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Clinical Observations

Cerebral Hemodynamics During Neonatal Cerebrospinal Fluid Removal

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ABSTRACT

Background: Standard treatment of neonatal posthemorrhagic hydrocephalus is cerebrospinal fluid removal. The aim of this study was to assess how much cerebrospinal fluid volume removal, by ventricular reservoir taps, is needed to improve cerebral hemodynamics and oxygenation in neonatal posthemorrhagic hydrocephalus.

Methods: Cerebral hemodynamics and oxygenation were continuously monitored by near-infrared spectroscopy in four newborns (one term and three preterm) during 28 ventricular reservoir taps. At each tap, 10 mL/kg of cerebrospinal fluid was removed. Near-infrared spectroscopy detected changes in the concentration of oxy-hemoglobin and total hemoglobin, considered as estimates of cerebral blood flow and volume, respectively. Cerebral tissue oxygenation index was also measured. During cerebrospinal fluid removal, variation in cerebral blood flow, volume, and oxygenation were analyzed by repeated measures analysis of variance. The associations between changes in cerebral hemodynamics and oxygenation, during cerebrospinal fluid removal and after its conclusion, were analyzed by Pearson's r correlation coefficient.

Results: A significant increase in cerebral blood flow and volume was already evident at 50% of targeted cerebrospinal fluid volume removal ($P < 0.001$). Although cerebral tissue oxygenation index absolute value remained unchanged, variations in cerebral blood flow and oxygenation were positively correlated, both during cerebrospinal fluid removal and after its conclusion ($r = 0.57$; $P = 0.002$).

Conclusions: On the basis of the results from this small cohort, the volume of cerebrospinal fluid removal associated with an improvement in cerebral hemodynamics and perfusion seems to be less than the traditional 10 mL/kg. Further research is needed to define the potential role of near-infrared spectroscopy monitoring to individualize cerebrospinal fluid removal.

Introduction

Posthemorrhagic hydrocephalus (PHH) complicates intraventricular hemorrhage, alters cerebral perfusion, and impairs neurodevelopment.[1,2] The usual treatment of PHH is the removal of cerebrospinal fluid (CSF), initially performed by either lumbar puncture or ventricular reservoir taps. The precise CSF volume needed to be removed to improve cerebral hemodynamics and oxygenation is unknown. Traditionally, the CSF volume removed is 10 mL/kg.[3,4]

Near-infrared spectroscopy (NIRS)[5] allows continuous noninvasive bedside monitoring of cerebral hemodynamics and oxygenation, and may potentially be used to individualize the treatment of PHH. In newborns with PHH, cerebral perfusion is modified by CSF removal, as cerebral blood flow, volume, and oxygenation increase after CSF drainage.[3,6-8] However, data on changes in cerebral hemodynamics and oxygenation during CSF removal are lacking.

The aim of our preliminary study was to assess how much CSF volume removal is needed to improve cerebral hemodynamics and oxygenation. We tested the hypothesis that cerebral hemodynamics and oxygenation would improve after the removal of lower CSF volumes than the standard 10 mL/kg.

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Conflict of interest: The authors declare no conflicts of interest.

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Methods

Participants

We studied cerebral hemodynamics and oxygenation during 28 ventricular reservoir taps, in four newborns with PHH and a ventricular reservoir. There were one term female and three preterm infants (one male and two females). Two preterm infants were born at 26 weeks of gestation and one at 30 weeks of gestation. Clinical data are reported in Table. The Independent Committee for Bioethics of our Institution approved the research. Informed consent was obtained from parents, after full technical and procedural explanation regarding the study.

NIRS monitoring

Cerebral hemodynamics and oxygenation during CSF removal were continuously monitored by NIRS.[5] A NIRO 200NX device (Hamamatsu Photonics, Hamamatsu City, Japan) was used. It emits near-infrared light at three wavelengths (735, 810, and 850 nm). By using the modified Beer-Lambert law,[9] it estimates changes in the concentration of oxy-hemoglobin (HbO_2) and deoxy-hemoglobin in units of micromoles per liter (μM/L). Total hemoglobin (HbTot) is calculated from the sum of oxy-hemoglobin and deoxy-hemoglobin. Cerebral tissue oxygenation index (CTOI) is measured using spatially resolved spectroscopy,[10] with a 3 cm distance between near-infrared light emitter and detector. A differential pathlength factor of 3.85 was assumed, as reported in newborns.[11] Reflected light was sampled once every second (1 Hz).

Procedure

CSF drainage was performed when lateral ventricle width exceeded the ninety-seventh percentile plus 4 mm[12] or when Doppler resistance index of anterior cerebral artery exceeded 0.86.[13] Before CSF removal, the NIRS probe was secured by an adhesive strip on one side of the infant's forehead, contralateral to the reservoir access. Continuous NIRS data acquisition was started one minute before CSF removal, continued throughout the procedure, and ended two minutes after the conclusion of CSF removal. CSF volume removed was 10 mL/kg of body weight (rate, 1 mL/minute), by accessing the ventricular reservoir. Peripheral oxygen saturation, heart rate, and respiratory rates were monitored and recorded continuously during the procedure.

