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Original Article

Intraoperative Variables and Cerebral Oxygen Monitoring in Pediatric Cardiac Surgeries

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Abstract

Objectives: The objective of this study was to evaluate the impact of combining near-infrared spectroscopy (NIRS) and bispectral index (BIS) for monitoring cerebral oxygenation and detecting ischemia during pediatric cardiac surgery with cardiopulmonary bypass (CPB).

Methods: A prospective, single-center study was conducted between March 01, 2024, and July 01, 2024, involving 50 pediatric patients undergoing congenital heart surgery. Cerebral oxygenation was continuously monitored using NIRS and BIS at 6 time points during surgery: T1 (entry), T2 (immediately after CPB initiation), T3 (deepest hypothermic temperature), T4 (post-rewarming), T5 (end of surgery), and T6 (postoperative intensive care unit [ICU]). Central venous saturation, hematocrit (Htc), temperature, mean arterial pressure (MAP), and lactate levels were also monitored. The primary outcomes included correlations between cerebral oxygenation parameters and neurological outcomes within 3 months.

Results: The study was conducted with a total of 50 children cases, of which 56% (n=28) were male, and 44% (n=22) were female. The age of the cases ranged from 6 to 200 months, with a mean 42.4±52.7 months. Weight measurements ranged from 14.2 to 65 kg, with a mean of 16.3±14.3 kg. The average CPB duration was 96.1±34.8 min. The cases had an average ICU stay of 3.2±2 days. Upon reviewing the final status, it was found that there were no mortality among the patients and only three patients experienced transient neurological complications, which resolved without long-term deficits. NIRS values remained stable between 55% and 65% during surgery. BIS monitoring detected no significant decreases, supporting the absence of severe ischemia.

Conclusion: Combining NIRS and BIS in pediatric cardiac surgery enhances cerebral perfusion monitoring and enables early detection of ischemic events, potentially reducing postoperative neurological complications. Larger studies are needed to validate these findings and further assess the role of intraoperative parameters such as Htc and MAP in preventing cerebral ischemia.

Keywords: Bispectral index; near-infrared spectroscopy; neuromonitoring; pediatric cardiac surgery.

Pediatrik Kalp Cerrahisinde İntraoperatif Değişkenler ve Serebral Oksijen Monitorizasyonu

Özet

Amaç: Kardiyopulmoner baypas (CPB) kullanılan pediatrik kalp cerrahisi sırasında serebral oksijenizasyonun izlenmesi ve iskeminin tespiti için Yakın Kızılötesi Spektroskopi (NIRS) ve Bispektral İndeks'in (BIS) birlikte kullanımının etkisini değerlendirmek.

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Gereç ve Yöntem: 1 Mart 2024 ve 1 Temmuz 2024 tarihleri arasında doğuştan kalp ameliyatı geçiren 50 pediatrik hastayı içeren tek merkezli, prospektif bir çalışma gerçekleştirildi. Ameliyat sırasında altı farklı zamanda (T1: giriş, T2: CPB başlatıldıktan hemen sonra, T3: en derin hipotermik sıcaklık, T4: yeniden ısınma sonrası, T5: ameliyat sonu, T6: postoperatif yoğun bakım) NIRS ve BIS kullanılarak sürekli serebral oksijenizasyon takibi yapıldı. Merkezi venöz satürasyon, hematokrit, sıcaklık, ortalama arter basıncı (MAP) ve laktat seviyeleri de takip edildi. Birincil sonuçlar, serebral oksijenizasyon parametreleri ile üç ay içindeki nörolojik sonuçlar arasındaki korelasyonları içeriyordu.

