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Original article

Comparison of changes in cerebral and systemic perfusion between appropriate- and small-for-gestational-age infants during the first three days after birth

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Abstract

Purpose: The aims of the current study were to compare changes in cerebral and systemic perfusion in appropriate-for-gestational-age (AGA) and small-for-gestational-age (SGA) infants immediately after birth. *Methods:* Cerebral blood volume (CBV), cerebral Hb oxygen saturation (cSO_2) and cerebral fractional tissue oxygen extraction (cFTOE) among 57 AGA infants and 30 SGA infants were monitored using a newly developed time-resolved spectroscopy system during the first 3 days of life. The left ventricular ejection fraction (LVEF), left ventricular cardiac output (LVCO) and E/e' values were determined by three-dimensional echocardiography and tissue Doppler imaging performed simultaneously. *Results:* There were significant differences between the body weights of both the AGA and SGA infants, but not between the gestational age and head circumferences in both groups. Although CBV showed no significant difference between the groups, cSO_2 was significantly higher and cFTOE was lower in SGA infants than in AGA infants. Hematocrit (Ht) levels were significantly higher and LVEF and LVCO were lower in SGA infants than in AGA infants. Negative correlation was observed between CBV and Ht levels in AGA infants, but not in SGA infants. *Conclusions:* The high Ht levels and vasoreactivity in SGA infants might be a compensatory mechanism in order to maintain oxygen delivery to the brain, which reflects the condition of chronic hypoxia during the fetal period and also reflects the weak contraction and low cardiac output of the left ventricle sustaining the relatively large brain from the fetal period to after birth.

Keywords: Intrauterine growth restriction (IUGR); Small-for-gestational-age (SGA); Near-infrared spectroscopy (NIRS); Time-resolved spectroscopy (TRS); Cerebral blood volume (CBV); Cerebral Hb oxygen saturation (cSO_2); Three-dimensional (3D) echocardiography

1. Introduction

Since neonates who are affected by intrauterine growth restriction (IUGR) and are small-for-gestational-age (SGA) suffer from respiratory difficulty, polycythemia, hypoglycemia, intraventricular hemorrhage and hypothermia [1], IUGR and SGA are associated with an increase in perinatal mortality. Moreover, some recent studies showed that increasing evidence points to a link between IUGR/SGA and obesity, diabetes mellitus, hypertension, metabolic syndrome and ischemic heart disease in the adult period [2]. Ultrasound is used to reveal IUGR, which is defined by the estimated fetal weight of less than −1.5 SD for gestational age (GA). Moreover, Doppler ultrasound is

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valuable in defining the degree of cardiovascular compromise in at-risk pregnancies [3]. IUGR associated with chronic fetal hypoxia and undernutrition due to placental insufficiency results in hemodynamic adaptation that allows preferential redistribution of blood flow to the brain; this is called the "brain sparing effect" [4]. The severity of fetal blood flow redistribution shows the degree of fetal adaptation and provides information on how long the pregnancy can be continued safety. The most widely used sign to identify placental insufficiency, and consequently to diagnose IUGR, is an increase in the resistance index (RI) in the umbilical artery (UA) and a decrease in the RI in the middle cerebral artery (MCA). It has been suggested that the cerebral/umbilical (C/U) ratio is a good predictor of neonatal outcome. However, whether this phenomenon indicates either a higher risk of brain injury or a protective mechanism remains uncertain [5–7]. Figueras et al. suggest that abnormal MCA Doppler findings reflect an advanced stage of brain injury with a higher risk of abnormal neurological maturation [4]. An SGA infant is defined by a birth weight of less than the 10th percentile for GA at birth. Some studies have investigated both cerebral and systemic perfusion in SGA infants during the early postnatal period [5,6,8,9]. However, the relationships between appropriate-for-gestational-age (AGA) and SGA infants and their cerebral and systemic perfusion during the immediate neonatal period are not well understood.

