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Head position change is not associated with acute changes in bilateral cerebral oxygenation in stable preterm infants during the first three days of life

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Abstract

Objective—Several recent intraventricular hemorrhage prevention bundles include midline head positioning to prevent potential disturbances in cerebral hemodynamics. We aimed to study the impact of head position change on regional cerebral saturations (SctO2) in preterm infants (< 30 weeks GA) during the first three days of life.

Study Design—Bilateral SctO2 was measured by near infrared spectroscopy. The infant's head was turned sequentially to each side from midline (baseline) in thirty-minute intervals while keeping the body supine. Bilateral SctO2 before and after each position change were compared using paired t-test.

Results—In relatively stable preterm infants (gestational age 26.5±1.7 weeks, birth weight 930±220g; n=20), bilateral SctO2 remained within normal range (71.1% - 75.3%) when the head was turned from midline position to either side.

Conclusion—Stable preterm infants tolerated brief changes in head position from midline without significant alternation in bilateral SctO2; the impact on critically ill infants needs further evaluation.

Keywords

near infrared spectroscopy; cerebral autoregulation; cerebral oxygenation; head positioning; premature infants

Introduction

Intraventricular hemorrhages (IVH) remain common in very preterm infants and contribute significantly to poor outcomes later in childhood[1]. A significant proportion of IVH (~50%) occurs in the first four days of life[2]. During this critical transition period, preterm infants have limited ability to autoregulate cerebral blood flow (CBF) and are at high-risk for brain

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Conflict of interest

The NIRS instrument and probes were partially provided by CAS Medical Systems, Inc [Branford, CT] without any contribution to any other phase of the study.

injury due to systemic hemodynamic instability[3-5]. Recent evidence suggests that abnormal cardiac function and cerebral hemodynamics during early postnatal days are associated with peri- and intraventricular hemorrhages[5]. Clinical interventions (e.g. ventilation strategies, transfusions, and pharmacological management of hypotension) profoundly affect cerebral hemodynamics (e.g. cerebral blood flow, cerebral oxygenation, etc.), which further elevate the risk of brain injury in preterm infants[3,6-9]. More recently, routine head position changes have been postulated to affect cerebral hemodynamics. Adult patients at risk for elevated cerebral pressure due to traumatic brain injury are routinely placed in head-neutral position to facilitate venous drainage[10]. Doppler studies in term infants have shown that turning the head towards one side functionally occluded jugular venous drainage on the ipsilateral side[11]. This is of concern in preterm infants in whom, there are currently no official guidelines or recommendations with regards to head positioning during early days of life. In particular, an intubated preterm infant's head may be turned towards one side (facing the ventilator, e.g. high frequency oscillator) for prolonged periods of time. Since impaired venous drainage and decreased cerebral tissue oxygenation are factors implicated in the pathogenesis of IVH [5,12,13], mid-line head positioning during early transitional period have been included in recent IVH prevention bundles in many institutions, albeit without strong data to support the practice[14-16].

The ability to non-invasively monitor cerebral hemodynamics at the bedside can be valuable in optimizing neonatal care. Near infrared spectroscopy (NIRS) technology non-invasively measures relative changes in oxygenated (HbO2) and deoxygenated hemoglobin (HbR) levels within brain tissues[17-19]. The cerebral tissue oxygen saturation (SctO2) can then be calculated as a ratio of HbO2 to total hemoglobin (total hemoglobin = HbO2 + HbR). The normal reference range of cerebral tissue oxygen saturation for preterm infants varies between 55-85% depending on multiple factors such as instrumentation design, clinical status, post-natal age as well as the precision of the instrument[18,20-22]. Unlike pulse-oximetry (also based on light spectroscopy) that approximates arterial oxygen saturation, NIRS measurements are heavily weighted (70-80%) towards the venous component [18]; therefore, NIRS is uniquely suited for detecting any potential venous drainage impairment associated with head turning. Previous studies involving preterm infants at varying postnatal ages have shown conflicting outcomes regarding the effect of head positioning on cerebral hemodynamics [23,25-27]. In addition, in light of evidence showing unilateral obstruction of venous drainage in response to head turning[11,21], potential bilateral regional differences in cerebral SctO2 in response to head turning have not been investigated [21]. Therefore, the aim of this study was to investigate regional SctO2 measures with the head in midline and the acute effect of changing head positioning on bilateral regional SctO2 in a cohort of preterm infants during the first three days of life, using non-invasive NIRS.

