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Effect of Fetal Hemoglobin on the Determination of Neonatal Cerebral Oxygenation by Near-Infrared Spectroscopy

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ABSTRACT. Near-infrared spectroscopy has been applied to the study of cerebral oxygenation and hemodynamics in the newborn. Fetal Hb is present in high concentrations in these infants. Because spectral absorption curves in the near-infrared range for fetal Hb are not identical to those for adult Hb, there is a potential for the measurements to be affected. This possibility has not previously been investigated. A quantitative analysis of cerebral oxygenation was undertaken in six newborn infants. The analysis used near-infrared spectroscopy multiplier coefficients derived from the absorption coefficients of both fetal and adult deoxygenated and oxygenated Hb. The results of both analyses were compared. It was concluded that the error in near-infrared spectroscopy analysis of neonatal cerebral oxygenation arising from the use of absorption coefficients derived from adult Hb is inconsequential, even in the presence of high concentrations of fetal Hb. (*Pediatr Res* 34: 15–17, 1993)

Abbreviations

NIRS, near-infrared spectroscopy
NIR, near infrared
[Hb], cerebral deoxyhemoglobin concentration
[HbO_2], cerebral oxyhemoglobin concentration
SaO_2, arterial oxygen saturation
CBF, cerebral blood flow
CBV, cerebral blood volume

The technique of NIRS has been used in the investigation of cerebral oxygenation and hemodynamics in the newborn (1–3). The preliminary investigations were based on changes in [Hb], [HbO_2], total cerebral Hb concentrations and cytochrome aa_3. These data were presented as relative changes due to the uncertainty of the estimation of optical path length. Scattering of light by tissues causes the optical path length to be much greater than the physical path length. Time-of-flight measurements through biologic tissue (4) now permit quantification of these changes as well as provide absolute values for CBF and CBV (5, 6). Such quantification is also dependent on accurate absorption coefficients for Hb.

Seventy-five percent or more of the Hb in the blood of newborn infants is fetal Hb, but this falls to around 5% by the age of 6 mo (7). The decline is much more rapid in premature infants who receive transfusions with adult blood. Spectrophotometric multicomponent analysis of Hb derivatives for fetal blood (8, 9) and the effects of fetal Hb on the analysis of Hb pigments by multiwavelength oximetry have been studied (10). Although the spectral absorption curves for adult and fetal Hb are of similar shape over the relevant spectral range of 450 to 100 nm, the small differences between them are of sufficient importance to suggest that they should be taken into account in multicomponent analysis of Hb derivatives (11). The purpose of this study was to determine whether it is necessary to modify the coefficients used in NIRS calculations when fetal Hb is present.

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MATERIALS AND METHODS

Theory. NIRS monitoring of cerebral oxygenation uses light in the range 775 to 990 nm (12, 13). The method requires knowledge of the absorption coefficients of HbO_2, Hb, and cytochrome aa_3. Changes in the concentrations of these chromophores can be expressed in terms of changes in the absorbance measured at 775, 845, and 904 nm (14). For example, the change in the [Hb] can be expressed as:

$$\Delta[\mathrm{Hb}] = (P\Delta A_{775} + Q\Delta A_{845} + R\Delta A_{904})/nd$$

where Δ refers to changes. The terms P, Q, and R are obtained by matrix inversion from the absorption coefficients of Hb, HbO_2, and cytochrome aa_3. The direct spacing between the transmitting and receiving optical fiber probes placed on the neonatal head is taken as d. The scattering of NIR light leads to an increase in optical path length in the tissue, and this path length multiplication factor (n) has been found to be 4.3 (4). Thus, the change can be expressed in μmol/L.

The results of the spectroscopic determination of absorption coefficients of fetal Hb and adult Hb, as measured by Zijlstra *et al* (11), and our coefficients for cytochrome aa_3 were used. Table 1 gives these absorption coefficients for the wavelengths used. Using these, we arrived at two sets (Table 2) of "NIR multiplier

Table 1. *Absorption coefficients of adult and fetal Hb and cytochrome aa_3**

Chromophore	Wavelength		
	775 nm	845 nm	904 nm
HbO_2a	0.68	1.00	1.20
Hba	1.16	0.76	0.84
HbO_2f	0.64	0.96	1.12
Hbf	1.16	0.72	0.80
Cyt	1.75	2.83	1.27

* a, adult; f, fetal; cyt, cytochrome aa_3.

