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The Differences of Cerebral, Abdominal, and Renal Oxygenation in Neonates with Hypothermia and Post-Rewarming Using NIRS at Dr. Soetomo Hospital

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ABSTRACT

Hypothermia significantly affects survival in neonates, as their thermoregulation is less effective than that in older children and adults. Hypothermia can worsen metabolic processes, leading to hypoglycemia, hypoxia, and metabolic acidosis. Near-infrared spectroscopy (NIRS) is useful for assessing regional tissue oxygenation (RSO2), providing insights into the oxygen supply-demand balance in vulnerable organs. This study aimed to demonstrate the differences of cerebral, abdominal, and renal oxygenation in neonates with hypothermia and post-rewarming using NIRS at Dr. Soetomo Hospital. An observational cross-sectional study was conducted from November 2019 to January 2020 at the neonatal intensive care unit (NICU) of Dr. Soetomo Hospital, Surabaya. Neonates were divided into hypothermia, rewarming, and normothermic groups. NIRS assessments were performed during hypothermia and post-rewarming. Statistical analyses were conducted using paired t-tests or Wilcoxon tests for the hypothermia group and independent t-tests or Mann-Whitney tests for comparisons between hypothermia and normothermic groups, with a significance level of $\boldsymbol{p < 0.05}$*. A total of 106 neonates met the inclusion criteria: 51 in the hypothermia and rewarming group and 55 in the normothermic group. The average birth weight was* $\mathbf{2261.96 \pm 832.26}$*grams for the hypothermia group and* $\mathbf{2009.09 \pm 676.87}$*grams for the normothermic group. Significant differences were noted in heart rates and renal tissue oxygenation (RrSO2) between conditions, with p-values of 0.014 and 0.023, respectively. This study found significant differences in renal tissue oxygenation between hypothermic conditions and post-rewarming.*

KEYWORDS *Neonates, hypothermia, rewarming, tissue oxygenation, NIRS.*

INTRODUCTION

Hypothermia is an important determinant of survival in neonates. The thermoregulatory mechanism in newborns is not as effective as in children or adults (Pinchefsky et al., 2021). Hypothermia in neonates can increase metabolism, leading to hypoglycemia, hypoxia, and metabolic acidosis (Lunze et al., 2013; Singer, 2021). Therapeutic hypothermia is used for neonates with hypoxic-ischemic encephalopathy (HIE). Cooling slows brain metabolism, reducing oxygen extraction; however, poor outcomes still occur frequently (Shellhaas et al., 2013).

The incidence of hypothermia in neonates in developed countries mostly occurs in low-birth-weight infants (BBLR) and small-for-gestational-age neonates. Research in the United States showed that 45% of very low-birth-weight (BBLSR) babies were hypothermic (body temperature <36.3°C) at birth. Studies in Australia indicated that 17% of babies born suffered from hypothermia (axillary temperature <36°C) during transport. In the United Kingdom, among babies born before 26 weeks of gestation who received intensive care, 66.7%, 80.0%, 58.3%, 42.7%, and 29.6% experienced hypothermia at 21, 22, 23, 24, and 25 weeks of

gestational age, respectively. Hypothermia in developing countries is more common, even in healthy babies and those with normal birth weight. Research in Nepal showed 85% neonatal hypothermia (body temperature <36°C) two hours after birth. Studies of babies born at home in northern India showed hypothermia (axillary temperature <35.6°C) in 19.1% and 3.1% during winter and summer, respectively, 24 hours after birth. A study of neonates treated in neonatal care units in Tanzania reported 22.4% hypothermia (axillary temperature <35.6°C); severe hypothermia (axillary temperature <32°C) occurred in 13%, and hypothermic infants had three times higher mortality and morbidity. A study of newborns admitted to the neonatal unit in Harare, Zimbabwe, found a hypothermia prevalence of 85%, with an average axillary temperature of 34.3°C. Research by Zayeri et al. (2007) showed that 7.8% of premature babies and 9.4% of full-term babies experienced hypothermia after admission to the neonatal unit. In Indonesia, the referral system is inadequate. Babies without pre-transport stabilization conforming to the STABLE (Sugar, Temperature, Airway, Blood, Laboratory, Emotional support) guidelines are more likely to develop hypothermia. Data from Dr. Soetomo General Hospital (RSDS) Surabaya in 2018 showed that 14% of BBLR neonates were hypothermic after birth (RSDS medical records, 2018).

