INTRODUCTION

In the United States, it is estimated that 87% of children that suffer unexpected cardiac arrest do not survive, whilst 50% of survivors suffer an unfavorable neurological outcome [1]. We previously reported that cerebral blood flow (CBF) disturbances after 9 minutes of pediatric asphyxial cardiac arrest (CA) are characterized by early hyperemia at 5 min followed by resolution of normal CBF in all brain regions except cortex, where early hypoperfusion is seen. Hyperemia and hypoperfusion are viewed as potential targets for therapies to improve neurological outcome after asphyxial cardiac arrest. Early hyperemia is regarded by some as essential for good neurological outcome [2], however other studies showed a benefit from reducing early hyperemia [3]. Reactive O₂ and N₂ species (ROS, RNS), are generated during CA and after resuscitation and can cause either vasoconstriction or vasodilatation depending on species generated. Scavenging ROS and RNS with polynitroxyl albumin (PNA), improved outcome in a model of focal brain ischemia [4]. The effect of resuscitation with colloid on CBF after CA remains to be defined.

Our research team has modified an adult model of asphyxial arrest, simulating the pediatric population using postnatal day (PN) 17 rats. This model allows for invasive physiological monitoring and acute resuscitation that closely mimics guidelines used in humans. We hypothesized that albumin or PNA given at resuscitation from pediatric asphyxial CA in immature rats would ameliorate regional CBF disturbances.

MATERIALS AND METHODS

PN 17 rats were used for this study. Isoflurane (1:1 O₂/N₂O) anesthetized rats were intubated, mechanically ventilated and femoral catheters were inserted. Isoflurane was discontinued and anesthesia was maintained by an infusion of Fentanyl and Vecuronium during which baseline CBF measurements were obtained. While on neuromuscular blockade, asphyxial cardiopulmonary arrest was produced by disconnecting the ventilator from the rats for 9 min. After this period, rats were then resuscitated with epinephrine, sodium bicarbonate, and either given saline (20 cc/kg), albumin 10% (10 cc/kg) or PNA containing 10% albumin (10 cc/kg), mechanical ventilation was reinitiated, and chest compressions performed until until restoration of spontaneous circulation (ROSC) returned. Perfusion spin-echo images were acquired in duplicate using the arterial spin-labeling technique [6] (TR/TE = 2000/10, 20, 30, summation of 3 echoes, 2 averages, 128 x 70 matrix) with labeling applied ± 2.5 cm from the imaging plane. CBF (cerebral blood flow) maps were generated from: CBF = α · (T₁obs · 2α)⁻¹, (M₀ – M₁) · (M₀)⁻¹, where M₀ and M₁ are the magnetization intensities from the control and labeled images, respectively. A spatially constant value of 0.9 mL · g⁻¹ · min⁻¹ was assumed for the blood brain partition coefficient for water (λ). The spin labeling efficiency (α) [7] was determined in each study with gradient echo images on the carotid arteries and spin-labeling applied at ± 11 mm (TR/TE = 100/9.6 msec, 45˚ flip angle, 8 averages, 256 x 256 matrix). CBF was quantified for 5 anatomical regions within each hemisphere for baseline measurements as well as 5 min, 10 min, 15 min, 30 min, 1 hr, 1.5 hr, 2 hr, and 2.5 hr post asphyxial arrest.

RESULTS AND DISCUSSION

PNA given at resuscitation prevented the early hyperemia at 5 min vs. saline in all regions except thalamus (p<0.05). In contrast, albumin treated rats had intense hyperemia in all ROI studied, with a maximum of 200% increase from baseline in thalamus. In this group, cortical regions also displayed hyperemia. Albumin treated rats also had prolonged hyperemia, compared to PNA and saline, sustained up to 60 min after ROSC in thalamus and cortex. In the delayed period after resuscitation, CBF was comparable in the three therapeutic groups.

In conclusion, PNA and albumin produced surprisingly divergent changes of CBF during the early period after asphyxial CA. PNA given at resuscitation from CA decreased the initial hyperemia, while albumin produced a more prolonged and intense hyperemic response in all brain regions. The mechanisms responsible for these CBF changes and the effects of albumin and PNA given at resuscitation on neurological outcome remain to be determined.

ACKNOWLEDGMENTS

The Pittsburgh NMR Center for Biomedical Research is supported by a grant from the National Institute of Biomedical Imaging and Bioengineering as an NIH-supported Resource Center (P41EB-001977). MDM is supported by NIH K08HD058798-01.

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