Material and Methods

This is a prospective observational study designed to investigate the short term effect of head position change on bilateral cerebral tissue oxygen saturations in a cohort of preterm infants.

Study Population

After obtaining parental consent, preterm infants (< 30 weeks estimated gestational age (EGA)) were prospectively recruited within the first 12 hours of life (Table 1) in the neonatal intensive care unit (NICU) at St. Louis Children's Hospital. Infants were not pre-screened based on initial head ultrasound findings since the timing of the clinical ultrasounds at the study site were not standardized for the first three of life. Exclusion criteria included infants: (1) whose parent(s) could not be reached for consent prior to 24 hours of age; (2) who were suspected to have chromosomal abnormalities or severe congenital abnormalities; or (3) who were clinically moribund and unlikely to survive as determined by the primary medical care team. The study was approved by the local institutional human research protection office (HRPO).

Cerebral tissue oxygen saturation (SctO2)

Regional SctO2 was measured by a commercially available near-infrared spectroscopy (NIRS) device [ForeSight, CAS Medical Systems, Branford, CT] which can simultaneously measure regional SctO2 from two separate channels[28]. This is a continuous wave, 4 wavelengths device that has been FDA-approved for neonatal applications. Data sampling rate is 0.5 Hz. Detailed specifications of this device have been previously published[28].

Head positioning

Regional SctO2 measurements were performed at the bedside. NIRS probes were placed over each fronto-parietal region of the head. At the start of the study, the infant was placed supine with head in midline. The head of the bed was elevated at approximately 30° which is a standardized practice at the study site. Simultaneous SctO2 from each side of the head were then recorded continuously in 4 consecutive head positions changed at 30-minute intervals:

(1) Head in the midline position (baseline)

(2) Head turned (45-60°) from midline towards the left side with the body remaining supine;

(3) Head returned to the midline position;

(4) Head turned (45-60°) from midline towards the right side with the body remaining supine.

We chose not to forcefully turn the head past 60° to either side. The chosen range of rotation represents typical head placement by nursing staff within the study NICU if the head is turned to either side. During the NIRS measurements, the heart rate, pulse-oximetry, and mean arterial blood pressure (via umbilical catheter when available), were continuously recorded and synchronized with the SctO2 measurements. A member of the research team stayed at the bedside during the study to note changes in physiologic parameters, clinical stability, and ensure proper head positioning. If an infant required changes in FiO2 after head turning and failed to wean back down to reference baseline FiO2 within 5 minutes, the bedside team member was instructed to reset the current head position measurements and a

new reference baseline (head back in midline position) was then obtained with the current FiO2.

Statistical Analysis

All data were collected using a customized data acquisition software (CAS Medical Systems, Branford, CT), which provided output in an Excel-compatible format. The statistical package IBM SPSS (version 20) was used to analyze the data. Time traces of bilateral SctO2, heart rate, blood pressure (when available), respiratory rate, systemic saturation (SpO2) were plotted to identify periods of instability. First, ten minutes of data immediately before each positioning change were averaged to reflect a baseline value for subsequent comparison. After the head was turned towards the side, the time traces were re-examined for clinical stability (e.g. without apnea, bradycardia, and desaturation). Once the infant was determined to be stable from observing the time traces, the first 10 minutes of data (after clinical stability) and the subsequent second 10 minutes of data were separately averaged to reflect progressive changes in SctO2 in response to the head positioning change. Two-tailed paired t-tests were used to compare the changes in averaged SctO2 within the same side of the head. Comparisons of averages were made between the same channels (measuring the same side of the head) due to inherent within-subject and inter-subject variabilities.

