NEAR-INFRARED SPECTROSCOPY MEASUREMENT OF ABDOMINAL TISSUE OXYGENATION IS A USEFUL INDICATOR OF INTESTINAL ISCHEMIA IN NEONATES

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ABSTRACT

Introduction. Neonatal intestinal ischemia is a frequent pathology, but unfortunately, often underdiagnosed. Current technique allows non-invasive investigation of splanchnic circulation, being capable of detecting early perfusion changes that occur at this level.

Objectives. The aim of this study was to determine the clinical value of infrared spectroscopy (NIRS) in early detection of ischemic bowel modifications in newborns from neonatal intensive care unit.

Material and methods. We performed a prospective observational study over a period of 18 months, on a group of 15 newborns with gestational age between 25-38 weeks. All infants included in the study had one or more clinical signs of digestive pathology.

Starting non-invasive continuous monitoring by cerebral and abdominal NIRS was performed according to the appearance of the first digestive changes between day 3 and 21 of life. Oxygen saturation was measured in the cerebral and abdominal regions (rSO_2-C and rSO_2-A) and cerebro-splanchnic oxygenation ratio (CSOR) was carried out. Meanwhile infants were monitored by biological and hemodinamyc methods.The monitoring period was variable, being between 1-5 days, the period required for establish the causal diagnosis.

Statistical significance was determined using statistical t-test. "p" was calculated for confidence interval of 95% (statistical significance $p < 0.05$). Also was evaluated the area under the receiver operating characteristic (ROC) curve to determine the suitability of this technique as a diagnostic tool.

Results. The study group included: 3 neonates with congenital heart disease(CHD) with significant decrease in aortic blood flow, 4 neonates with necrotizing enterocolitis (NEC) stage II, 3 pacients with intrauterine growth retardation (IUGR) severe form, 1 newborn with intestinal atresia and secondary peritonitis, 1 newborn with Rh incompatibility anemia with placental anasarca and 3 pacients with sepsis and associated gastrointestinal pathology without NEC criteria.

In all 15 patients, NIRS measurement values were significantly lower compared to the normal range, with different values depending on the severity of the condition. Mean rSO_2-A value was 41.85 (interquartile range15-85) compared to an average value, considered normal. Also the average value of the CSOR ratio was significantly lower compared to the normal. The lowest values of rSO_2-A at the beginning of simptoms has had the group of patients with CHD followed by those with NEC. The area under the ROC curve was 0.95 (95% CI 0.88 to 1.02) for the CSOR ratio. Considering a limit value of ROCS for prediction of intestinal ischemia < 0.75, this ratio proves to be an excellent indicator of changes in bowel circulation.

Conclusion. NIRS method has the potential to detect the occurrence of alterations in intestinal oxygenation and perfusion, allowing early detection of bowel ischemia, just before the modification of other hemodynamic parameters. NIRS is a non-invasive, highly accurate method, to follow in evolution the changes in tissue perfusion under the treatment instituted, also being able to guide treatment, proving helpful in clinical practice.

Keywords: near infrared spectroscopy, neonates, regional oxygen saturation, intestinal ischemia

INTRODUCTION

Near-infrared spectroscopy (NIRS) is a feasible, noninvasive and beneficial technology to assess regional tissue oxygenation reflecting perfusion status. NIRS has the ability to continuously and simultaneously monitor tissue perfusion in different organ systems at the bedside without interrupting routine care.

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In 1977, Jobsis described NIRS for the first time for medical use (1), and since then it was used in adults. Research has demonstrated its benefit in monitoring cerebral, intestinal and renal perfusion to detect potential ischemic episodes.

The use in neonates to measure cerebral oxygenation was first reported by Brazy et al (2) and Delpy (3), and since then NIRS started to become more popular in neonates.

Various NIRS technologies have already been used by a number of biomedical engineers and interested physicians (4-7). Several different NIRS devices are currently available: FORE-SIGHT, INVOS, NIRO, InSpectra, O2C, OM-220, OxiplexTS, TOx and TRS-20 (8,9). These devices use different near-infrared light sources (laser/LED), wavelengths, optode distances, and algorithms to calculate cerebral and somatic oxygen saturation.

NIRS utilizes light wavelengths (700-1,000 nm) similar to pulse oximetry for measuring tissue oxygenation. Pulse oximetry depends on pulsatile blood flow and measures only the oxyhemoglobin in arterial blood as it leaves the heart. NIRS measures the difference between oxyhemoglobin and deoxyhemoglobin, which reflects oxygen uptake in the tissue bed. This measurement is reported as the regional oxygen saturation (rSO_2). NIRS measures the balance of oxygen that is deliverd minus what is extracted at the tissue level, thus clinicians can directly monitor fluctuations in tissue oxygenation as they occur (10,11).

