Frontal Lobe Oxygenation Is Maintained During Hypotension Following Propofol-Fentanyl Anesthesia

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Near-infrared spectroscopy (NIRS) assesses cerebral oxygen saturation (ScO2) as a balance between cerebral oxygen delivery and consumption. In 71 patients, we evaluated whether marked reduction in mean arterial pressure (MAP) during propofol-fentanyl anesthesia induction affects frontal lobe ScO2. The NIRS-determined arm muscle oxygenation (Smo2), heart rate (HR), and cardiac output (CO) were monitored, end-tidal carbon dioxide tension was controlled at 3.5 to 4.5 kPa, and central blood volume was maintained.

Before anesthesia, the median (range) MAP, HR, and CO were 93 mm Hg (61-126 mm Hg), 76 beats/min (50-96 beats/min), and 5.3 L/min (2.4-9.0 L/min), respectively, but immediately following intravenous administration of fentanyl and propofol, MAP decreased to 63 mm Hg (37-109 mm Hg), HR to 63 beats/min (40-103 beats/min), and CO to 4.1 L/min (1.9-7.0 L/min) (P < .05).

When blood pressure decreased, the median (range) NIRS-determined SmO2 also decreased (73% [54%-94%] to 71% [52%-87%]), whereas ScO2 increased from 67% (46%-93%) to 74% (48%-95%) (P < .05), independent of age and gender. After anesthesia induction, variables recovered and remained at preanesthetic levels during surgery. The findings implicate that even an approximately 30% drop in MAP at the induction of anesthesia does not typically affect cerebral oxygenation.

Keywords: Anesthesia, blood pressure, cerebral autoregulation, heart rate, near infrared spectroscopy.

Because it is not possible to communicate with patients during general anesthesia, it is most often unknown whether cerebral oxygenation is maintained. It can be assumed only that maintaining mean arterial pressure (MAP) within what is considered the cerebral autoregulation range of approximately 60 to approximately 140 mm Hg1 secures cerebral blood flow. Yet, for example, cerebral ischemia has been reported during shoulder surgery in the beach-chair position, leading to a catastrophic outcome,2 and the clinical relevance of the Bezold-Jarisch reflex in that regard has been addressed.3

On the other hand, cerebral oxygenation can be monitored by the noninvasive method of near-infrared spectroscopy (NIRS) to indirectly measure oxygenation of the frontal lobe (ScO2).4 Frontal lobe oxygenation, as determined by NIRS, integrates arterial, regional capillary, and venous oxygenation and follows the calculated capillary oxygen saturation of the brain during manipulation of arterial oxygen and carbon dioxide tensions.5 Frontal lobe oxygenation, as determined by NIRS, also responds to decreased cerebral perfusion as a result of lowering the central blood volume and reducing cardiac output (CO).6 When cerebral perfusion declines markedly, indicated by decreased MAP and the development of presyncopal symp-
fentanyl (0.15-0.25 mg) and propofol (1.5-2.5 mg/kg) and maintained with bolus injections of fentanyl (0.05-0.1 mg) in addition to propofol 4-12 mg/kg per hour. For patients undergoing mastectomy (n = 37), a laryngeal mask was used, while for operations on the neck (n = 26), the patients were orally intubated after the administration of cisatracurium (1.5 mg/kg). Controlled ventilation was established to ensure an end-tidal carbon dioxide tension (PETCO₂) between 3.5 and 4.5 kPa (median, 3.8 kPa) (1 kPa = 7.5 mm Hg), and oxygen and atmospheric air were mixed to establish an inspired oxygen fraction of 0.8. The arterial oxygen saturation was monitored by using a finger pulse oximeter (SpO₂) and kept at more than 97%.

To maintain the central blood volume, the legs were elevated approximately 10 cm and an intravenous infusion of isotonic saline was started before anesthesia and maintained at 3 mL/kg. Hemodynamic monitoring included the recording of HR from a 3-lead electrocardiogram. The arterial blood pressure was determined by using a Finapres device (Ohmeda 2300, Englewood, Colorado) with the cuff applied to the third finger, which has been validated to report even a small decrease in MAP. The Finapres apparatus was connected to a computer that, based on the pressure wave, calculates stroke volume (SV) of the heart by simulating a nonlinear 3-element model of the arterial input impedance.

Beat-to-beat CO was estimated from the arterial pressure wave with the Modelflow method. The method uses a nonlinear 3-element model of the aortic input impedance and simulates aortic flow waveforms from a peripheral arterial pressure signal. Of the 3 model elements, 2 (aortic characteristic impedance and arterial compliance) depend on the elastic properties of the aorta and are computed by using a built-in database of arctangent aortic pressure-area relationships given age and gender of the patient. Integrating the aortic flow waveform per beat provides left ventricular SV. The CO is computed by multiplying SV and HR. The third model element, peripheral vascular resistance, is calculated for each heart beat as the quotient of measured arterial pressure and computed SV. The software used is an online real-time version of Beatsope (FMS, Amsterdam, the Netherlands). The consequently derived CO has been validated against a thermodilution estimate of CO during a deliberate reduction in the central blood volume induced by head-up tilt in healthy subjects, during cardiac surgery, and in intensive care medicine.