Results

We recruited a total of 26 infants of whom complete head turning data sets were available in 22 infants. In the remaining 4 infants, data was available only with head in the midline position because the primary care teams preferred the heads of these infants to remain in the head midline position for the first three days of life; hence these infants were excluded from further analyses. Two additional infants with severe IVH (24 and 26 weeks of gestation at birth, respectively, Table 1) were first excluded from analyses in order to present data on a cohort of infants with no apparent or mild (grade I) IVH. Severe grade IVH is defined as grades III and/or IV on either side, based on clinical ultrasounds during the first seven days of life. Only one infant developed IVH (grade I) in the remaining cohort. Out of those four infants without complete head turning dataset mentioned above, one was found to have a Grade IV IVH shortly upon admission and prior to the NIRS study. The clinical characteristics of the recruited subjects are summarized in Table 1. The final cohort (n=20) had a mean (SD) gestational age of 26.5±1.7 weeks and birth weight of 930g ± 220g. Eighteen infants were studied on the 2nd day of life, with a range of 1-3 days. The average clinical risk index for babies score was 3.6 ± 3.1. Most infants (n=13, 65%) did not require mechanical ventilation at the time of the study. None received medical/surgical treatment for patent ductus arteriosus at the time of the study; however, eight infants did later require treatment.

The regional SctO2 are shown in Table 2. When infants with severe grade IVH were first excluded, the baseline bilateral SctO2 with the head in midline ranged between 72.3-75.0%. There was a statistically significant decrease (−1.5% in the first 10-min epoch after head position change (p=0.050); −1.7% in the second 10-min epoch (p=0.04)) in SctO2 on the left

side of the brain when the head was turned towards the left side from a midline position. When the two infants with grade IV IVH (clinical characteristics are shown in Table 1) were included in the analyses, similar amount of decreases (−1.6% (p=0.041 and 0.050) in both 10-min epochs) in SctO2 were noted again only on the left side when the head was turned towards the left.

No statistically significant changes were noted in any other channels, during either 10-min epochs, on either side of the brain when the head was turned towards the right side (Table 2). Statistical comparisons were made only within the same channels (measuring the same side of the brain) due to the inherent within-tissue and within subject variabilities. Furthermore, when the cohort was stratified by a cut-off birth weight of 800g (n=9), there was no statistically significant difference in SctO2 associated with head positioning change observed in any channel during any epoch (Table 3).

No statistical differences were found in heart rate, transcutaneous oxygen saturation via pulse oximeter, and mean arterial blood pressure during this period. While most infants tolerated the head position change without significant apnea, bradycardia, or desaturation episodes, 4 infants required up to 80 seconds to allow for initial transition between head position changes. None of the infants received inotropic agents during the study period or received fluid bolus within 4 hours of the study period.

Given the current sample size and observed data distributions between the two NIRS channels, a *post hoc* analysis shows sufficient power (96%) to detect a SctO2 difference of 10% between the left and right channels (with $\alpha = 0.05$). A 10% difference in SctO2 between the left and right side of the brain is arbitrarily chosen to be clinically significant, considering the precision of the instrument.

Discussion

Neutral head-positioning in the very preterm infants during early transitional periods is being explored as a potential method for IVH prevention[14-16,29]. In this cohort of relatively stable very preterm infants during the first three days of life, we describe the normal, bilateral regional SctO2 levels with the head in midline. Although we noted a statistically significant decrease in SctO2 on the ipsilateral side of the brain when the head was turned towards the left, this small decrease in SctO2 (<2%) is likely not clinically significant given the precision of the NIRS instrument, potentially small changes in PaO2, cerebral perfusion/autoregulation, and cerebral metabolism, etc. over this period of time. Interestingly, when the study cohort is further stratified by a birthwieght of 800g, no significant decrease in SctO2 associated with head turning was noted in any channels during any epoch. It is important to note that the overall SctO2 remaining within the expected normal range regardless of head position, even in those infants with birth weight <800g. Thus, brief changes in head position (which may occur as part of normal neonatal nursing care) do not seem to affect regional saturations in this cohort of stable infants.

