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Influence of variations in systemic blood flow and pressure on cerebral and systemic oxygen saturation in cardiopulmonary bypass patients

A. Moerman[1]*, W. Denys[1], F. De Somer[2], P. F. Wouters[1] and S. G. De Hert[1]

[1] Department of Anesthesiology and [2] Department of Cardiac Surgery, Ghent University Hospital, De Pintelaan 185, Gent 9000, Belgium

* Corresponding author. E-mail: annelies.moerman@ugent.be

Editor's key points

- Maintenance of adequate tissue perfusion and oxygenation is important during anaesthesia.
- In patients undergoing cardiopulmonary bypass, the authors independently manipulated blood flow and systemic arterial pressure.
- Cerebral and systemic oxygenation were positively correlated with flow but not with pressure.

Background. Although both pressure and flow are considered important determinants of regional organ perfusion, the relative importance of each is less established. The aim of the present study was to evaluate the impact of variations in flow, pressure, or both on cerebral and whole-body oxygen saturation.

Methods. Thirty-four consenting patients undergoing elective cardiac surgery on cardiopulmonary bypass were included. Using a randomized cross-over design, four different haemodynamic states were simulated: (i) 20% flow decrease, (ii) 20% flow decrease with phenylephrine to restore baseline pressure, (iii) 20% pressure decrease with sodium nitroprusside (SNP) under baseline flow, and (iv) increased flow with baseline pressure. The effect of these changes was evaluated on cerebral (Sc_{O_2}) and systemic (Sv_{O_2}) oxygen saturation, and on systemic oxygen extraction ratio (OER). Data were assessed by within- and between-group comparisons.

Results. Decrease in flow was associated with a decrease in Sc_{O_2} [from 63.5 (7.4) to 62.0 (8.5) %, $P<0.001$]. When arterial pressure was restored with phenylephrine during low flow, Sc_{O_2} further decreased from 61.0 (9.7) to 59.2 (10.2) %, $P<0.001$. Increase in flow was associated with an increase in Sc_{O_2} from 62.6 (7.7) to 63.6 (8.9) %, $P=0.03$, while decreases in pressure with the use of SNP did not affect Sc_{O_2}. Sv_{O_2} was significantly lower ($P<0.001$) and OER was significantly higher ($P<0.001$) in the low flow arms.

Conclusions. In the present elective cardiac surgery population, Sc_{O_2} and Sv_{O_2} were significantly lower with lower flow, regardless of systemic arterial pressure. Moreover, phenylephrine administration was associated with a reduced cerebral and systemic oxygen saturation.

Keywords: cardiopulmonary bypass; oximetry; phenylephrine; spectroscopy, near-infrared

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Decreases in arterial pressure during anaesthesia are often managed by vasopressor use. However, vasoconstrictors may impair regional organ perfusion, which might go undetected when monitoring solely arterial pressure.[1] Cerebral oximetry, a non-invasive technology using near infra-red spectroscopy (NIRS), enables an estimation of systemic venous oxygen saturation, thereby providing a means for real-time monitoring of adequacy of organ perfusion.[2 3]

In a proposed algorithm to correct for decreases in NIRS-derived cerebral oxygen saturation (Sc_{O_2}), increasing mean arterial pressure (MAP) with the use of vasopressors was suggested as one of the initial measures to correct for low Sc_{O_2}.[4] However, recent published data demonstrated that vasopressors such as phenylephrine may negatively affect Sc_{O_2}.[5–9] This negative effect on Sc_{O_2} was not observed when increase in arterial pressure was obtained by vasopressor agents which also increase cardiac output, such as ephedrine.[5 6 10] Also, studies in healthy subjects demonstrated an increase in Sc_{O_2} during exercise,[7 11] whereas in patients not capable of increasing cardiac output, such as in patients with heart failure, the ability to augment Sc_{O_2} during exercise was limited.[12] These data suggest that cardiac output might contribute to the preservation of cerebral oxygenation. However, it should be acknowledged that it is debated whether the distinctive effects of phenylephrine and ephedrine represent genuine differences in Sc_{O_2}, explained by their distinctive effects on cardiac output,[5 6] or if the decrease in Sc_{O_2} is a measurement artifact because of cutaneous vasoconstriction by vasopressors and the inability of cerebral oximeters to deal with extracranial contamination.[13]

The aim of the present study was to determine the impact of variations in flow, in pressure, and in both variables at the same time on cerebral and whole-body oxygen saturation. We hypothesized that not only pressure, but also flow would have a major contribution in preservation of cerebral and systemic oxygenation.

A major problem in evaluating physiologic processes is that pressure and flow are intertwined and modifications to one also alter the other. Cardiopulmonary bypass (CPB) represents a unique clinical circumstance in which different aspects of perfusion can be modified independently and in a controlled manner. Therefore, we chose CPB as the model to test our hypothesis. To separate the effect of flow and pressure on cerebral and systemic oxygenation, we independently modified these parameters in patients on CPB.

