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Utility of Cerebral Oxymetry for Assessing Cerebral Arteriolar Carbon Dioxide Reactivity during Cardiopulmonary Bypass

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ABSTRACT

Background: Our study evaluated changes in cerebral arterial oxygen saturation (rSO_2) during cardiopulmonary bypass (CPB) that were caused by changes in arterial carbon dioxide tension ($PaCO_2$).

Methods: A group of 126 patients undergoing routine, elective, first-time coronary artery bypass graft surgery (CABG) was entered into a prospective study using bilateral near-infrared spectroscopy (NIRS) before anesthetic induction (T1), after anesthetic induction (T2), and continuing at 5-minute intervals during moderate hypothermic (32°C) CPB. Pump flows were set at 2.5 L/min/m^2 and adjusted to maintain mean arterial pressure (MAP) within 10 mmHg of the MAP recorded at the initial fifth minute of CPB (T3). Thirty-two patients were excluded from data collection because MAP could not be stabilized within the target range of 60-90 mmHg. In the remaining 94 patients, after obtaining steady state flow, MAP, and oxygenation, a trial period of hypocarbia (mean $PaCO_2$ of 30 mmHg) was induced by increasing oxygenator fresh gas flow rate (FGFR) to 2.5 L/min/m^2 (T4). A reciprocal period was then measured at reduced FGFR (0.75 L/min/m^2) (T5).

Results: After 20 minutes of a higher (2.75 L/min/m^2) (FGFR), mean PaCO2 decreased from a baseline of 38 ± 4 mmHg to 30 ± 2 mmHg. This was associated with a parallel decrease (–10±9%) in mixed cerebral oxygen saturation without alteration of mean arterial oxygen tension (PaO_2), lactate, MAP, CPB flow, or other parameters implying increased cerebral oxygen extraction.

Conclusion: Parallel changes in $PaCO_2$ and rSO_2 occur during CPB when other variables remain constant, and are due to the effects of carbon dioxide on cerebral arterioles. Cerebral oxygen saturation measured by NIRS may be a useful indirect measure of $PaCO_2$ when continuous blood gas analysis is not possible during open-heart surgery. Cerebral oximetry values may be useful measurements for setting an optimum gas flow rate through the oxygenator.

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INTRODUCTION

Cerebral blood flow (CBF) and distribution are highly sensitive to changes in the arterial carbon dioxide tension ($PaCO_2$) [Laffey 2002a]. Elevated $PaCO_2$ (hypercapnia) leads to decreased cerebrovascular resistance and consequent increases in CBF and cerebral oxygen delivery (DO_2), whereas hypocapnia leads to increased cerebrovascular resistance and related decreases in CBF and DO_2 [Laffey 2002a]. This local control process, known as cerebrovascular carbon dioxide reactivity, provides a vital homeostatic function that helps regulate not only the peripheraic arterial pH, but also the resistance of cerebral arterioles, which directly affects CBF and DO_2. In the normothermic life state, this control process usually maintains adequate arterial flow to the brain. During open-heart surgery, a patient's body temperature, continuous blood flow, fresh gas flow, and arterial blood-gas concentrations shift due to alterations related to cardiopulmonary bypass (CPB); consequently, maintaining adequate CBF and cerebral oxygenation during CPB is more complex than in the normal life state.

Near-infrared spectroscopy (NIRS) has become popular for monitoring the balance of cerebral oxygen supply and demand during cardiac surgery. Use of NIRS during open-heart surgery is associated with reduced neurologic complications and reduced postoperative neurocognitive dysfunction [Tan 2008; Slater 2009]. A recent study revealed a strong correlation between NIRS and transcranial Doppler (TCD) assessments of CBF autoregulation in 23 patients with sepsis [Steiner 2009].

In this study, our aim was to evaluate the utility of NIRS monitoring of cerebral regional oxygen saturation (rSO_2) as a method for assessing how changes in $PaCO_2$ affect CBF during CPB.