NIRS has been used extensively in monitoring cerebral hemodynamics in the neonatal population[18,22]. It may be even better suited for evaluating processes that alter regional

SctO2 due to significant venous drainage disturbance (assuming stable arterial oxygen supply and tissue consumption) because SctO2 measurements are heavily weighted towards the venous compartment. While the development of IVH is certainly multifactorial, the primary aim of this study is to evaluate whether short-term head position changes are associated with acute SctO2 difference due to potential ipsilateral venous congestion.

There is currently no consensus on proper head positioning when caring for very preterm infants during the early days of life. Small studies suggest that lower SctO2 is associated with brain injury[5] and head turning alters cerebral hemodynamics (more specifically, ipsilateral venous drainage) in term-born infants[11]. However, studies aimed at investigating the potential effect of head/body positioning in preterm infants thus far have shown discrepant results likely due to the differences in study designs and the cerebral hemodynamic measurements reported [23,25,26]. Pellicer *et al* evaluated a heterogeneous group of 21 infants (24-37 weeks EGA, studied on days of life 1-33) [26] and found an acute and significant increase (up to 37%) in cerebral blood volume (CBV; parameter extrapolated from traditional NIRS measures) when the head was turned laterally. Infants in this study who weighed less than 1200g showed higher variability in CBV (perhaps, due to venous congestion) compared to those who were heavier and presumably more mature in gestational age. The change in CBV is not surprising as premature infants have been shown to have significant impairment in cerebral autoregulation, especially early in the postnatal course [30]. Since only frontal-midline measurements of CBV are available in this study, it is not clear whether the head turning exerts a global or more regional effect. Ancora *et al* (2011) studied cerebral tissue oxygenation in midline frontal region in 24 non-mechanically ventilated infants (27.5 ± 2.8 weeks EGA) in the second week of life [25]. They found no significant differences in cerebral tissue oxygenation in these infants with changes in body position (in either prone or supine), head rotation, and bed elevation (with or without elevating the head of the bed). Since measurements were taken only from the midline frontal region, potential changes in regional cerebral saturation differences were not explored. The effect of body positioning on cerebral oxygenation was studied by Bembich *et al* (2012) who used a multi-channel NIRS system to study 20 preterm infants (25-34 weeks EGA) between 2-48 days of life [23]. They noted a higher overall cerebral oxygenation in the supine/head midline position than in the prone position with head towards the side. These measurements at each body position were performed 1 day apart, but there were no significant differences in capillary pCO2, blood pressure, heart rate, and transcutaneous oxygen saturation between the two consecutive days. More mature infants (i.e. later gestational age at birth and older post-natal age) were included in this study and the effect on the younger subgroups were not explored.

In contrast to these studies, our study included a relatively more homogeneous group of preterm infants (26.5 ± 1.7 weeks EGA) monitored exclusively during the early postnatal period (first 3 days of age) when the incidence of IVH is high. It is also important to point out that our cohort of very preterm infants were relatively stable at the time of study (Table 1) as the majority did not require significant mechanical ventilatory support and none required inotropes or fluid boluses for hypotension; only one of the twenty infants analyzed in this study had any IVH. The inclusion of two infants with severe IVH did not alter the changes in ipsilateral regional SctO2 noted on turning the head to the left.