Changes in the central blood volume were assessed by thoracic electrical admittance (TA) measured in millisiemens (mS). At a low-frequency (1.5 kHz) and a high-frequency (100 kHz) current, TA distinguishes between the extracellular (TA₁₅) and total water (TA₁₀₀) content. Accordingly, changes in the difference between the high and the low frequency current were considered to reflect changes in the intracellular water content (TAICW).

The ScO₂ and arm muscle oxygenation (SmO₂) were measured by the NIRS (INVOS Cerebral Oximeter, Somanetics, Troy, Michigan) that determines the absorption of near-infrared light at 733 and 808 nm and reports an index of the ratio of oxymyoglobin to deoxyhemoglobin. The NIRS optodes are designed with 1 light-emitting diode and 2 separate optodes whereby changes in light absorption relate predominantly to hemoglobin in blood vessels positioned deeper than the skin and the skull. The optodes were attached on the forehead above the frontal sinuses and above the biceps muscle on the arm used for pulse oximetry, and both optodes were covered to shield external light.

Changes over time for all data were evaluated by analysis of variance for repeated measures and the Fisher test for post-hoc comparisons to identify when changes occurred. Statistical significance was set at the 95% confidence limit (P < .05), and data are presented as median with range. To evaluate whether the lower limit of cerebral blood flow autoregulation was surpassed, for each patient, the ScO₂ value was plotted against MAP, and a separate evaluation was made for 3 age groups (16-40 years, n = 19; 41-60 years, n = 31; and 61-91 years, n = 21) considering that the cerebral circulation might be more vulnerable at advanced age. Thus, the influence of age on ScO₂ was evaluated by correlation analysis (Spearman rho). With inclusion of males and females in the study, an influence of gender on ScO₂ and changes in ScO₂ were evaluated by using the Mann-Whitney test.

**Results**

With the patients resting on the operating table before anesthesia, HR and MAP were stable and within the normal range. However, following the intravenous administration of fentanyl and propofol, there was a drop in MAP from 93 mm Hg (61-126 mm Hg) to 63 mm Hg (37-109 mm Hg) concomitant with a decrease in HR from 76 beats/min (50-95 beats/min) to 63 beats/min (40-103 beats/min; Figure 1). At the same time, SV decreased from 71 mL (37-118 mL) to 65 mL (31-89 mL) and, consequently, CO decreased from 5.3 L/min (2.4-9.0 L/min) to 4.1 L/min (1.9-7.0 L/min). This decrease in CO took place despite an increased or stable central blood volume as assessed by the intracerebral fluid content of the thoracic region as TA₁₅ mS (172 mS) [169-325 mS] to 178 mS [113-333 mS]) and TA₁₀₀ (227 mS [95-400 mS] to 232 mS [132-400 mS]) increased, and, therefore, there was no significant change in TAICW (54 mS [108-113 mS]). During this hypotensive episode following the induction of anesthesia, there were only small changes in the NIRS-determined tissue oxygenation: decreased in SmO₂ (73% [54%-94%] to 69% [48%-87%]), while the ScO₂ increased from 67% (46%-93%) to 72% (48%-95%). Furthermore, neither the recorded values nor the changes...
in $\text{ScO}_2$ were related to the age of the patients (Figure 2). Also there was no significant influence of gender on $\text{ScO}_2$ or on the change in $\text{ScO}_2$.

Intubation of patients or the placement of a laryngeal mask increased MAP from 63 mm Hg (37-109 mm Hg) to 81 mm Hg (52-127 mm Hg), more so in intubated patients (65 mm Hg [109-37 mm Hg] to 98 mm Hg [123-54 mm Hg]) than in patients provided with a laryngeal mask.
mask (61 mm Hg [86-48 mm Hg] to 76 mm Hg [127-52 mm Hg]), while HR increased from 63 beats/min (40-103 beats/min) to 69 beats/min (40-120 beats/min). The SV also increased, and, therefore, CO attained a value of 4.6 L/min (2.3-9.3 L/min). A fraction of inspired oxygen of 0.8 increased the \( \text{Sco}_2 \) to 99% (92%-100%). The \( \text{Smo}_2 \) increased from 67% (46%-93%) to 72% (52%-92%), while \( \text{Sco}_2 \) and the variables derived by electrical admittance remained stable. After the airway was secured, all variables remained stable during the period of surgery lasting 1 hour, 28 minutes (25 minutes to 2 hours, 35 minutes).

