*Original Article*

# THE RELATIONSHIP BETWEEN CEREBRAL OXYGEN SATURATION CHANGES AND POST OPERATIVE NEUROLOGIC COMPLICATIONS IN PATIENTS UNDERGOING CARDIAC SURGERY

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**ABSTRACT**

***Objective:*** To study the relationship between cerebral oxygen saturation changes and postoperative neurologic complications.

***Methodology:*** Seventy two adult patients with ASA class II, III who were scheduled for elective cardiac surgery, were randomized into three groups: Group I: with CPB (on –pump) Group II: without CPB (off- pump) Group III: valve surgery. Neuropsychological outcome was assessed by the Mini-Mental State Examination (MMSE). Cerebral oxygen saturation was also measured.

***Results:*** There was no statistical difference in desaturation of more than 20% among three groups (P=0.113) but it was significant between group I and II (P=0.042). Changes of $rSO_2$ in different hours of surgery was significant in group I and group II (P=0.0001 in both ) but it was not significant in group III ( P=0.075) .

***Conclusion:*** Although cerebral oximetry is a noninvasive and useful method of monitoring during cardiac surgery, it has low accuracy to determine postoperative neurologic complications.

**KEYWORDS:** Cerebral Oxygen Saturation, Cardiopulmonary Bypass, Neurologic Complication.

**Pak J Med Sci May - June 2007 Vol. 23 No. 3 380-385**

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* Received for Publication: July 13, 2006

* Accepted: January 25, 2007

## INTRODUCTION

Neurologic complications after cardiac surgeries specially cardiopulmonary bypass (CPB) are important problems in intensive care units.[1] When these complications including CVA, seizure, mild neurologic disturbance are associated with cardiac surgery, they cause cognitive dysfunction.[2]

Neurologic disorders based on type, time of neurologic test and accuracy of results, range from 19% to 80%.[3] The highest risk is seen in elderly patients with predisposing factors such as atherosclerosis, hypertension, genetic background, neurologic pathology and diabetes. Neurologic complications occur in these groups nine times that of patients younger than 65 years old.[3] Seizure, developmental disorders and low intelligence have been seen in neonates and children who have undergone cardiac arrest[3] with DHCA (Deep hypothermic circulatory arrest). Severe complications such as CVA (Cerebrovascular accident) have been reported in 0.8% to 6% of them.[2,3]

Improvement of surgical techniques such as, off pump surgery and use of cerebral and hemodynamic monitoring have important roles in prevention of neurologic complications.[4-6] There are different methods to monitor cerebral blood flow. One of them which has been recently introduced is measurement of cerebral oxygen saturation ($rSO_2$) with cerebral oximetry, which is noninvasive and easy to use.[7-9] Since it measures mostly venous blood oxygen saturation and does not require pulsatile signal, it can be used as a measure of global perfusion during cardiac surgery.[2]

Normal $rSO_2$ ranges from 55% to 75%. $rSO_2$ below 50% for a long period, below 40% or change more than 20% of baseline values for a short period is associated with neurologic complication.[3] Cerebral oxygen saturation decreases with cerebral blood flow decline due to increasing of oxygen extraction from tissue. Cerebral oximeter passes two wavelengths of near-infrared light into the patient's forehead. By measuring returned light at two distances (3cm and 4cm) from the light source, the hemoglobin oxygen saturation in frontal cortex can be determinded.[2]

According to the laboratory data, cerebral oximetry shows insuffiency of cerebral blood flow prior to EEG. The Brain can increase oxygen extraction even when its blood flow is low and this continues until it is not able to compensate flow decline. Thus, cerebral oximetry is an almost specific and sensitive indicator for the efficacy of cerebral blood flow from the area under the sensor of oximeter. The main problem is that the lowest acceptable value of regional oxygen saturation is unknown, because it differs from one patient to another and is influenced by anaesthetic drugs. The purpose of this study was to examine the relationship between cerebral oxygen saturation changes and neuropsychological dysfunction after cardiac surgery.