During hemodynamic stability, tissue oxygenation uptake differs between regions of the body. Cerebral uptake is higher due to higher metabolic demands, while renal and splanchnic uptake is lower indicating less metabolic activity. In NIRS measurements, this translates to normal cerebral readings being generally lower than somatic measurements (60-80) and splanchnic/renal measurements being generally higher than cerebral (65-90) (10,11). Baseline trends must be obtained in all infants monitored with NIRS. The objective in NIRS measurements is to observe persistent and/or frequent changes from baseline that are greater than 15% (10). It was suggested that interpretation of NIRS measurements in ratio format provides a relative comparison between differential regional perfusion. Known as a cerebro-splanchnic oxygenation ratio (CSOR), values less than 0.75 have been correlated with an increased risk for mesenteric ischemia (12).

NIRS technology is currently use in cardiac intensive care units, in operating rooms to monitor vascular and cerebral oxygenation, in neonatal intensive care units, showing significant potential to further understanding of tissue perfusion pathology not reflected in current routine bedside monitoring modalities (13-18). Current methods employed to evaluate oxygen delivery and tissue consumption are frequently nonspecific. For neonates in the intensive care unit (NICU), these methods include urine output, lactate measurements, capillary refill time, blood presure, oxygen saturation and others. Because of the immaturity of the vasculature tree, coupled with a narrow range of pressure autoregulation, even slight fluctuations in tissue perfusion can potentially result in ischemia leading to end organ damage (19,20). Previous studies that applied NIRS to the abdomen of neonates demonstrated that neonates with an acute abdomen have lower cerebro-splanchnic NIRS ratios (12).

NIRS can augment current physiologic monitoring to increase awarness of abnormal perfusion status in the neonates and potentially reduce risks associated with many diseases that may lead to ischemic injury. NIRS may evolve into an important diagnostic, monitoring and prognostic tool for neonatal treatment and outcome.

PURPOSE

In the Neonatal Intensive Care Units (NICUs) there is need for a non-invasive clinical tool in order to evaluate the regional perfusion at diferent sites and possibly prevent a series of pathologies. Thus, the aim of this study is to determine the clinical value of NIRS in early detection of ischemic bowel changes in neonates from NICU.

MATERIAL AND METHODS

The study had a prospective observational design and the local ethical committee approval was obtained. Also the parental consent was sought and acquired on all subjects. The study included 15 infants born in a third level maternity in Romania over a period of 18 months. Gestational age (GA) was between 25-38 weeks (with a medium of 29.60 ± 2.26) and birth weight (BW) was between 750 g – 3250 g.

All infants included in the study had one or more clinical signs of digestive pathology (abdominal distension, bilious gastric residue or with digest milk, absence of digestive tolerance, digested bloody stool, lethargy).

Starting non-invasive continuous monitoring by cerebral and abdominal NIRS was performed according to the appearance of the first digestive

changes, between day 3 and 21 of life. Routine care of infants was not interrupted. Meanwhile infants were monitored by biological and hemodinamyc methods (blood count, C-reactive protein, blood gas analysis, serum lactate, glucose, arterial oxygen saturation, blood pressure, heart rate, temperature). The monitoring period was variable, being between 1-5 days, the period required for causal diagnosis determination, and then to follow the changes in the intestinal perfusion under the therapy instituted.

For measuring the regional oxygen saturation we used Somanetics 5100 INVOS System device. Sensors were placed over the forehead for cerebral regional saturation (rSO_2-C) and infraumbilical abdomen for abdominal regional saturation (rSO_2-A) (Fig. 1). rSO_2 was measured every day for at least 8 hours. Measured values were recorded as an average, with a minimum and a maximum (Fig. 2). This measurements were then combined as a ratio of abdominal rSO_2 over cerebral rSO_2 (rSO_2-A/rSO_2-C) to produce a cerebro-splanchnic oxygenation ratio (CSOR).

Statistical analysis was performed using SPSS Version 17 Program. Results are expressed as mean ± SD. In order to compare the significant differences on rSO2-A and CSOR values at the study group, compared to the values considered normal (rSO2-C: 60-80% rSO2-A: 65-95%), it was used statistic t-test for independent samples. All p values < 0.05 were considered statistically significant for an confidence interval (CI) of 95%. Also was evaluated the area under the receiver operating characteristic (ROC) curve to determine the suitability of this technique as a diagnostic tool.

FIGURE 1. *Pacient A.I., 5 days old, monitorised by cerebral and abdominal spectroscopy. Position of optodes on head and abdomen.*

FIGURE 2. *Aspect of INVOS device*

RESULTS

The study group included:

- 3 newborns with congenital heart disease (CHD) with significant decrease in aortic blood flow
- 4 newborns with stage II NEC
- 3 newborns with IUGR severe form
- 1 newborn with intestinal atresia and secondary peritonitis
- 1 newborn with Rh incompatibility anemia and placental anasarca
- 3 newborns with sepsis associated with digestive pathology without NEC criteria.

