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Original Article / Özgün Makale

An evaluation of bilateral cerebral oxygen saturation during cyanotic and non-cyanotic cardiac surgery

Siyanotik ve non-siyanotik kardiyak cerrahide iki taraflı serebral oksijen satürasyonunun değerlendirilmesi

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ABSTRACT

Background: This study aims to investigate cerebral oxygenation differences between cyanotic and non-cyanotic pediatric cardiac surgery patients using near-infrared spectroscopy.

Methods: Between January 2013 and May 2013, a total of 25 pediatric patients (10 boys, 15 girls) were included in this prospective study. Cyanotic group (group C) included 11 patients who received total correction for tetralogy of Fallot, while the non-cyanotic group (group NC) included 14 patients whose simple congenital heart disease was surgically repaired. Bilateral near-infrared spectroscopy values at varying time points: post-induction (T_1), pre-bypass (T_2), on cross-clamp (T_3), after removal of cross-clamp (T_4), rewarming (T_5), off bypass (T_6), and end of the operation (T_7) were recorded. Also, hemodynamic variables, body temperature, blood gas parameters, lactate, oxygen content, hematocrit values, mechanical ventilation duration, and length of intensive care unit and hospital stay were noted.

Results: There was no significant difference in the right and left cerebral oxygenation values between the groups. Similarly, no significant difference was observed in the right and left cerebral oxygenation in each individual group. None of the patients experienced morbidity or mortality following surgery.

Conclusion: Although hematocrit, arterial oxygen, and carbon dioxide pressure may alter in cyanotic cardiac diseases, bilateral cerebral oxygenation values appear to be similar between cyanotic and non-cyanotic patients. Although there were significant physiopathological differences between the groups, NIRS values did not differ.

Keywords: Cardiac surgery; cerebral oxygenation; cyanotic heart disease; near-infrared spectroscopy; non-cyanotic heart disease; pediatric congenital heart disease.

ÖZ

Amaç: Bu çalışmada yakın kızılötesi spektroskopi kullanılarak siyanotik ve asiyanotik kalp cerrahisi yapılan pediatrik hastalar arasında serebral oksijenasyon farklılıkları araştırıldı.

Çalışma planı: Bu prospektif çalışmaya Ocak 2013 - Mayıs 2013 tarihleri arasında toplam 25 pediatrik hasta (10 erkek, 15 kız) alındı. Siyanotik grup (C grubu) Fallot tetralojisi nedeniyle total düzeltme yapılan 11 hastadan oluşurken, asiyanotik grup (NC grubu) basit doğuştan kalp hastalığı cerrahi olarak tamir edilen 14 hastadan oluşuyordu. Çeşitli zaman noktalarında iki taraflı yakın kızılötesi spektroskopi değerleri kaydedildi: indüksiyon sonrası (T_1), baypas öncesi (T_2), kros-klemp sırası (T_3), kros-klemp çıkarıldıktan sonra (T_4), baypas sonrası (T_6) ve cerrahi sonrası (T_7). Hemodinamik parametreler, vücut ısısı, kan gazı parametreleri, laktat, oksijen içeriği, hematokrit değerleri, mekanik ventilasyon süresi ve yoğun bakım ünitesi ve hastanede kalış süreleri de kaydedildi.

Bulgular: Gruplar arasında sağ ve sol serebral oksijenasyon değerleri açısından anlamlı bir fark yoktu. Benzer şekilde, grup içinde de sağ ve sol serebral oksijenasyon değerleri açısından anlamlı bir fark gözlenmedi. Hastaların hiçbirinde cerrahi sonrası morbidite veya mortalite gelişmedi.

Sonuç: Siyanotik kalp hastalıklarında hematokrit, arteriyel oksijen ve karbondioksit basıncı değişiklik gösterse de iki taraflı serebral oksijenasyon değerleri siyanotik ve asiyanotik hastalarda benzer görünmektedir. Bu çalışmada gruplar arasında önemli fizyopatolojik farklar olmasına rağmen NIRS değerleri farklı bulunmadı.

Anahtar sözcükler: Kalp cerrahisi; serebral oksijenasyon; siyanotik kalp hastalığı; yakın kızılötesi spektroskopi; asiyanotik kalp hastalığı; pediatrik doğuştan kalp hastalığı.

