Journal of Biomedical Optics 5(3), 283–286 (July 2000)

Changes in cerebral hemoglobin concentration and oxygen saturation immediately after birth in the human neonate using full-spectrum near infrared spectroscopy

Kenichi Isobe
Takashi Kusaka
Kagawa Medical University
Department of Pediatrics and Maternal and Children's Center
Mikicho, Kitagun, Kagawa 761-0793, Japan

Yuka Fujikawa
Masatoshi Kondo
Kou Kawada
Saneyuki Yasuda
Susumu Itoh
Konomu Hirao
Shoju Onishi
Kagawa Medical University
Department of Pediatrics
Mikicho, Kitagun, Kagawa 761-0793, Japan

Abstract. Using full-spectrum near infrared spectroscopy (fsNIRS), we measured changes in oxy- and deoxyhemoglobin (HbO_2 and Hb), total hemoglobin (T-Hb) concentration, and hemoglobin oxygen saturation (SbO_2) in the brain tissue of seven neonates immediately following birth. It was found that HbO_2 rose rapidly within 2–3 min after birth. During the same time, there was a transient increase in T-Hb concentration, after which it decreased together with Hb. SbO_2 increased rapidly after birth, from 18% at 1.5 min to about 55% at 5–6 min, followed by a gradual increase of about 10%. Oxygenation in the brain occurred much sooner in three subjects given oxygen for a short time immediately after birth than in those who did not receive oxygen. This preliminary study indicated that dynamic changes occur in cerebral circulation and oxygenation as part of the physiological changes taking place soon after birth. *© 2000 Society of Photo-Optical Instrumentation Engineers.* [S1083-3668(00)00203-3]

Keywords: near infrared spectroscopy; full spectrum; cerebral hemoglobin concentration; cerebral hemoglobin oxygen saturation; neonate.

Paper JBO 109923 received Apr. 12, 1999; revised manuscript received Sep. 10, 1999 and Dec. 13, 1999; accepted for publication Dec. 23, 1999.

1 Introduction

Arterial partial oxygen pressure in normal neonates rises rapidly from an extremely low value of 20–25 Torr during the fetal period to approximately 60 Torr at 10 min after birth,[1,2] because of the shift to pulmonary respiration with birth as the turning point. Adaptation of the respiratory system to extrauterine life immediately after birth gives rise to rapid oxygenation of the organs and tissues. Research on the changes in the state of brain oxygenation just after birth is limited to a single report by Peebles et al.[3] dealing with one patient. We therefore undertook this study, using full-spectrum near infrared spectroscopy (fsNIRS), of the cerebral hemoglobin concentration and oxygenation state immediately after birth.

2 Subjects

The subjects were seven neonates (Table 1). Informed consent was obtained in all cases. Subject 4 had complications of polycythemia and pneumomediastinum, and subjects 5, 6, and 7 received oxygen inhalation treatment for a short time after birth. First breathing in all subjects had commenced by the time the fsNIRS measurements were started.

3 Methods

The fsNIRS apparatus was an IMUC-7000 (Otsuka Electronics, Osaka, Japan), which measured the full spectrum of 614–900 nm. The system used three quartz optical fibers, one of which was connected to a stabilized 300 W halogen lamp for the light source, and the other two were used as the light receiving fibers. One of the light receiving fibers was set with an interoptode distance of 10 mm to obtain a reference spectrum, and the other at an interoptode distance of 20 mm to obtain a measurement spectrum. The light intensity of the reference and the measurement side amplified by the image intensifier in IMUC-7000 were regulated to the same extent by changing the sampling time. The sampling time for each scan for the reference and the measured spectrum was set at 0.25 and 2 s, respectively. Immediately after birth a probe was attached to either the left or right forehead. Measurements were begun at 70 s–4 min after birth, and continued until 15 min after birth. The relative concentration of hemoglobin in brain tissue was calculated using a previously reported method,[4–6] which had been modified as described below.

According to Fantini et al.,[7] with the distance between fibers that we are using, the influence of the scattering coefficient will be large and accurate analysis will be difficult. However, with the full-spectrum measurement method that we are using, the variations in optical path length due to the influence of light scattering can be recognized as variations in the shape of the spectrum. We thus selected the method of applying the diffusion correction equation described below to normalize the optical path length across the wavelengths.

The following occur when measurements are made through a light-diffusing body, such as living tissue:

This paper was originally scheduled to appear in the October 1999 special section on Medical Near-Infrared Spectroscopy, but was not available in time. Address all correspondence to Kenichi Isobe. Tel: 81-87-898-5111; Fax: 81-87-891-2172; E-mail: isobe@kms.ac.jp

Table 1 Newborn infants studied by full-spectrum NIRS.

