The influence of systemic hemodynamics and oxygen transport on cerebral oxygen saturation in neonates after the Norwood procedure

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Supplemental material is available online.

Objectives: Ischemic brain injury is an important morbidity in neonates after the Norwood procedure. Its relationship to systemic hemodynamic oxygen transport is poorly understood.

Methods: Sixteen neonates undergoing the Norwood procedure were studied. Continuous cerebral oxygen saturation was measured by near-infrared spectroscopy. Continuous oxygen consumption was measured by respiratory mass spectrometry. Pulmonary and systemic blood flow, systemic vascular resistance, oxygen delivery, and oxygen extraction ratio were derived with measurements of arterial, and superior vena cava and pulmonary venous gases and pressures at 2- to 4-hour intervals during the first 72 hours in the intensive care unit.

Results: Mean cerebral oxygen saturation was 66% ± 12% before the operation, reduced to 51% ± 13% on arrival in the intensive care unit, and remained low during the first 8 hours; it increased to 56% ± 9% at 72 hours, still significantly lower than the preoperative level ($P < .05$). Postoperatively, cerebral oxygen saturation was closely and positively correlated with systemic arterial pressure, arterial oxygen saturation, and arterial oxygen tension and negatively with oxygen extraction ratio ($P < .0001$ for all). Cerebral oxygen saturation was moderately and positively correlated with systemic blood flow and oxygen delivery ($P < .0001$ for both). It was weakly and positively correlated with pulmonary blood flow ($P = .001$) and hemoglobin ($P = .02$) and negatively correlated with systemic vascular resistance ($P = .003$). It was not correlated with oxygen consumption ($P > .05$).

Conclusions: Cerebral oxygen saturation decreased significantly in neonates during the early postoperative period after the Norwood procedure and was significantly influenced by systemic hemodynamic and metabolic events. As such, hemodynamic interventions to modify systemic oxygen transport may provide further opportunities to reduce the risk of cerebral ischemia and improve neurodevelopmental outcomes.

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There has been a dramatic reduction in mortality after surgery for complex congenital heart defects. Consequently, much attention is now being directed to neurologic outcomes among survivors.[1] The incidence of measurable neurologic sequelae is as high as 25%, including both early postoperative seizures[2,3] and long-term neurodevelopmental impairment such as cognitive, attentional, behavioral, and neuromuscular disabilities.[4-8] Studies on neurologic outcomes have largely focused on specific intraoperative risk factors, such as hemodilution, pH management,[9] and deep hypothermic circulatory arrest.[2-5,8,10] Others have reported preoperative reduction of cerebral blood flow and ischemic injury (in turn related to anatomic and functional features), being most severe in neonates with hypoplastic left heart syndrome.[11-14] Postoperative hemodynamic instability may further affect

Abbreviations and Acronyms

CPB = cardiopulmonary bypass
Do_2 = oxygen delivery
ERo_2 = oxygen extraction ratio
ICU = intensive care unit
NIRS = near-infrared spectroscopy
Pao_2 = arterial oxygen tension
Qp = pulmonary blood flow
Qs = systemic blood flow
Sco_2 = cerebral oxygen saturation
SVR = systemic vascular resistance
Vo_2 = oxygen consumption

the vulnerable brain. Prolonged stay in the intensive care unit (ICU) has been found to be associated with poorer neurologic outcomes.[15] Ischemic lesions early after cardiac surgery, in the form of periventricular leukomalacia, have been seen in more than 50% of neonates and have been attributed to postoperative hypoxia and diastolic hypotension.[16,17]