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The blood flow rate of normal brain perfusion can be regulated by the help of several factors, such as perfusion pressure, temperature, hematocrit, arterial oxygen-carbon dioxide pressure, and cannula position.[1] In recent years, the importance of cerebral oxygenation monitoring in neonates, babies, and children during cardiopulmonary bypass (CPB) has been increasing. Although cardiorespiratory data are routinely monitored throughout cardiac surgery, standards for brain monitoring have not yet to be established in cardiac operations.[1,2] Effective brain monitoring improves cerebral homeostatic regulation, decreases neurological injury inherent in CPB, which results in improved functional outcomes.[1,2] The most frequent causes for brain damage in pediatric cardiac surgery are CPB, low flow rate, hypothermia, and global hypoperfusion, which is a result of the variation in cerebral hemodynamics.[1,2] To avoid hypoxia-, ischemia-, emboli-, or electrophysiological deteriorations-related brain damages, several intraoperative monitoring techniques have been developed. These techniques include near-infrared spectroscopy (NIRS), transcranial Doppler ultrasound, measurement of arterial flow and resistance, and electroencephalography.[4] Near-infrared spectroscopy, which is based on the Beer-Lambert Law, is a noninvasive, continuous, portable, and compact measurement technique, which does not depend on pulse, pressure, or temperature.[4] It enables the real-time monitoring of brain oxygenation with a turnaround time of 0.1 sec thanks to its advanced measurement, calculation, and imaging systems.[3] Both in children and adults, based on the clinical data, when the cerebral oxygenation is lower than 40 to 50% or when there is 20% or more variation compared to baseline, hypoxic-ischemic neural injury may occur.[4]

Cyanotic heart disease is a group-type of congenital heart defects which occurs due to deoxygenated blood bypassing the lungs and entering the systemic circulation or a mixture of oxygenated and deoxygenated blood entering the systemic circulation. There is a possibility that physiopathological events associated with deoxygenated mixture and various compensatory mechanisms (i.e., polycythemia, low oxygen saturation) may affect the NIRS measurements.

In the present study, we aimed to investigate cerebral oxygenation differences between cyanotic and non-cyanotic pediatric cardiac surgery patients using the NIRS.

PATIENTS AND METHODS

The study protocol was approved by the Türkiye Yüksek Ihtisas Training and Research Hospital Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

A total of 25 patients (10 boys, 15 girls) were included in this prospective study. The cyanotic group (group C, n=11) included only patients who received total correction of tetralogy of Fallot (TOF), while non-cyanotic group (group NC, n=14) included patients whose atrial septal (n=8), ventricular septal (n=3), atrioventricular canal (n=1), or subaortic membrane defects (n=1), or aortic stenosis (n=1) were surgically repaired. Exclusion criteria were as follows: the presence of another complex shunt, more than one prior surgery, previous complex surgical procedure, syndromes affecting the functions of organs, and extra-cardiac anomalies.

Intraoperative anesthesia management

The patients were pre-medicated 30 min before anesthesia induction by oral 0.3 mg/kg midazolam. Then, electrocardiography, pulse oximetry, and non-invasive blood pressure monitoring were performed. Anesthesia was induced by inhalation of sevoflurane in the mixture of oxygen 50% and air 50%. When an intravenous line was inserted, we switched to total intravenous anesthesia with midazolam-fentanyl-rocuronium bromide. Ventilator settings were adapted to maintain normocapnia. All patients received dexamethasone at a dose of 1 mg/kg. Following anesthesia induction and intubation, radial artery and jugular vein catheters were inserted to all patients and head positions were arranged as midline. Body temperature was monitored by thermal sensors placed both in the nasopharynx and the rectum. Cerebral oxygenation monitoring was performed by connecting pediatric probes which were placed on the right and left frontal forehead region to the NIRS (INVOS Somanetics, 5100, Troy MI, USA). Values measured during the post-induction were marked as baseline NIRS values, and subsequent cerebral oxygenation changes were evaluated. Anesthesia maintenance was achieved by hourly administration of fentanyl 5 to 10 μg/kg with regular administration of midazolam 0.1 mg/kg and rocuronium bromide 0.05 mg/kg.

Intraoperative surgery management

Following heparinization, an arterial cannula on the ascending aorta and selective vena cava cannulas were placed. Then, CPB was initiated. The body temperature was reduced to 28 to 32 °C. Deep hypothermic circulatory arrest was not performed in any patient. In group NC, the patients were cooled down to a minimum of 30 °C, while the patients in group C were cooled down to a minimum of 28 °C.