Near-infrared spectroscopy (NIRS) is used to assess the effects of therapeutic hypothermia in neonates with HIE. NIRS provides quantitative measurements of brain blood volume, reflecting regional tissue oxygen perfusion and oxygen saturation (rSO_2), which represents brain metabolism (Shellhaas et al., 2013). Hypothermia causes vasoconstriction, while rewarming induces vasodilation, increasing perfusion and oxygen delivery to tissues (Chock et al., 2018). Regional tissue oxygen saturation provides useful information about perfusion in susceptible organs (i.e., cerebral and somatic circulation) and oxygen supply status compared to ongoing cellular oxygen requirements (Bailey et al., 2013; Samraj and Nicolas, 2015). Pulse oximetry measures arterial oxygen saturation (SpO_2), reflecting only oxygen supply to tissues, whereas NIRS measures rSO_2, reflecting the balance of oxygen supply and demand in local tissues. NIRS complements pulse oximetry (Sood et al., 2015). NIRS examination can also reflect renal, splanchnic, and peripheral tissue perfusion in critically ill infants (Shellhaas et al., 2013), aiding hemodynamic management and potentially improving outcomes through early detection of organ dysfunction (Samraj and Nicolas, 2015).

Despite the growing body of literature on therapeutic hypothermia for neonatal HIE, significant gaps remain in understanding regional tissue oxygenation dynamics in neonates experiencing accidental or pathological hypothermia. Most existing NIRS research has focused exclusively on therapeutic hypothermia protocols for HIE, where controlled cooling and rewarming occur under highly standardized conditions (Mitra et al., 2016; Wu et al., 2018). However, accidental hypothermia—which accounts for the majority of cases in developing countries—presents different physiological challenges, including variable cooling rates, delayed recognition, and diverse underlying pathologies. Furthermore, while cerebral oxygenation during therapeutic hypothermia has been extensively studied due to concerns about neuroprotection, responses in other vulnerable organs, particularly the kidneys and

splanchnic circulation, remain understudied in accidental neonatal hypothermia (Chock et al., 2018).

Previous studies have established baseline NIRS values for healthy term neonates (Bailey et al., 2014; Bernal et al., 2010) and demonstrated cerebral autoregulation preservation during therapeutic hypothermia in HIE patients (Shellhaas et al., 2013). Research by Wu et al. (2018) showed significant changes in renal oxygenation during rewarming in therapeutic hypothermia protocols, with $RrSO_2$ increasing and rFTOE decreasing post-rewarming. Similarly, Chock et al. (2018) documented that renal saturation was consistently lower than cerebral saturation during therapeutic hypothermia and improved after rewarming. However, these findings emerged from controlled therapeutic settings with full-term neonates experiencing HIE, limiting generalizability to broader hypothermic neonate populations, including preterm infants and those with diverse hypothermia etiologies.

The research gap this study addresses is the lack of comprehensive, multi-organ NIRS data in neonates experiencing hypothermia across the gestational age spectrum, including accidental and pathological causes. Unlike previous studies focused on single organs or specific populations, this research simultaneously examines cerebral, abdominal, and renal oxygenation patterns in hypothermic neonates of varying gestational ages, comparing them before and after rewarming and against normothermic controls. This multi-organ approach is critical because differential responses of vital versus non-vital organs to hypothermia and rewarming may have important implications for clinical management.

