compared to the intervention group. In the intervention group the rSO_2 mainly responded to an increase in mean arterial pressure. The area under the curve below threshold rSO_2 was significantly more ($P < 0.0001$) in the control group compared to intervention group and a significant decrease in the MMSE and ASEM scores occurred in control group at one week and three months postoperatively. **Conclusions:** Monitoring of rSO_2 during CPB can significantly decrease the incidence of postoperative neurocognitive decline.

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Key words: Cardiopulmonary bypass, Cerebral oximetry, Cognitive dysfunction, Mini-mental state examination, Antisaccadic eye movement test

INTRODUCTION

There is a continued need for monitoring adequacy of cerebral perfusion during cardiac surgery, as adverse cerebral outcomes still remain a major cause of morbidity. The incidence of stroke is up to 6%; whereas, neuropsychological dysfunction occurs more frequently in 40-50% patients.[1] Several studies have shown that postoperative cognitive dysfunction after cardiac surgery are associated with perioperative cerebral oxygen desaturation.[2,3] Cerebral microembolism and hypoperfusion resulting in cerebral oxygen desaturation have been proposed to be a major mechanism for cognitive dysfunction after cardiac surgeries done on cardiopulmonary bypass (CPB).[2,4] Murkin and colleagues[5] demonstrated that monitoring and treatment of cerebral oxygen desaturation prevented prolonged desaturation and was associated with a shorter stay in the Intensive Care Unit (ICU) and a significantly reduced incidence of major organ morbidity and mortality. Cerebral oximetry monitoring with near infrared reflectance spectroscopy (NIRS) is increasingly used to monitor bifrontal regional cerebral oxygen saturation (rSO_2).[6] Cerebral oximetry works on the principle of the Beer-Lambert's law. The measurement is thought to reflect 16% arterial and 84% venous contributions.[7] In this study, we evaluated the usefulness of rSO_2 monitoring and the beneficial effects of measures utilized to correct rSO_2 on neurocognitive function and length of ICU stay.

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MATERIALS AND METHODS

After obtaining Institutional Ethics Committee approval and written informed consent, 100 patients undergoing cardiac surgery using CPB were selected for the study. Patients with pre-existing neuropsychiatric disorders, inability to correctly perform the neurocognitive tests, and mini-mental state examination (MMSE) scores of less than 23, were excluded from the study. The selected patients were randomly allocated to either control group or intervention group. All patients received premedication with oral diazepam (0.1-0.2 mg/kg). Upon arrival in the operating room standard monitors were connected, including five-lead electrocardiogram, pulse oximeter, capnography, and radial artery catheter. Prior to induction of anesthesia, all the patients in both the groups had Nonin Equanox (model 7600) cerebral oximeter sensors (model 8000CA) placed bilaterally over the fronto-temporal area, and the baseline rSO_2 values were measured. This system has a dual emitter and dual detector sensor topology. It has been proven to provide an accurate measure of trends in cerebral oxygen saturation.[8] Anesthesia was induced with midazolam (1-3 mg), propofol (0.5 mg/kg) and fentanyl (5-10 μg/kg). Muscle relaxation was provided with vecuronium bromide. Anaesthesia was maintained with fentanyl and midazolam boluses, and isoflurane in O_2, air mixture. Minute ventilation was adjusted to maintain an end tidal carbon dioxide concentration of 30-35 mmHg. The conduct of CPB was standard and included flow rates of 2.2 to 2.4 l/minute, a mean arterial pressure (MAP) greater than 60 mmHg, hematocrit above 22% and a partial pressure of carbon dioxide of 40 mmHg or greater by alpha-stat management. Antegrade or retrograde blood cardioplegia was utilized for myocardial protection.