The ascending aorta was cross-clamped and cardiac arrest was, then, achieved by antegrade hypothermic crystalloid cardioplegia. A roller pump with membrane oxygenator was used and standard pump flow rate was set to 150 to 200 mL/kg/min. Proportional with the body surface area, pump prime solution was composed of blood, blood products, isolyte, and mannitol. Blood was not added to the prime solution of the group C. Hemofiltration was performed, if needed. To preserve myocardium, blood cardioplegia was performed in 15 to 20 min intervals during cross-clamping. After cross-clamping, topical cooling was employed in all patients. Alpha-stat arterial blood gas monitoring and activated clotting time monitoring were performed during CPB. Subsequent to the completion of surgical repair, when the body temperature was normothermic and hemodynamic variables were stable, CPB was terminated. In all patients, intraoperative evaluation was carried out using transesophageal echocardiography.

Data acquisition

Bilateral NIRS values for post-induction term (T_1), pre-cardiopulmonary bypass (T_2), on cross-clamp (T_3), after removal of cross-clamp (T_4), rewarming (T_5), off cardiopulmonary bypass (T_6), and at the end of the operation (T_7); hemodynamic variables, body temperature, blood gas parameters, lactate, oxygen content, and hematocrit values, and cross-clamp and operation durations were recorded. As the main objective of the present study was to investigate the effects of several parameters, such as oxygen saturation, oxygen pressure, and hematocrit level, baseline (T_1) SO_2 measurement was performed while the patients was breathing 50% oxygen. Morphine and midazolam were administered during mechanical ventilation during the intensive care unit stay. The patients who met the extubation criteria were extubated, based on their clinical conditions and blood gas values. The duration of mechanical ventilation and length of hospital and intensive care unit stays were also recorded for all patients.

Statistical analysis

Statistical analysis was performed using SPSS for Windows version 15.0 (SPSS Inc., Chicago, IL, USA). Normally distributed continuous variables were expressed in mean ± standard deviation, while categorical variables were expressed in number and percentage. Demographic features and perioperative variables were compared by the Mann-Whitney U and chi-square tests. The right and left rSO_2 values recorded at seven time points during the operation were compared by the Mann-Whitney U test for both all patients and individually for each group. A p value of less than 0.05 was considered statistically significant.

RESULTS

Demographic and perioperative data of all patients are presented in Table 1. The mean age was 6.4±2.2 years

Table 1. Demographic characteristics and perioperative data of patients

	Group NC (n=14)		Group C (n=11)		
	n	Mean±SD	n	Mean±SD	*p*
Age (years)		6.4±2.2		4.3±3.0	>0.05
Weight (kg)		22.6±8.8		14.6±6.2	0.018
Gender					>0.05
Male	5		5		
Female	9		6		
Cardiac diagnosis			Tetralogy of Fallot		
Atrioventricular septal defect	8				
Ventricular septal defect	3				
Atrioventricular canal defect	1				
Aortic stenosis	1				
Subaortic membrane	1				
Cross-clamp time (min)		48.4±16.2		85.4±15.5	<0.001
Operation time (h)		3.4±0.6		5.0±0.6	<0.001
Mean nadir temperature (°C)		32.8±1.6		30±1.9	<0.05
Extubation time (h)		3.4±2.4		11.5±2.3	<0.001
Days in intensive care unit		1.1±0.3		2.4±1.5	<0.05
Days in hospital		6.5±1.7		8.9±1.9	<0.05

NC: Non-cyanotic; C: Cyanotic; SD: Standard deviation.

in group NC and 4.3±3.0 in group C. There was a significant difference in the body weight between the groups; the body weight of the children in group C was lower compared to the children in group NC. As different surgical procedures were performed in each group, there was a significant difference in the cross-clamp time, and duration of surgery and extubation between the groups. In addition, the length of intensive care unit and hospital stays were longer in group C, compared to group NC (Table 1).

On the other hand, we observed no difference in the mean arterial pressure and heart rate between the groups; there were expected differences between the measurement times due to CPB. Although there was a significant difference in the pH values at T_1 (p=0.016) and T_2 (p=0.023) between the groups, the values were clinically within normal ranges. Partial oxygen pressure also differed between the groups, as expected (Table 2). However, we found no significant difference in the partial carbon dioxide pressure. In addition, there was a difference in the arterial oxygen saturation, hematocrit values, and oxygen content between the groups (as shown in footnotes in Table 2), indicating the compensation mechanisms in cyanotic cardiac disease.