The majority of newborns were preterms, 73.3% being under 37 weeks of gestation and 53.3% under 32 weeks, and 93.4% had birth weight below 2,500 g. The details concerning GA, BW, diagnosis and NIRS measurements of the pacients are shown in Table 1. In 8 (60%) cases the onset of the symptoms was before 10 days of life.

NIRS measurements were performed continuously since the first appearance of clinical signs until the diagnosis has been established, and further, to follow the changes in intestinal perfusion under the treatment. In all 15 pacients, NIRS measurement values were significantly lower compared to normal values, with different values depending on the severity of the condition. The lowest values of abdominal rSO_2 at the begining of simptoms has had the group of patients with CHD followed by those with NEC. Individual cerebral and abdominal rSO_2 range values and the CSOR for each pacient, at the time of simptoms onset, are shown in Table 1. Mean rSO_2-A value was 41.85 (interquartile range 15-85) compared to an average of 76.22 (65-88) ($p = 0{,}000$; $t = -9.764$), considered normal value. Also the average value of the CSOR ratio was significantly lower compared to the normal: 0.58 to 1.10 ($p = 0{,}000$, $t = -9.782$).

TABLE 1. *The details concerning GA, BW, diagnosis and NIRS measurements of the pacients*

No	GA	BW	Diagnosis	Range rSO_2-C	Average	Range rSO_2-A	Average	CSOR
1.	28	1120	Sepsis	15-95	84	15-89	53	0.63
2.	28	730	Sepsis	63-77	69	15-68	46	0.66
3.	32	1750	Sepsis	55-95	77	15-88	57	0.74
4.	37	1840	IUGR	15-95	57	72-89	85	1.49
5.	37	2050	IUGR	66-94	79	61-88	75	0.94
6.	34	1280	IUGR	24-72	52	17-73	49	0.94
7.	38	2350	CHD	52-83	70	15-95	30	0.42
8.	32	1640	CHD	54-95	82	15-75	42	0.51
9.	39	3250	CHD	52-83	70	22-82	55	0.78
10.	28	1060	NEC	77-87	81	15-74	37	0.45
11.	34	1540	NEC	56-95	79	15-95	59	0.74
12.	32	1260	NEC	69-95	86	15-74	37	0.43
13.	26	1000	NEC	50-92	80	15-75	42	0.52
14.	25	720	Small bowel atresia	53-95	75	15-95	24	0.32
15.	33	2160	Severe anemia, anasarca	15-55	41	15-58	15	0.36

IUGR = intrauterine growth retardation, CHD = congenital heart disease, NEC = necrotising enterocolitis, rSO_2-C = cerebral regional oxygen saturation, rSO_2-A = abdominal regional oxygen saturation, CSOR = cerebro-splanchnic oxygenation ratio

To determine the suitability of this technique as a diagnostic tool, we have generated a receiver operating characteristic (ROC) curve (Fig. 3 and Fig. 4). In this analysis we examined the ability of rSO_2-A and CSOR to discriminate between the neonates with and without intestinal ischemia. The area under the ROC curve was 0.94 (95% CI 0.87-1.02) for rSO_2-A and 0.95 (95% CI 0.88 to 1.02) for the CSOR ratio. Taking a threshold value for CSOR of 0.75 to demarcate the boundary between a positive and negative study, these parameters proves to be excellent indicators of intestinal pathology, showing intestinal ischemia.

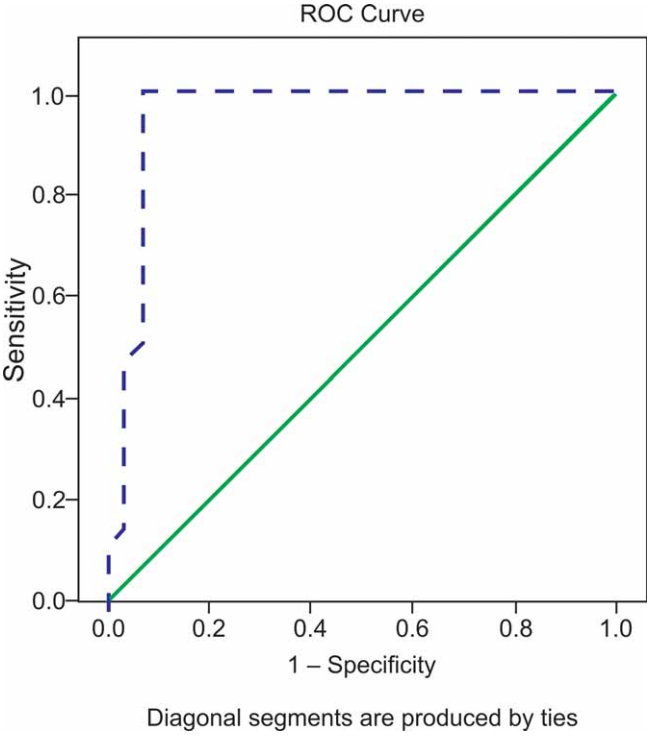

FIGURE 3. *ROC curve (dotted line) for rSO_2-A for prediction of intestinal ischemia. The area under the curve is 0.94 (95% CI 0.87-1.02)*