In the control group rSO_2 was recorded continuously, but the attending anesthesiologist was blinded. In the intervention group specific interventions were done in case of cerebral desaturation. Cerebral desaturation was defined as a decrease in saturation values below 80% of the baseline or an absolute value below 50% for one minute or longer.[9] However, interventions were started when the rSO_2 fell to 85% of the baseline value to prevent significant desaturation. The interventions included the following: Repositioning of the head or perfusion cannulae; Increasing arterial CO_2 tension; Increasing systemic arterial blood pressure; Adjusting the pump flow rate; Adjusting the anesthetic depth; Reduction of temperature; Vasodilatation; and, Increase in the hematocrit. We followed the algorithm proposed by Denault *et al*.,[9] for managing the decrease in rSO_2. The MAP was maintained between 60-70 mmHg by using vasopressors (phenylephrine) and increasing the pump flow rate up to a maximum of 3 l/min. PCO_2 was maintained between 40-45 mmHg on CPB by adjusting the oxygenator fresh gas sweep speed. Hematocrit was maintained between 22-25%. Depth of anesthesia was increased with fentanyl and midazolam boluses and using isoflurane on CPB. At the end of surgery patients were transferred to ICU. The extubation and ICU discharge were decided by the intensivists and they were blinded to the interventions carried out in the operating room for increasing the rSO_2.

Neurologic assessment: Neurocognitive testing was done preoperatively in all patients using the MMSE and simplified antisaccadic eye movement test (ASEM). These tests were repeated at one week and three months postoperatively. The standard MMSE assesses orientation (10 points), registration (3 points), attention and calculation (5 points), recall (3 points), and language (9 points). The maximum score of MMSE is 30 points.[10] Postoperative MMSE impairment was defined as a decrease in scores by more than 20% of the preoperative values.[11] The clinical protocol for ASEM described by Currie *et al*,[12] was followed. ASEMs are eye movements deliberately made in the direction opposite to that of a suddenly presented peripheral stimulus and require the suppression of any reflexive eye movement toward that stimulus. The patient is seated facing the examiner, who positions his hands equidistant from the midline in the patient's left and right visual fields, with each index finger extended in the manner commonly used to test the visual fields by confrontation. The stimulus for each trial consists of two to five rapid, repeated flexions of one or the other of the examiner's index fingers. The correct antisaccadic response is an initial eye movement to the side opposite to that of the moving finger, and any initial eye movement across the midline toward the moving finger is recorded as an error, even if a subsequent correction toward the non-moving finger is made. Twenty trials were done for each patient. The total numbers of correct responses was used as the score. Postoperative ASEM impairment was defined as a decrease of scores to more than 30% of preoperative values.

All the collected data were statistically analyzed using the SPSS version 14 software. Categorical data were analyzed using the Chi-square test and the unpaired *t*-test was used to compare the variables between the groups. A *P*-value of less than 0.05 was considered statistically significant.

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RESULTS

The demographic data, perioperative characteristics, and surgical procedures performed are shown in Tables 1 and 2. Both the groups were comparable with respect to the demographic variables and CPB and aortic cross clamp (AoX) times. The clinical parameters such as heart rate, MAP, PO_2, PCO_2, Hb%, and temperature monitored during the perioperative period were comparable between the two groups. The rSO_2 measured throughout the intraoperative period is shown in Figure 1. The rSO_2 increased during induction in both the groups. There was a fall in rSO_2 during CPB in both the groups. The decrease in rSO_2 was significant ($P < 0.001$) in the control group compared to the intervention group. The rSO_2 values remained below the baseline throughout CPB in both the groups. The rSO_2 values gradually reached the baseline once the patients were weaned off bypass. However, in the intervention group, as specific interventions were given, the rSO_2 values were maintained above 80% of the baseline. Seventy-six percent ($n = 38$) patients required intervention. Most of the patients ($n = 29$) responded to an increase in the MAP either by increasing pump flow rate or using phenylephrine. Remaining nine patients required multiple interventions. Four patients responded to an increase in the hematocrit, and the remaining five to further increase in the depth of anesthesia. The area under the curve below threshold rSO_2 represented as min.% was significantly more ($P < 0.0001$) in the control group (Rt- 92.48 ± 58.31 min.% and Lt- 92.74 ± 58.61 min.%) compared to the intervention group (Rt- 2.993 ± 8.87 min.% and Lt- 3.056 ± 8.96 min.%). Time for extubation and length of ICU stay in the control group showed a statistically significant prolongation compared to the intervention group. The results of the neurocognitive assessment are summarized in Table 3. Sixty-eight percent ($n = 34$) and 44% ($n = 22$) patients in the control group showed a significant decrease in the MMSE and ASEM scores at one week and three months postoperatively. All these patients showed a significant fall in rSO_2 (> 20% fall from baseline) during CPB. Two patients in the intervention group showed significant neurocognitive impairment one week postoperatively, both had a fall in rSO_2 (> 20% fall from the baseline) for a brief period and none of them had cognitive impairment three months postoperatively. The relationship between neurocognitive impairment and the extent of cerebral oxygen desaturation is depicted in Tables 4 and 5. Patients with a neurocognitive decline showed a significantly greater area under curve below threshold rSO_2 than the patients without a decline. Two patients in the control group had neurological damage. One patient had left fronto-parietal infarct and the other had bilateral multiple cerebral infarct. Both the patients showed a significant fall in rSO_2 during CPB (absolute value < 40%).