Nonetheless, there was no significant difference in the right and left cerebral oxygenation values between the groups. Similarly, no significant difference was observed in the right and left cerebral oxygenation in each individual group (Table 3). The minimum cerebral oxygenation value in group NC was 42 and 48 for the right and left, respectively. The minimum cerebral oxygenation value in group C was 40 and 47 for the right and left, respectively. In group C, there was a significant difference in the right NIRS values between T_1 and T_2 (p=0.041), as well as T_6 and T_7 (p=0.012). Similarly, we found a difference in the left NIRS values between T_1 and T_2 (p=0.040), as well as T_5 and T_6 (p=0.040) in group C. Moreover, between baseline (T_1) and termination (T_7), no significant difference in the left and right NIRS values was observed (right p=0.688, left p=0.503). In group NC, there was a difference in the right NIRS values between T_1 and T_2 (p=0.018), as well as T_5 and T_6 (p=0.043). In group NC, there was a difference in the left NIRS values between T_1 and T_2 (p=0.048), as well as T_5 and T_6 (p=0.003).

Table 2. Physiological variables

	MAP (mmHg)	HR	Hct (%)	pH	PaO_2 (mmHg)	$PaCO_2$ (mmHg)	SaO_2 (%)	Lactate (mmol/L)	O_2 Content (unit)
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
T_1*,†,‡,§									
Group NC	76.6±4.8	103.5±19.4	35.3±3.5	7.4±3.6	167.3±37.2	31.4±4.3	99.3±0.7	1.4±0.5	16.2±1.9
Group C	67.4±14.9	98±17.9	46.5±5.7	7.4±1.8	70.2±20.6	34.1±1.7	85.7±13.4	1.1±0.2	18.2±1.9
T_2*,†,§									
Group NC	54.0±8.9	107.7±11.3	30.4±4.9	7.4±4.2	160.5±42.8	34.9±4.2	98.8±0.9	2.0±1.0	14.2±2
Group C	50.1±8.7	99.6±13.6	36.4±7.9	7.4±5.2	89.4±23.7	34±2.5	91.5±10.1	1.9±0.9	14.7±2.3
T_3*									
Group NC	51.8±8.0		26.1±5.4	7.4±4.5	176.2±31.6	36.8±7.1	99.4±0.5	4.3±0.9	13±2.9
Group C	47.8±8.2		29.5±6.9	7.4±5.4	139.0±5.1	36.9±5	99.6±0.5	3.9±1.2	13±2.5
T_4†									
Group NC	57.9±8.5	105.5±8.7	26.7±3.8	7.4±3.8	159.9±33.8	36.8±5.7	98.5±1.1	4.0±1.1	13.2±2.7
Group C	52.9±6.2	99.8±9.3	27.6±5.2	7.4±2.7	144.4±27.8	33.2±4.9	99.5±0.6	4.5±1.6	11.8±1.6
T_5									
Group NC	58.7±6.3	106.1±18.8	26.4±2.4	7.4±4.4	153.3±24.1	33.4±3.3	98.7±1.1	4.5±1.3	12.5±1.15
Group C	60.4±10.1	114.9±14.7	29±4.7	7.4±4.2	129.7±27.6	36.6±4.7	97.9±1.8	4.5±1.3	13±1.8
T_6*,‡									
Group NC	64.6±9.0	111.4±11	28.3±3.8	7.4±3.3	165.2±24.3	33.3±3.1	98.7±1.4	3.9±1.0	12.8±1.2
Group C	60.3±4.9	120.1±8.2	32.5±4.8	7.4±3.2	113.4±25.5	32.8±2.9	98.1±1.7	4.7±1.5	14.2±2.9
T_7*,‡									
Group NC	66.6±8.5	113.4±10	29.4±2.9	7.4±3.0	164.8±25.6	33.4±3.3	98.7±1.5	3.6±0.9	13.0±1.7
Group C	61.7±6.1	121±7.9	32.8±4.2	7.4±2.0	114.6±9.7	32.9±2	98.4±1.5	4.2±1.1	14.3±2.4

MAP: Mean arterial pressure; HR: Heart rate; Hct: Hematocrit; PaO_2: Partial arterial oxygen pressure; $PaCO_2$: Partial arterial carbondioxyde pressure; SaO_2: Oxygen saturation; O_2: Oxygen; SD: Standard deviation; * PO_2 T_1, T_2, T_3, T_6, T_7 p<0.001; † SaO_2 T_1, T_2, T_4 p<0.05; ‡ Hematocrit T_1, T_2, T_6, T_7 p<0.05; § Oxygen content T_1 p=0.014.