No.	B.W. (g)	G.A. (w)	Delivery	Apgar score (1/5 min)
1	3010	38	Elective c.s.	8/9
2	2864	39	v.d.	7/8
3	3334	41	Emergency c.s.	8/9
4†	3254	36	v.d.	8/9
5*	1962	37	Emergency c.s.	8/9
6*	3188	38	Elective c.s.	8/9
7*	2874	39	Elective c.s.	8/9

B.W., birth weight; G.A., gestational age; v.d., vaginal delivery; c.s., cesarean section.

† This infant had polycythemia and pneumomediastinum.

* O_2 inhalation.

(1) Dispersion of optical path length, which depends on the magnitude of the molecular extinction coefficient $[d_{\text{const}} \Rightarrow d(\lambda)]$.

(2) Optical loss effect due to scattering, which depends on the magnitude of the optical path length (the loss effect itself is independent of wavelength).

Thus when the incident intensity is $I_0(\lambda)$, the measured intensity $I(\lambda)$ is expressed as follows:

$$I(\lambda) = I_0(\lambda) \times 10^{-\epsilon_1(\lambda)\cdot c_1 \cdot d(\lambda)} \times 10^{-\epsilon_2(\lambda)\cdot c_2 \cdot d(\lambda)} \times \ldots \times 10^{-\alpha_{\text{const}} \cdot d(\lambda)},$$

where $\epsilon_1(\lambda)$, $\epsilon_2(\lambda)$ are the molecular extinction coefficients which depend on the molecular species, c_1 and c_2 are the molar concentrations of the respective molecular species, and α_{const} is the optical loss effect constant, which depends on the optical diffusion conditions of the measured object.

When the optical path length is changed by Δd, the above equation becomes

$$I'(\lambda) = I_0(\lambda) \times 10^{-\epsilon_1(\lambda)\cdot c_1 \cdot (d(\lambda)+\Delta d(\lambda))} \times 10^{-\epsilon_2(\lambda)\cdot c_2 \cdot (d(\lambda)+\Delta d(\lambda))} \times \ldots \times 10^{-\alpha_{\text{const}} \cdot (d(\lambda)+\Delta d(\lambda))}.$$

Since $I_0(\lambda)$ is usually extremely difficult to measure, the absorption spectrum is determined from the difference of the above two equations (self-reference)

$$\frac{I(\lambda)}{I'(\lambda)} = \frac{I_0(\lambda) \times 10^{-\epsilon_1(\lambda)\cdot c_1 \cdot d(\lambda)} \times 10^{-\epsilon_2(\lambda)\cdot c_2 \cdot d(\lambda)} \times \ldots \times 10^{-\alpha_{\text{const}} \cdot d(\lambda)}}{I_0(\lambda) \times 10^{-\epsilon_1(\lambda)\cdot c_1 \cdot (d(\lambda)+\Delta d(\lambda))} \times 10^{-\epsilon_2(\lambda)\cdot c_2 \cdot (d(\lambda)+\Delta d(\lambda))} \times \ldots \times 10^{-\alpha_{\text{const}} \cdot (d(\lambda)+\Delta d(\lambda))}}$$
$$= 10^{\epsilon_1 \cdot c_1 \cdot \Delta d(\lambda)} \times 10^{\epsilon_2 \cdot c_2 \cdot \Delta d(\lambda)} \times \ldots \times 10^{\alpha_{\text{const}} \cdot \Delta d(\lambda)},$$

$$Abs(\lambda) = \log\left(\frac{I(\lambda)}{I'(\lambda)}\right) = \epsilon_1(\lambda)\cdot c_1 \cdot \Delta d(\lambda) + \epsilon_2(\lambda)\cdot c_2 \cdot \Delta d(\lambda) + \ldots + \alpha_{\text{const}} \cdot \Delta d(\lambda).$$

At this point, the spectrum is distorted because of the wavelength dependence of the optical path due to the effect of (1) mentioned above.

This distortion is corrected by the diffusion correction equation (the wavelength dependence of the optical path is resolved to obtain a spectrum that is proportional to the molecular extinction coefficients)[8–10]

$$Abs'(\lambda) = \beta(\lambda)(\epsilon_1(\lambda)\cdot c_1 \cdot \Delta d_{\text{const}} + \epsilon_2(\lambda)\cdot c_2 \cdot \Delta d_{\text{const}} + \ldots + \alpha_{\text{const}} \cdot \Delta d_{\text{const}}),$$

where $\beta(\lambda)$ is the correction factor.