Furthermore, this study's novelty lies in its examination of a heterogeneous neonatal population that reflects real-world clinical scenarios in resource-limited settings where accidental hypothermia remains prevalent. By including preterm neonates (28–36 weeks gestational age) alongside term infants and examining various hypothermia causes rather than solely therapeutic hypothermia for HIE, this research provides clinically relevant data for at-risk neonates. This is particularly significant for Dr. Soetomo Hospital and similar tertiary referral centers in developing countries, where inadequate pre-transport stabilization and referral system challenges contribute to high rates of admission hypothermia.

The practical significance of this research extends beyond descriptive characterization of regional oxygenation patterns. Understanding which organs show the most significant oxygenation changes during rewarming can inform clinical protocols on rewarming rates, monitoring priorities, and intervention thresholds. For instance, if renal oxygenation is more sensitive to temperature changes than cerebral oxygenation, this suggests prioritizing renal NIRS monitoring during rewarming to guide individualized protocols. Additionally, establishing whether post-rewarming oxygenation normalizes to levels comparable with normothermic neonates across organs can validate current practices or identify needed modifications. Given that NIRS monitoring is non-invasive, continuous, and increasingly available in neonatal intensive care units, this research has potential to translate into improved clinical care through evidence-based strategies. Based on this problem, research is necessary to prove differences in regional tissue oxygenation of organs under hypothermic conditions and after rewarming using NIRS in neonates as an early marker of organ dysfunction.

The problem formulation in this study focuses on differences in cerebral, abdominal, and renal regional tissue oxygenation during hypothermia and after rewarming, measured using near-infrared spectroscopy (NIRS). The main question is whether differences exist in oxygenation in each of these tissues in neonates experiencing hypothermia and after rewarming. This study aims to prove these differences, with the general objective of understanding how regional tissue oxygenation is affected by hypothermia and rewarming. Specific objectives include proving differences in cerebral, abdominal, and renal regional tissue oxygenation in neonates using NIRS. The benefits of this research are significant, both theoretically and practically. Theoretically, it is expected to deepen understanding of tissue oxygenation during hypothermia and rewarming and validate NIRS as an effective tool. Practically, results can contribute directly to hypothermia management for research subjects and provide evidence for institutions to improve care at Dr. Soetomo Hospital. Additionally, the findings can support further research in science and technology focused on enhancing neonatal hypothermia management.

METHOD

This study employed an observational cross-sectional design, in which research subjects who met the criteria underwent examination. The research was conducted at the NICU of Dr. Soetomo Regional General Hospital Surabaya from November 2019 to January 2020. The study population consisted of neonates born at the hospital or referred from other facilities, and samples were selected consecutively from those meeting inclusion and exclusion criteria until the required number was reached based on sample size calculations.

Samples were divided into three groups based on condition: the hypothermic group, the rewarming group (hypothermic neonates post-rewarming), and the normothermic group. Each group was subdivided by gestational age. The sample size was estimated using a formula for a two-tailed hypothesis test, yielding a minimum of 106 neonates. Inclusion criteria included neonates less than 3 days old (preterm or full-term) with parental consent. Exclusion criteria encompassed genetic abnormalities, congenital defects, low Apgar scores, hydrocephalus, and early-onset sepsis.

Data collection involved multiple methods, including physical examinations to measure body temperature, heart rate, and weight, as well as secondary data from medical records. Tissue oxygenation was assessed using near-infrared spectroscopy (NIRS) and pulse oximetry, along with blood sampling for glucose analysis. Independent variables were hypothermia and rewarming; dependent variables included cerebral, abdominal, and renal tissue oxygenation. Operational definitions were detailed in a table specifying definitions and measurement tools for each variable.

