CHD

Brain magnetic resonance imaging abnormalities after the Norwood procedure using regional cerebral perfusion

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Objectives: Neurologic deficits are common after the Norwood procedure for hypoplastic left heart syndrome. Because of the association of deep hypothermic circulatory arrest with adverse neurologic outcome, regional low-flow cerebral perfusion has been used to limit the period of intraoperative brain ischemia. To evaluate the effect of this technique on brain ischemia, we performed serial brain magnetic resonance imaging in a cohort of infants before and after the Norwood operation using regional cerebral perfusion.

Methods: Twenty-two term neonates with hypoplastic left heart syndrome were studied with brain magnetic resonance imaging before and at a median of 9.5 days after the Norwood operation. Results were compared with preoperative, intraoperative, and postoperative risk factors to identify predictors of neurologic injury.

Results: Preoperative magnetic resonance imaging (n = 22) demonstrated ischemic lesions in 23% of patients. Postoperative magnetic resonance imaging (n = 15) demonstrated new or worsened ischemic lesions in 73% of patients, with periventricular leukomalacia and focal ischemic lesions occurring most commonly. Prolonged low postoperative cerebral oximetry (<45% for >180 minutes) was associated with the development of new or worsened ischemia on postoperative magnetic resonance imaging ($P = .029$).

Conclusions: Ischemic lesions occur commonly in neonates with hypoplastic left heart syndrome before surgical intervention. Despite the adoption of regional cerebral perfusion, postoperative cerebral ischemic lesions are frequent, occurring in the majority of infants after the Norwood operation. Long-term follow-up is necessary to assess the functional effect of these lesions.

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Neurologic and developmental abnormalities are common in children with hypoplastic left heart syndrome (HLHS) after the Norwood procedure.[1-5] Although the cause of brain injury in these infants is likely multifactorial, with contributions from preoperative, intraoperative and postoperative events, the use of deep hypothermic circulatory arrest (DHCA) appears to play a role in poor neurologic and developmental outcome.[6-10] Ischemic brain lesions have been documented on pathologic brain specimens[11] and on magnetic resonance imaging (MRI)[12] in neonates after surgical palliation with DHCA.

Because of these concerns, many centers have adopted the technique of regional low-flow cerebral perfusion (RLFP) during aortic arch reconstruction in lieu of DHCA. RLFP decreases the period of cerebral ischemia by limiting decreases in cerebral blood volume and oxygen saturation.[13] Although RLFP has been associated with better neurologic outcome in animal models,[14] such studies have not been performed in human subjects. In the present study we compare preoperative and postoperative brain MRI

Abbreviations and Acronyms

BT = Blalock-Taussig
CHD = congenital heart disease
CICU = cardiac intensive care unit
CPB = cardiopulmonary bypass
DHCA = deep hypothermic circulatory arrest
EEG = electroencephalography
HLHS = hypoplastic left heart syndrome
MRI = magnetic resonance imaging
NIRS = near-infrared spectroscopy
PVL = periventricular leukomalacia
RFLP = regional low-flow cerebral perfusion
rSO_2 = regional cerebral oxygen saturation
Sao_2 = arterial oxygen saturation
Svo_2 = venous oxygen saturation

findings in neonates undergoing the Norwood procedure with RLFP.

Methods

With institutional review board approval and informed consent, all infants with HLHS or its variants admitted to the cardiac intensive care unit (CICU) at Cincinnati Children's Hospital Medical Center between September 2003 and March 2005 were evaluated for study inclusion. Inclusion criteria included term gestational age ($\geq$36 weeks) and an intention to undergo surgical intervention (Norwood operation with aortic arch reconstruction) with RLFP. Infants were excluded if they had (1) a history of birth asphyxia (5-minute Apgar score $<$5), (2) a genetic anomaly associated with neurodevelopmental abnormalities, or (3) preoperative cardiac arrest.