Near-infrared spectroscopy (NIRS) has been used in some clinical fields with various measuring devices using several different wavelengths. These light-based non-invasive approaches are very useful in neonates because the newborn brain is accessible by near-infrared light owing to the thin scalp and skull. Although conventional commercially available NIRS systems can only detect changes in cerebral Hb owing to being based on the modified Beer–Lambert law, a recently developed near-infrared time-resolved spectroscopy (TRS) device enables the assessment of quantitative hemodynamics, absolute values of cerebral blood volume (CBV), and cerebral hemoglobin oxygen saturation (cSO_2) [10,11].

The aims of the current study were to compare changes in cerebral and systemic perfusion in AGA and SGA infants during the early neonatal period in order to understand the pathophysiological background of SGA infants.

2. Methods

2.1. Subjects

Fifty-seven AGA infants (birth weight within the 10th percentile for GA) and 30 SGA infants (birth weight less than the 10th percentile for GA with a head circumference within ±2 SD for GA) who were admitted to the neonatal intensive care unit of Tokyo Medical University Hospital from October 1, 2009 to August 31, 2011 were enrolled in this study. Infants with congenital anomalies, congenital heart disease, intracranial hemorrhage, asphyxia and extremely low birth weight were excluded.

The study was approved by the research ethics committee of the university, and written informed consent for participation in this study was obtained from the parents of all infants.

2.2. NIRS measurement

Hemodynamic data were acquired using a NIR-TRS system (TRS-20, Hamamatsu Photonics K.K., Shizuoka, Japan) employing the TCSPC method to obtain a temporal profile of the detected photons. This system features improved optical sensitivity compared with the TRS-10 system [12,13] employing a GaAs photocathode photomultiplier tube (H7422P-50MOD, Hamamatsu Photonics K.K.), with a quantum efficiency above 12% at approximately 800 nm. The TRS-20 is computer controlled through a digital input/output (I/O) interface, consisting of a 3-wavelength (761, 801 and 834 nm) picosecond light pulser (PLP, Hamamatsu Photonics K.K.) as the light source, a photon-counting head (composed of a fast-response, highly sensitive photomultiplier tube and high speed amplifier) with a 9-step optical attenuator for single photon detection, and signal processing circuits (which consist of a constant fraction discriminator, time-to-amplitude converter, analog/digital (A/D) converter and histogram memory) for time-resolved measurements. The PLP generates a light pulse with a pulse width of 100 ps, a pulse rate of 5 MHz, and an average power of approximately 80 μW. Three PLPs emit light pulses sequentially, and the 3-wavelength light pulses are guided into one illuminating optical fiber by a fiber coupler (NTT Advanced Technology Corporation, Tokyo, Japan). A grated index type single optical fiber with a numerical aperture (NA) of 0.25 and a core diameter of 200 μm was used for irradiation of the tissue. An optical bundle fiber (Moritex Corporation, Tokyo, Japan) with an NA of 0.26 and a bundle diameter of 3 mm was used to collect diffused light from the tissue for light detection [14].

To calculate the values of μ_a, and μ'_s for the three wavelengths, the temporal profile obtained from the TRS measurement is fitted with that obtained from the theoretical solution of the diffusion equation by Patterson et al. using the non-linear least squares fitting method [15]. Subsequently, oxyHb and deoxyHb levels were calculated from the μ_a of the three wavelengths (761, 801 and 834 nm) using the following equations:

$$\mu_{a\,761\,\mathrm{nm}} = \epsilon_{\mathrm{oxyHb}\,761\,\mathrm{nm}} C_{\mathrm{oxyHb}} + \epsilon_{\mathrm{deoxyHb}\,761\,\mathrm{nm}} C_{\mathrm{deoxyHb}} + \epsilon_{\mathrm{H_2O}\,761\,\mathrm{nm}} C_{\mathrm{H_2O}}$$