Data were presented in tables and text, with statistical analysis performed using SPSS version 26.0 to assess sample distribution and intergroup differences. The research schedule was outlined in a table mapping activities from literature search to results presentation. The research flow was illustrated through diagrams depicting sampling, NIRS sensor placement, and data collection. Instruments included monitoring sheets, medical equipment, and NIRS

devices borrowed from providers. Ethical approval was obtained from the health research ethics committee, and subject confidentiality was strictly maintained. The research budget covered all necessary costs, totaling Rp 25,269,900.

RESULT AND DISCUSSION

Characteristics of Research Subjects

The study subjects consisted of 46 male neonates (43.4%) and 60 female neonates (56.6%). The average birth weight of the hypothermia group was 2261.96 □ 832.26 grams and the normothermic group was 2009.09 □ 676.87 grams. By temperature

body was lowest 34□C in 3 neonates, moderate hypothermia 32-35.9□C in 51 neonates. Neither hypothermia nor normothermic neonates showed hypoglycemia, the mean GDA in the hypothermia group was 80.47 □ 15.27 mg/dl, in the normothermic group 81.02 □ 15.98. Hemoglobin levels in the hypothermia group were 15.95 □ 2.15, in the normothermic group 15.99 □ 2.79. There were no significant differences in sex, birth weight, blood sugar and hemoglobin levels in both groups, but there was a significant difference in the heart rate (HR) of the hypothermia group (132.47 □ 12.87) compared to the normothermic group (139.33 □ 15.09) with a p of 0.014 and a difference in the number of samples according to gestational age. In the gestational age group of 28-336/7 weeks, there were more samples in the normothermic group, namely 26 neonates compared to 13 neonates in the hypothermia group, while in the gestational age group of 37-40 weeks, there were more samples in the hypothermia group, namely 24 neonates compared to 12 neonates in the normothermic group.

Regional Oxygenation of the Hypothermia Group

RcSO2 examination in the hypothermia group showed no significant difference between RcSO2 during hypothermia and after rewarming with p 0.72 and no significant difference between cFTOE during hypothermia and after rewarming with p 0.68. The examination of RaSO2 in the hypothermia group showed no significant difference between RaSO2 during hypothermia and after rewarming with p 0.61 and no significant difference between aFTOE during hypothermia and after rewarming with p 0.12. Examination of RrSO2 in the hypothermia group showed a significant difference between RrSO2 during hypothermia and after rewarming with p 0.02 and a significant difference between rFTOE during hypothermia and after rewarming with p 0.03. Data on the differences between RSO2 and FTOE hypothermia groups before and after rewarming are shown in table 5.2.

Table 1. Differences between RSO2 and FTOE hypothermia groups before and after Reheating

	Quantity (n)	Hypothermia (Mean□SD)	Rewarming (Mean□SD)	p
RcSO2	51	73.92 ± 8.84	73.68 ± 9.29	0,72
RaSO2	51	67.92 ± 11.32	67.47 ± 14.09	0,61
RrSO2	51	88.44 ± 6.76	89.56 ± 5.7	0,02
cFTOE	51	0.24 ± 0.09	0.24 ± 0.09	0,68
aFTOE	51	0.3 ± 0.11	0.29 ± 0.11	0,12

rFTOE	51	0.09 ± 0.07		0.08 ± 0.06	0.03

No significant differences were found in the results of the RcSO2 and cFTOE examination of the hypothermia group and after reheating at all gestational ages.

Table 2. Cerebral oxygenation according to gestational age

Age	**RcSO2**	**RcSO2**		**cFTOE**	**cFTOE**	
Gestasis (Sunday)	hypothermia (Mean□SD)	*Rewarming* (Mean□SD)	p	Hypothermia (Mean□SD)	*Rewarming* (Mean□SD)	P
28 – 336/7	73,58□11,19	72,46□9,55	0,37	0,24□0,11	0.25□0.1= 0.51	
34 – 366/7	78,57□7,73	80,5□6,85	0,28	0,2□0,08	0.18□0.070.29	
37 – 40	70,87□8,09	70,86□7,65	0,99	0,27□0,08	0,27□0,080,9	

No significant differences were found in the results of the RaSO2 and aFTOE examination of the hypothermia group and after reheating at all gestational ages.