Our findings suggest that head positioning change in the first three days of life does not acutely nor progressively lead to clinically significant changes in cerebral hemodynamics in relatively stable preterm infants. The head-turning intervention was limited to only 30 minutes at each position in this study. Based on our experience, certain infants (especially infants requiring high frequency ventilation) may have their heads placed in one position for much longer periods of time. Therefore, it is unclear whether prolonged head turning may lead to bigger changes in SctO2. Furthermore, we cannot extrapolate the current finding to infants with higher acuity levels. Transient bilateral cerebral tissue oxygenation differences (unrelated to head rotation) were previously seen in preterm infants during systemic desaturations[31] but not in stable term and preterm infants without brain injury[21]. It may be reasonable to postulate that sicker preterm infants may exhibit wider differences in regional SctO2 with changes in head position, due to factors that may combine to exacerbate venous congestion (therefore alter SctO2). These factors may include prolonged head turning, impaired cerebral autoregulation, signs of early neonatal sepsis, hypotension requiring fluid resuscitation and/or inotropic support, symptomatic patent ductus arteriosus (PDA), and/or significant respiratory insufficiency requiring high ventilatory support which can lead to high mean airway pressures.

This study is the first to demonstrate the steady and normal bilateral regional SctO2 levels with head in midline and to investigate the acute effects of head-turning in a relatively homogenous cohort during the critical period when the incidence of IVH is high. While similar to aforementioned studies, our study is limited by a small sample size. *Post-hoc* analysis showed the current sample size to have sufficient power to detect larger and more clinical meaningful differences in bilateral cerebral tissue oxygenation. Second, there are other potential confounders that may be difficult to address in an observational study, e.g. inter-subject differences in ventilation requirement, PCO2, cardiac function, and cerebral autoregulation, *etc*. Nevertheless, the effects of inter-subject variability might be minimized because the pre- and post- head turn measurements in each infant were made by the same probe, at the same spot on the head, and only within a relatively brief period of time during which no dramatic differences in some of these physiologic variables were expected. Furthermore, none of the infants in our cohort experienced significant changes in arterial blood pressure, and none required ventilatory setting changes during our brief study period. The four infants who required transient increase in FiO2 support after head position change returned quickly to baseline FiO2 (without changes in ventilator setting changes). Other factors such as cardiac function[5], and the direction of blood flow across the ductus arteriosus may influence cerebral hemodynamics, particularly as preterm infants have been reported to have asymmetrical cerebral injury patterns, with the left side more frequently and/or more severely injured than the right side [32]. Since the ductus arteriosus is anatomically closer to the left than to the right carotid artery, a symptomatic PDA early in the postnatal period may functionally steal more blood away from the left side of the brain[33,34], leading to the asymmetrical injury patterns. This is an interesting finding given our data in relatively stable, non-injured preterm infants. We did not obtain concurrent echocardiograms to evaluate for PDA, but presumably most infants during the early days of life would have had a PDA and indeed 8 infants in our cohort later required intervention. While no infant in this study received medical or surgical PDA treatment at the time of our study, the dynamic

nature of PDA during early postnatal age is hard to control given the limits of the study design.

Conclusions

In summary, clinically stable preterm infants appeared to maintain stable bilateral SctO2 levels with their head in midline and also tolerated short-term head positioning changes well based on bilateral NIRS monitoring. Although we found a statistically significant decrease in ipsilateral SctO2 from baseline in response to turning the head to the left from midline, these may not be clinically significant in this cohort of relatively stable very preterm infants during the first three days of life. While previous IVH prevention bundles (including neutral head positioning) have shown improvement in various outcomes[14,15], our future research efforts will focus specifically on the effect of head positioning in infants with higher acuity (e.g. hypotensive, pressure passive states, etc.) as well as explore the effect of patent ductus arteriosus on cerebral hemodynamics.

