Colloid Based Resuscitation following Asphyxial Cardiac Arrest: ASL_MRI Assessment of Regional Cerebral Blood Flow.

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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 aspyxial 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 O_2 and N_2 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 (PND) 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

PND 17 rats were used for this study. Isoflurane (1:1 O_2/N_2O) 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 restoration of spontaneous circulation (ROSC) returned. During each MRI study, $PaCO_2$, PaO_2, MABP, HR and rectal temperature were monitored.

MR studies were performed on a 7-Tesla, 21cm bore Bruker Biospec system, equipped with a 12 cm diameter shielded gradient insert and a 72 mm volume RF coil. For all imaging experiments, a slice thickness of 2 mm and FOV = 3 cm were used. Maps of T_{1obs} [5] were generated from a three-parameter exponential fit to a series of spin-echo images with variable *TR* (*TR* = 8000, 4300, 2300, 1200, 650, 350, 185, 100 msec, 2 averages, 128 x 70 matrix). 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: $CBF = \lambda \cdot (T_{1obs} \cdot 2\alpha)^{-1} \cdot (M_C - M_L) \cdot (M_C)^{-1}$, where M_C and M_L are the magnetization intensities from the control and labeled images, respectively. A spatially constant value of 0.9 mL · g^{-1} was assumed for the blood brain partition coefficient for water (λ). The spin labeling efficieny (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.

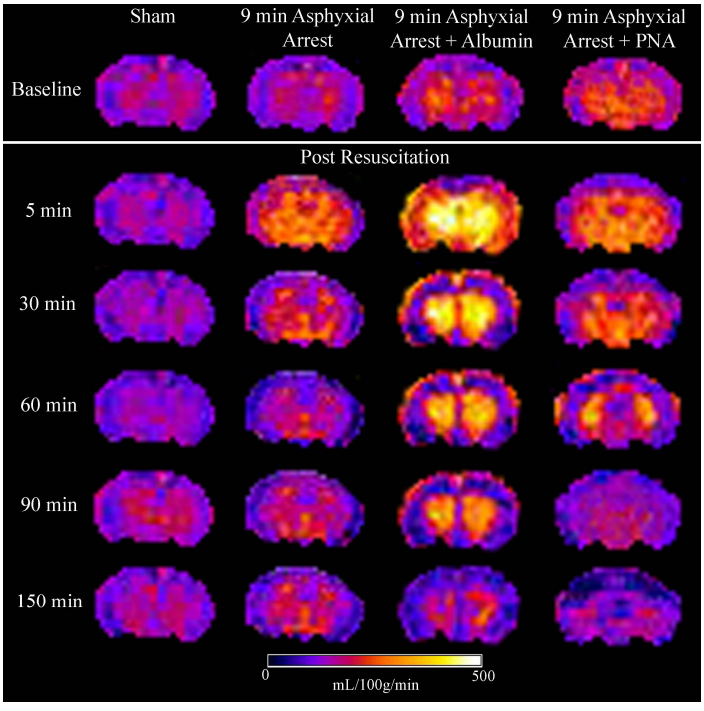

Figure 1: Representative CBF maps of PND 17 rats before and after return of spontaneous circulation following 9 mins of asphyxial cardiac arrest

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.

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REFERENCES

1. Young KD and Seidel JS. *Ann. Emerg. Med.* **33**, 195-205 (1999).
2. Safar, P., Xiao, F., Radovshky, A., Tanigawa, K., Ebmeyer, U., Bircher, N., Alexander, H. and Stezoski, S. W. *Stroke* **27**, 105-113 (1996).
3. Zhao,H., Sapolsky, R. M. and Steinberg, G. K. *J. Cereb. Blood Flow Metab.* **26**, 1114-1121 (2006).
4. Beaulieu C, Busch E, Rother J, de Crespigny A, Hsia CJ, Moseley ME. *J Cereb Blood Flow Metab* **18**,1022-1031 (1998).
5. Hendrich KS, Kochanek PM, Williams DS, Schiding JK, Marion DW and Ho C. *Magn. Reson, Med.* **42**, 673-681 (1999).
6. Detre JA, Leigh JS, Williams DS and Koretsky AP. *Magn. Reson. Med.* **23**, 37-45 (1992).
7. Zhang W, Williams DS and Koretsky AP. *Magn. Reson. Med.* **29**, 416 421 (1993).