Table 3. Abdominal oxygenation according to gestational age

Age	**RaSO2**	**RaSO2**		**aFTOE**	**aFTOE**	
Gestasis (Sunday)	**Hypothermia (Mean□SD)**	**Rewarming (Mean□SD)**	**P**	**Hypothermia (Mean□SD)**	**Rewarming (Mean□SD)**	**p**
28 – 336/7	60,35□10,35	63,08□11,03	0,21	0,37□0,1	0,34□0,1	0,07
34 – 366/7	**76,29□9,4**	71,07□21,1	0,82	0,22□0,09	0,22□0,11	0,88
37 – 40	**67,14□9,86**	67,75□9,84	0,6	0,31□0,1	0,3□0,1	0,7

Significant differences were found in the results of the RrSO2 and rFTOE examination in the hypothermia group and after reheating the gestational age group of 37-40 weeks shown in table 4.

Table 4. Renal oxygenation according to gestational age

Age	**RrSO2**	**RrSO2**		**rFTOE**	**rFTOE**
Gestasis (Sunday)	**Hypothermia (Mean□SD)**	**Rewarming (Mean□SD)**	**P**	**Hypothermia (Mean□SD)**	**Rewarming p (Mean□SD)**
28 – 336/7	90,54□4,24	88,92□6,02	0,438	0,06□0,05	O,08□0,070,76
34 – 366/7	88,21□7,13	89,5□6,24	0,210	0,09□0,07	0.08□0.060.06
37 – 40	87,43□7,59	89,94□5,4	0,04	0,1□0,07	0.08□0.060.05

Difference between Regional Oxygenation of Hypothermia Group and Normothermia Group

No significant difference was found between RcSO2 during hypothermia and normothermic with p 0.248 and no significant difference between cFTOE during hypothermia and normothermic with p 0.13. The examination of RaSO2 in the hypothermia group showed that there was no significant difference between RaSO2 during hypothermia and normothermia with p 0.66 and no significant difference between aFTOE during hypothermia and normothermic with p 0.46. Examination of RrSO2 in the hypothermia group showed no significant difference between RrSO2 during hypothermia and normothermic with p 0.91 and no significant difference between rFTOE during hypothermia and normothermic with p 0.39.

The data on the difference between RSO2 and FTOE of the hypothermia and normothermic groups is shown in table 5.6.

Table 5. Differences between RSO2 and FTOE of the hypothermia group and the normothermic group

Total		**Hypothermia**	**NormotermiaP**	
(n)		**(Mean□SD)**	(Mean□SD)	
RcSO2	51	73,68 □ 9,29	75.87 □ 10.09	0,25
RaSO2	51	67.92 □ 11.32	68.26 □ 15.26	0,66
RrSO2	51	88,44 □ 6,76	87,85 □ 9,38	0,91
cFTOE	51	0,24 □ 0,09	0,21 □ 0,1	0,13
aFTOE	51	0,3 □ 0,11	0,29 □ 0,16	0.46
rFTOE	51	0,09 □ 0,07	0,09 □ 0,1	0.39

This study aims to prove the difference between oxygenation of cerebral, abdominal and renal regional tissues in hypothermia and after reheating using NIRS in neonates at Dr Soetomo Hospital Surabaya. The research design used was cross sectional. The subjects of the study were neonates born at the Dr. Soetomo Regional General Hospital Surabaya or referred to hypothermia or normothermia. The data obtained were analyzed to prove the difference between oxygenation of cerebral, abdominal and renal regional tissues of the neonatal condition of hypothermia and after rewarming using NIRS.