Neonates with hypoplastic left heart syndrome undergoing the Norwood procedure, which involves reconstruction of the aortic arch to maintain unobstructed systemic blood flow (Qs) and limiting pulmonary blood flow (Qp) with a modified Blalock–Taussig shunt, may be particularly prone to neurologic insult, with hypoxic–ischemic lesions seen preoperatively in nearly half of these neonates.[12,17] Intraoperatively, the already vulnerable neonatal brain will be exposed to the effects of prolonged cardiopulmonary bypass (CPB), circulatory arrest, and variable hemodynamic and metabolic events. The effects of regional brain perfusion strategies remain to be demonstrated, but it is likely that intraoperative neuroprotection is less than complete.[18] In addition to these preoperative and intraoperative risk factors, our group has shown that the early postoperative period after the Norwood operation is characterized by hemodynamic instability with marginal systemic oxygen delivery (Do_2), with the injured neonatal single right ventricle supplying the parallel circulations and arterial oxygen desaturation.[19,20] At the same time, systemic oxygen consumption (Vo_2) increases,[19,20] thus further impairing systemic oxygen transport and placing the cerebral circulation at risk. It has been recently reported that low systemic venous oxygen saturation is associated with childhood neurodevelopmental abnormality.[21] Clearly, a systematic assessment of the effects of systemic hemodynamics and oxygen transport on cerebral oxygenation during the early postoperative period is needed to understand the mechanisms of neurologic ischemic injury and to improve postoperative management and long-term neurologic outcomes.

Near-infrared spectroscopy (NIRS) provides a noninvasive, continuous method to monitor regional tissue oxyhemoglobin saturation.[22,23] It has been extensively used during CPB to determine the risk factors for poor cerebral perfusion.[16,18,24] In the present study, we hypothesized that cerebral oxygen transport might be influenced by systemic hemodynamics and oxygen transport during the early postoperative period after the Norwood procedure. We used NIRS to continuously measure cerebral oxygen saturation (Sco_2) and respiratory mass spectrometry to continuously measure Vo_2 and to derive measurements of Qp and Qs, Do_2, and oxygen extraction ratio (ERo_2). We examined the effects of each of the systemic hemodynamic indices and oxygen transport variables on Sco_2 during the first 72 hours after the Norwood procedure.

Patients and Methods

Patients

This study was approved by the Research Ethics Board at the Hospital for Sick Children, Toronto, Canada. Written informed consent was obtained from the parents of 16 neonates (14 boys, age range 4–16 days, median 7 days) undergoing the Norwood procedure between April 2004 and November, 2006. Patient demographics are shown in Table E1. Data from some of these patients were reported previously on systemic hemodynamics and oxygen transport early after the Norwood procedure.[19,20]

Operative Procedure

Neonates were intubated with a cuffed endotracheal tube (Microcuff-Heidelberg-Pediatric; Microcuff GmbH, Weinheim, Germany). General anesthesia was maintained with inhaled isoflurane, intravenous fentanyl, and pancuronium bromide. A standard Norwood procedure with regional cerebral circulation was used. All neonates had a 3.5-mm right modified Blalock–Taussig shunt with the distal anastomosis placed centrally on the intramediastinal pulmonary artery. CPB management consisted of a target flow of 125 $mL \cdot min^{-1} \cdot kg^{-1}$ and a hematocrit value of 25% to 30% with modified pH-stat blood gas management for uniform cooling (18°C–20°C) at the esophageal site. Selected cerebral perfusion was performed in all neonates at pump flows of 30 to 35 $mL \cdot min^{-1} \cdot kg^{-1}$. All neonates received aprotinin 1.7×106 KIU/m^2 and methylprednisolone 10 mg/kg before CPB. Phenoxybenzamine 0.25 mg/kg was added to the pump prime. Separation from CPB occurred after initiation of infusions of milrinone ($0.66\ \mu g \cdot min^{-1} \cdot kg^{-1}$) and dopamine ($5\ \mu g \cdot min^{-1} \cdot kg^{-1}$). Modified ultrafiltration was used in all neonates immediately after separation from CPB. A pulmonary venous line was inserted into the orifice of the right upper pulmonary vein. The sternal incision was left open routinely in all the patients.

Critical Care

Infants received time-cycled pressure control/pressure support ventilation. Sedation and analgesia were given as a continuous intravenous infusion of morphine ($20–40\ \mu g \cdot h^{-1} \cdot kg^{-1}$), intermittent injections of lorazepam (0.1 mg/kg), and pancuronium (0.1 mg/kg). Pancuronium was discontinued when the patient achieved satisfactory hemodynamic stability.

The central esophageal temperature was monitored continuously and maintained at 36°C–37°C. Vasoactive agents (milrinone,