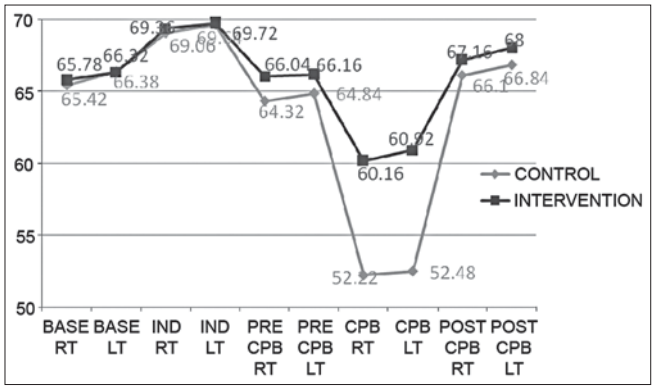

Figure 1: Comparison of rSO_2 between the groups (RT - right; LT - left; IND - induction; CPB - cardiopulmonary bypass

Table 1: Comparison of demographic and perioperative characteristics between the groups

Factor	Control (n = 50)	Intervention (n = 50)	P value
Age (Years)	38.05 ± 15.81	34.60 ± 16.28	0.49
Sex (Male/Female)	28/22	30/20	0.68
BMI	21.29 ± 4.73	20.11 ± 3.13	0.20
CPB Time (minutes)	91.18 ± 61.36	86.28 ± 35.80	0.62
AoX Time (minutes)	64.22 ± 28.43	65.00 ± 28.74	0.89
Time for extubation (hours)	7.96 ± 2.00	6.43 ± 2.41	0.01
Length of ICU stay (hours)	40.81 ± 11.81	35.88 ± 9.27	0.02

CPB: Cardiopulmonary bypass, ICU: Intensive care unit

Table 2: Comparison of surgeries between the groups

Surgeries	Control (n=50)	Intervention (n=50)
ASD	7	11
VSD	0	2
AVR	14	12
DVR	5	5
MVR	11	13
MV REPAIR	6	3
LA MYXOMA	4	1
BENTALL	1	2
PUL.END	2	1

Table 3: Comparison of MMSE and ASEM scores between the groups

Factor	Control	Intervention	P value
MMSE Base	29.28 ± 0.83	29.26 ± 0.78	0.902
One week	25.42 ± 7.54	28.58 ± 2.29	< 0.001
Three months	26.50 ± 6.31	28.88 ± 1.88	< 0.001
ASEM Base	17.90 ± 0.76	17.94 ± 0.74	0.791
One week	15.04 ± 4.80	17.46 ± 1.99	< 0.001
Three months	15.69 ± 3.99	17.68 ± 1.79	< 0.001

MMSE - Mini-mental state examination; ASEM - antisaccadic eye movement

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DISCUSSION

Adverse central nervous system (CNS) outcomes following cardiac surgery are classified into two categories: Type 1 (cerebral death, nonfatal stroke, focal injury, stupor, encephalopathy, coma, and new transient ischemic attack); and, Type 2 (deterioration in cognitive function, deficit memory, or seizures).[13] The causes are multifactorial. Mild cerebral hypoxia (rSO_2 40-49%) may be well-tolerated for a long period without significant clinical signs and symptoms or with only subclinical dysfunction. Moderate cerebral hypoxia (rSO_2 30-39%) continuing for a certain period may cause neuron damage; whereas severe cerebral hypoxia (rSO_2 < 30%), continuing even for a short time, may result in both acute neuron necrosis and apoptotic neuron death.[2]

