BRAIN INJURY PATTERN AND INFLUENCING FACTORS DURING NEONATAL HYPOTHERMIC LOW-FLOW CARDIOPULMONARY BYPASS

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Introduction: Hypothermic low-flow cardiopulmonary bypass (LF-CPB) and deep hypothermic circulatory arrest (DHCA) facilitate surgical repair of complex congenital heart defects. Since outcome studies in neonates have shown advantages of LF-CPB compared with DHCA, it is becoming more popular, but is still associated with neurobehavioral sequelae.(1) Whereas the injury pattern has been described for DHCA, it remains uncertain for LF-CPB.(2) This study examines function and histopathology after LF-CPB in neonatal piglets.

Methods: Piglets (n=22, age 3-5 days) were anesthetized with ketamine/acepromazine and fentanyl/droperidol, intubated, and ventilated. Carotid artery and external jugular vein were cannulated for CPB. Arterial blood pressure (MAP), pH, blood gases, hematocrit, and blood glucose were monitored throughout the experiment. Brain, esophageal, and rectal temperatures were recorded, cortical cerebral blood flow (CBF) was measured (laser Doppler). Animals underwent CPB with ph-stat management until 22 C (brain), followed by LF-CPB for 150 min, rewarming, separation from CPB, extubation and recovery for 2 or 9 days. Weight gain and neurological status were assessed daily. Histopathology (H) was assessed after 2 days.

Results: During LF-CPB, MAP was 9 mmHg (range 6-14) and pump flow was 9 ml/kg/min (range 4-19). Cerebral cortical blood flow during LF-CPB was 8±7% of pre-CPB (n=14, range 1-23%). Thirteen animals survived, 5 animals died a cardiovascular, 2 a neurologic death, and 1 of hyperthermia. One day after CPB functional impairment was mild in 21%, moderate in 29%, severe in 14%; 36% showed no disability. Two days after CPB function improved to no disability in 70%, mild disability in 15%, and moderate in 15% animals; no animal was rated as severely impaired. However, all animals showed histological brain damage. Neuronal damage was moderate to severe in neocortex and hippocampus, mild in basal ganglia, thalamus, white matter, and cerebellum, and not observed in brain stem. Cell death appeared as selective neuronal necrosis, less so apoptosis, in layers 4-6 in neocortex and CA1-4 sections in hippocampus, without cerebral infarction. Neocortical, hippocampal, and white matter damage inversely correlated with arterial pCO2 during LF-CPB or rewarming, not MAP, pump flow, or CBF. Higher blood glucose during LF-CPB was associated with less hippocampal damage and a higher hematocrit post-CPB with less functional impairment and less damage in basal ganglia.

Discussion: Brain damage following LF-CPB is similar yet different from DHCA. Vulnerable areas in both include neocortex and hippocampus, appearing as selective neuronal death and rarely infarction. Neuronal death after LF-CPB appeared as necrosis most often in deep gray matter (layer 4-6), a watershed area. Conversely, neuronal death after DHCA appeared apoptotic, typically in superficial gray matter (layers 2 and 3). Even with pH-stat management, higher pCO2 during LF-CPB and rewarming reduces brain damage; possibly by a mechanism independent of arterial pressure, pump flow, or cortical cerebral blood flow. Higher hematocrit and blood glucose are also beneficial.

References:
1. Circulation 1999; 100(5): 526