Table 2. *Two sets of NIR multiplier coefficients: NIRA obtained using absorption coefficients of adult Hb and NIRF using those of fetal Hb*

	NIRA			NIRF		
Concentration	775 nm	845 nm	904 nm	775 nm	845 nm	904 nm
[HbO_2]	−1.023	−0.0028	1.415	−1.014	−0.055	1.52
[Hb]	1.541	−0.896	−0.126	1.465	−0.862	−0.098
[Hb tot]*	0.518	−0.899	1.289	0.451	−0.917	1.422

* [Hb tot], total cerebral Hb concentration.

coefficients": NIRF, obtained using fetal Hb absorption coefficients; and NIRA, obtained using adult Hb absorption coefficients.

Subjects. Six infants were studied. They were all receiving additional oxygen therapy for respiratory distress syndrome or transient tachypnea of the newborn. To ensure high levels of fetal Hb, the studies were all performed during the 1st wk of life and before any blood transfusion. In some of these infants, the percentage of fetal Hb was measured from preoxygenated arterial or venous blood samples, using an OSM3 hemoximeter (Radiometer, Copenhagen, Denmark). To determine the effects of decreasing levels of fetal Hb, three studies were performed in one baby over a period of 48 d. During this time, the baby received four transfusions with adult blood, and the resulting change in fetal Hb was measured.

Procedure. The NIRS probes were placed on the infant's head and held in place a measured distance apart using double-sided adhesive rings and elastic webbing.

In all studies, the direct spacing between the optical probes was more than 4 cm. Each study consisted of an induced fall in SaO_2 by 10 to 15% from resting values of 95 to 98% by altering the inspired oxygen for a period of 5 min, then returning it to the initial value. This allows changes in the oxygenated Hb and Hb to be calculated during the fall in SaO_2. SaO_2 and heart rate were monitored using an N200 pulse oximeter (Nellcor-Inc., Hayward, CA) with the sensor attached to the foot.

This study was approved by the local ethical committee, and informed consent was obtained from the parents of the subjects.

RESULTS

The results of performing the calculation using both the adult and fetal Hb absorption coefficients were investigated for [HbO_2] and [Hb]. Here, [HbO_2]A and [Hb]A refer to changes in the concentration of oxy- and deoxyhemoglobin calculated using NIRA multiplier coefficients, whereas [HbO_2]F and [Hb]F refer to values obtained using NIRF multiplier coefficients (Table 2). The relationship between the results obtained using the different coefficients was tested for both [HbO_2] and [Hb], using linear regression analysis to examine the slope and intercept. For [HbO_2], the average values for slope and intercept were found to be 0.971 ± 0.01 and 0.003 ± 0.0028, respectively; r was 0.998 ± 0.0023. For [Hb], the average values for the slope and intercept were 1.049 ± 0.002 and 0.002 ± 0.0009, respectively; average value for r was 0.999 ± 0.0007. Figure 1 shows a scatter diagram with the line of identity for change in [HbO_2] during a desaturation study calculated using two different sets of NIR coefficients as given in Table 2.

Table 3 gives the results of the analysis in which the same baby was studied using NIRS after a blood transfusion. There was not any significant difference between the calculated values under different percentages of fetal Hb. The closeness to unity of the slope and to origin of the intercept for both [HbO_2] and [Hb] clearly shows that the error in NIRS analysis resulting from the use of adult Hb absorption coefficients in the presence of varying concentrations of fetal Hb is inconsequential.

