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The effect of continuous propofol versus dexmedetomidine infusion on regional cerebral tissue oxygen saturation during cardiopulmonary bypass

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Abstract

Background: Cerebral oxygen desaturation can arise during various durations of cardiopulmonary bypass (CBP), thus continuous monitoring is necessary. This desaturation may account for distinct neuropsychological deficits. Near-infrared spectrophotometry (NIRS) is a non-invasive method that offers many advantages for monitoring cerebral oxygenation.

Objectives: The aim of this study was to compare the outcome of propofol and dexmedetomidine on cerebral regional oxygen saturation ($rScO_2$) during CPB and on postoperative cognitive dysfunction.

Patients and Methods: 50 patients anticipated for open heart surgeries were encompassed in the study. Patients were divided into 2 groups, group P (receiving propofol) and group D (receiving dexmedetomidine) during CPB. Both groups were studied for variations in right and left $rScO_2$ as well as postoperative cognitive dysfunction using the Mini Mental State Examination Score (MMSE) test.

Results: The results showed no significant difference in both groups of the study, with an increase in $rScO_2$ on the right and left side in T1 compared to T0 and maximum increase in T3-4-5, then a decrease in T6-7. With regard to the cognitive dysfunction there was a decrease in the values at 1 h in both groups without significant difference; after 1 week MMSE values returned to baseline values.

Conclusion: Propofol and dexmedetomidine infusion used during CPB preserve the $rScO_2$ and do not affect the neurological outcome.

Keywords: cerebral oxygen saturation, cardiopulmonary bypass, dexmedetomidine, propofol

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Introduction

Neuropsychological and neurological deficits are still the most considerable reasons of morbidity and mortality after cardiac surgery [1]. These complications are thought to be provoked by embolisms and cerebral hypoxia [2]. Cerebral oxygen desaturation can take place during different periods of cardiac surgery; thus continuous monitoring is fundamental [3]. (NIRS) is a non- invasive method that shows many advantages for monitoring cerebral oxygenation [4].

Maintaining ($rScO_2$) higher than 50% has been found to reduce postoperative neurological dysfunction and accomplish with improved clinical outcomes in patients undergoing cardiac surgery [5]. Cerebral oxygen desaturation can happen at the initiation of CBP because of hemodilution or during the low perfusion and rewarming stages [6].

Propofol is a sterically hindered phenol (2,6 diisopropylphenol) that was introduced in 1989. It has a very short half-life with a short postoperative recovery period [7]. Propofol produces a dose-dependent decline

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in the cerebral blood flow (CBF) and the cerebral metabolic rate (CMR).

Dexmedetomidine is an imidazole-derivative adrenoceptor agonist presenting high selectivity for α_2 adrenergic agonist [8]. It has a sedative, analgesic and induces suppression of central sympathetic outflow [9]. It selectively stimulates presynaptic α_2 receptors with dose dependent reduction in arterial pressure, heart rate, cardiac output and norepinephrine release [10]. Dexmedetomidine decrease the CBF without change in CMR, which may influence the cerebral oxygen delivery.

The aim of this study was to compare the effect of propofol and dexmedetomidine infusion on $rScO_2$ during different stages of CPB and its influence on postoperative cognitive dysfunction.

Patients and Methods

This prospective, randomized, double blind study was conducted between June 2016 and May 2017 after obtaining the approval of the Ethical Committee Board. A written informed consent was taken from patients scheduled for open heart surgery over 1 year, either valve surgeries or pump coronary artery bypass grafting surgeries, either males or females. After exclusion of emergency cases, patients with cervical spine pathology (cervical stenosis, cervical disc herniation, carotid stenosis), patients with cerebral pathology (cerebral strokes, ischemic attacks), patients with Mini Mental State Examination Score (MMSE) of 23 or less, complicated cases with prolongation of the cardiopulmonary bypass period, patients needing moderate hypothermia, 50 patients remained and were included in the study.

Based on a computer-generated randomization list, patients were divided into 2 groups (group P and group D) of 25 patients each, group P patients receiving propofol infusion, group D patients receiving dexmedetomidine infusion.