## PATIENTS AND METHODS

In this clinical trial, 72 adult patients who were scheduled for elective cardiac surgery in Shahid Madani Research Center were randomized into three 24- person groups. Group I underwent CABG with pump, group II underwent CABG without pump and group III underwent valve surgery. Exclusive criteria were history of CVA, Mental retardation and being unable to speapk native language. After institutional review board approval and obtaining informed consent, the Mini-Mental state Examination (MMSE) was performed to evaluate patient's neuropsychological state. 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] The score less than 25 shows possibility of disorder and less than 20 shows definite cognitive disorder.

In this study, 20% decrease in postoperative score for all patients and scores less than 20 for educated patients were considered abnormal. The total number of correct responses was used as the score and percentage change in score before and after surgery and was calculated as follows:

$$\frac{\text{Preoperative score - Postoperative score}}{\text{Preoperative score}} \times 100$$

Post operative impairment was defined as scores decreased by more than 20% and one standard deviation (SD) of preoperative values. This test was performed by anaesthesiology resident before and after surgery. Anaesthesia was induced with midazolam (0.1-0.2mg/kg), fentanyl (5-10μg/kg) and pancuroniom (0.2mg/kg), and was maintained with fentanyl boluses (1-5μg/kg), midazolam boluses (2mg to total of 10-15mg) and halothane. Patients were ventilated by a mixture of air (30%) and oxygen (70%). Cerebral oximetry was used to determine cerebral oxygen saturation (INVOS 4100). Two disposable sensors were applied to the forehead on the right and the left sides. $rSO_2$ was measured in awake situation, before induction and every 15 minutes after that. The lower values of either side were collected for analysis. Lower values are clinically more important because mean values or higher values may mask the existing hypoxia, which may contribute to postoperative neuropsychological dysfunction. Flow rates were set at 2 and 2.4L/min/m$^2$ during cooling (28$^{0c}$) and warming, respectively. Core body temperature was measured by nasopharyngeal prob. Mean arterial blood pressure was maintained at 50-90mmHg during pump and 20% of baseline value in patients without pump. Cerebral oximetry was continued until the end of surgery. MMSE was performed 24 hours after operation for all patients and their scores were compared and assessed. Data were analyzed by SPSS 12 statistical package. Quantitative data were compared by oneway ANOVA test among three groups. Mean quantitative data were compared by students' t-test between group I and II. Comparisom of nominal data was performed by chi-square test between group I and II. Fisher's exact test was used when expected numbers were less than 5. Change of $rSO_2$ during surgery was analyzed by repeated measures ANOVA in each group. P<0.05 was considered statistically significant.

## RESULTS

Patients' demographic characteristics are listed in Table-I. Two patients of group III had decline of postoperative score more than 20% of preoperative values. Desaturation more than 20% and areas of $rSO_2$<50% was seen in both of them and sings of CVA was seen in one of them. Other patients of this group with more than 20% desaturation didn't have significant change in MMSE score.

One patient of group II had decline of post-operative MMSE score more than 20% of pre-operative values which was accompanied by desaturation more than 20% but neurologic complications was not seen in this patient. Other patients of this group with desaturation more than 20% didn't have significant change in MMSE score, but signs of CVA was seen in one of them three days after surgery. In group I, from 14 patients with desaturation more than 20%, only two patients had decline of post operative MMSE score more than 20% of pre-operative values.

Comparison of $rSO_2$ change, MMSE score, pre and post operative variables is listed in Table-II. Comparison of $rSO_2$ change during different hours of surgery is listed in Table-III. Repeated measures ANOVA was performed for patients of each group which the follwing results were seen:

Group I or on –pump: F (6,57) =6.45; P=0.0001

Group II or off –pump: F (6,36) =10.36; P=0.0001

Group III or valve surgery: F (6,42)=2.09; P=0.074

As it is seen, cerebral oximetry changes during various hours of operation were significant in group I and II but were not significant in group III. Comparing more than 20% cerebral oxygen desaturation and MMSE difference among three groups, more than 20% desaturation and lack of more than 20% desaturation were accompanied by average decrease of 1.45 and 0.7 in MMSE score, respectively, which was not statistically different (P=0.264) .