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Table 1

Subject clinical characteristics (infants included in final analyses; n=20)

	Infants without severe* IVH (n=20)	Infants with IVH (n=2)	
Estimated gestational age at birth (weeks, mean ± sd)	26.5 ± 1.7	24 (n/a)	26 (n/a)
Median post-natal age at the time of study (days)	2 [1-3]	2	2
Gender			
Male	6	√	√
Female	14		
Race			
African American	16	√	√
Caucasian	4		
Birthweight (grams, mean ± sd)	930 ± 220		
CRIB scores (mean ± sd)	3.6 ± 3.1	5	6
Respiratory support at the time of study			
None	1		
Biphasic/NCPAP	12		
SIMV	7	√	√
Inotropic support at the time of study	0		
PDA (*none treated during study monitoring)			
- Not clinically significant/never treated	12		
- Treated with indomethacin alone	5	√	√
- Surgical ligation	3		
Proven sepsis in the first 7 days of life	0		0
Intraventricular hemorrhage			
None	19		
Grade I	1		
Grade IV	0	√	√

(CRIB = clinical risk index for babies, NCPAP = nasal continuous positive airway pressure, SIMV = synchronized intermittent mandatory ventilation, PDA = patent ductus arteriosus)

*severe IVH is defined as grade III and/or grade IV IVH on either sides of the brain based on routine clinical ultrasounds within the first 7 days of life.

Table 2

Regional cerebral tissue oxygen saturations (SctO2) in different head positions averaged across 20 infants (two additional infants with severe IVH were excluded)

	NIRS channel position	Averaged SctO2 (n=20)	SD	Sig (2-tailed paired t-test)
Head turned from midline to the left	L SctO2 (head midline)	72.7	6.4	**n/a**
	L SctO2 (head turned left) during the 1st 10-min epoch	71.1	6.1	**0.05**
	L SctO2 (head turned left) during the 2nd 10-min epoch	71.7	4.8	**0.04**
	R SctO2 (head midline)	75.0	7.3	n/a
	R SctO2 (head turned left) during the 1st 10-min epoch	74.4	7.5	0.49
	R SctO2 (head turned left) during the 2nd 10-min epoch	75.3	6.9	0.62
Head turned from midline to the right	L SctO2 (head midline)	72.3	6.1	n/a
	L SctO2 (head turned right) during the 1st 10-min epoch	73.1	5.3	0.19
	L SctO2 (head turned right) during the 2nd 10-min epoch	74.2	5.5	0.13
	R SctO2 (head midline)	73.3	6.9	n/a
	R SctO2 (head turned right) during the 1st 10-min epoch	73.8	6.8	0.58
	R SctO2 (head turned right) during the 2nd 10-min epoch	74.3	5.6	0.73

IVH – intraventricular hemorrhage; NIRS – near-infrared spectroscopy; SctO2 – cerebral tissue oxygen saturation; SD – standard deviation; L – left side of the head (NIRS probe position); R – right side of the head

Table 3

Regional cerebral tissue oxygen saturations (SctO2) in different head positions averaged across 9 infants whose birth weights were less than 800g

	NIRS channel position	Averaged SctO2	SD	Sig (2-tailed paired t-test)
Head turned from midline to the left	L SctO2 (head midline)	70.3	6.2	n/a
	L SctO2 (head turned left) during the 1st 10-min epoch	68.0	5.1	0.09
	L SctO2 (head turned left) during the 2nd 10-min epoch	68.7	3.9	0.09
	R SctO2 (head midline)	72.2	8.1	n/a
	R SctO2 (head turned left) during the 1st 10-min epoch	71.1	7.8	0.42
	R SctO2 (head turned left) during the 2nd 10-min epoch	73.1	7.7	0.71
Head turned from midline to the right	L SctO2 (head midline)	70.1	5.5	n/a
	L SctO2 (head turned right) during the 1st 10-min epoch	70.4	4.4	0.75
	L SctO2 (head turned right) during the 2nd 10-min epoch	72.2	5.1	0.34
	R SctO2 (head midline)	70.7	5.6	n/a
	R SctO2 (head turned right) during the 1st 10-min epoch	70.3	5.8	0.76
	R SctO2 (head turned right) during the 2nd 10-min epoch	71.7	3.6	0.79

IVH – intraventricular hemorrhage; NIRS – near-infrared spectroscopy; SctO2 – cerebral tissue oxygen saturation; SD – standard deviation; L – left side of the head (NIRS probe position); R – right side of the head