MRI scans of the brain were performed preoperatively (day of the operation) and in the early postoperative period. The scans were performed on a Signa LX 1.5-T scanner (GE Medical, Milwaukee, Wis). The following sequences were performed: (1) sagittal T1-weighted spin-echo images, (2) axial T1-weighted inversion-recovery images, (3) axial and coronal T2-weighted fast spin-echo images, (4) axial diffusion-weighted images, and (5) short echo proton magnetic resonance spectroscopy in the basal ganglia. All MRI scans were reviewed by a single neuroradiologist blinded to the subjects' clinical status. MRI scans were reviewed for congenital and acquired lesions, including general or focal atrophy, periventricular leukomalacia (PVL), cerebral edema, delayed myelination, intraparenchymal hemorrhage, intraventricular hemorrhage, and infarction. All lesions were classified as mild, moderate, or severe. PVL, infarction, and intraparenchymal hemorrhage were considered to represent ischemia.

Clinical Management

Preoperative clinical management was provided in the CICU. Infants were maintained on a continuous prostaglandin infusion. Pulmonary overcirculation was managed with administration of subambient oxygen (fraction of inspired oxygen, 0.17-0.20) or addition of inhaled CO_2. Inotropic medication was administered at the discretion of the attending physician. As an assessment of overall status, a preoperative inotropic score was calculated as the sum of all inotrope doses, correcting for potency.[15,16] Preoperative neurologic evaluation included electroencephalography (EEG) and examination by a pediatric neurologist directed at level of consciousness, motor tone, response to stimuli, and deep tendon reflexes. Regional cerebral oxygen saturation (rSo_2) was monitored continuously by using near-infrared spectroscopy (NIRS; Somanetics INVOS 5100A, Troy, Mich), with the probe placed on the right side of the patient's forehead. Monitoring commenced 12 hours before the operation. Data were recorded at 1-minute intervals. An rSo_2 value of less than 45% was considered to represent cerebral desaturation. Cumulative time spent with rSo_2 values of less than 45% was recorded. Management was not altered on the basis of cerebral oximetry readings.

For the preoperative MRI, anesthesia was induced with fentanyl (5 μg/kg), midazolam (0.1 mg/kg), and vecuronium (0.2 mg/kg). In patients not already mechanically ventilated, nasotracheal intubation was performed. Patients were monitored during the MRI with continuous pulse oximetry, capnography, electrocardiography, and blood pressure measurements. After the MRI, patients were transported to the operating suite for cardiac surgery. Surgical repair consisted of aortic arch reconstruction, ascending aorta–to–pulmonary artery anastomosis, and creation of an unrestrictive atrial septal communication. Pulmonary blood flow was provided by either a systemic–to–pulmonary artery shunt or a right ventricle–to–pulmonary artery conduit.

Cardiopulmonary bypass (CPB) and surgical management followed our usual institutional practice. Whole blood was added to the primer to yield a goal hematocrit value of 28% to 30% during CPB. Arterial blood gas-pH management followed the alpha-stat strategy on CPB initiation, with switch to pH-stat strategy during cooling. The alpha-stat strategy was resumed during rewarming. All patients were cooled to deep hypothermia (18°C). During reconstruction of the aortic arch, continuous RLFP was provided through the innominate shunt at 30 $mL \cdot kg^{-1} \cdot min^{-1}$. Before separation from CPB, patients received a loading dose of milrinone (37.5 μg/kg). Dopamine and epinephrine infusions were instituted and titrated to achieve adequate blood pressure and systemic vascular resistance.

Postoperative management was provided in the CICU. Inotropic medication was adjusted at the discretion of the attending physician. Sodium nitroprusside was added as tolerated for afterload reduction and to improve cardiac output. Management targets included mean arterial pressure of 45 mm Hg or greater, mixed venous oxygen saturation (Svo_2) of 50% or greater, arterial oxygen saturation (Sao_2) of 70% or greater, and a hematocrit value of greater than 40%. Blood for Svo_2 measurement was sampled from a catheter placed intraoperatively in the superior vena cava. Svo_2 was measured on admission and every 4 hours. Cerebral rSo_2 monitoring continued for 48 hours after the operation. Postoperative inotrope scores were calculated every 6 hours.

The postoperative MRI was performed when the patients were deemed suitable for transport, generally between 5 and 14 days after the operation. Sedation was provided with oral pentobarbital (5 mg/kg) in spontaneously breathing patients and with inhaled anesthesia in intubated patients. Patients were monitored in similar fashion as the preoperative scan. Postoperative EEG and neuro-