The sensitivities of the NIR multiplier coefficients to the measured absorption coefficients were calculated by differentiating the equations derived by Cramer's Rule for matrix inversion

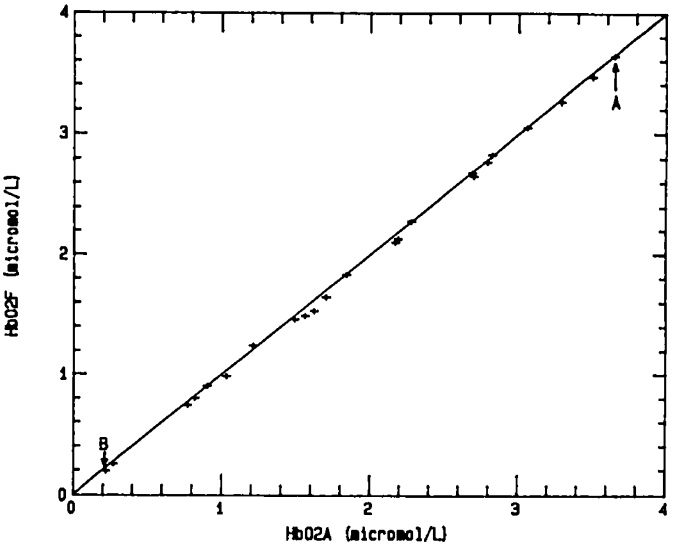

Fig. 1. Scatter diagram of data points, with line of identity for [HbO_2] calculated using adult (NIRA) and fetal (NIRF) NIR multiplier coefficients (*HbO2A* and *HbO2F*, respectively). The change was caused by a transient fall in SaO_2. At *A*, the saturation was 93.8%, falling to 85.7% at *B*.

Table 3. *Same baby (birth weight 1080 g; RDS) studied after blood transfusion, when the fetal Hb had fallen from 100% (d 6) to 23% (d 48)**

	Slope	SEM	Intercept	SEM	r
[HbO_2]A and [HbO_2]F					
Age 6 d (100%)†	0.960	0.014	−0.0001	0.004	0.998
Age 7 d (75%)	0.989	0.006	0.006	0.002	0.999
Age 48 d (23%)	0.992	0.004	−0.003	0.001	0.999
[Hb]A and [Hb]F					
Age 6 d (100%)	1.052	0.003	0.003	0.0006	0.999
Age 7 d (75%)	1.052	0.002	−0.0008	0.0009	0.999
Age 48 d (23%)	1.051	0.001	0.001	0.0005	0.999

* Results show that adult Hb coefficients can be applied to infants irrespective of the levels of fetal Hb present without introducing a significant error. RDS, respiratory distress syndrome; A, adult; F, fetal.

† Number in parentheses indicates percentage of fetal Hb.

(15). All sensitivities were <3. This means that for a given increment in any one absorption coefficient, no multiplier changes by more than three times that increment. This shows that the system of equations relating NIR absorbance changes to chromophore concentration changes is well conditioned. Thus, it has been demonstrated experimentally that the effects of small changes in absorption coefficients will be small.

DISCUSSION

Application of spectrophotometric multicomponent analysis to the determination of Hb derivatives in neonatal blood may theoretically lead to incorrect results due to the presence of fetal Hb. This is because of the difference in absorption spectra of adult and fetal Hb derivatives. The magnitude of the error depends on the wavelength of light that is used for different monitoring techniques. The contribution of varying concentrations of fetal Hb on pulse oximeter readings has been studied and has been found not to influence the accuracy of the results (16). However, it cannot be assumed that this applies to NIRS because different wavelengths of light are used. The fact that in clinical investigations NIRS uses absorption coefficients obtained from adult Hb has raised the question of whether this could lead

to errors when NIRS is applied to investigations in the neonate or fetus.

Clinical use of NIRS to monitor cerebral oxygen sufficiency, CBF and CBV in the neonate and fetus is increasing. Measurements of change in CBV have been compared with results obtained using jugular venous occlusion plethysmography (6) and measurements of CBF have been compared with results obtained by xenon clearance (17), thus providing a sound basis for further studies. If the presence of fetal Hb were to lead to errors in the quantified NIRS parameters when such studies are carried out, then account would have to be taken of this in the analysis. A series of coefficients would be necessary to allow for varying concentrations of fetal Hb. The percentage of fetal Hb present in the subject would also need to be determined before the data could be analyzed, which would limit the application of NIRS in the neonatal field.

This study has clearly demonstrated that adult Hb coefficients can be applied to infants, irrespective of the level of fetal Hb present, without introducing a significant error. This is particularly important for serial measurements in infants during the early weeks of life.

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