The anaesthetic technique was standardized to all patients. On arrival to the operating room patients were connected to the monitor (Aisys; Datex-Ohmeda, Inc., a General Electric Company, doing business as GE Healthcare, Madison, Wisconsin, USA), 5 leads electrocardiogram (ECG), oxygen saturation (SPO_2), non-invasive blood pressure (NIBP). Regional cerebral oxygen saturation ($rScO_2$) was continuously monitored using near-infrared spectroscopy (NIRS) with an INVOS® 5100C cerebral oximeter (Somanetics, Troy, MI). After cleansing the skin area with alcohol, sensors for cerebral oximeter were placed bilaterally on the right and left sides of the forehead according to the manufacturer's instructions with the caudal border about 1 cm above the eyebrow with the medial edge at the midline. This position takes the light source and sensors away from the frontal sinus and temporalis muscle. The $rScO_2$ values from the right and left frontal lobes were averaged to determine cerebral oxygenation, and a baseline of $rScO_2$ was recorded. Electrodes for the intra-aortic balloon pump (IABP) (Maquet, Sweden) were placed. Temperature was controlled through a heating cooling unit (Stockert-T3, Germany) and measured continuously through oro-pharyngeal and rectal probes.

Patients received 0.02 $mg.kg^{-1}$ midazolam i.v. (Midazolam Labesfal, 15 mg/3 ml) through a peripheral cannula 20 G that was inserted in the station before arriving at the operating room. Radial arterial cannula, either right or left was inserted under aseptic technique after injecting lidocaine 1 $mg.kg^{-1}$ as local anaesthesia and connected to a pressure transducer (GE Healthcare, Madison, Wisconsin, USA) for continuous monitoring of invasive blood pressure. The pressure transducer was referenced to the mid-axillary level, and a base line arterial oxygen saturation (SaO_2) was recorded. Ultrasound guided (portable Sonosite, linear probe 10-5 MHz, Fujifilm, Sonosite, inc, USA) right Internal Jugular central venous catheter was inserted under complete aseptic technique, a baseline venous oxygen saturation ($ScvO_2$) was taken.

After pre-oxygenation for 3 min, anesthesia was induced by fentanyl 5-10 $mcg.kg^{-1}$ (50 µg/ml, 2 ml) and cisatracurium 0.15 $mg.kg^{-1}$ (10 ml, 2 mg/ml). 3 min later patients were intubated with a cuffed endotracheal tube, the cuff pressure maintained at 20 cm H_2O, the position of the endotracheal tube was checked by chest auscultation and end-tidal CO_2 once the patient was connected to the anaesthesia machine. The lungs were mechanically ventilated with 100% oxygen which was minimized gradually according to the arterial blood gases (ABG) to 60% oxygen in air. Anaesthesia was maintained by 0.5-1% end-tidal sevoflurane in 60% oxygen in air flow, cisatracurium infusion at a rate 0.1 $mg.kg.h^{-1}$ (2 ampoules 40 mg /20 ml, diluted in 50 ml syringe, with aconcentration of 0.8 mg/ml), fentanyl infusion at a rate of 1-3 $mcg.kg.h^{-1}$ (500 mcg /10 ml ampoule, diluted in 40 ml normal saline 0.9%, concentration 10 µg/ml) and lactated ringer solution at a rate of 8-10 $ml.kg.h^{-1}$. Routine continuous monitoring in the form of invasive blood pressure, heart rate, SPO_2, end-tidal CO_2, oro-pharyngeal and rectal temperature, $rScO_2$, urine output, sevoflurane, air and oxygen were measured with gas analyzer, arterial blood gases and venous blood gases were recorded on demand.

