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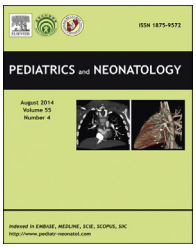

ORIGINAL ARTICLE

Changes in Amplitude-integrated Electroencephalograms in Piglets During Selective Mild Head Cooling After Hypoxia-ischemia

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Background: Amplitude-integrated electroencephalogram (aEEG) is a simplified, alternative means of monitoring cerebral function and may be more useful clinically in some situations than conventional EEG. The aim of this study is to evaluate newborn piglets as an animal model to examine the effect of selective mild head cooling (HC) on aEEG after hypoxia-ischemia (HI).
Methods: Thirty-four piglets were randomly allocated to the following treatment groups: normothermic control group (NC, $n = 7$), selective HC control group (HC, $n = 9$), normothermic HI group (NHI, $n = 9$), and selective HC HI group (SHC-HI, $n = 9$). HI was induced by temporary occlusion of both carotid arteries and simultaneous reduction of the concentration of inspired oxygen to 6% for 30 minutes. Mild hypothermia (35°C) was induced after HI using a HC cap and was maintained for 24 hours. Changes in aEEG were monitored for 6 days after these treatments and the incidence of abnormalities analyzed. Physiological parameters were also measured during this period.
Results: In the two HI groups, animals exhibited severely abnormal aEEGs [continuous low voltage (CLV), burst-suppression, or flat tracing (FT)] 20 minutes after the beginning of HI.

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At 2 hours, the aEEG returned to normal in most of these animals. From 12 hours to 6 days, all animals in the NHI group exhibited severely abnormal aEEGs. Fewer animals in the SHC-HI group exhibited severe abnormal aEEGs during this time period, and four out of nine (44.4%) animals had continuous normal voltage (CNV) at 6 days.
Conclusions: Selective mild HC decreases the incidence of severe abnormal aEEGs at late times after HI in newborn piglets.

1. Introduction

Perinatal hypoxic-ischemic brain damage (HIBD) is a major cause of perinatal mortality and long-term neurodisability.[1] Evidence from both human and animal studies has shown that hypothermia provides neuroprotection from hypoxia-ischemia (HI) in adults and young/newborns,[2,3] and it can reduce the incidence of cerebral palsy.[4–6] Clearly, hypothermia is a promising treatment for perinatal HIBD.

Monitoring changes in electrocortical brain activity during HIBD can help assess the degree of brain damage and predict neurological outcome. For many years, conventional electroencephalography (EEG) has been used for intermittent and continuous assessment of brain function and for the prediction of neurological outcomes in infants. However, conventional EEG is of limited applicability in the neonatal intensive care unit. The use of multichannel EEG to monitor cerebral function in newborn infants who are in a critical condition is impractical.[7,8] Amplitude-integrated EEG (aEEG) is a simplified, alternative means of monitoring cerebral function.[9] Advantages of aEEG are that it is easy to use and analyze, shows less interference from artefacts such as muscle contraction, and positions the electrodes over the parietal zone, above an area known to be sensitive to ischemia. This recording approach has been shown to be one of the most accurate bedside methods for predicting neurological outcomes in term infants after HI.[10,11] Indeed, this non-invasive technique has been increasingly used to identify infants suitable for hypothermic neuroprotection following severe HI.[12]

To date, there is little information available regarding the use of aEEG to monitor changes in brain electrical activity in newborn animals after induction of HI and hypothermia. Therefore, we carried out an experiment in newborn piglets to examine aEEG and corresponding physiological data before and up to 6 days after the induction of HI and subsequent 24-hour mild hypothermia. We hypothesized that aEEG would be abnormal after the induction of HI and that mild hypothermia would promote normalization.

2. Materials and methods

2.1. Animals

Thirty-four healthy newborn white piglets of either sex were obtained from an experimental animal nursery in Shanghai. They were aged between 5 days and 7 days (term delivery) and weighed from 2.10 kg to 2.71 kg (mean: 2.35 $\pm$ 0.18 kg).

Piglets were randomly allocated to one of the following four groups: (A) normal temperature with rectal temperature maintained at approximately 39°C [normothermic control group (NC), $n = 7$]; (B) selective head cooling (HC) without HI, with nasopharyngeal temperature maintained at 35°C and rectal temperature maintained at 36°C [HC without HI group (HC), $n = 7$]; (C) HI insult without selective HC and rectal temperature maintained at 39°C [normothermic HI group (NHI), $n = 9$]; and (D) HC (mild hypothermia) after HI insult, with nasopharyngeal temperature maintained at 35°C and rectal temperature maintained at 36°C [selective HC after HI group (SHC-HI), $n = 9$].

This study was approved by the Animal Ethics Committee of the Children's Hospital of Fudan University, Shanghai, China.

2.2. Animal surgical preparation and postsurgical treatment

In all groups, anesthesia was initiated with intramuscular ketamine (10 mg/kg) and maintained with an infusion of ketamine (10 mg/kg/hour). Maintenance fluid (Na 50 mEq/L, K 20 mEq/L, Cl 50 mEq/L, 5% glucose) was infused at a rate of 5 mL/kg/hour. An ear vein was cannulated for continuous infusion of maintenance fluids and administration of medication. Endotracheal intubation and mechanical ventilation (Newport 200, Newport Medical Instruments Inc., Costa Mesa, CA, USA) were then initiated. A Judkins number 4 catheter (Utal Medical Products, Inc USA) was inserted into the left axillary artery to monitor blood pressure and for repeated blood sampling. This artery is the continuation of the left subclavian artery in the region of the shoulder joint and left front leg. Bilateral carotid arteries were isolated for cerebral ischemic insult. Ketamine administration was terminated at the end of this surgery. Ventilation was adjusted as necessary to maintain synchronized intermittent mandatory ventilation: fraction of inspired oxygen, 30%; peak inspiratory pressure, 12—15 cmH_2O; respiratory rate, 20—30 breaths/minute; inspiratory time, 0.5 seconds; positive end-expiratory pressure, 3 cm H_2O; flow, 8 L/minute; and $PaCO_2$, 40—50 mmHg. Piglets were then placed on a radiant warmer bed in a prone position for 2 hours to stabilize vital signs.

During the 6-day postsurgical period, animals were maintained with milk containing chloral hydrate for mild sedation (1 mL/kg of milk containing 10% chloral hydrate) administered by gastric tube. Chloral hydrate at this dose has no effect on aEEG. The protocol called for vasopressors to treat hypotension [mean arterial pressure (MAP) $<$ 40 mm Hg] and sodium bicarbonate to treat