METHODS AND MATERIALS

Patient Selection

The study was prospective and the Ethics Committee of Acıbadem University approved the protocol. Volunteers were selected from among 126 adults who underwent elective, isolated, first-time coronary artery bypass grafting of 3 or more vessels. Patients who had a mean arterial pressure (MAP) outside the 60–90 mmHg range after 5 minutes

of CPB were excluded. The remaining 94 patients were enrolled in the study.

Protocol

As part of our routine practice, patients were hospitalized 1 day prior to surgery and underwent a standardized preoperative workup. All surgeries were performed under general anesthesia with CPB, and through a midsternal incision. Anesthetic management and CPB strategies were tailored to each patient. Prior to anesthetic induction, arterial cannulation, peripheral venous cannulation, and central venous cannulation were performed, and electrodes and sensors were applied for electrocardiography and monitoring of peripheral arterial oxygen saturation ($sPaO_2$). The rSO_2 of the right and left cerebral hemispheres ($RrSO_2$ and $LrSO_2$) was monitored via NIRS throughout each operation (see detailed methods to follow).

After anesthesia induction, CPB pump flow was set at 2.5 L/min/m^2 and was adjusted as needed to maintain MAP within 10 mmHg of the MAP recorded after 5 minutes of CPB. To reduce $PaCO_2$, the fresh gas flow rate (FGFR) was set at 2.5 L/min/m^2 for 5 minutes after the fifth minute of initiation of CPB. After the tenth minute of CPB, FGFR was reduced to 0.75 L/min/m^2 to increase $PaCO_2$. Moderate hypothermia (32ºC) was maintained during CPB, and rewarming was initiated during left internal mammary artery grafting. When body temperature reached 36.5°C and the patient was hemodynamically stable, CPB was discontinued.

Data Collection

Demographic characteristics and operative data (cross-clamp time, total bypass time, and volume balance) were recorded for each patient. Intraoperative data ($PaCO_2$, arterial oxygen tension [PaO_2], lactate concentration, MAP, $LrSO_2$, and $RrSO_2$) were recorded at 5 time points:

T1: Before anesthetic induction (baseline)
T2: After anesthetic induction
T3: Fifth minute of CPB (FGFR 2.5 L/min/m^2)
T4: Tenth minute of CPB (FGFR 2.5 L/min/m^2)
T5: Twentieth minute of CPB (after 10 minutes with FGFR 0.75 L/min/m^2)

Percentage change from baseline was calculated for each $LrSO_2$ and $RrSO_2$ measurement after baseline.

Near-Infrared Spectroscopy

The NIRS method was performed using an in vivo optical spectroscopy (INVOS) system (Somanetics Invos 5100C; Somanetics Corp, Troy, MI, USA) consisting of sensors placed on the right and/or left side of the patient's forehead, one or two preamplifiers, reusable sensor cables, and a monitor. The probe for this unit has one light source and two photo detectors. The photo detector close to the light source absorbs light reflected from superficial tissues. The second photo detector located far from the light source absorbs light reflected from deeper tissues, such as watershed zones of the brain.

Statistical Analysis

Data were calculated as percentages or as means ± standard deviation. Analyses were performed using the Statistical Package for the Social Sciences (SPSS Inc; Chicago, IL, USA). Results were compared using the paired Student t test or the Wilcoxon signed-rank test. Differences with *P* values less than .05 were considered significant.

RESULTS

Table 1 summarizes the patients' demographic and operative data, and Table 2 highlights the results for intraoperative variables. The mean $PaCO_2$ at T3 was significantly higher than that at T4 (35 vs 30 mmHg, respectively; $P < .0001$). The mean $LrSO_2$ at T3 was significantly higher than that at T4 (59±7% vs 56±7%, respectively; $P < .0001$), and identical

Table 1. Demographic and operative data*

Female sex, n (%)	26 (27.6)
Body surface area, m^2	2.32 ±1.9
Cross-clamp time, min	41 ± 16
Bypass time, min	67 ± 16
Fluid volume status, mL	878 ± 525

*Data are presented as the mean ± SD where indicated.