Once patients were connected to the heart-lung machine, sevoflurane was discontinued and the patient disconnected from the anaesthesia machine. Propofol infusion at a rate of 0.3-4 $mg.kg.h^{-1}$ (500 mg in 50 ml syringe) started and dexmedetomidine infusion at a rate

of 0.2-0.7 mcg.kg.h^{-1} (200 mcg dexmedetomidine diluted in 48 ml of 0.9% normal saline injection for a final concentration of 4 mcg/ml) together with fentanyl infusion at a rate of 1-3 mcg.kg.h^{-1}. The $rScO_2$ was recorded before induction of anaesthesia T0 then 10 min after inductionT1 then 5 min after starting cardiopulmonary bypass T2, then 5 min after reaching the desired temperature T3, then every 30 min T4, and T5 of CPB, then 5 min after reaching the desired temperature T6, then 5 min after weaning of the cardiopulmonary bypass T7.

During the cardiopulmonary bypass period, the flow was kept between 2.2-2.6 L/m^2 to maintain a MBP between 60-70 mmHg, the temperature kept at 34°C during cooling, the $PaCO_2$ between 36-42 cmH_2O, the PH above 7.36, and the hematocrit around 30. Any changes in these parameters were managed by the perfusionist.

Baseline $rScO_2$ was defined as the average saturation value over a 1-min period before induction of general anaesthesia. Cerebral desaturation was defined as a reduction of $rScO_2$ more than 20% of baseline for more than 15 s, which should be treated by the attending perfusionist and anaesthesiologist by adjusting the perfusion pressure to keep a mean arterial blood pressure (MAP) between 60-70 mmHg through the manipulation of the infused drugs or giving vasopressors as phenylephrine 100-200 mcg, and increasing FiO_2. Once patients weaned from cardiopulmonary bypass propofol and dexmedetomidine infusion were discontinued, patients reconnected to the anaesthesia machine, with 0.5-1% sevoflurane in 100% oxygen flow, re-expansion of the lungs manually, and then anaesthesia was maintained till closure of skin.

Once the patients were extubated in cardiac surgical unit (CSU), they were neurologically assessed by the intensivist for gross motor and sensory neurologic evaluation and gross cognitive evaluation (orientation in time and space, recall of name, date of birth, and address). Any side effects were recorded.

Cognitive function of the patients was assessed using the MMSE test the day before surgery and then reassessed 1 hour after extubation then 1 week after the operation. The mini-mental state examination (MMSE) or Folstein test is a brief 30-point questionnaire test that is used to screen for cognitive impairment. The MMSE test includes simple questions and problems in a number of areas: the time and place of the test, repeating lists of words, arithmetic, language use and comprehension, and basic motor skills. Postoperative cognitive dysfunction (POCD) was considered when there was decrease in MMSE score 2 points or more from preoperative value (Table 1).

Statistical analysis

Using PASS for sample size calculation, it was calculated that a sample size of 25 patients per group would achieves 82% power to detect a mean of paired differences in the regional cerebral oxygen of 20.0 with an estimated standard deviation of differences of 20.0 and with a significance level (alpha) of 0.05.

The statistical analysis was executed using a standard SPSS software package version 20 (IBM, Armonk, NY, United States of America). Data were expressed as mean values ± SD, numbers (%), Student's t-test was used to analyze the parametric data, and categorical variables were analyzed using the χ^2 test, with p values < 0.05 considered statistically significant.

Results

With regard to the demographic data there was no significant difference between the 2 groups of the study regarding age, sex, type of surgery (Table 2).

As regards the right $rScO_2$ (Table 3, Figure 1) there was no significant difference between both groups at T0 (71.44 ± 3.7) in group P compared to (71.72 ± 3.59) in group D. There was an increase in $rScO_2$ in both groups at T1 with no significant difference, (72.4 ± 3.6) in group P and (72.7 ± 3.6) in group D. There was

Table 1. Mini-mental state examination

Category	Possible points	Description
Orientation to time	5	From broadest to most narrow. Orientation to time has been correlated with future decline
Orientation to place	5	From broadest to most narrow. This is sometimes narrowed down to streets and sometimes to floor
Registration	3	Repeating named prompts
Attention and calculation	5	Serial sevens or spelling "world" backwards. It has been suggested that serial sevens may be more appropriate in a population where English is not the first language
Recall	3	Registration recall
Language	2	Naming a pencil and a watch
Repetition	1	Speaking back a phrase
Complex commands	6	Varies. Can involve drawing figure shown