With a spectrum of this form, the component spectra, which are measured from transparent solution systems and are in accordance with the wavelength dependence of molecular extinction coefficients, can be fitted to the spectrum.

Here, since the $\alpha_{\text{const}} \cdot \Delta d_{\text{const}}$ term, which corresponds to the optical loss effect, is not dependent on the wavelength at all and can be considered to take on a fixed value, a base line of value 1.000000 is added as a component in the fitting.

As a result, the following values are determined:

$$\beta(\lambda)\cdot c_1 \cdot \Delta d_{\text{const}}, \beta(\lambda)\cdot c_2 \cdot \Delta d_{\text{const}}, \ldots, \beta(\lambda)\cdot \alpha_{\text{const}} \cdot \Delta d_{\text{const}}.$$

Since Δd_{const} may differ for each spectrum due to variation of blood volume, etc., different spectra cannot be compared accurately at this point.

Normalization of the measured volume (optical path length) is thus performed with $\beta(\lambda)\cdot \alpha_{\text{const}} \cdot \Delta d_{\text{const}}$, which depends only on Δd_{const} and does not depend on the concentration of the absorbing body.

The final results obtained by this normalization are as follows:

$$\frac{c_1}{\alpha_{\text{const}}}, \quad \frac{c_2}{\alpha_{\text{const}}}, \quad \ldots.$$

The respective spectra for 0.1 mM oxy- and deoxyhemoglobin (HbO_2 and Hb), 0.1 mM cytochrome *c* oxidase in the

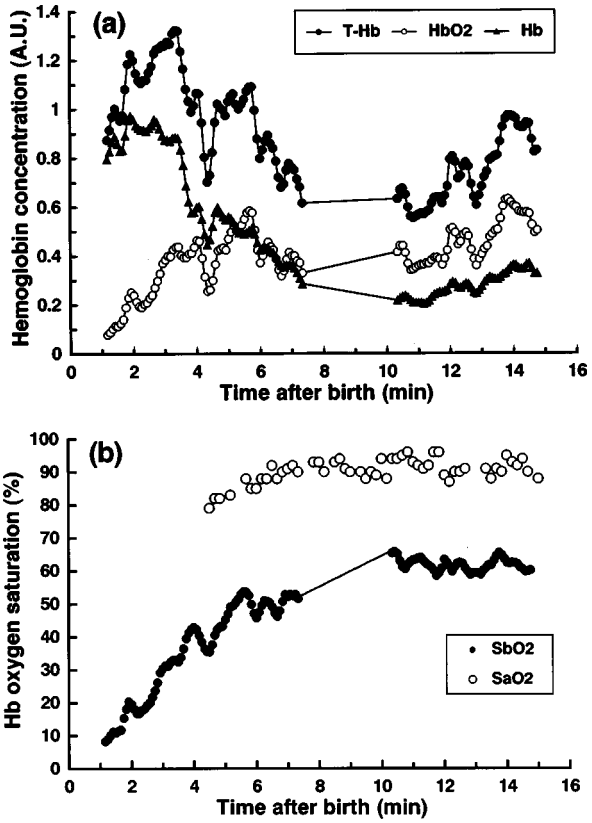

Fig. 1 (a) Changes in cerebral oxyhemoglobin (HbO_2), deoxyhemoglobin (Hb) and total hemoglobin (T-Hb) concentration. (b) Arterial oxygen saturation (SaO_2) measured by pulse oximeter and cerebral hemoglobin oxygen saturation (SbO_2) during first 15 min after birth.

oxidized and reduced state and water, and base line were used as components in performing the curve fitting. The cerebral total hemoglobin (T-Hb) concentration and cerebral hemoglobin oxygen saturation (SbO_2) were calculated as follows:

$$[\text{T-Hb}]=[\text{HbO}_2]+[\text{Hb}],$$

$$\text{SbO}_2=[\text{HbO}_2]/([\text{HbO}_2]+[\text{Hb}])\times 100,$$

where [ ] indicates concentration relative to α.

At the same time, arterial oxygen saturation (SaO_2) in the right hand was measured using a pulse oximeter (Nellcor model N-180).