Table-I: Patient's demographic data before and during surgery

| | *Group I On pump* | *Group II off pump* | *Group III Valve* | *Pvalue 3 groups* | *Pvalue 2 groups (I-II)* |
|---|---|---|---|---|---|
| Sex M/F | 23/1 | 21/3 | 14/10 | 0.0001 | 0.602 |
| Age (year) | 54.3±9.6 | 53.9±10.4 | 33.7±13.3 | 0.0001 | 0.886 |
| EF | 48.7±10.2 | 49.1±10 | 55.8±7.1 | 0.015 | 0.910 |
| Hct(before surgery) | 41.1±4.9 | 40.2±4.5 | 40.8±5.9 | 0.836 | 0.520 |
| Hct(during Surgery) | 27.1±2.9 | 35.5±5.3 | 25.6±3.9 | 0.0001 | 0.0001 |
| Diabetes | 5 | 5 | 1 | 0.18 | 1 |
| Education | 12 | 16 | 17 | 0.288 | 0.380 |

Table II: Comparison of MMSE Score and rSO2 during surgery

| | *Group I On pump* | *Group II Off pump* | *Group III Valve* | *Pvalue 3 groups* | *Pvalue 2 groups(I-II)* |
|---|---|---|---|---|---|
| $MMSE_1$(before) | 24.29±3.77 | 24.67±4.64 | 24.58±5.01 | 0.955 | 0.760 |
| $MMSE_2$(after) | 22.67±3.79 | 23.46±3.83 | 24.25±4.6 | 0.529 | 0.476 |
| Hours of post.op. Intubation | 8.8±4.8 | 10.5±4.8 | 19.4±33.4 | 0.142 | 0.235 |
| ICU stay (day) | 2.4±0.6 | 2.4±0.5 | 3.3±4 | 0.321 | 1 |
| NeurologicComplication | 1 | 1 | 1 | - | - |
| MMSE<20(educated) | 1 | 0 | 0 | - | - |
| $rSO_2$<40% | 0 | 0 | 3 | 0.044 | - |
| $rSO_2$>20% | 14 | 7 | 12 | 0.113 | 0.042 |
| $rSO_2$ <50% | 4 | 2 | 10 | 0.015 | 0.247 |
| MMSE >20% | 2 | 1 | 2 | 0.807 | - |
| Base Line $rSO_2$ | 77.3±8.3 | 75.6±7.9 | 70.8±9.6 | 0.03 | 0.478 |
| Awake $rSO_2$ | 74.4±7.7 | 72.1±6.8 | 68.8±11.8 | 0.197 | 0.361 |
| MMSE >20%Educated | 1 | 0 | 0 | 0.245 | - |

Comparing this variable between group I and II, more than 20% desaturation and lack of more than 20% desaturation is accompanied by avarage decrease of 1.17 and 0.96 in MMSE score, respectively, which was not statistically difference (p=0.740).

## DISCUSSION

The mechanism of postoperative neuropsychological dysfunction is probably multifactorial. Cerebral microembolism, hypoperfusion or the combination of both has been proposed. Nevertheless, all of these cause tissue ischemia and hypoxia, resulting in neurodegeneration. Neurodegeneration is accompanied by both acute necrotic neuron death and delayed apoptotic neuron death.

In this clinical trial, more than 58% of group I 29%of group II and 50% of group III and had desaturation more 20%. $rSO_2$ below prepump values in group I was because of hemodilution from non- blood priming solution, hypotension, lower pump flow and severe inflammatory responses. The initial drip in cerebral oxygen saturation at the beginning of CPB was because of low pump flow, which improved slightly once adequate pump flow was established. But generally desaturation was seen during CPB in group I and during heart elevation in group II. There was not significant relationship between decline of MMSE score with desaturation more than 20%, which can be because of low number of patients and low sensitivity of MMSE test. Awake cerebral oxygen saturation was in normal range of 52-82% in three groups, which was similar to other studies. There was statistically difference in baseline values of $rSO_2$ after induction among three groups, but since all of these values were in normal range, this difference was not clinically important. $rSO_2$ less than 50% and 40% in group III can be due to low baseline values of $rSO_2$, but because of their youth and good neurologic reserve, no significant neurological disorder was seen in this group.