Patients were studied for $rScO_2$ as primary outcome and MMSE as secondary outcome

Table 2. Demographic data in both groups

	Group P (n = 25)	Group D (n = 25)	p-value
Age (years)	60.32 ± 7.004	60.52 ± 5.96	0.94
Sex (M/F)	14/11	16/9	0.77
Type of surgery			
• Valve surgery	4	3	1
• Coronary artery bypass grafting	21	22	

Data were expressed as mean ± SD or number of patients
P-value > 0.05 is considered statistically non-significant

an increase in $rScO_2$ in both groups at T2 with no significant difference (73.44 ± 3.7) in group P and (73.64 ± 3.63) in group D. At T3, T4, and T5 there was a maximum increase in $rScO_2$ in both groups with no significant difference, at T3 (77 ± 3.37) in group P and (78.1 ± 4) in group D, at T4 (76.88 ± 3.4) in group P and (78 ± 3.7) in group D, and at T5 (76.84 ± 3.4) in group P and (77.96 ± 3.7) in group D. There was a decrease of the $rScO_2$ in both groups at T6 then at T7 without significant difference; at T6 (73.44 ± 3.66) in group P and (73.6 ± 3.62) in group D, and (72.2 ± 3.8) in group P and (72.8 ± 3.7) in group D at T7.

Table 3. Changes of right regional cerebral tissue oxygen saturation in both the P group (propofol) and D group (dexmedetomidine)

Time intervals	Group P (n = 25)	Group D (n = 25)	p-value
T0	71.44 ± 3.7	71.72 ± 3.59	0.786
T1	72.4 ± 3.6	72.7 ± 3.6	0.78
T2	73.44 ± 3.7	73.64 ± 3.63	0.847
T3	77 ± 3.37	78.1 ± 4	0.269
T4	76.88 ± 3.4	78 ± 3.7	0.271
T5	76.84 ± 3.4	77.96 ± 3.7	0.273
T6	73.44 ± 3.66	73.6 ± 3.62	0.872
T7	72.2 ± 3.8	72.8 ± 3.7	0.574

Data were expressed as mean ± SD
P-value > 0.05 is considered statistically non-significant

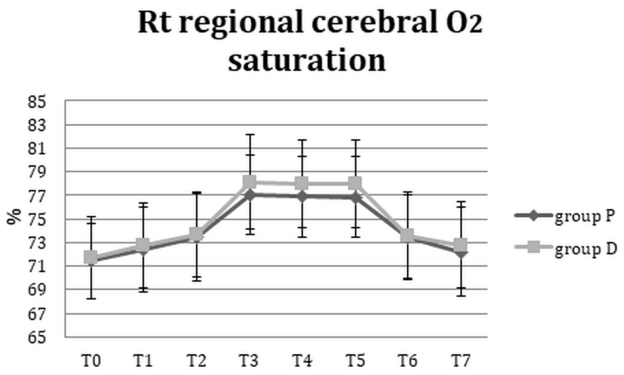

Fig. 1. Changes of right regional cerebral tissue oxygen saturation

As regards the left $rScO_2$ (Table 4, Figure 2) there was no significant difference between both groups at T0 (71.72 ± 3.58) in group P compared to (71.48 ± 3.71) in group D. There was increase in $rScO_2$ in both groups at T1 with no significant difference, (72.7 ± 3.6) in group P and (72.5 ± 3.7) in group D. There was increase in $rScO_2$ in both groups at T2 with no significant difference, (73.64 ± 3.63) in group P and (73.5 ± 3.68) in group D. At T3, T4, and T5 there was a maximum increase in $rScO_2$ in both groups with no significant difference, at T3 (78.12 ± 3.37) in group P and (77.1 ± 3.43) in group D, at T4 (78 ± 3.7) in group P and (77 ± 3.38) in group D, and at T5 (77.96 ± 3.74) in group P and (76.9 ± 3.44) in group D. There was a decrease of the $rScO_2$ in both groups at T6 then at T7 without significant difference; at T6 (73.6 ± 3.6) in group P and (73.5 ± 3.7) in group D, and (72.8 ± 3.7) in group P and (72.1 ± 3.86) in group D at T7.