Table 2. Arterial blood gas findings and near-infrared spectroscopy measurements*

	T1	T3	T4	T5
$PaCO_2$ (mmHg)	38 ± 4	35 ± 3†‡	30 ± 2†§	41 ± 4§‡
$LrSO_2$ (%)	63 ± 7	59 ± 7†	56 ± 7 †§	60 ± 7§
$LrSO_2$ (% change from baseline)	—	-6 ± 9†	-10 ± 9 †§	-5 ± 9§
$RrSO_2$ (%)	63 ± 7	59 ± 7†	56 ± 7 †§	60 ± 7§
$RrSO_2$ (% change from baseline)	—	-6 ± 9†	-10 ± 9 †§	-4 ± 9§
Lactate (mmol/L)	1 ± 0.3	0.9 ±0.3	0.9 ± 0.3	0.9 ±0.3
Mean arterial pressure (mmHg)	79 ± 13	65 ± 13	69 ± 13	70 ± 13
PaO_2 (mmHg)	83 ± 34	167 ± 39	153 ± 34	120 ± 40
Hb (g/dL)	11.3 ± 2.4	—	—	—

*Data are presented as the mean ± SD where indicated. Hb indicates hemoglobin; $LrSO_2$: left cerebral hemisphere arterial oxygen saturation; $PaCO_2$: arterial carbon dioxide tension; PaO_2: arterial oxygen tension; $RrSO_2$: right cerebral hemisphere arterial oxygen saturation.
T1: Before anesthetic induction (baseline); T2: After anesthetic induction; T3: Fifth minute of CPB (fresh gas flow rate of 2.5 L/min/m^2); T4: Tenth minute of CPB (fresh gas flow rate of 2.5 L/min/m^2); T5: Twentieth minute of CPB (after 10 minutes with fresh gas flow rate of 0.75 L/min/m^2).
†: $P < .001$ for T3 vs T4.
‡: $P < .05$ for T3 vs T5.
§: $P < .001$ for T4 vs T5.

findings were observed for $RrSO_2$. At T5, $PaCO_2$ was higher than that at T3 and T4 ($P < .05$ and $P < .001$, respectively) and $LrSO_2$ and $RrSO_2$ were both higher than the corresponding values at T4 ($P < .001$ for both).

DISCUSSION

Low MAP, low hematocrit, and changes in oxygenation during CPB are thought to alter the limits of normal CBF autoregulation during open-heart surgery [Moraca 2006; Gottesman 2006]. This is particularly important for patients with cerebral vascular disease, a group that constitutes a large proportion of those who need open-heart surgery [Moraca 2006; Gottesman 2006]. In addition, the changes in body temperature that occur during CPB complicate the autoregulation of cerebral oxygen delivery, and the rewarming phase, in particular, is reported to be a period of increased risk for brain injury [Boodhwani 2007].

