Monitoring Extremely Premature Newborns with IVH using NIRS: One Patient Case Study

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Abstract

The present study investigates the possibility of detecting changes in cerebral oxygenation and consequently of intraventricular hemorrhage (IVH) in preterm children using paired data from the NIRS-monitor and the patient vital signs monitor. During the study, one patient's data were analyzed. The patient was born at the gestational age of 25+6 weeks. He was monitored for a period of 72 hours. IVH was first detected by the ultrasound diagnostics in 1000 minutes after birth. Analysis of the paired data showed that HR is not a useful IVH indicator. Comparison of the regional cerebral (cSrO2) and peripheral blood oxygen saturation (SpO2) changes and cerebral fractional oxygen extraction (OEF) with its second derivative represents a more beneficial method. It shows the tissue oxygen absorption changing (ie, periods of great change in hemodynamic, at the beginning or end of IVH). By comparing the calculated results and the medical records of the IVH course, it can be argued that this method can be efficiently used to determine the start and end of the bleeding into the brain ventricles. (Int J Biomed. 2016; 6(4):290-293.)

Key Words: near-infrared spectroscopy • extremely premature newborns • intraventricular hemorrhage • blood oxygen saturation

Introduction

Each year about 15 million babies are born prematurely worldwide (before 37 completed weeks of gestation), and this number is steadily growing. One of the most frequent and serious complications observed in prematurely born children (<28 weeks) is intraventricular hemorrhage (IVH).[1]

IVH is a bleeding into the central nervous system that occurs most frequently in premature infants in the cerebral ventricles, because the blood vessels in these areas are very fragile, and adaptive changes in the bloodstream of newborns and fluctuations in blood pressure may cause a rupture of the blood vessels and subsequent bleeding. Other risk factors are mechanical ventilation, hypercapnia, patent ductus arteriosus, volume expansion in the first days of life, and fetal growth retardation. About 90% of cases of bleeding in the brain ventricles occur during the first 72 hours after childbirth, hence this period must be closely monitored.[1-4]

Clinical manifestations most often include convulsions, worsening of breathing difficulties, fontanelle bulging, and coma. Asymptomatic IVH is no exception.

There are 4 grade of IVH:
- Grade 1 - subependymal hematoma;
- Grade 2 - bleeding into the brain ventricles, ventricles have normal volume;
- Grade 3 - bleeding into the brain ventricles, ventricles are expanded;
- Grade 4 - bleeding into the brain parenchyma accompanied or not accompanied with the presence of blood in the ventricles (periventricular hemorrhagic infarction). Infarction is typically one-sided, large, probably venous origin.[3, 4]

Bleeding of Grades 1 and 2 is limited to the ventricles and in most cases is spontaneously absorbed without any consequences and with favorable prognosis for the child’s further development. Hemorrhage of Grade 3 is bleeding into the ventricles on a larger scale, which is usually healed without any residual effects, but in this case there is a greater risk, for example obstruction of the blood brain pathways, blood clot formation, and hydrocephalus. IVH Grade 4 is the cause of brain tissue damage, usually with serious consequences for the further development of the child. Severe psychomotor retardation affects are observed in up to 90% of the children with Grade 4 bleeding. Bleeding is not always isolated. Bleeding of this grade is usually associated with the cerebral lesions such as periventricular leukomalacia, pontosubikulární necrosis etc., which contribute to an unfavorable prognosis.[3, 4]

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In most cases, bleeding is diagnosed by ultrasound diagnostics, which is usually done with a long interval (4-6 hours) between particular diagnostics. Ultrasound diagnostics cannot detect the start time of bleeding. The grade of IVH is determined by the extent of the bleeding.

Treatment of bleeding is possible. In most cases the blood is spontaneously absorbed and the rupture heals itself. An important point is a regular monitoring of bleeding and timely diagnosis of complications (e.g., the development of hydrocephalus). Complications such as hydrocephalus are resolved surgically. Therefore, ultrasound is useful for diagnosis and also in the subsequent period during the monitoring of the healing process, but does not allow continuous monitoring because of the large intervals between the times of diagnosis. \[1-4\]

Near-infrared spectroscopy (NIRS) is a noninvasive spectroscopic method widely used in research. It is an instrument for continuous measurement of tissue oxygen saturation that uses the infrared region of the electromagnetic spectrum. The method is not very sensitive, but NIRS is able to penetrate deeper into the sample. The method is very popular in neonatology, particularly in premature babies. It enables monitoring of the regional tissue oxygenation, for example oxygenation of the brain tissue. \[5,6\]

At the beginning of the 21st century in Drexel University (PA), Alper Bozkurt and his research team, having researched the principle of NIRS, assumed a possible correlation between cerebral blood flow, cerebral oxygenation, and subsequent occurrence of intraventricular / brain hemorrhage in premature infants. \[7\]

Ying Zhang and his team analyzed the 3-hour records of 5 preterm infants with IVH and 12 preterm infants without IVH. The main conclusion of this study was that infants with IVH had lower coherence between arterial blood pressure (BP) and deoxygenated hemoglobin (HHb) illative from NIRS. Parameters derived from the analysis of transfer function, however, did not show significant deviation from the norm. Because of this, the hypothesis that IVH could be detected by analyzing changes in BP was rejected. \[8\]

The aim of this study was to verify the possibility of detecting the period of time with large changes in hemodynamics and consequently the beginning or end of IVH using the values of regional cerebral (cSrO2) and peripheral blood oxygen saturation (SpO2), cerebral fractional oxygen extraction (OEF) and its second derivative.

Methods

During the study, one patient’s data were analyzed. The study was approved by the Czech Technical University Ethics Committee. Written informed consent was obtained from the child’s parents. The patient was born at the gestational age of 25+6 weeks. He was monitored for a period of 72 hours. IVH was first detected by the ultrasound diagnostics in 1000 minutes after birth (Table 1).

