Letter to the Editor

Neuroprotective effects of pre-treatment with systemic steroids in a neonatal piglet model of cardiopulmonary bypass with deep hypothermic circulatory arrest

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Received 10 July 2000; accepted 11 September 2000

We read with great interest the paper of Langley et al. [1] on attenuation of cerebral response to deep hypothermic circulatory arrest by pre-treatment with preoperative high-dose methylprednisolone in a neonatal piglet model. We have just finished our initial studies of a similar model of neonatal piglets and deep hypothermic circulatory arrest to evaluate the neuroprotective effects of pre-treatment with methylprednisolone in the same dose. We would like to note our comments and concerns with regard to the protocol and conclusion of the Langley study.

Conflicting results have been reported in the literature with regard to the neuroprotective effects of steroids [2–5]. The improvement of the cerebral metabolic rate and regional brain perfusion in the short reperfusion phase on bypass may not necessarily indicate a neuroprotective advantage at all. The animals only underwent 60 min of deep hypothermic circulatory arrest without a longer period of reperfusion after weaning from bypass. This time may not provoke significant neuronal injury to evaluate the protective effects.

Langley et al. [1] did not perform neuropathological studies to evaluate the possible occurrence of brain injury and the possible neuroprotective effects after pharmacological interventions. We have evaluated the mode of neuronal cell injury in neonatal piglets with respect to hypothermic circulatory arrest duration and the possible neuroprotective effects after pre-treatment with high-dose methylprednisolone. Eleven neonatal piglets (age <10 days; weight, 1.9 ± 0.5 kg BW) were included in this study. Five animals received no pharmacological intervention and six animals were pre-treated with high-dose methylprednisolone (30 mg/kg/BW) and all of the animals underwent cooling on full-flow CPB (200 ml/kg/min) and deep hypothermic circulatory arrest for 120 min after the establishment of a minimum rectal temperature of 14°C. After re-warmed reperfusion and the establishment of stable cardiac ejection, the animals were weaned from CPB and monitored for 6 h. Then the animals were sacrificed and the brain was immediately removed, cut in standardised sections and fixed for histological and immunohistochemical studies. Neuronal cells (540 ± 20 cells) were counted in sector CA4 of each animal and sectors CA1–CA3 and dentate gyrus were verified for necrotic and apoptotic neuronal cell injury.

The main preliminary findings in our model were the quantitative evaluation of cell injury, which included perivascular astroglial swelling and necrotic and apoptotic neuronal cell injury. The pre-treatment with methylprednisolone produced a mild to moderate decrease of perivascular oedema, but failed to reduce the number of necrotic neuronal cells [2]. In addition, apoptotic neuronal cell injury was seen more pronounced in the steroid pre-treated animals, which raises concern with regard to the routine use of methylprednisolone during paediatric cardiac surgery [4]. Thus, we suggest that the conclusion of the study by Langley et al. [1] of possible neuroprotective effects after pre-treatments of methylprednisolone is not justified and should await further experimental and clinical trials before a recommendation for routine use in neonates and infants can be made.

References