Table 3. Near-infrared spectroscopy values

	Right	Left	*p* (between groups)	*p* (in groups)
	Mean±SD	Mean±SD	Mean±SD	Mean±SD
T_1				
Group NC	67.0±6.4	66.0±6.5	>0.05	>0.05
Group C	68.9±6.6	70.8±7.9	>0.05	>0.05
T_2				
Group NC	59.5±9.1	59.6±6.0	>0.05	>0.05
Group C	57.5±12.3	62.6±6.2	>0.05	>0.05
T_3				
Group NC	55.3±5.9	56.3±6.6	>0.05	>0.05
Group C	58.2±6.8	57.1±4.9	>0.05	>0.05
T_4				
Group NC	58.9±10.6	61.2±10.5	>0.05	>0.05
Group C	58.4±9.4	60.1±8.7	>0.05	>0.05
T_6				
Group NC	67.5±8.9	67.3±8.2	>0.05	>0.05
Group C	66.4±5.9	69.0±6.5	>0.05	>0.05
T_7				
Group NC	68.8±8.3	67.3±8.2	>0.05	>0.05
Group C	67.1±5.5	69.0±6.5	>0.05	>0.05

NC: Non-cyanotic; C: Cyanotic; SD: Standard deviation.

In group NC, between baseline (T_1) and termination (T_7), no significant difference in the right and left NIRS values was observed (p=0.682, left p=0.140) (Figures 1). None of the patients experienced morbidity or mortality following surgery.

DISCUSSION

In the present study, in cyanotic cardiac diseases, bilateral cerebral oxygenation values were found similar to those of non-cyanotic cardiac pediatric patients in all time points. Preoperative physiological data showed substantial physiopathological compensatory differences, such as hematocrit values, arterial oxygen, and carbon dioxide pressure; however, no significant difference in the NIRS cerebral oxygenation values was observed between the groups during the whole procedure.

Neurological complications are still significant concerns in pediatric cardiac surgery.[5] Several etiological factors, such as previous unrecognized neurological abnormality, embolic events, hypoxic insult, low cardiac output syndrome, systemic inflammatory response, altered cerebral blood flow, and cerebral metabolism, have been suggested to play a role.[5] Cerebral ischemia may occur, when oxygen supply is insufficient to meet the global/regional cerebral consumption.[5] During cardiac surgery, cerebral blood flow and metabolism may be also affected by several factors including arterial PCO_2, hemoglobin level, temperature, depth of anesthesia, and pump perfusion flow rate.[5]

It is well-established that 21 to 69% of neonates and infants undergoing cardiac surgery with CPB

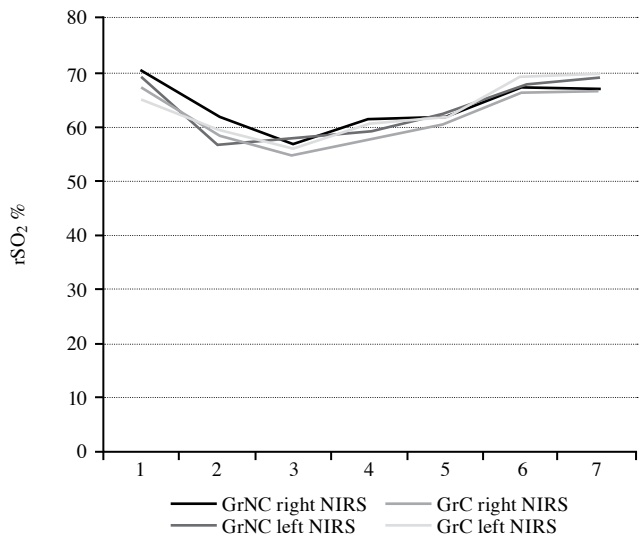

Figure 1. Right near-infrared spectroscopy values in both groups.
NC: Non-cyanotic; C: Cyanotic; NIRS: Near-infrared spectroscopy.

suffer from long-term adverse neurodevelopmental complications.[6-8] The reasons are multi-factorial, and many authors have claimed that abnormal brain development resulting from a cardiac lesion can be blamed for brain injury.[6,9,10]

Coagulation during cyanotic coronary heart diseases may be due to the consumption of factors by intravenous coagulation, or liver dysfunction caused by polycythemia and stasis.[11] Due to platelet dysfunction, these patients are extremely susceptible to intravascular thrombosis and hemorrhage,[11] which can also explain why babies with TOF experience slow growth and development. Mental development may be also slow due to cerebral hypoxia in these patients. As reported in the literature, the incidence of thromboembolic factors-related cerebrovascular events is 4%; however, hemiplegia and paraplegia in children with TOF occur rather with very low hematocrit values, which may indicate that these lesions occur due to hypoxia-related anemia, rather than due to thromboembolism.[11,12] All these factors indicate the critical role of oxygenation monitoring in congenital pediatric cardiac surgery. During the progress of the disease, contribution of several factors, such as CPB, hypothermia, cannula malposition, and hemodilution, may be chaotic. In the present study, baseline cerebral oxygenation values of both children with TOF and children with non-cyanotic defects were found similar.