1. Characteristics of Research Subjects

This study used premature and full-term neonatal research subjects, as many as 39 (36.8%) neonatates of gestational age 28-336/7 weeks, 31 (29.2%) neonatates of gestational age 34-366/7 weeks and 36 (34%) neonatates of gestational age 37-40 weeks. The male gender was 46 (43.4%) and 60 (56.6%) females, the proportion of females was more than males with a male: female ratio = 1 : 1.3. Previous research by Mitra et al. in 2016 on cerebral oxygenation during rewarming in neonates with therapeutic hypothermia used a sample of full-term neonates with an average gestational age of 39 (38-41) weeks with a male: female ratio = 1.3:1 (Mitra et al., 2016). Another study by Chock et al. in 2018 on renal saturation and the incidence of Acute Kidney Injury (AKI) in neonates during therapeutic hypothermia used a sample of full-term neonatates with an average gestational age of 38 □ 2 weeks and non-AKI of 39 □ 2 weeks (Chock et al., 2018).

In this study, a significant difference in HR was found in the hypothermia and normothermic groups (p = 0.014). This is in accordance with a 2018 study by Wu et al., on hemodynamic changes during reheating after therapeutic hypothermia in full-term neonates (38.8 ± 2 weeks) with HIE. There was a significant change in cardiovascular function during reheating, namely with an increase in HR with p = 0.001 (Wu et al., 2018).

2. Regional Network Oxygenation in Neonates with NIRS Examination

Monitoring of arterial oxygen saturation using pulse oximetry (SpO2) is not sufficient to guarantee the adequacy of perfusion or oxygenation of the brain, as SpO2 only reflects arterial

oxygen saturation, and not oxygen saturation in tissues. Disorders of tissue perfusion and oxygen delivery can be detected indirectly by decreased SpO2, capillary filling time, increased blood lactate, metabolic acidosis, hypotension, or oliguria according to their severity. However, by the time signs of this tissue perfusion disorder appear, it indicates that tissue damage has already occurred and it will be too late to recover. NIRS can be used for early detection of tissue perfusion disorders to prevent tissue damage. RcSO2 is usually lower than RrSO2 or RaSO2 because the brain's metabolic activity and oxygen demand are higher than those of other organs. The brain is an organ that has self-regulation so that brain blood flow and pressure can be maintained in the normal range even when there are fluctuations in systemic blood pressure. However, in critically ill neonates and premature neonates with immature brain vessels, brain autoregulation stops so that perfusion disorders can occur that will result in hypoxic ischemic brain injury (Jeon, 2019).

In this study, the results of the RcSO2 examination in the normothermic group were 75.87 □ 10.09%, RaSO2 68.26 □ 15.26% and RrSO2 87.85 □ 9.38% (table 5.6). RSO2 in the renal is the highest compared to cerebral and abdominal RSO2, while the abdominal RSO2 is the lowest compared to cerebral and renal. This result is according to a study by Bailey et al in 2014, in healthy neonates of full term it showed that the average RcSO2 was 78.2 □ 7.9% on the first day and 78.3 □ 6.1% on the second day. The average RrSO2 was 92.1 □ 5.3% on the first day and 88.9 □ 5.9% on the second day. The average RaSO2 was 69.9 □ 12.1% on the first day and 75.3 □ 12.4% on the second day. The kidneys are the organs with the highest RSO2 values that gradually decline over time. RcSO2 values are quite consistent while RaSO2 is lowest on the first day of life, but increases and is similar to RcSO2 on the second day. RaSO2 is lower than RcSO2, with averages below the normal range of adults, the average decrease in RrSO2 begins to approach pediatric and adult data by the end of the second day. An increase in RaSO2 over time resulted in average values similar to normal data of children and adults at the end of the second day (Bailey et al., 2014).

