Cerebral Ischemia Caused by Obstructed Superior Vena Cava Cannula is Detected by Near-Infrared Spectroscopy

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Objective: Bicaval venous cannulation is being used with increasing frequency in neonates and infants to avoid circulatory arrest. However, superior vena cava (SVC) cannula obstruction may result in cerebral ischemia with no change in blood pressure or mixed venous O₂ saturation. The authors hypothesized that near-infrared spectroscopy (NIRS) would allow noninvasive detection of SVC cannula obstruction.

Methods: Fifteen Yorkshire piglets (9.07 ± 0.20 kg) underwent total cardiopulmonary bypass (CPB) (100 mL/kg/min, pH-stat strategy, hematocrit of 20%) with ascending aortic and bicaval cannulations. Femoral arterial and SVC pressure were monitored as well as mixed venous O₂ saturation. NIRS monitoring of tissue oxygenation index (TOI) as well as oxyhemoglobin and deoxyhemoglobin (HHb) was undertaken. Animals were cooled to an esophageal temperature of 25°C over 20 minutes. CPB flow was reduced to 50 mL/kg/min for 20 minutes. Animals then underwent a 60-minute study period of continuous CPB at 50 mL/kg/min with manipulation of the SVC cannula: group 1, open; group 2, partial occlusion; and group 3, complete occlusion. Animals were rewarmed to 37°C at full flow with the SVC cannula open. Cerebral blood flow was assessed at onset of CPB, at end of cooling, at end of low flow, at end of SVC manipulation period, and at end of rewarming using radioactive microspheres.

Results: CBF decreased to 27.9 ± 1.5 mL/min/100 g with complete occlusion (p < 0.01) group 1: 39.7 ± 1.9, group 2, 38.3 ± 2.0 mL/min/100 g with no change in arterial pressure or mixed venous saturation. There were also significant differences in cerebral oxygen delivery between group 3 and other groups (p < 0.01). SVC pressure increased to 19.5 ± 4.5 and 32.5 ± 3.1 mmHg with partial and complete occlusion. NIRS indicated significant cerebral ischemia with a decrease in TOI (p < 0.05; group 3 v group 1 and 2) and an increase in HHb (p < 0.05; group 3 v group 1). At the end of the study, significant acidosis was found in group 3 compared with group 1 (p < 0.05).

Conclusion: SVC cannula obstruction causes cerebral ischemia with no change in blood pressure or venous oxygen saturation. In view of the difficulties and risks of CVP monitoring in babies, it is recommended to use other monitoring modalities such as NIRS to assess adequacy of cerebral perfusion if bicaval cannulation is used in neonates and infants.

KEY WORDS: SVC obstruction, cardiopulmonary bypass, cerebral ischemia, near-infrared spectroscopy

THE SURGICAL OUTCOME FOR congenital cardiac anomalies has improved in recent years. However, children undergoing surgical repair of congenital cardiac anomalies remain at significant risk of brain injury. Estimates of the incidence of neurologic complications in children after cardiac surgery vary between 2% and 25%.1 Many reports have contributed to a reduced incidence of neurologic impairment after cardiopulmonary bypass (CPB) with deep hypothermic circulatory arrest.2,3 However, in general, the use of circulatory arrest has been minimized in recent years. Although CPB without circulatory arrest is considered safe, bicaval venous cannulation carries a risk of nonuniform blood flow distribution because of poor superior vena cava (SVC) drainage. Furthermore, the standard monitoring parameters may not reflect obstructed SVC flow. Poor venous drainage may result in cerebral ischemia with no change in blood pressure or mixed venous O₂ saturation.

Near-infrared spectroscopy (NIRS) has the potential to detect venous obstruction and offers distinct advantages over other indirect methods of monitoring brain physiology.4,5 In the current study, cerebral blood flow (CBF) and oxygenation were examined with manipulation of the SVC cannula.