Knowledge gained about CBF during CBP has led cardiovascular surgeons and anesthesiologists to monitor CBF autoregulation in order to reduce cerebral complications during and after open-heart surgery. Several methods have been used to monitor the cerebral effects and changes in CBF that occur during CPB. Continuous monitoring with electroencephalography (EEG), rSO_2 recording, and TCD imaging may be used individually [Edmonds 2000] or in combination with traditional monitoring devices [Sorteberg 1989]. It is well documented that the reliability of EEG for monitoring cerebral status is questionable, as several potential issues during CPB (ie, cerebral perfusion/oxygenation, insufficient or excess anesthetic depth, and gaseous or particulate emboli) can affect EEG results [Austin 1997]. Clinical methods of monitoring CBF autoregulation involve evaluating changes in measures of CBF in response to arterial blood pressure perturbations. Time-domain analysis of slow-wave changes in TCD-derived CBF velocity in response to spontaneous changes in arterial blood pressure has been validated as a means for continuous monitoring of CBF autoregulation [Minhas 2004; Reinhard 2005]. A previous study that evaluated subjects at rest revealed a significant positive correlation between TCD-derived blood flow velocity in the middle and anterior cerebral arteries (MCA and ACA, respectively) and the corresponding regional CBF [Moehle 2001]. Similarly, Sorteberg and Hyung-sik assessed TCD findings in healthy patients who had undergone GV20 acupuncture sessions and concluded that alterations in MCA and ACA blood flow velocity due to carbon dioxide reactivity can be easily and reliably monitored via TCD [Sorteberg 1989; Hyung-sik 2011]. Zui et al applied TCD monitoring in 7 astronauts and found this modality to be effective for monitoring gravity-induced changes in CBF, CBF autoregulation, and cerebral carbon dioxide reactivity [Zui 2012]. In contrast, Giller et al and Willie et al observed that carbon dioxide reactivity causes alterations in TCD findings that do not reflect the oxygenation of the brain tissue [Giller 1993; Willie 2012].

It is important to determine whether methods such as TCD and EEG are safe for monitoring CBF under CPB conditions. It is well known that CPB affects hematocrit, flow autoregulation in the cerebral vascular bed (thus altering perfusion pressure), $PaCO_2$, and arterial oxygen content [McCusker 2006]. Arterial carbon dioxide tension and arterial oxygen content can profoundly influence CBF velocity and cerebral arterial blood flow velocity [Brown 1985] during CPB. In addition, body temperature changes during open-heart procedures can interfere with CBF [Brijen 2010]. Despite this knowledge, for practical reasons, cardiovascular anesthesiologists and surgeons tend to increase MAP during CPB. One study concluded that raising MAP targets during CPB in order to reduce risk of cerebral hypoperfusion might inadvertently increase the risk of cerebral injury in some patients [Hogue 2006]. Furthermore, in patients who have significant inflammation due to CPB or have intracerebral hemorrhage, increased CBF caused by higher MAP could lead to cerebral edema [Laffey 2002b].

Mean arterial blood pressure, body temperature, $PaCO_2$, PaO_2, and electrical activity of the brain (as monitored by EEG) are important parameters to track during cardiovascular operations performed under CPB, and have been monitored for many years. Monitoring of CBF alterations during CPB has been a more recent research focus, and this is more complex than monitoring CBF in normal life conditions. Cerebral blood flow velocity derived from TCD data may not be an accurate indication of brain cell oxygenation during CPB, as the oxygen demand/supply ratio changes due to the above-noted effects of CPB. Previous studies on NIRS monitoring have proven that CBF is pressure-passive during CPB [Newman 1994], and this finding makes NIRS monitoring a particularly valuable tool.

Maintaining FGFR at 2.5 L/min/m^2 during CPB causes $PaCO_2$ to drop below physiologic levels; therefore, it is very important to monitor and optimize FGFR carefully during CPB [Toraman 2007]. In our study of NIRS monitoring of cerebral rSO_2 with controlled $PaCO_2$ alterations, we found that cerebral rSO_2 decreased as $PaCO_2$ decreased, and that cerebral rSO_2 increased when $PaCO_2$ increased.

We suggest that the parallel direction of changes in $PaCO_2$ and rSO_2—during the period of CPB when CPB pump flow, MAP, PaO_2, lactate, body temperature, and hemoglobin remain constant—reflects the effects of carbon dioxide on cerebral arterioles. Based on this, and considering that $PaCO_2$ alterations during CPB depend on multiple factors (ie, body temperature, CPB flow, FGFR, body surface area), NIRS monitoring of cerebral rSO_2 may be a valuable technique for identifying negative cerebral affects of carbon dioxide.

Using NIRS to monitor cerebral rSO_2 may be particularly important additional to blood gas analysis or when continuous blood gas analysis is not possible during open-heart surgery.

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