In the present study, rSO_2 decreased during CPB in both the groups and it remained below the baseline throughout CPB. The initial dip in rSO_2 after institution of CPB is believed to be due to hemodilution and low perfusion pressure which usually improves once adequate flow on CPB is established. Similar results were observed by Yao, *et al.*,[2] and Negargar, *et al.*[14] In this study, in the intervention group the rSO_2 values improved in majority of the cases with an increase in the MAP. Few cases required multiple interventions like increasing the depth of anesthesia and increasing the hematocrit. Earlier, Murkin, *et al.*,[5] reported that increase in the pump flow and mean arterial pressure were sufficient to rapidly return rSO_2 to the baseline in many patients, but few required multiple interventions, with an overall success rate of 80%. We also observed that the rSO_2 decreased during rewarming, which may be attributed to the imbalance between oxygen supply and demand.[15] The increase in rSO_2 above the baseline, after induction of anesthesia could be due to the effect of preoxygenation and anesthesia-induced reduction in the cerebral oxygen demand.

We used MMSE and ASEM tests for assessing neurocognitive function, as these tests can be performed as a bedside test even in the ICU. The MMSE is considered as the quantitative screening test for the assessment of cognitive function and has been accepted for assessing cognitive function after general anesthesia, in elderly patients.[16] The ASEM test is a simple and reliable test of higher cortical function.[11] It is thought that ASEM uses the corticotectal pathways that originate from several areas of the prefrontal cortex, including frontal eye fields.[17] As cerebral oximetry monitors oxygenation in the microvasculature of the frontal lobes, ASEM appears well-suited to corroborate the effects of oxygen desaturation measured by the oximeter.[2]

The incidence of early postoperative neurocognitive decline observed in our study was 36%. However, when individual groups were considered, the control group showed an increased incidence of early cognitive impairment (68%) than the intervention group (4%). This showed that effective management of cerebral oxygen desaturation could decrease the incidence of cognitive impairment. Slater, *et al.*,[6] reported a 60% incidence of early postoperative cognitive decline; the cerebral desaturation rates observed in their study in both the control and intervention groups were nearly identical probably due to poor compliance to the treatment protocol in the intervention group.

The time for extubation and the length of ICU stay were prolonged in the control group. The neurological damage that occurred in two patients in the control group had a moderate degree of cerebral hypoxia during CPB, which could have resulted in the CNS insult.

The absence of rSO_2 monitoring in the postoperative period is a limitation of our study. Although, the postoperative hemodynamic changes can affect rSO_2, these factors were not taken in to account since we have aggressively and effectively maintained

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Table 4: Relationship between intraoperative rSO_2 and neurocognitive impairment in the control group

	Decline at one week (*n* = 34)	No decline at one week (*n* = 16)	*P* value	Decline at three months (*n* = 22)	No decline at three months (*n* = 28)	*P* value
AUC (min.%) Rt	129.2 ± 26.12	14.47 ± 7.81	< 0.0001	141.4 ± 24.61	54.07 ± 47.14	< 0.0001
AUC (min.%) Lt	129.6 ± 26.40	14.39 ± 7.59	< 0.0001	141.5 ± 25.50	54.47 ± 47.70	< 0.0001

Table 5: Relationship between intraoperative rSO_2 and neurocognitive impairment in the intervention group

	Decline at one week (*n* = 2)	No decline at one week (*n* = 48)	*P* value	Decline at three months (*n* = 0)	No decline at three months (*n* = 50)	*P* value
AUC (min.%) Rt	42.95 ± 10.82	1.33 ± 2.96	< 0.0001	-	2.99 ± 8.87	-
AUC (min.%) Lt	42.90 ± 13.29	1.39 ± 3.09	< 0.0001	-	3.06 ± 8.96	-

the hemodynamics, which could have resulted in insignificant changes in rSO_2.

In conclusion, cerebral oximetry is a useful noninvasive tool to monitor rSO_2 during the non-pulsatile flow conditions of CPB. Intraoperative monitoring of rSO_2 especially during CPB and treatment of decreases in rSO_2 can significantly decrease the incidence of postoperative neurocognitive decline.

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