MATERIALS AND METHODS

Fifteen 5- or 6-week-old Yorkshire piglets were used for this study. They were sedated with ketamine (20 mg/kg) and xylazine (4 mg/kg) and intubated with a 5-mm cuffed endotracheal tube. Each animal was ventilated at a peak inspiratory pressure of 20 cmH₂O, an inspired oxygen fraction of 0.21, and a rate of 12 to 18 breaths/min, by means of a pressure-controlled ventilator (Healthdyne model 105; Healthdyne Technologies, Marietta, Ga.) to achieve a normal pH and arterial carbon dioxide tension. The skin was completely shaved before application of optodes to avoid the possible “light piping” by hair. A pair of fiberoptic optodes for NIRS was placed on the head over the frontal lobes, with an interoptode distance of 4.0 cm. For intraoperative monitoring and blood sampling, arterial and venous catheters were placed in the left femoral artery and vein, respectively. After an intravenous bolus injection of fentanyl (25 µg/kg) followed by pancuronium (0.5 mg/kg), anesthesia was maintained by a continuous infusion of fentanyl (25 µg/kg/h), midazolam (0.2 mg/kg/h), and pancuronium (0.2 mg/kg/h) throughout the entire experiment. A median sternotomy was performed to expose the ascending aorta, right atrium, and SVC for cannulation. A single-lumen catheter was placed in the jugular vein through a pursestring in the innominate vein and was used to monitor the jugular venous pressure and to draw the jugular venous blood. After systemic heparinization (300 IU/kg), ascending aortic and SVC + right atrial cannulations were performed and the SVC was taped for total bypass. Bilateral subclavian arteries and aygous vein were ligated. The CPB circuit consisted of a roller-pump, membrane oxygenator (Minimax; Medtronic, Inc, Anaheim, CA) and sterile tubing, with a 40-µm arterial filter (Olson Medical, Ashland, MA). Methylprednisolone (30 mg/kg), furosemide (0.25 mg/kg), sodium bicarbonate (10 mL), fentanyl (25 µg/kg), and pancuronium (0.5 mg/kg) were added to the prime. The pH-stat strategy was used, and hematocrit was maintained at a pressure-controlled ventilator (Healthdyne model 105; Healthdyne Technologies, Marietta, Ga.) to achieve a normal pH and arterial carbon dioxide tension. The skin was completely shaved before application of optodes to avoid the possible “light piping” by hair. A pair of fiberoptic optodes for NIRS was placed on the head over the frontal lobes, with an interoptode distance of 4.0 cm. For intraoperative monitoring and blood sampling, arterial and venous catheters were placed in the left femoral artery and vein, respectively. After an intravenous bolus injection of fentanyl (25 µg/kg) followed by pancuronium (0.5 mg/kg), anesthesia was maintained by a continuous infusion of fentanyl (25 µg/kg/h), midazolam (0.2 mg/kg/h), and pancuronium (0.2 mg/kg/h) throughout the entire experiment. A median sternotomy was performed to expose the ascending aorta, right atrium, and SVC for cannulation. A single-lumen catheter was placed in the jugular vein through a pursestring in the innominate vein and was used to monitor the jugular venous pressure and to draw the jugular venous blood. After systemic heparinization (300 IU/kg), ascending aortic and SVC + right atrial cannulations were performed and the SVC was taped for total bypass. Bilateral subclavian arteries and aygous vein were ligated. The CPB circuit consisted of a roller-pump, membrane oxygenator (Minimax; Medtronic, Inc, Anaheim, CA) and sterile tubing, with a 40-µm arterial filter (Olson Medical, Ashland, MA). Methylprednisolone (30 mg/kg), furosemide (0.25 mg/kg), sodium bicarbonate (10 mL), fentanyl (25 µg/kg), and pancuronium (0.5 mg/kg) were added to the prime. The pH-stat strategy was used, and hematocrit was maintained at...
maintained at 20%. Full bypass flow was set at 100 mL/kg/min. CPB was started, a left ventricular vent was placed, and animals were perfused for 10 minutes at normothermia. During CPB, SVC and inferior vena cava (IVC) flows were measured every 5 minutes by individual magnetic flow meters that were interposed in the venous drainage lines. Blood gases were checked from SVC, IVC, and mixed venous blood as well as arterial blood.