Furthermore, polycythemia is secondary to TOF and is a mechanism developed by the system to meet the systemic oxygen demand. When the hematocrit level increases by 55 to 65%, systemic oxygen delivery increases. When the hematocrit level increases by 70 to 75%, then oxygen delivery decreases.[12] It can be explained by hyperviscosity developed in relation with high hematocrit values and, thereby, reduced cardiac output. In the present study, the hematocrit level of group C was found to be higher, compared to group NC (46.5% vs 35.3%). Since the value obtained via cerebral oximetry is the ratio of oxyhemoglobin to total hemoglobin, secondary erythrocytosis is assumed to have an effect on the rSO_2 level. In two previous reports in the literature, no effects of polycythemia on rSO_2 have been reported. In one of these studies, Liem et al.[13] studied neonatal patients with high fetal hemoglobin levels, and reported hematocrit levels as >65. The mean hematocrit level was also reported as 54% by Sunghee et al.[14] In another study, the baseline hematocrit level was reported as 63.9% for pediatric patients with cyanotic heart disease, and the authors concluded that it was not unlikely to obtain rSO_2 values using the NIRS device (invos 5100), as the device did not read any values.[15] In the aforementioned study, as the hematocrit level decreased, the device gradually yielded results: in five patients, after reaching 61% and in four patients, after reaching 35% by hemodilution following CPB, and rSO_2 was successfully measured. In the present study, baseline hematocrit values of the cyanotic patients were much lower than those reported in the aforementioned studies, and no problem was experienced in the measurements performed by NIRS. Higher baseline hematocrit levels of group C may have increased the amount of oxyhemoglobin molecules falling in the cerebral area to be measured by the light-emitting diode (LED) beam of the NIRS device. Moreover, the oxygen content of the blood may have increased by the globally increasing hemoglobin levels. In addition, the oxygen content of group C was found to be higher in the present study. The venous component comprises about 70 to 80% of the values obtained by NIRS, which may be another reason why arterial desaturation did not adversely affect the rSO_2 rates in the cyanotic patients. The compensation of the low arterial oxygen saturation by the mechanisms presented in our may have caused both groups to have similar baseline rSO_2 values. The severity of the disease in cyanotic heart disease is closely associated with the degree of arteriovenous mixture, the amount of compensation mechanisms, and hemodynamic and hemostatic variables. In patients with higher hematocrit values, cardiac flow decreases due to the increased blood viscosity, which degenerates tissue oxygenation.[13] We believe that further studies on cerebral oxygenation in patients with severe cardiac cyanotic disease would be helpful in daily practice.

In pediatric cardiac surgery, anesthesia induction, intubation, positioning of the vascular lines, sternotomy, and CPB are risky phases for cerebral ischemia.[16] In the present study, at T_2 (pre-cardiopulmonary bypass), T_3 (on cross-clamping), and T_4 (after removal of cross-clamp) measurements, there were no significant decreases in the cerebral oxygenation values. The decreases in arterial blood pressure and hypothermia in these time points were probably responsible for these reductions. In several studies, reduced cerebral oxygenation values were reported to be caused by several reasons, such as cardiac manipulation, dissection of surrounding tissues, pericardial suspension, and cannulation of vena cava and aorta, particularly during the pre-bypass period.[17-19] In the present study, cerebral oxygenation data of the pre- and post-bypass periods were similar in all time points in both groups.

Furthermore, the mean arterial pressure has an impact on the cerebral perfusion pressure, as

a part of the autoregulation mechanism.[20] Brain perfusion is assumed to be stabilized within a mean blood pressure range of 50 to 150 mmHg. However, the exact timing of full autoregulation in pediatric patients is still controversial. Hayashida et al.[20] reported that, in congenital cardiac surgery, children younger than four years old were more sensitive to cerebral ischemia due to insufficient autoregulation. In the present study, the mean age of both groups was over four years; therefore, their autoregulation system might be more developed. Furthermore, in both groups, the differences in the right and left NIRS values at several time points (T_1-T_2, T_5-T_6, T_6-T_7) were found to be correlated with the mean arterial pressure differences in these time points. However, these differences were not considered to be clinically relevant.