Table 4. Changes of left regional cerebral tissue oxygen saturation in both P groups (propofol) and D group (dexmedetomidine)

Time intervals	Group P (n = 25)	Group D (n = 25)	p-value
T0	71.72 ± 3.58	71.48 ± 3.71	0.817
T1	72.7 ± 3.6	72.5 ± 3.7	0.846
T2	73.64 ± 3.63	73.5 ± 3.68	0.91
T3	78.12 ± 3.37	77.1 ± 3.43	0.31
T4	78 ± 3.7	77 ± 3.38	0.33
T5	77.96 ± 3.74	76.9 ± 3.44	0.311
T6	73.6 ± 3.6	73.5 ± 3.7	0.91
T7	72.8 ± 3.7	72.1 ± 3.86	0.53

Data were expressed as mean ± SD
P-value > 0.05 is considered statistically non-significant

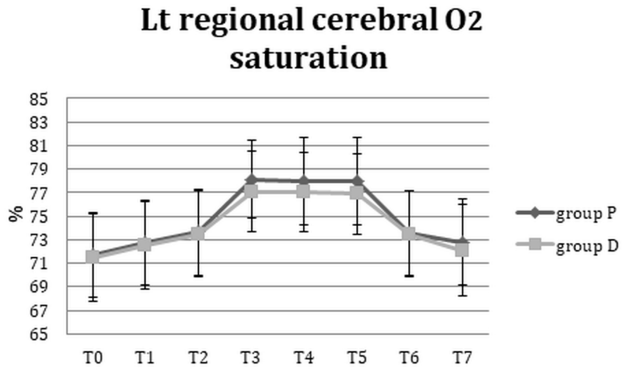

Fig. 2. Changes of left regional cerebral tissue oxygen saturation

As regards the MMSE (Table 5) there was no significant difference between both groups at the preoperative value (30) in group P and (30) in group D. As regard MMSE at 1 h there was a decrease in the values compared to the baseline with no significant difference in both groups (23.3 ± 0.408) in group P

and (23.2 ± 0.41) in group D. After 1 week the MMSE returned back to baseline value with no significant difference between both groups (30) in group P and (30) in group D.

Table 5. Changes of mini-mental state examination in both the P group (propofol) and D group (dexmedetomidine)

	Group P (n = 25)	Group D (n = 25)	p-value
MMSE preoperative	30	30	1
MMSE 1 h	23.3 ± 0.408	23.2 ± 0.41	1
MMSE 1 week	30	30	1

Data were expressed as mean ± SD or number of patients
P-value > 0.05 is considered statistically non-significant

Discussion

This prospective randomized double-blind study was designed to compare the effects of propofol and dexmedetomidine infusion during CPB on $rScO_2$. The success of cardiac surgery is related to the neurological outcome of the patients, which can be adversely affected by cerebral oxygen desaturation [11]. During CPB, cerebral oxygen desaturation occurs at different time, such as the beginning of bypass due to hemodilution, during low perfusion and during rewarming. Correcting the cause of desaturation is an important issue in anaesthetic management, and preserving $rScO_2$ is a major concern in cardiac surgery [6].

In our current study the factors influencing the $rScO_2$ were kept constant throughout the procedure. In the literature, 20% decrease in the baseline value of $rScO_2$ has been suggested as the best threshold value to predict cerebral ischemia. However, performed studies have shown that $rScO_2$ values decreasing below 50 even for a short period of time, resulted in significant cognitive or neurological damage [12].