4 Results

SaO_2 was found to be 35%–60% at 2 min after birth, 70%–88% at 5 min, 83%–93% at 7 min, and 93%–99% at 15 min. These values are similar to values reported by Harris et al.[11] 1–7 min after birth. Figure 1 shows the changes in HbO_2, Hb, and T-Hb concentrations in the brain (a), and SbO_2 and SaO_2 (b), in subject 1 between 70 s and 15 min after birth. Measurements were temporarily halted from 7.5 to 10 min after birth in order to save fsNIRS data in a personal computer. There was a rapid rise in cerebral HbO_2 accompanying the

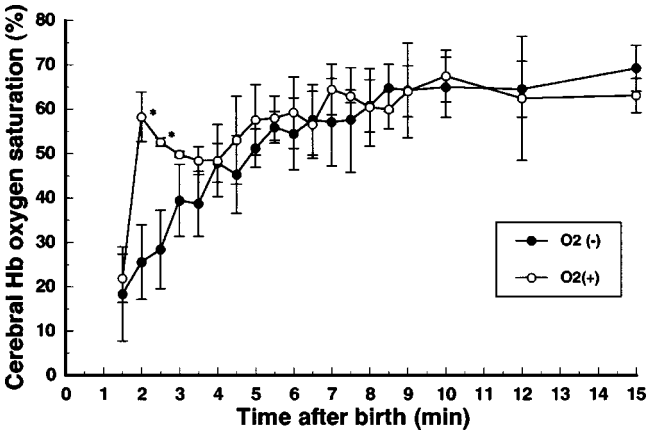

Fig. 2 Cerebral hemoglobin oxygen saturation (SbO_2) in four infants who did not receive oxygen (●) and in three infants who inhaled oxygen (○) during first 15 min after delivery. Vertical bars are ±SD.*, $p<0.01$ unpaired t test.

establishment of respiration. There was a concurrent, transient increase in T-Hb in brain tissue, followed by a decline together with a reduction in Hb. HbO_2, Hb, and T-Hb in brain tissue all increased from the time measurements were resumed at 10 min after birth. SbO_2 increased rapidly from 8% at the start of measurements to about 50% at 5 min after birth, and approximately 60% at 10 min. There was a transient increase in cerebral T-Hb in the other six subjects similar to that seen in this subject within 2–3 min after birth, followed by a decline. However, cerebral T-Hb in subject 4, who had complications from polycythemia and pneumomediastinum, was higher than in the other subjects.

The SbO_2 levels of three subjects who inhaled oxygen and the other four subjects who did not are shown in Figure 2. SbO_2 in the neonates who did not receive oxygen rose rapidly from 18±11 (mean ±SD)% at 1.5 min after birth to 51±4% 5 min later, then increased gradually to 69±5% at 15 min after birth. Three patients were given oxygen transiently for 30 s starting 1.5 min after birth. The oxygen inhalation caused a rapid rise in SaO_2 to 75% from the initial level of 32% in subject 5. SbO_2, reflecting the increase in SaO_2, also rose rapidly from the initial level of 22±5% to 58±6% within 0.5 min. Afterward, following a transient decline after oxygen administration was discontinued, it increased gradually in parallel with the changes in SaO_2.

5 Discussion

Adaptation of the respiratory system to extrauterine life after birth causes rapid oxygenation of organs and tissues. Little is known about the effect on cerebral oxygenation and hemodynamics of the physiologic changes that occur in the first minutes after birth. We have developed a new analytical system, which allows optical spectroscopic measurements of semiquantitative cerebral hemoglobin concentration and cerebrovascular saturation.

Our results concerning SbO_2 immediately after birth in healthy term infants are the first reported data. We found that HbO_2 increased rapidly within 2–3 min after birth, and during

the same time, there was a transient increase in T-Hb concentration, after which it decreased together with Hb. Furthermore, we found a rapid rise in mean SbO_2 from 18% to 51% from 1.5 to 5 min after birth, and thereafter it increased slowly to 69% at 15 min after birth. Because SaO_2 falls to as low as zero at birth,[12] it is thought that brain tissue becomes hypoxic, causing dilatation of the arterioles. During the first several minutes of extrauterine life, a rapid rise in SaO_2 occurs. These results therefore suggest that cerebral blood flow increases after birth, and the arterioles contract due to the increase in oxygen concentration of arterial blood flowing into the brain. The decrease in cerebral blood flow due to the increase in oxygen concentration is supported by Lundstrom, Pryds, and Greisen.[13]

Oxygen inhalation for 30 s caused a rapid rise in SbO_2 to $58\pm6\%$ from the initial level of $22\pm5\%$ SbO_2. This shows clearly that the administration of oxygen for a short time immediately after birth accelerates oxygenation of brain tissue. This quick increase in oxygenation after birth may have adverse effects not only in preterm infants but also in term infants.[13]

The mean value for SbO_2 at 15 min after birth obtained in this study (69%) is similar to that measured by NIRS using the water spectrum (63%) reported by Cooper et al.[14]

The continuous measurements of SbO_2 in human neonates after birth may become a sensitive clinical parameter of adequate cerebral oxygen delivery. Using fsNIRS, we have demonstrated the state of cerebral oxygenation and the hemodynamic changes in the very early stages after birth.

