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Original article

Simultaneous measurement of cerebral hemoglobin oxygen saturation and blood volume in asphyxiated neonates by near-infrared time-resolved spectroscopy ☆

Shinji Nakamura [a], Kosuke Koyano [a], Wataru Jinnai [a], Satoshi Hamano [a], Saneyuki Yasuda [b], Yukihiko Konishi [a], Toru Kuboi [c], Kenji Kanenishi [b], Tomoko Nishida [d], Takashi Kusaka [a,*]

[a] *Department of Pediatrics, Faculty of Medicine, Kagawa University, Kagawa, Japan*
[b] *Maternal Perinatal Center, Faculty of Medicine, Kagawa University, Kagawa, Japan*
[c] *Department of Neonatology, Shikoku Medical Center for Children and Adults, Kagawa, Japan*
[d] *Department of Education for Children with Special Needs, Faculty of Education, Kagawa University, Kagawa, Japan*

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Abstract

Background: Hypoxic-ischemic encephalopathy (HIE) usually results in a poor clinical outcome even when treated with hypothermic therapy (HT). Early postnatal changes in cerebral blood oxygenation and hemodynamics may be critical determinants of brain injury and the efficacy of HT.

Objectives: We measured cerebral hemoglobin oxygen saturation (ScO_2) and cerebral blood volume (CBV) by near-infrared time-resolved spectroscopy (TRS) in HT-treated and non-HT-treated neonatal HIE patients to assess the influence of these parameters on clinical outcome.

Methods: We retrospectively compared ScO_2, CBV, and clinical outcomes of 11 neonates with HIE: 5 were treated by HT (HT-treated; 33.5 °C ± 0.5 °C for 72 h starting approximately 6 h after delivery) and 6 were not (non-HT-treated). Both CBV and ScO_2 were measured by TRS at 6, 24, 48, and 72 h after birth. Magnetic resonance imaging (MRI) was performed 1–2 weeks after birth to assess brain injury.

Results: Five neonates had adverse outcomes (3 HT-treated, 2 non-HT-treated). Of these, 1 died within 3 days of birth and 4 had abnormal MRI findings, including basal ganglia, white matter, and/or thalamic lesions. The other 6 neonates had normal MRI findings (favorable outcome). At 6 h after birth, CBV was significantly higher in neonates with adverse outcomes compared with those with a favorable outcome. At 24 h after birth, ScO_2 was significantly higher in neonates with adverse outcomes. Furthermore, we found that combined CBV at 24 h after birth plus ScO_2 had the best predictive ability for neurological outcome: sensitivity, specificity, positive predictive value, and negative predictive value were all 100%.

Abbreviations: CBV, cerebral blood volume; DeoxyHb, deoxyhemoglobin; HIE, hypoxic-ischemic encephalopathy; Hb, hemoglobin; HT, hypothermic therapy; MRI, magnetic resonance imaging; NICU, neonatal intensive care unit; NIRS, near-infrared spectroscopy; OxyHb, oxyhemoglobin; ScO_2, cerebral hemoglobin oxygen saturation; TRS, near-infrared time-resolved spectroscopy

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* Corresponding author at: Department of Pediatrics, Faculty of Medicine, Kagawa University, 1750-1 Mikicho, Kitagun, Kagawa 761-0793, Japan. Tel.: +81 87 891 2171; fax: +81 87 891 2172.

E-mail address: kusaka@med.kagawa-u.ac.jp (T. Kusaka).

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Conclusion: Early postnatal CBV and ScO_2 elevations were predictive of a poor outcome in HIE. Therefore, measuring combined CBV plus ScO_2 at 24 h after birth can allow more precise prediction of neurological outcome. Control of postnatal CBV and ScO_2 is critical for effective HIE treatment.

Keywords: Cerebral blood volume; Cerebral hemoglobin oxygen saturation; Hypothermic therapy; Hypoxia-ischemic encephalopathy; Near-infrared time-resolved spectroscopy

1. Introduction

Hypoxic-ischemic encephalopathy (HIE) is a relatively common birth complication, with an incidence of approximately a few cases per 1000 live births and results in death or an adverse neurodevelopmental outcome in most cases [1]. Hypothermic therapy (HT) is now the standard treatment for neonates with HIE. However, the clinical outcome remains poor, suggesting that HT as currently applied may not alter certain critical neurological variables necessary for survival and preservation of function. It is thus necessary to precisely assess HT-associated changes and subsequent brain injury in HIE neonates to identify alternative therapies.