Methods

This prospective clinical study was approved by the Institutional Ethics Committee and written informed consent was obtained from all subjects. The trial is registered at ClinicalTrials.gov (NCT01424800). Thirty-four adult patients undergoing elective cardiac surgery (CABG, valve surgery, or both) on moderately hypothermic CPB without blood transfusion were recruited. Patients with history of cerebrovascular disease or significant carotid artery stenosis (>60%) and patients necessitating vasopressor or inotropic therapy before surgery were excluded.

On the morning of surgery, patients were allowed to take their routine medication, except for angiotensin-converting enzyme inhibitors. Patients were premedicated with oral diazepam (5–10 mg). Standard monitoring was used throughout the procedure, including ECG, pulse oximetry, end-tidal oxygen, carbon dioxide and sevoflurane concentrations, bispectral index (BIS), invasive arterial and central venous pressure measurement, and temperature measurement (AS3, Datex, Helsinki, Finland). Arterial pressure was recorded continuously via the right radial artery catheter. Two disposable NIRS sensors were applied on each side of the forehead for continuous registration of Sc_{O_2} of the corresponding brain hemisphere (INVOS 5100, Somanetics Corporation, Troy, MI, USA). All data were recorded continuously and integrated digitally with the RUGLOOP® software (Demed, Temse, Belgium). Anaesthesia was induced with fentanyl 5 $\mu g\ kg^{-1}$, diazepam 0.1 $mg\ kg^{-1}$, and rocuronium 1 $mg\ kg^{-1}$. The lungs were ventilated mechanically with oxygen enriched air (fractional inspired oxygen 0.6) adjusted to keep the end-tidal carbon dioxide ~5 kPa. Anaesthesia was maintained with boluses of fentanyl up to a total dose of 25–35 $\mu g\ kg^{-1}$ and sevoflurane at a minimum concentration of 1.5%.

CPB was performed with a roller pump (Stöckert S5, Sorin group, München, Germany) providing non-pulsatile flow. The priming consisted of 1200 ml colloids (Geloplasma®, Fresenius Kabi, Schelle, Belgium), heparin 5000 IU and mannitol 0.5 g kg^{-1}. Systemic heparinization maintained an activated clotting time of >480 s. Moderately hypothermic CPB (blood temperature 30 °C) was initiated at flow rates of 2.5 litre $min^{-1}\ m^{-2}$. During CPB, Pa_{O_2} and Pa_{CO_2} were maintained ~25 and 5 kPa, respectively. Arterial blood gases were measured at 37°C, independent of body temperature (alpha-stat blood gas management). Blood was sampled after 3 min during steady state, I1 and I3. Temperature, Pa_{CO_2}, Pa_{O_2}, haemoglobin (Hb), and sevoflurane concentrations were kept constant during the measurements.

Interventions

The study used a randomized cross-over design where the subjects served as their own controls. Subjects were randomly allocated, based on computer generated codes, to start with the flow-related interventions, or with the pressure related interventions. In all subjects, response to variations in flow, in pressure, and to the combined variation of flow and pressure was investigated. With the interventions, a change of 20% in pressure, flow, or both was aimed. Changes in arterial pressure were obtained by the use of vasoactive agents, sodium nitroprusside (SNP) for arterial pressure decrease and phenylephrine for arterial pressure increase. Flow was regulated by control of the pump flow.

Baseline (BL) values of MAP, flow, Sc_{O_2}, and systemic oxygen saturation (Sv_{O_2}) were determined at steady state. Steady state was defined as the presence of a stable (<10% change) MAP over a period of 5 min on CPB. After reaching steady state, four different haemodynamic states were simulated: 20% flow decrease (I1), 20% flow decrease with administration of phenylephrine to restore baseline MAP (I2); then haemodynamics were allowed to return to BL values after which SNP was administered until 20% MAP decrease under baseline flow (I3) followed by restoration of baseline MAP by increasing pump flow (I4). The order of variations in pressure and flow was assigned randomly by the use of a computer generated randomization code. Subjects were randomly assigned to undergo first the flow-related interventions and then the pressure related interventions (Group F), or first the pressure related interventions and then the flow-related interventions (Group P). All changes were sustained for 5 min. In Group F, the sequence of interventions was BL, I1, I2, BL, I3, I4. In Group P, the sequence of interventions was BL, I3, I4, BL, I1, I2 (Fig. 1). Interventions were separated by a time period of ~2 min for finalizing computer data registration and preparation of the next intervention.

Outcome variables

To analyse the effect of changes in flow and pressure on changes in Sc_{O_2}, right and left Sc_{O_2} were averaged. We calculated both the change in absolute values in Sc_{O_2}, as the relative change in Sc_{O_2}, defined as the percentage difference between the Sc_{O_2} value at the start of the intervention and the value exactly 5 min later, at the end of the intervention. To evaluate the effect of changes in flow and pressure on whole-body oxygen balance, Sv_{O_2} was measured, and systemic oxygen delivery (DO_2) and oxygen extraction ratio (OER) were calculated according to standard formulae. Arterial oxygen