After extubation following surgery, all variables were at the levels established before induction of anesthesia (see Figure 1). However, on the transition to spontaneous ventilation when mechanical ventilation was stopped, the \( \text{Sco}_2 \) increased to 77% (50%-97%) concomitant with an increase in PET\( \text{CO}_2 \) (5.7 kPa [4.5-7.0 kPa]). The HR also increased (to 68 beats/min [44-109 beats/min]), as did SV (83 mL [33-125 mL]) and, thus, CO (5.7 L/min [1.4-9.8 L/min]).

To evaluate whether there was any individual change in \( \text{Sco}_2 \) in response to a lowering of MAP at induction of anesthesia, for each patient, \( \text{Sco}_2 \) was correlated to MAP. A statistically significant correlation between \( \text{Sco}_2 \) and MAP could not be established, except for 3 patients. For these 3 patients, the correlation between \( \text{Sco}_2 \) and MAP was established because of an elevation in \( \text{Sco}_2 \) at a high MAP (and Pa\( \text{CO}_2 \)) in transition to spontaneous ventilation and not because of a decrease in \( \text{Sco}_2 \) at a low MAP.

Discussion
This study demonstrates, in contrast with our hypothesis, that a drop in blood pressure at the induction of anesthesia to below what is considered the lower limit of cerebral autoregulation did not affect the NIRS-determined \( \text{Sco}_2 \). After the induction of anesthesia, blood pressure decreased nearly 30%, but that did not appear to have any consequence on cerebral oxygenation as \( \text{Sco}_2 \) became slightly elevated. In 26 patients, MAP was less than 60 mm Hg, which is often considered to represent the lower level of cerebral autoregulation. The study was designed to evaluate the effect of a reduction in MAP as induced by propofol/fentanyl anesthesia on cerebral oxygenation. To separate the effect of arterial pressure itself from that of central blood volume and CO, the study was performed under conditions in which these variables were secured. Accordingly, we consider that the ability of
patients to maintain ScO$_2$ even at a low MAP (lowest value, 37 mm Hg) relates to the maintained central blood volume (Figure 3). Thus, during hemorrhage in a patient anesthetized with propofol and fentanyl, the lower limit of cerebral autoregulation, as evaluated by ScO$_2$, was approximately 60 mm Hg, similar to the values in studies carried out in healthy subjects using lower body negative pressure or head-up tilt, in which the central blood volume is reduced deliberately.

Collectively, the present findings and the evidence from lower body negative pressure and head-up tilt indicate that the lower limit of cerebral autoregulation depends on the central blood volume or the ability to increase CO, possibly by way of an increase of sympathetic activity.

A role of sympathetic activity for cerebral perfusion in humans is made during exercise. In that situation, ScO$_2$ increases together with the middle cerebral artery flow velocity. However, in patients with atrial fibrillation, the increase in middle cerebral artery flow velocity with exercise depends on the ability of the patients to increase CO. Furthermore, when in healthy subjects the ability to increase CO during exercise is restricted by β-adrenergic receptor blockade, the ability to increase middle cerebral artery flow velocity also becomes limited. This limitation is due to sympathetic activity as middle cerebral artery flow increases with a stellate block. In other words, it seems that human brain circulation is influenced significantly by sympathetic activity.

A limitation to this study is that we did not measure cerebral blood flow or, eg, middle cerebral artery flow velocity, but rather oxygenation of the brain. However, under circumstances ranging from hypovolemic shock to maximal exercise, there is a parallel change in ScO$_2$ and middle cerebral artery flow velocity. Furthermore, it may be considered that the main purpose of cerebral blood flow is to provide adequate oxygenation of the brain.

It may further be considered also that the individual variation in the NIRS-derived ScO$_2$ was large. We accept that the initial value is somewhat arbitrary in that we did not know which cerebral vessels were appreciated, and we consider changes in ScO$_2$ more important than the absolute values. From that perspective, the present data suggest that with maintained central blood volume, the lower limit of cerebral autoregulation is at a MAP that is lower than the often considered value of 60 mm Hg, and it is definitely lower than the 80 mm Hg that is derived when the central blood volume is restricted in humans deliberately or because of hemorrhage.

For anesthesia, the implication of this study is that it remains unknown whether a given low MAP is sufficient for adequate perfusion of the brain. A reduction in MAP induced by hemorrhage may affect ScO$_2$, while the finding of this study is that the same MAP may be of no consequence for ScO$_2$ if the central blood volume is maintained. We recommend that the central blood volume be monitored during anesthesia and that brain oxygenation be monitored under circumstances in which the circulation of the brain may be endangered, eg, when hemorrhage is suspected or when hypotensive anesthesia is planned.

REFERENCES


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