Another study by Bernal et al. examined RcSO2 and RrSO2 during the first 5 days of life in 26 full-term neonates, with a mean age of 44 ± 28 hours. The overall mean of RcSO2 was 77.9% ± 8.5%, RrSO2 was 86.8% ± 8.1%, and the somatic-cerebral RSO2 difference was 8.9% ± 9.4%. During breastfeeding, RcSO2 experienced minimal decrease (78.6% ± 8.4% compared to 78.0% ± 9.0%, $p = 0.023$), RrSO2 remained unchanged (87.0% ± 8.1% compared to 87.3% ± 8.0%, $p = 0.31$). During the first 120 hours after birth, RcSO2 decreased on average ($p < 0.01$), and RrSO2 remained relatively unchanged. In general, RrSO2 is 10%-15% higher than RcSO2 (Bernal et al., 2010).

RcSO2 is usually lower than RrSO2 or RaSO2 because the brain's metabolic activity and oxygen demand are higher than those of other organs. Standard brain RcSO2 differs in several studies, reported 57%-77% by McCormick et al. (1991), 62%-78% by Lemmers et al. Lemmers et al., (2006), 56%-76% by Petrova and Mehta, (2006), and 66%-83% by McNeill S et al. (McNeill S et al., 2011). In general, standard RcSO2 values in neonates are 60% - 80%. The results of cerebral RcSO2 examination can be influenced by changes in blood flow caused by arteriovenous malformations, superior sagittal sinuses, or epidural hemorrhage, by

extracranial structures and by the placement of sensors on the front head (Jeon, 2019). Pichler et al., reported that low RcSO2 at birth then increased for a few minutes and became stable. In contrast, high cFTOE at birth then decreases for a few minutes and becomes stable (Pichler et al., 2013).

Montaldo et al. in 2015 researched the oxygenation of non-vital organs such as kidneys and mesenteric tissue during the neonatal transition period. The results showed that RrSO2 and RaSO2 increased more slowly than RcSO2 in the first 7 minutes of life. RcSO2 is stable at 7 minutes from birth while RrSO2 and RaSO2 are stable at 10 minutes of life. The transition immediately after childbirth is a very complex process that involves almost every organ.

After cord clamping at birth, significant changes occur in the cardiovascular system. During childbirth there is a surge of hormones that determine the increased production and release of catecholamines, renin-agiotensin and vasopressins. One of the main functions of the cardiovascular system is the delivery of oxygen to meet the oxygen needs of the tissues. The most likely explanation for the low RrSO2 and RaSO2 findings in early neonatal transitions is due to a right-to-left shunt by the ductus arteriosus to the lower part of the body. Pre ductal SpO2 was significantly higher than post ductal SpO2 up to 9 minutes after birth reflecting the persistence of ductal transients from right to left and/or atrial shunts leading to high rFTOE and aFTOE compared to cFTOE (Montaldo et al., 2015). According to Urlesberger et al., the low RrSO2 and RaSO2 findings in early neonatal transition occur due to vasoconstriction in certain non-vital organs (kidneys and mesenteric tissues) to maintain oxygen delivery to the brain circulation (Urlesberger et al., 2010).

RaSO2 values are 5% - 15% higher than RcSO2 (McNeill et al., 2011). Preterm neonates with RaSO2 ≤ 56% 11 times increased risk of developing necrotizing enterocolitis (NEC) compared to preterm neonates with RaSO2 > 56% (Patel et al., 2014). A study in neonates showed that the ratio of RcSO2 and RaSO2 called cerebro-splanchnic oxygenation ratio (CSOR) was shown to have a 90% sensitivity in detecting abdominal ischemia based on the assumption that cerebral autoregulation minimizes changes in RcSO2 during events affecting abdominal perfusion (Sood et al., 2014). Another study in neonates showed that CSOR <0.75 was associated with an eight-fold greater risk of NEC and was reported to be able to predict the need for surgical intervention.