Data analysis

NIRS signal was filtered for movement artifacts. As previously reported,[3] all changes in NIRS signal larger than 2 μM/L and with a duration less than two seconds were excluded from statistical analysis. NIRS data collected when peripheral oxygen saturation was less than 85% were excluded from statistical analysis as well.

During CSF removal, HbO_2 (as estimate of cerebral blood flow),[14] HbTot (as estimate of cerebral blood volume),[14] and CTOI values were analyzed by repeated measures analysis of variance. Four time points were considered for statistical analysis, as 10 second averages of each detected variable, at (1) baseline (10 seconds before starting CSF removal), (2) 50% CSF removal, (3) completion of CSF removal, and (4) two minutes after the completion of CSF removal. Paired *t* test was used for *post hoc* analysis.

We analyzed correlations between changes in cerebral hemodynamics and oxygenation, during CSF removal and after its conclusion. Changes in cerebral blood flow, volume, and oxygenation during CSF removal were quantified as the difference of HbO_2, HbTot, and CTOI values at 50% CSF removal and at baseline ($\Delta_{50\%}HbO_2$, $\Delta_{50\%}$HbTot, and $\Delta_{50\%}$CTOI, respectively). Then, $\Delta_{50\%}$CTOI was correlated both to $\Delta_{50\%}HbO_2$ and to $\Delta_{50\%}$HbTot by Pearson's *r* correlation coefficient. Similarly, changes in cerebral blood flow, volume, and oxygenation after ending the CSF removal were quantified as the difference of HbO_2, HbTot, and CTOI values at CSF removal completion and at baseline (ΔHbO_2, ΔHbTot, and ΔCTOI, respectively). Then, ΔCTOI was correlated both to ΔHbO_2 and to ΔHbTot by Pearson's *r* correlation coefficient. Statistical analyses were conducted using SPSS version 22.0 for Windows (IBM Corp, Armonk, NY, USA). A *P* value of <0.05 was considered significant.

Results

A total of 28 ventricular reservoir taps were monitored in four newborns. Their distribution among participants is reported in Table. Average percentage reduction in lateral ventricle width was 20% and in resistance index was 25.2%.

During CSF removal, we observed an increase in HbO_2 ($F_{(3,81)} = 9.601$; $P < 0.001$) and HbTot ($F_{(3,81)} = 21.416$; $P < 0.001$). *Post hoc* paired *t* test revealed that all hemoglobin concentrations were significantly increased, compared with baseline, at 50% of CSF removal (HbO_2, $t_{(27)} = -4.115$; $P < 0.001$; HbTot, $t_{(27)} = -4.304$; $P < 0.001$), at completion of CSF removal (HbO_2, $t_{(27)} = -6.218$;

TABLE.
Participants' Clinical Data. (Clinical Characteristics of Our Study Population)

GA (weeks + days)	BW (g)	IVH (Grade)	Diagnosis	VR Placement (days)	Age (days) at first NIRS Monitoring	Age (days) at Last NIRS Monitoring	No. of Monitored CSF Removal
37 + 0	2890	III	Thalamic hemorrhage	45	52	66	8
26 + 2	560	III	Prenatal IVH	30	31	42	5
26 + 5	886	IV	Prenatal IVH	10	11	23	9
30 + 3	1770	IV	Prenatal IVH	14	15	23	6

Abbreviations:
BW = birth weight
CSF = cerebrospinal fluid
GA = gestational age
IVH = intraventricular hemorrhage
NIRS = near-infrared spectroscopy
VR = ventricular reservoir

$P < 0.001$; HbTot, $t_{(27)} = -9.289$; $P < 0.001$), and two minutes after the completion of CSF removal (HbO_2, $t_{(27)} = -5.345$; $P < 0.001$; HbTot, $t_{(27)} = -4.950$; $P < 0.001$). Hemoglobin concentrations significantly increased also between 50% of CSF removal and completion of CSF removal (HbO_2, $t_{(27)} = -4.495$; $P < 0.001$; HbTot, $t_{(27)} = -5.907$; $P < 0.001$), but did not differ between the time of completion of CSF removal and the last time point, 2 minutes later (HbO_2, $t_{(27)} = 0.024$; $P = 0.98$; HbTot, $t_{(27)} = 0.934$; $P = 0.36$) (Fig). CTOI remained unchanged ($F_{(3,81)} = 0.746$, $P = 0.528$) at all time points.

With regard to correlations between changes in cerebral hemodynamics and oxygenation, $\Delta_{50\%}HbO_2$ resulted significantly and positively correlated with $\Delta_{50\%}$CTOI ($r = 0.57$; $P = 0.002$), and ΔHbO_2 resulted significantly and positively correlated with ΔCTOI ($r = 0.57$; $P = 0.002$). On the contrary, correlations between $\Delta_{50\%}$HbTot and $\Delta_{50\%}$CTOI ($r = 0.35$; $P = 0.067$) and between ΔHbTot and ΔCTOI ($r = 0.09$; $P = 0.64$) were not significant. Therefore both during CSF removal and after its conclusion, changes in cerebral blood flow and oxygenation were positively correlated.