After stabilization, animals were cooled to an esophageal temperature of 25°C over 20 minutes. Ventilation was stopped after the establishment of CPB. CPB flow was reduced to 50 mL/kg/min corresponding to a flow index of approximately 1.2 L/min/m² at 25°C for 20 minutes. Each group underwent 60 minutes of continuous CPB with 50 mL/kg/min flow according to assigned protocol (SVC line: open, partially occluded, or completely occluded). Rewarming was begun at 100 mL/kg/min without SVC occlusion, and animals were warmed to 37°C over 30 minutes. Then animals were euthanized by injection (FatalPlus; Vortech Pharmaceuticals, Dearborn, MI).

All animals received humane care in compliance with the “Principles of Laboratory Animal Care” formulated by the National Society for Medical Research and the “Guide for the Care and Use of Laboratory Animals” prepared by the Institute of Laboratory Animal Resources and published by the NIH (NIH publication No. 86-23, revised in 1985).

Animals were randomized into 3 groups according to SVC cannula manipulation: (1) group 1: SVC cannula was left open, (2) group 2: SVC cannula was partially occluded to reduce SVC flow by 50%, and (3) group 3: SVC cannula was completely clamped.

Arterial and jugular blood gas values, including electrolyte, glucose, and lactate concentrations, were measured before CPB (baseline) and during CPB, particularly before each microsphere injection. The measurements were performed by a blood gas analyzer (Stat Profile 9; Nova Biomedical, Waltham, MA). Hemoglobin, saturation, and oxygen content were calculated by the device.

A pair of fiberoptic optodes was attached to the head of the animal with a probe holder after induction of anesthesia. The optode spacing was 4.0 cm in a coronal plane. These 2 optodes, one a transmitter and one a receiver of laser light of near-infrared wavelength, were connected to a NIRS device (NIRO300; Hamamatsu Photonics K.K., Japan). The NIRO 300 device uses 4 wavelengths, 775, 810, 850, and 910 nm, to measure and calculate the relative concentration changes in oxygenated hemoglobin (HbO₂), deoxygenated hemoglobin (HHb), total hemoglobin, and oxidized cytochrome aa₃ as well as tissue oxygenation index (TOI), which is a calculated ratio of oxygenated to total hemoglobin. TOI is an index of average tissue hemoglobin saturation and is calculated independently from the change in HbO₂ and HHb. It is measured by 3 different detectors and is calculated by using the spatially resolved spectroscopy method. This value is also quite different from percutaneous arterial oxygen saturation measured by pulse oximetry. Data were recorded every 10 seconds after the induction of anesthesia through the termination of CPB.

Regional blood flow to the brain was measured by radioactive microspheres (1) at 10 minutes after initiation of CPB (baseline, 37°C), (2) at 20 minutes after the start of cooling with full flow (25°C), (3) at 20 minutes after the beginning of low flow (25°C), (4) at the end of SVC cannula manipulation (25°C), and (5) at the end of experiment (37°C). Microspheres (15 μm in diameter) labeled with one of the following radioactive nuclides: ⁴¹Ce, ⁵¹Cr, ⁹⁹Ru, ⁹⁵Nb, and ⁴⁶Sc suspended in 2 mL of 0.9% saline followed by 2 mL of 0.9% saline were injected into a side port on the arterial tubing 1 m from the tip of the arterial cannula to ensure complete mixing. Each microsphere injection consisted of approximately 2.5 × 10⁶ microspheres. A measured quantity of blood (approximately 5 mL) as reference was withdrawn at a constant rate by a syringe pump (model 551143; Harvard Apparatus) from the arterial catheter placed in the left femoral artery. Arterial blood was withdrawn before, during, and after the microsphere injection for a total of 90 seconds. At the termination of the experiment, the brain was removed and weighed. Three samples were taken from the left and right frontal cortex. Additional samples were taken from the left and right parietal and occipital cortex, the left and right cerebellum, pons, and medulla oblongata. Radioactivity was counted with a gamma counter (Cobra II autogamma; Packard Instrument, Downers Grove, IL) with a spillover correction between the nuclides. The reference blood flow was also analyzed for radioactivity. The regional blood flow calculated from the rate of withdrawal of the reference blood and the ratio of the radioactivity of the brain to the reference blood. Average cerebral blood flow was derived by adding the average regional blood flows and dividing them by number of regions.