3. Difference between Regional Tissue Oxygenation Hypothermia and After Reheating

Several previous studies have conducted regional tissue oxygenation in HIE neonates who have received therapeutic hypothermia and there have been no previous studies on regional tissue oxygenation in neonates with hypothermic conditions. In this study, the lowest body temperature was measured at 34□C in 3 neonates, a total of 51 neonates with moderate hypothermia (32□C-35.9□C). Examinations conducted in the hypothermia group showed no difference between RSO2 and FTOE in the cerebral and abdominal during hypothermia and after reheating, but there was a difference between RrSO2 during hypothermia and after rewarming (p 0.02) and rFTOE during hypothermia and after rewarming (p 0.03). RrSO2 test results were lower (88.44 □ 6.76% compared to 89.56 □ 5.7%) with higher rFTOE (0.09 □

0.07% compared to 0.08 □ 0.06%) during hypothermia and after rewarming. The difference in RrSO2 and rFTOE is significant in the gestational age group of 37-40 weeks, this can be due to the large number of hypothermia samples in that age group.

Wu et al.'s 2018 study of full-term neonates with moderate to severe HIE showed no significant changes in RcSO2 and cFTOE during the rewarming period. In contrast, RrSO2 increased ($p = 0.01$) and rFTOE decreased ($p = 0.002$) at the time of rewarming. The oxygenation ratio of kidney-brain tissue increased from 0.93 ± 0.1 to 1.01 ± 0.1 after reheating ($p = 0.006$).

An increase in body core temperature during reheating is associated with an increase in the brain's metabolic rate and oxygen needs. Cerebral blood flow or cFTOE or both increases to meet the increased oxygen needs of the brain. The systolic peak velocity of the middle cerebral artery (MCA) measured by transcranial Doppler increased with RcSO2 and cFTOE unchanged after rewarming showing an improvement in brain blood flow and good cerebral flow metabolism during and after rewarming. In non-vital organs such as the kidneys, RrSO2 is shown to increase and rFTOE decreases during rewarming. In response to reheating, there is an increase in cardiac output which leads to an increase in systemic blood flow and an increase in the oxygenation ratio of kidney-brain tissue due to the redistribution of systemic blood flow to all organs (vital and non-vital). During therapeutic hypothermia, vasoconstriction and decreased perfusion of the kidneys (non-vital organs) occur to maintain cerebral perfusion so that the flow of cerebral metabolism is maintained (Wu et al., 2018).

Chock et al's 2018 study showed that RrSO2 was lower than RcSO2 during therapeutic hypothermia ($p < 0.01$), RrSO2 increased after rewarming, with rFTOE decreased ($p < 0.0001$). The kidneys have poor self-regulation and experience disturbances or fluctuations in perfusion in the event of systemic hypotension when compared to the brain. Oxygenation of the kidneys can be affected during the process of therapeutic hypothermia and rewarming than brain oxygenation. During hypothermia, decreased cardiac output is evidenced by decreased HR and peripheral vasoconstriction. Vasodilation occurs and an increase in HR after reheating leads to increased renal perfusion and oxygen delivery so that RrSO2 increases. In contrast, rFTOE tends to increase during therapeutic hypothermia to maintain sufficient tissue oxygen levels when there is a decrease in perfusion and oxygen delivery to the kidneys (Chock et al., 2018).

The limitations of this study are that the number of samples from each gestational age group is not the same and NIRS examination is carried out at the same chronological age can affect the results of the study.

CONCLUSION

In conclusion, this study demonstrates a significant improvement in renal tissue oxygenation (RrSO2) following rewarming in hypothermic neonates, while cerebral and abdominal oxygenation remained stable. This finding suggests that renal perfusion is particularly sensitive to temperature changes and that rewarming effectively enhances renal oxygen delivery. For future research, it is recommended to conduct longitudinal studies with larger, more balanced sample sizes across gestational ages and causes of hypothermia to better characterize organ-specific responses. Additionally, future investigations should explore the

correlation between changes in NIRS-derived oxygenation parameters during rewarming and specific clinical outcomes, such as the incidence of acute kidney injury (AKI) or neurodevelopmental status, to determine the prognostic value of NIRS monitoring in guiding neonatal hypothermia management.

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