In this research, we used data of regional oxygenation obtained with the device INVOS 5100C. The INVOS 5100C is a system that enables real-time monitoring of changes in regional blood oxygen saturation in the brain (cSrO2) or other tissues under the sensor for adults, children, infants and newborns. The NIRS device had the sampling rate set to approximately 6 times per minute. \[9\] We used also a patient vital signs monitor, Delta, with the sampling rate set to 1 sampling per minute. Subsequent data processing was done in MATLAB.

### Tab. 1.

<table>
<thead>
<tr>
<th>Basic patient’s data and parameters of monitoring</th>
<th>(\frac{SpO2 - cSrO2}{SpO2})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>male</td>
</tr>
<tr>
<td>Gestational age at birth</td>
<td>25 + 6 weeks</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>IVH Grade 1</td>
</tr>
<tr>
<td>First detecting IVH by UZ</td>
<td>The 2nd day of life (≈1000 minutes after birth)</td>
</tr>
<tr>
<td>Character of bleeding</td>
<td>unilateral, small size</td>
</tr>
<tr>
<td>Symptoms</td>
<td>no</td>
</tr>
<tr>
<td>The period of monitoring</td>
<td>4320 minutes (72 hours)</td>
</tr>
<tr>
<td>Monitored parameters</td>
<td>cSrO2, SpO2, HR</td>
</tr>
</tbody>
</table>

**Data processing**

Using MATLAB, a summary table for a patient was created, which contained minute paired data from two devices. The table contains the values of HR (heart rate), SpO2 and cSrO2 and calculated OEF for each minute of recording. Dropouts of measured signals were checked and complemented by linear approximation. OEF was calculated according to the equation:

\[
OEF = \frac{SpO2 - cSrO2}{SpO2}
\]

Fig. 1 shows changes in time of cSrO2 (blue) and SpO2 (yellow) oxygen saturation. The sudden decrease in cerebral oxygen saturation (from the 419th minute) presumably marks the start of the IVH. The patient had IVH Grade 1, which was absorbed during the return to the normal hemodynamic, which happened around the 1320th minute of life. There was a sharp increase in regional cerebral oxygen saturation. The red line shows the time-point of US diagnostics, when IVH was first detected.

OEF values are directly proportional to the difference between SpO2 and cSrO2, and indirectly proportional to peripheral blood oxygen saturation (Fig. 2). The OEF coefficient is a normalized value that increases considerably after the expected IVH start (i.e., from the 419th minute). The red line shows the time-point of US diagnostics when IVH was first detected.

To detect great changes in hemodynamics, which could indicate the beginning or the end of bleeding, we used the method of second difference. This method determines the time of the changes in the tissue oxygen absorption according to the equation:

\[
2.\ diff f_i = |x_i - x_{i-20}| - |x_{i-20} - x_{i-40}|
\]

where \(i\) is a minute of life, and \(x\) is a value of OEF.
It is assumed that at the point where the second derivative of OEF is greater than 0.25, there is a significant change in hemodynamics that may indicate the beginning or the end of hemorrhage.

Fig. 3 is a graphical representation value of the second derivative of OEF. The first time period when the second differential values are greater than 0.25 (the 74th minute of life) can be omitted because of its origin; interference is the result of mechanical operations at the beginning of monitoring. Considering the medical records of the IVH course, presented above, other places where the second derivative of OEF is greater than 0.25 (432th and 1320th minutes of life) are probably the beginning and the end times of bleeding. The red line shows the time-point of US diagnostics when IVH was first detected.

The HR dynamic is shown in Fig. 4. These changes cannot be combined with the process of IVH. The HR values obtained before the 739th minute of life were subtracted from SpO2, and values obtained starting from the 740th minute were subtracted from ECG. HR values did not show significant deviation from the norm.

To determine the possibility of IVH detection by HR, we performed a correlation analysis of HR and OEF. The correlation coefficient was calculated as Pearson's correlation coefficient according to the equation 3:

$$ r = \frac{\sum(x - \bar{x})(y - \bar{y})}{\sqrt{\sum(x - \bar{x})^2 \sum(y - \bar{y})^2}} $$

where $x$ and $y$ are each minute values of HR and OEF, and $\bar{x}$ and $\bar{y}$ are mean values of HR and OEF. The correlation coefficient is $r_{4320 \text{ min}} = -0.03476$, which means that there is no correlation between the HR and OEF values recorded during 4320 minutes.

Correlation analysis was also performed for the HR and OEF values recorded during the period of 120 minutes. The interval chosen was from the 359th minute to the 479th minute of after birth, so that the expected start of IVH (the 419th minute of life) was in the middle section of the correlated signals. The correlation coefficient is $r_{120 \text{ min}} = -0.01497$, which means that there is no correlation between the records of HR and OEF taken during the 120-minute period, wherein the putative start of IVH (the 419th minute of life) was in the middle of the correlated signals. The hypothesis that IVH could be detected by changes in HR analysis was rejected.
In conclusion, changes in regional cerebral oxygenation changes and subsequent IVH can be detected in preterm children using paired data from NIRS and the patient vital signs monitor. Analysis of the paired data showed that HR is not a useful IVH indicator because it does not correlate with the changes of cSrO2. Comparison of cSrO2 and SpO2 changes and OEF with its second derivative represents a more beneficial method. It shows the tissue oxygen absorption changing (ie, periods of great change in hemodynamic, at the beginning or end of IVH). By comparing the calculated results and the medical records of the IVH course, it can be argued that this method can be efficiently used to determine the start and end of the bleeding into the brain ventricles.

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References