Discussion

We monitored cerebral hemodynamics and oxygenation during 28 CSF ventricular reservoir taps in four newborns with PHH. The concentrations of both HbO_2 and HbTot increased, reflecting an increase in cerebral blood flow and volume, respectively.[14] Changes in cerebral oxygenation during CSF removal were positively correlated with changes in cerebral blood flow, but not with changes in cerebral blood volume. Both the improvement in cerebral hemodynamics and the positive correlation between changes in cerebral oxygenation and cerebral blood flow were statistically significant after removing 50% of the targeted CSF volume.

Previous studies on neonatal cerebral blood flow and volume, collected before performing CSF removal and after concluding the procedure, found similar improvements in cerebral hemodynamics.[3,7,8] Such results have been interpreted as a decrease in cerebrovascular resistance and a consequent improvement in cerebral perfusion.[3]

The exact CSF volume needed to be removed, to improve cerebral hemodynamics and outcomes in infants with PHH, is unknown. A volume of 10 mL/kg of body weight is commonly chosen.[3,4] However, the hemodynamic impact of a standard volume removal might differ among patients, according to individual differences in the extent of PHH and its effect on cerebral perfusion and oxygenation. In our patients, an increase in cerebral perfusion was already present after removing 50% of the targeted CSF volume of 10 mL/kg.

We did not observe any change in cerebral oxygenation absolute value. In this regard, previous reports yielded inconsistent results. One study found no changes in cerebral oxygenation after CSF removal,[8] whereas two other studies observed an increase, but only after the first CSF drainage (i.e., on the day when the ventricular drainage was inserted).[6,7] The device we used measures hemoglobin concentration and CTOI with different algorithms (the Beer-Lambert law and the diffusion equation, respectively). This finding may at least partially explain why we observed improved hemodynamics, but no increase in CTOI. However, the improvement in cerebral blood flow during CSF removal was positively correlated with changes in cerebral oxygenation.

The main limitation of this study was its sample size of only four patients. Although all 28 CSF procedures were monitored by NIRS on these patients, our results need to be confirmed in larger samples.

In conclusion, bedside monitoring of cerebral neonatal hemodynamics and oxygenation, during CSF removal in PHH, may allow to tailor such intervention. On the basis of the results from this small cohort, improved cerebral hemodynamics and a positive correlation between changes in cerebral blood flow and oxygenation were observed at 50% of planned CSF removal volume. Further research is warranted to assess a possible role of NIRS in individualized CSF removal.

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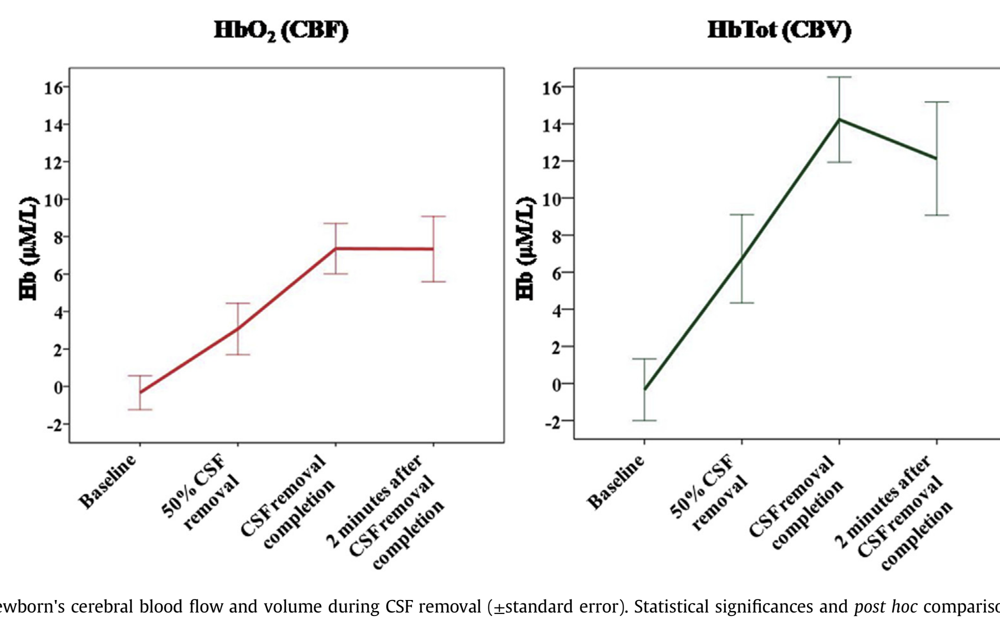

FIGURE. Increase in newborn's cerebral blood flow and volume during CSF removal (±standard error). Statistical significances and *post hoc* comparisons are reported in Results section. CBF, cerebral blood flow; CBV; cerebral blood volume; CSF, cerebrospinal fluid; HbO_2, oxy-hemoglobin; HbTot, total hemoglobin. The color version of this figure is available in the online edition.

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