Fun- Sun F Yao et al proposed that mild cerebral hypoxia ($rSO_2$ 40% -49%) may be well tolerated for a long period of time without significant clinical signs and symptoms or with only subclinical dysfunction. Moderate cerebral hypoxia ($rSO_2$ 30% -39%) for a certain period

TableIII: Comparison of $rSO_2$ , MMSE Score and variables after surgery

| | Group I (On pump) | Group II (Off pump) | Pvalue |
|---|---|---|---|
| First hour $rSO_2$ | 73.5±9.4 | 70.8±8.3 | 0.302 |
| 2nd hour $rSO_2$ | 71.7±8.3 | 69.1±8.3 | 0.288 |
| 3rd hour $rSO_2$ | 65.9±10.9 | 67.5±8 | 0.579 |
| 4th hour $rSO_2$ | 67.5±1.3 | 65.8±9.1 | 0.558 |
| 5th hour $rSO_2$ | 70.4±12.8 | 62.5±7.1 | 0.059 |

of time may cause neuron damage. logically, severe cerebral hypoxia ($rSO_2$ <30%) even for a short period of time may result in both acute neuron necrosis and apoptotic neuron death.[2] In our study, because of low numbers of moderate cerebral hypoxia and lack of sever cerebral hypoxia there was not a criterion to compare with above study. However, our results of mild cerebral hypoxia were similar to above study. In study of Fun- Sun F Yao, embolic factors have been considered to be the main cause of postoperative neurologic disorder in on-pump method and cerebral hypoperfusion secondary to decrease of CPP (cerebral perfusion pressure) seems to be the cause of neurologic disorders in off-pump method.[2] In our study, we could not evaluate cerebral embolies because of limited facilities. Cerebral hypoxia may be caused by any or a combination of the following conditions: hyperthermia, hypotension below the autoregulation threshold, anemia, arterial desaturation, low $Paco_2$ or cerebral vasoconstriction.[2] The limitation of this study is that MMSE test is not a standard test for evaluation of cognitive function. The incidence of postoperative neuropsychological dysfunction detected by MMSE was lower than other reports. This test was used because it can be performed as a bedside test even in the ICU.

According to Anthony et al, the MMSE was 87% sensitive and 82% specific in detecting dementia and delirium. However, the MMSE was found to have only 52% sensitivity and 87% specifity in predicting cognitive impairment after cardiac surgery.[11]

NIRS cerebral oximetry has been used to describe the cerebral oxygen supply–demand relation in critically ill patients. However, it is not able to measure total lack of cerebral blood flow. In most cases, oxygen saturation may correlate with cerebral blood flow but not always.[5]

Nemoto et al have shown that oxygen saturation values of infarcted brain tissue can be in the normal range; whereas the penumbra area, where oxygen extraction continues, is much lower.[12] Because 2 single- patient- use sensors were applied to the forehead of the patient, the NIRS measurements reflect only local oxygenation of the frontal brain and the signal might be affected by scalp and skull. The oxygen saturation measured by NIRS is closely related to the oxygen saturation in the jugular bulb, which represents the venous oxygenation of the whole brain. Furthermore, there is evidence that the influence of scalp and skull, both tissues with low oxygen metabolism, is below 5% of the signal.

However during CPB with mild hypothermia, and especially during periods of hypoperfusion, extracranial blood volume would be expected to be declining, thereby reducing the absorption of light by extracranial hemoglobin and allowing the NIRS signal to penetrate even deeper into the brain.[2] In the study of Chen CS et al on 15 patients, no relationship was seen between cerebral oxygen saturation and jugular bulb oxygen saturation.[13] They showed that temperature change during rewarming was very important for cerebral oxygen balance. Furthermore, cerebral oximetry (INVOS 3100) is not able to monitor cerebral oxygen saturation and is not recommended.

Study of Dauboney PE et al on 18 children undergoing cardiopulmonary bypass, showed that NIRS was a good device for monitoring of supply to demand ratio of oxygen especially during cardiac arrest.[14] According to Taillefer MC and Denault Ay, NIRS criteria didn't correlate with jugular bulb oxygen saturation.[15]

In this clinical trial, there was not a statistically significant relationship between cerebral oxygen desaturation, neurologic complications and MMSE change. However, patients who had neurologic complications showed cerebral oxygen desaturation and none of the patients who had normal cerebral oxygen saturation during operation, showed neurologic complications. We believe that considering small numbers of microembolies which either are absorbed or cause only subclinical brain damage, use of cerebral oximetry can be useful.

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