6 Conclusion

Although there were few subjects in this preliminary investigation, we were able to demonstrate using fsNIRS that dynamic changes occur in cerebral circulation and oxygenation immediately after birth. With further investigation of a greater number of subjects, fsNIRS may prove to be a valuable tool in elucidating the pathophysiological condition of diseases causing brain damage in the neonatal period.

Acknowledgments

This research was supported by Grants-in-Aid for Scientific Research (C) Nos. 09671193, 09671194 and 11671070, and Encouragement of Young Scientists Nos. 08770906 and 09770866, from the Ministry of Education of Japan (Science and Culture Division).

References

1. N. J. Eastman, ''Mount Everest in utero,'' *Am. J. Obst. Gynec.* **67**, 700–711 (1954).
2. R. Tunell, ''The influence of different environmental temperatures on pulmonary gas exchange and blood gas changes after birth,'' *Acta Paediatr. Scand.* **64**, 57–68 (1975).
3. D. M. Peebles, A. D. Edward, J. S. Wyatt, M. Cope, D. T. Delpy, and E. O. R. Reynolds, ''Changes in human fetal cerebral oxygenation and blood volume during delivery,'' *Am. J. Obst. Gynec.* **167**, 1916–1917 (1992).
4. S. Onishi, S. Itoh, T. Imai, M. Nanba, T. Kunikata, Y. Ohtaki, K. Kawada, K. Isobe, and K. Hirao, ''Application of an innovative equation to near infrared spectroscopy analysis which converts the flattened and nonlinear diffusion spectrum of chromophores in the biological tissue to the transmission spectrum,'' *Photomed. Photobiol.* **15**, 57–60 (1993).
5. K. Isobe, T. Kusaka, S. Onishi, T. Kunikata, M. Ono, K. Kawada, S. Sugihara, Y. Ohtaki, T. Imai, S. Itoh, and K. Hirao, ''Cerebral oxygen saturation measured by continuous nir spectroscopy relating to oxygen saturation and oxygen partial pressure of blood in the internal jugular vein and artery,'' *Photomed. Photobiol.* **16**, 55–57 (1994).
6. T. Kusaka, K. Isobe, K. Kawada, Y. Ohtaki, S. Itoh, K. Hirao, and S. Onishi, ''Postnatal changes in the cerebral oxygenation in normal and asphyxiated neonates,'' *Proc. Photon Propagation in Tissues III SPIE* **3194**, 92–102 (1998).
7. S. Fantini, D. Hueber, M. A. Franceschini, E. Gratton, W. Rosenfeld, P. G. Stubblefield, D. Maulik, and M. R. Stankovic, ''Non-invasive optical monitoring of the newborn piglet brain using continuous-wave and frequency-domain spectroscopy,'' *Phys. Med. Biol.* **44**, 1543–1563 (1999).
8. K. Hirao and H. Inamoto, ''Method and apparatus for measuring the inside information of substance with the use of light scattering,'' US Patent No. 5,057,695 (15 Oct. 1991).
9. K. Hirao, ''Absorption spectrum determining method and spectrometric measuring apparatus for light-diffusive object using the method,'' US Patent, No. 5,333,610 (2 Aug. 1994).
10. T. Kitai, A. Tanaka, A. Tokuka, K. Tanaka, Y. Yamaoka, K. Ozawa, and K. Hirao, ''Quantitative detection of hemoglobin saturation in the liver with near-infrared spectroscopy,'' *Hepatology* **18**, 926–936 (1993).
11. A. P. Harris, M. J. Sendak, and R. T. Donham, ''Changes in arterial oxygen saturation immediately after birth in the human neonate,'' *J. Pediatr. (St. Louis)* **109**, 117–119 (1986).
12. T. K. Oliver, J. A. Demis, and G. D. Bates, ''Serial blood gas tensions and acid-base balance during the first hour of life in human infants,'' *Acta Paediatr. (Stockholm)* **50**, 346–360 (1961).
13. K. E. Lundstrom, O. Pryds, and G. Greisen, ''Oxygen at birth and prolonged cerebral vasoconstriction in preterm infants,'' *Arch. Dis. Child.* **73**, F81–F86 (1995).
14. C. E. Cooper, C. E. Elwell, J. H. Meek, S. J. Matcher, J. S. Wyatt, M. Cope, and D. T. Delpy, ''The noninvasive measurement of absolute cerebral deoxyhemoglobin concentration and mean optical path length in the neonatal brain by second derivative near infrared spectroscopy,'' *Pediatr. Res.* **39**, 32–38 (1996).