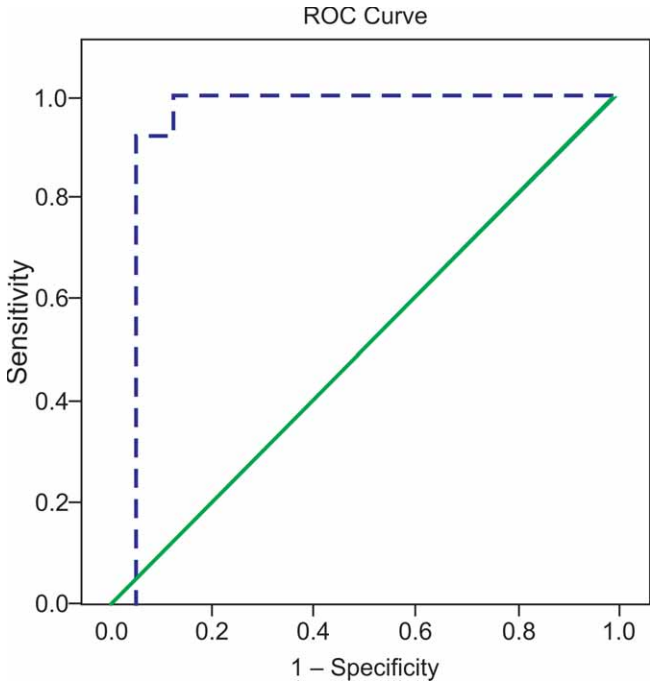

FIGURE 4. *ROC curve (dotted line) for CSOR for prediction of intestinal ischemia. The area under the curve is 0.95 (95% CI 0.88 to 1.02)*

In evolution the group with CHD presented the lowest value, followed by NEC group. Under the treatment the measurements values have improved in the groups with sepsis, IUGR, NEC and in the case with severe anemia, while in the other cases has remained unchained (with small oscillations under the medical treatment), the cases requiring surgery to cure the disease.

DISCUSSION

Near-infrared spectroscopy has been extensively used up today to study cerebral and somatic perfusion initially in adults and then to infants especially in newborns (21,22).

This study was an observational study, which aimed to evaluate the ability of NIRS method in detecting ischemic bowel in neonates. The evaluation of intestinal oxygenation and blood flow in the superior mesenteric artery may help in early diagnosis of clinical changes that occur secondary to cardiac pathologies with decreased aortic flow, necrotising enterocolitis, severe anemia or severe hypoxia and other diseases.

Our study shows that in all 15 pacients, NIRS measurement values were significantly lower, being an early diagnostic method, together with other clinical and imaging methods (eg ultrasound Doppler in cardiac pathology, radiography in abdominal pathology).

For example, necrotising enterocolitis is a common and potentially fatal condition seen in neonatology, for which there is very little availble in terms of a monitor to help determine whether bowel ischemia is improving or worsening. Despite the prevalence of this condition, no diagnostic technique with sufficient sensitivity is available to aid in the diagnosis and management of suspected cases (23,24). Using abdominal NIRS we was able to detect lower rSO_2-A and CSOR values in all the neonates diagnosed with NEC. This method has proved useful in establishing early diagnosis and initiating treatment as soon as it is possible in order to prevent the damage of the small intestine. Previous studies of abdominal NIRS measurement have provided hints that technology may be useful in detecting the early onset of NEC in infants, as the study of Fortune et al (12). Similar results concerning the values of regional oxygen saturation in neonates with necrotising enterocolitis had also the study done by Cortez and colegues (11).

Also the NIRS method is suitable to follow in evolution the changes in tissue perfusion under the treatment instituted, being able to guide the treatment (25).

CONCLUSIONS

In conclusion, this study suggests that NIRS method has the potential to detect the occurrence of alterations in intestinal oxygenation and perfusion, allowing early detection of bowel ischemia, just before the modification of other hemodynamic parameters. By comparing the regional oxygen saturation between somatic and cerebral regions may be possible to establish the presence of normal splanchnic perfusion and detect when intestinal ischemia developed. NIRS is a non-invasive, highly accurate method, to follow in evolution the changes in tissue perfusion under the treatment instituted, also being able to guide treatment, proving helpful in clinical practice.

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