Near-infrared spectroscopy (NIRS) allows for noninvasive monitoring of cerebral oxygenation and circulation in the neonatal intensive care unit (NICU) [2–4]. It has been reported that cerebral Hb oxygen saturation (ScO_2) on postnatal day 1 is predictive of HIE outcome [2–4]. Near-infrared time-resolved spectroscopy (TRS) is a simple noninvasive technique that can continuously and simultaneously measure the absolute values of ScO_2 and cerebral blood volume (CBV). It can be used at the bedside of neonates. We previously reported simultaneous measurement of CBV and ScO_2 using TRS in both a hypoxic piglet model [5,6] and human neonates [7,8], and suggested that combined evaluation of CBV and ScO_2 may be superior to ScO_2 measurements alone for revealing pathological changes in cerebral hemodynamics leading to brain injury. To our knowledge, no previous study has reported simultaneous measurement of ScO_2 and CBV in asphyxiated neonates during the early postnatal period using TRS. The aim of this study was to measure both CBV and ScO_2 by TRS in neonates with HIE (HT-treated or non-HT-treated) during the first 72 h after birth to evaluate the influence of these parameters on clinical outcome.

2. Patients and methods

We conducted a retrospective study of 11 neonates admitted to our NICU from April 2005 to October 2013 with a diagnosis of mild, moderate, or severe HIE as graded by the Sarnat scale. We performed HT in 5 of the neonates according to established criteria [9]: (A) >35 weeks gestation with at least one of (i) Apgar score <5 at 10 min after birth, (ii) continued need for resuscitation including endotracheal or mask ventilation at 10 min after birth, or (iii) acidosis within 60 min of birth (any occurrence of umbilical cord, arterial, venous, or capillary pH <7.00 or base deficit $\geqslant$16 mmol/L); and (B) moderate to severe encephalopathy with altered state of consciousness (lethargy, stupor, coma) and at least one of (i) hypotonia, (ii) abnormal reflexes including oculomotor or papillary abnormalities, (iii) absent or weak suckle, or (iv) clinical seizure.

Whole-body hypothermia was achieved using a cooling blanket (Arctic sun 2000, Medivance, USA). Neonates were cooled to 33.5 °C ± 0.5 °C for 72 h and then rewarmed at 0.5 °C/h using the blanket. Normothermia was usually reached in about 6 h.

The parents of all neonates enrolled in this study provided informed consent after receiving a full explanation of the study.

2.1. Near-infrared time-resolved spectroscopy monitoring

We used a portable three-wavelength TRS system (TRS-10; Hamamatsu Photonics K.K., Hamamatsu, Japan) with the probe attached to the forehead. The light emission and detection optodes were positioned on the parietal region at a 30-mm inter-optode distance. The TRS system, which uses a time-correlated single-photon-counting technique for detection, has been described in detail elsewhere [5–8]. The oxyhemoglobin (oxyHb) and deoxyhemoglobin (deoxyHb) concentrations were calculated from the absorption coefficients of oxyHb and deoxyHb assuming that background absorption was due to 85% water content (by volume). The total cerebral Hb concentration [totalHb], ScO_2, and CBV were calculated as follows:

$$[\text{totalHb}] = [\text{oxyHb}] + [\text{deoxyHb}],$$
$$ScO_2(\%) = \{[\text{oxyHb}]/([\text{oxyHb}] + [\text{deoxyHb}])\} \times 100, \text{ and}$$
$$\text{CBV (mL/100 g brain)} = [\text{totalHb}] \times MW_{Hb} \times 10^{-6}/(\text{tHb} \times 10^{-2} \times D_t \times 10),$$

where square brackets indicate the Hb concentration (μM), MW_{Hb} is the molecular weight of Hb (64,500), tHb is the venous Hb concentration (g/dL), and D_t is the brain tissue density (1.05 g/mL).