Cerebral oxygen delivery (CDO₂), cerebral metabolic rate for oxygen (CMRO₂), and oxygen extraction ratio (OER) as well as cerebral metabolic rate for glucose and lactate were calculated by using a standard formula.

All results were expressed as mean ± standard error of the mean. Repeated measures of analysis of variance were used for sequential, time-based measurements such as CBF, CD0₂, CMRO₂, or OER.
NIRS data were also analyzed in the same manner. In cases in which multiple t tests were used on the same data, a Bonferroni correction was applied for the number of t tests used. Data were further compared by a Student t test if analysis of variance was significant. A p value <0.05 was considered statistically significant. All data were analyzed by a statistical analysis software package (Stat View 5.0; Abacus Concepts, Berkeley, CA).

RESULTS
Preoperative data are shown in Table 1. There were no significant differences among the groups. During the experiment, there were also no significant differences in esophageal and rectal temperatures, perfusion pressure, mixed venous saturation, hematocrit, and arterial blood gas among the groups.
Fig 2. Change in (A) SVC flow and (B) IVC flow.
SVC flow in group 2 was controlled to be half that in group 1 (SVC flow in group 3 was 0 mL/kg/min) (Fig 2A). IVC flow was also recorded as it responded to manipulation of the SVC catheter (Fig 2B). Jugular venous pressure was recorded for each group (Fig 3).

CBF and CDO$_2$ decreased significantly with complete occlusion (group 3 v group 1) (Fig 4). However, there were no significant differences in CMRO$_2$ and OER among the groups (Fig 5). Also, there were no significant differences in cerebral metabolic rate for glucose and lactate among the groups (Fig 6). There was a significant decrease in TOI during SVC occlusion in group 3 (Fig 6E). There was a tendency for jugular venous saturation in group 3 to be lower than that in the other 2 groups, although it did not reach statistical significance.

**DISCUSSION**

This study has shown that partial or even complete occlusion of the SVC cannula during hypothermic reduced flow bypass results in no change in mean perfusion pressure or mixed venous oxygen saturation. This is an important finding because perfusion pressure and mixed venous oxygen saturation are the 2 principal means that are relied on for monitoring adequacy of perfusion during CPB. The study has also shown that complete occlusion of the SVC cannula results in a significant decline in cerebral blood flow as well as cerebral oxygen delivery. Because cerebral metabolic rate for oxygen consumption is unchanged, there is a risk of critical cerebral ischemia. This can be detected by NIRS, which is shown by this study to be a sensitive monitoring modality for detecting SVC occlusion. There is a significant increase in deoxyhemoglobin with SVC occlusion. The tissue oxygenation index also is helpful in indicating a state of relative cerebral ischemia.

Jugular venous pressure monitoring was a sensitive indicator of partial and complete SVC cannula occlusion in this animal model. In clinical practice, monitoring of SVC pressure above the level of SVC cannulation can be technically challenging and carries significant risk. A combination of relatively small vessel size, vessel injury through repeated unsuccessful cannulation attempts, as well as prolonged usage beyond several days, particularly if combined with infusion of hyperosmolar solution, can set the stage for a high risk of SVC thrombosis. This is an extremely serious complication in the neonate or small infant. For this reason, many groups prefer to rely on direct cannulation of the right atrium with a transthoracic monitoring catheter for monitoring of central venous pressure postoperatively.