In previous studies, in room air, cerebral oxygenation values of children with non-cyanotic cardiac disease were found to be very close to healthy children (68%±10%), while it was found to be lower in children with TOF (57%±12%).[13,14] In our study, baseline values at post-induction showed a right cerebral oxygenation value of 68% and a left cerebral oxygenation value of 70% in children with TOF under 50% oxygen. Improved oxygenation due to mechanical ventilation may have increased these values. Similarly, no asymmetry was observed between the right and left values. There was also no significant difference between pre- and post-correction phases. In group C, pre-correction NIRS values were expected to be different compared to group NC, due to non-physiological state of cyanotic disease. However, there was no significant difference in the pre-correction values between the groups. Therefore, it is not surprising that post-correction values were also similar between the groups. The asymmetry in the baseline values may have been resulted from several reasons which rarely occur, such as intracranial artery stenosis, intracranial space-occupying lesion, or infarction. However, any asymmetry in cardiac surgery may indicate a problem related with aortic or venous cannulation which occurs more frequently.[21] One of the important benefits of NIRS monitoring is that it allows early detection of a mal-positioned cannula. The cerebral oxygenation values can serve as a guide to manipulate the modifiable factors, if any, such as cannula placement.

In recent years, many health care centers have adopted the NIRS monitoring for congenital heart surgery as a standard monitoring method.[22,23] In pediatric heart surgery, cerebral hemodynamic and oxygenation alterations may pose additional problems in terms of brain damage development. Therefore, real-time neurological monitoring is fundamental for neuroprotective strategies. In the literature, potential brain damage in pediatric heart surgery has been reported to have been avoided by NIRS.[22,23] It has been also shown that higher arterial saturation and narrower arterial-cerebral rSO_2 saturation differences are associated with improved motor performance in pediatric heart surgery.[23] Cardiopulmonary bypass time, total length of hospital stay, and tube feedings are the main risk factors for abnormal neurodevelopment.[24] However, recent technologies should be carefully reviewed according to diseases and surgeries, and their effectiveness should be supported by evidence to yield satisfactory outcomes.

On the other hand, the present study has some limitations. During the preparation of the pediatric patients for surgery, the NIRS monitoring was unable to be performed, as the motions of the patient made intense interference. Therefore, the baseline measurements were performed after the anesthesia induction, similar to other studies.[24] In addition, the small sample size, although consistent with the previous studies reported in the literature, can be deemed as a limitation. However, considering that a 10-unit difference between each group's NIRS values was significant, the power of the study was calculated as 92%. Because rSO_2 monitoring was not a routine process, the number of patients was limited to the number of pellets obtained as part of the study. Another limitation was the lack of multiple cerebral monitoring. Along with cerebral oxygenation monitored by the NIRS, evaluation of blood flow velocity in the cerebral vasculature by transcranial Doppler ultrasound would have been more useful to gain a better insight on the cerebral hemodynamics and viscosity increase.

In conclusion, although hematocrit, arterial oxygen, and carbon dioxide pressure may alter in cyanotic cardiac diseases, bilateral cerebral oxygenation values found to be similar between cyanotic and non-cyanotic patients. As the cyanotic patients were not critically ill in our study, we believe that an active compensatory mechanism to protect cerebral oxygen saturation may be present in these patients.