In our current study no $rScO_2$ value as cerebral desaturation was detected in both groups during the procedure. Propofol leads to an increase in cerebrovascular resistance while it decreases cerebral blood flow and cerebral metabolic rate [13]. It has been demonstrated that dexmedetomidine in a dose dependent manner, leads to a decrease in the cerebral blood flow [14]. Studies concerning the effect of both drugs on $rScO_2$ have conflicting results in the literature.

In the current study and after induction of anaesthesia there was an increase in the $rScO_2$ in both groups compared to the baseline with no significant value. 5 min after starting the CPB there was a non-significant increase in the $rScO_2$ in both groups although it is well known from other studies that hemodilution at the start of CPB causes a decline in $rScO_2$ which may be due to the constant hematocrit which is kept at 30% throughout the procedure.

Once cooling started, the cerebral metabolic rate and oxygen consumption decreased. Thus saturation can decrease during the initial part of CPB as well as during the rewarming stage, which correlates to the current study showing a non-significant increase in $rScO_2$ in both groups of the study and then it decreased again during the period of rewarming and after CPB [15].

Regarding both groups of the study, there was no significant difference between them throughout the procedure, regardless the variation of $rScO_2$ which was mainly due to the effect of hemodilution, temperature, $PaCO_2$, and PH.

Michenfender [16] showed that following the administration of propofol, the relationship between cerebral flow and metabolism was preserved, and $rScO_2$ remained unchanged. Le Blanc et al., in the study on children with cardiac surgical operations, showed that propofol did not interfere with cerebral oxygenation and metabolism in which it was suggested that it was due to the effect of propofol on the stabilization of energy balance in mitochondrial level [17]. Drummond measured cerebral tissue oxygenation during the administration of dexmedetomidine for neurovascular surgery and determined that dexmedetomidine disturb neither cerebral oxygenation nor cerebral metabolism [18]. Rooyen et al. found that dexmedetomidine decreased cerebral tissue oxygenation, but they reported that this situation was clinically non-significant [19]. Padmanabhan et al. assessed cerebral oxygenation levels in children during the sedation process out of the operation room, and did not recognize any decrease in cerebral oxygenation in children with both medications [20].

The minimal difference in oxygen saturation between the right and left sides was correlating with the study of Güçlü et al., and skin hair follicles, forehead shape and arterio-venous anatomy might have been responsible for the difference [6].

The MMSE was used for evaluating cognitive function as it has many advantages regarding its high validity and reliability, ease of use and suitability for bedside use. Also MMSE is very appropriate for repeated cognitive assessments overtime [21]. There are other sensitive and specific scores as regards the assessment of cognitive functions. However, they have major drawbacks of lengthy, complex administration guidelines and duration in its application [22].

In the current study there was no significant difference in MMSE between both groups of the study. MMSE was lower at 1 h postoperative in comparison to baseline value which might be due to the effect of CPB and sedation, and it reaches the baseline value

after 1week. Maghawry et al., who studied the effect of dexmedetomidine and esmolol on $rScO_2$ during hypotensive anaesthesia in shoulder arthroscopy, found that there was no significant difference in both groups within group comparison or in between group comparison [23]. Townes and colleagues reported there were no neuropsychological changes or decrease in the MMSE score after induced hypotension in healthy young adults [24]. Güçlü et al., who compared the effect of sevofurane and fentanyl-midazolam combination on $rScO_2$ during open heart surgery, found that there was a superiority of the sevoflurane group but they have several limitations in their study, as they did not use any neurocognitive or neuropsychiatric tests after surgery to identify neurological outcomes [6].

Proper intraoperative management and prevention of any cerebral oxygen desaturation could explain the absence of any significant difference between the preoperative and the postoperative MMSE values.

Conclusion

Monitoring the $rScO_2$ during open heart surgery is an important tool to identify any cerebral desaturation during CPB. Its variation throughout the procedure was not related to propofol or dexmedetomidine infusion, but it is mainly related to the variation in hematocrit, PH, $PaCO_2$ and temperature variation. Propofol and dexmedetomidine infusion used during CPB preserve the $rScO_2$ and does not affect the neurological outcome.

Conflict of interest

Nothing to declare

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