An important technical difficulty with central venous pressure monitoring in the neonate or small infant is that the tip of the catheter is likely to extend below the level of SVC cannulation. It is not uncommon for the surgeon to note the tip of the catheter in the right atrium when an internal jugular catheter of standard length has been placed in a neonate. Under these circumstances, a
Fig 4. (A) CBF and (B) CDO₂.

(A) CBF (mL/min/100g tissue)

(B) CDO₂ (mL/min/100g tissue)

* *P* < 0.01 vs Group I, II

* *P* < 0.05 vs Group II
jugular venous catheter would be falsely reassuring to the operative team regarding the absence of SVC occlusion.

Previous reports from this group have documented both the utility as well as the limitations of NIRS monitoring during CPB. Ideally, the technique would allow monitoring of the redox state of cytochrome a,a3. This is important in the setting of CPB in which the conditions of hypothermia and relative alkalinity shift oxyhemoglobin dissociation leftward. Under these circumstances, mixed venous oxygen saturation may be falsely reassuring when high. Because cytochrome a,a3 is the terminal cytochrome of the electron transport chain that hands off electrons to oxygen, a change of redox state in an appro-

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**Figure 5.** (A) CMRO and (B) OER.
Fig 6. NIRS data during the experiment. Changes in (A) oxygenated hemoglobin (HbO₂), (B) HHb, (C) total hemoglobin (HbT), (D) oxidized cytochrome a,a₃ (CytO₂), and (E) TOI are shown.

A

HbO₂ (μM*DPF)

B

HHb (μM*DPF)

Fig 6. NIRS data during the experiment. Changes in (A) oxygenated hemoglobin (HbO₂), (B) HHb, (C) total hemoglobin (HbT), (D) oxidized cytochrome a,a₃ (CytO₂), and (E) TOI are shown.
Figure 6. (Cont’d)
appropriate direction would be a helpful monitor of successful oxygen delivery to the internal milieu of cerebral neurons. Unfortunately, however, a study using cyanide performed by this group has failed to validate the cytochrome signal in the setting of CPB. The signal is overwhelmed by the major changes that occur in the hemoglobin signal during CPB.

Although the cytochrome signal is not currently reliable for monitoring during CPB, the oxyhemoglobin and deoxyhemoglobin signals have proven to be very useful. For example, the oxyhemoglobin nadir duration has proven to be a useful predictor of safe duration of hypothermic circulatory arrest. In a study using a piglet model, it was also shown that the new tissue oxygenation index is a reliable predictor of neurologic injury. The present study adds further evidence that the tissue oxygenation index is a helpful indicator of cerebral ischemia. Furthermore, in the setting of SVC cannula obstruction, the mechanism of cerebral ischemia, namely venous congestion, results in an increased level of HHb. In contrast, during hypothermic circulatory arrest, there is a decline in oxyhemoglobin with a simple reciprocal increase in HHb unlike the pattern seen in the current study. In the current study, oxyhemoglobin remained stable, but there was an important increase in deoxyhemoglobin.

A limitation of the current study is the dissimilarity between the vessel anatomy of the piglet relative to humans. Piglets have essentially a bovine trunk in which both carotid arteries arise from the aortic arch. In addition, the SVC is relatively smaller than that in humans, suggesting that alternative venous collateral pathways, possibly paraspinal, may be available to decompress the brain in the setting of SVC occlusion. If this is the case, however, the findings of this study would be even more dramatic in humans.

In conclusion, NIRS is a helpful monitoring technique for detecting venous cannula occlusion during hypothermic CPB. Traditional monitoring methods such as perfusion pressure and venous oxygen saturation may show little evidence of either partial or complete superior vena caval occlusion.

ACKNOWLEDGMENTS

The authors thank Patricia Dunning from the Department of Radiology, Children’s Hospital, Boston, MA, for her technical support. Laura Young is also thanked for preparation of the manuscript.

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