Declaration of conflicting interests

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REFERENCES

1. Jonas RA, Newburger JW, Volpe JJ. Brain injury and pediatric cardiac surgery. Boston: Butterworth-Heinemann; 1995.
2. Sakamoto T, Hatsuoka S, Stock UA, Duebener LF, Lidov HG, Holmes GL, et al. Prediction of safe duration of hypothermic circulatory arrest by near-infrared spectroscopy. J Thorac Cardiovasc Surg 2001;122:339-50.
3. Dunham CM, Sosnowski C, Porter JM, Siegal J, Kohli C. Correlation of noninvasive cerebral oximetry with cerebral perfusion in the severe head injured patient: a pilot study. J Trauma 2002;52:40-6.
4. Hoffman GM, Ghanayem NS, Tweddell JS. Noninvasive assessment of cardiac output. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2005:12-21.
5. Nelson DP, Andropoulos DB, Fraser CD Jr. Perioperative neuroprotective strategies. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2008:49-56.
6. Wernovsky G, Shillingford AJ, Gaynor JW. Central nervous system outcomes in children with complex congenital heart disease. Curr Opin Cardiol 2005;20:94-9.
7. Bellinger DC, Wypij D, duPlessis AJ, Rappaport LA, Jonas RA, Wernovsky G, et al. Neurodevelopmental status at eight years in children with dextro-transposition of the great arteries: the Boston Circulatory Arrest Trial. J Thorac Cardiovasc Surg 2003;126:1385-96.
8. Majnemer A, Limperopoulos C, Shevell M, Rosenblatt B, Rohlicek C, Tchervenkov C. Long-term neuromotor outcome at school entry of infants with congenital heart defects requiring open-heart surgery. J Pediatr 2006;148:72-7.
9. du Plessis AJ. Mechanisms of brain injury during infant cardiac surgery. Semin Pediatr Neurol 1999;6:32-47.
10. Wernovsky G, Newburger J. Neurologic and developmental morbidity in children with complex congenital heart disease. J Pediatr 2003;142:6-8.
11. Tempe DK, Virmani S. Coagulation abnormalities in patients with cyanotic congenital heart disease. J Cardiothorac Vasc Anesth 2002;16:752-65.
12. Swan L, Birnie DH, Hillis WS. The haematological management of patients with cyanotic congenital heart disease. A time for consensus? Eur Heart J 1997;18:1973-6.
13. Liem KD, Hopman JC, Oeseburg B, de Haan AF, Kollée LA. The effect of blood transfusion and haemodilution on cerebral oxygenation and haemodynamics in newborn infants investigated by near infrared spectrophotometry. Eur J Pediatr 1997;156:305-10.
14. Sunghee H, Hyon BJ, Young-Seok O, Moon HB, Ho-Gol R. Changes in cerebral oxygenation during normovolemic hemodilution in patients with polycythemia. Anesthesiology 96: Abstract 280; 2002.
15. Gottlieb EA, Mossad EB. Limitations of cerebral oxygenation monitoring by near-infrared spectroscopy in children with cyanotic congenital heart disease and profound polycythemia. J Cardiothorac Vasc Anesth 2014;28:347-9.
16. Amigoni A, Mozzo E, Brugnaro L, Tiberio I, Pittarello D, Stellin G, et al. Four-side near-infrared spectroscopy measured in a paediatric population during surgery for congenital heart disease. Interact Cardiovasc Thorac Surg 2011;12:707-12.
17. Hoffman GM, Stuth EA, Jaquiss RD, Vanderwal PL, Staudt SR, Troshynski TJ, et al. Changes in cerebral and somatic oxygenation during stage 1 palliation of hypoplastic left heart syndrome using continuous regional cerebral perfusion. J Thorac Cardiovasc Surg 2004;127:223-33.
18. Daubeney PE, Smith DC, Pilkington SN, Lamb RK, Monro JL, Tsang VT, et al. Cerebral oxygenation during paediatric cardiac surgery: identification of vulnerable periods using near infrared spectroscopy. Eur J Cardiothorac Surg 1998;13:370-7.
19. Vavilala MS, Lee LA, Lam AM. The lower limit of cerebral autoregulation in children during sevoflurane anesthesia. J Neurosurg Anesthesiol 2003;15:307-12.
20. Hayashida M, Kin N, Tomioka T, Orii R, Sekiyama H, Usui H, et al. Cerebral ischaemia during cardiac surgery in children detected by combined monitoring of BIS and near-infrared spectroscopy. Br J Anaesth 2004;92:662-9.
21. Kussman BD, Wypij D, DiNardo JA, Newburger J, Jonas RA, Bartlett J, et al. An evaluation of bilateral monitoring of cerebral oxygen saturation during pediatric cardiac surgery. Anesth Analg 2005;101:1294-300.
22. Guzmán-Pruneda FA, Fraser CD Jr. Neuroprotective strategies--what do we really need to know? Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2014;17:77-80.
23. Sood ED, Benzaquen JS, Davies RR, Woodford E, Pizarro C. Predictive value of perioperative near-infrared spectroscopy for neurodevelopmental outcomes after cardiac surgery in infancy. J Thorac Cardiovasc Surg 2013;145:438-45.
24. Hoffman GM, Brosig CL, Bear LM, Tweddell JS, Mussatto KA. Effect of Intercurrent Operation and Cerebral Oxygenation on Developmental Trajectory in Congenital Heart Disease. Ann Thorac Surg 2016;101:708-16.