Bulgular: Çalışma, %56'sı (n=28) erkek ve %44'ü (n=22) kız olan toplam 50 çocuk olgu ile gerçekleştirildi. Olguların yaşı 6 ile 200 ay arasında değişmekte olup, ortalama yaş 42.4±52.7 aydı. Ağırlık ölçümleri 14.2 ile 65 kg arasında değişmekte olup, ortalama ağırlık 16.3±14.3 kg idi. Kardiyopulmoner baypas (CPB) süresi ortalama 96.1±34.8 dakika olarak kaydedildi. Olguların yoğun bakım ünitesinde (YBÜ) kalış süreleri ortalama 3.2±2 gün olarak bulundu. Nihai durum incelendiğinde, hastalar arasında mortalite olmadığı ve yalnızca üç hastada geçici nörolojik komplikasyonlar görüldüğü, ancak bu komplikasyonların uzun vadeli bir defisit bırakmadan düzeldiği tespit edildi. NIRS değerleri ameliyat sırasında %55 ile %65 arasında sabit kaldı. BIS takibi ise şiddetli iskeminin olmadığını destekleyerek anlamlı bir düşüş göstermedi.

Sonuç: Pediatrik kalp cerrahisinde NIRS ve BIS'in birlikte kullanımı, serebral perfüzyon takibini artırmakta ve iskemik olayların erken tespitini sağlamaktadır; bu da postoperatif nörolojik komplikasyonları potansiyel olarak azaltabilir. Bu bulguları doğrulamak ve hematokrit ile MAP gibi intraoperatif parametrelerin serebral iskemi önlemedeki rolünü daha fazla değerlendirmek için daha geniş çaplı çalışmalara ihtiyaç vardır.

Anahtar sözcükler: Bisktral indeks; NIRS; nöromonitorizasyon; pediatrik kardiyak cerrahi.

Introduction

In pediatric cardiac surgeries, hemodynamic changes and cardiopulmonary bypass (CPB) can lead to cerebral perfusion disorders, cerebral ischemia, and irreversible damage. While survival rates in pediatric cardiac surgery cases have reached up to 90%, nearly 50% of these cases experience long-term neurodevelopmental problems.[1] In a cohort study by Majnemer et al., involving 94 patients who underwent complex congenital heart surgery and were tested at age 5, 49% showed significant gross motor delay, and 39% had fine motor delay.[2] In advanced centers, where survival rates for pediatric cardiac surgery exceed 95%, the incidence of serious neurological outcomes has dramatically improved over time, shifting the focus to long-term functional morbidity, particularly neurodevelopmental disorders.[3] Perioperative neurological injuries can result from cerebral hypoxia/ischemia due to cyanosis, prolonged deep hypothermic circulatory arrest, surgical or CPB techniques, cerebral emboli, low cardiac output, and cardiac arrest. Cerebral oxygen supply-demand imbalances, caused by cerebral hypoperfusion, are major contributors to brain damage.[4] During CPB, non-physiological conditions such as hypothermia, hypotension, hemodilution, and pulseless blood flow disrupt the normal cerebral oxygen supply-demand balance.[5,6]

Currently, methods for monitoring cerebral perfusion in pediatric cardiac surgery include processed electroencephalography (EEG) (bispectral index [BIS]), cerebral oximetry (near-infrared spectroscopy [NIRS]), and Doppler ultrasound techniques. Perioperative NIRS usage has become the gold standard in cardiac surgeries.[7,8] NIRS offers advantages as a non-invasive, real-time dynamic indicator that does not require a pulsatile method like pulse oximetry, and it is beneficial during hypothermia, CPB, and resuscitation after cardiac arrest. Cerebral NIRS provides reliable measurements of venous saturation under the sensors, especially in neonatal patients with small skulls. In piglets exposed to hypoxia, NIRS has shown strong correlations with neurocognitive dysfunction and cerebral blood flow.[3] However, during cardiac surgery, hemoglobin levels and partial pressure of carbon dioxide have significant effects on NIRS monitoring. Hemodilution, transfusion, hypocapnia, and hypercapnia can cause significant variations in cerebral oximetry, making NIRS a continuous monitoring alarm that should be compared with other data before making any management changes.[9]

The BIS, especially when used alongside NIRS to indicate cerebral tissue oxygenation, allows for the detection of cerebral ischemia and hypnotic states.[10,11] A sudden and deep BIS decrease occurs when acute EEG slowing develops due to cerebral ischemia, even if the depth of anesthesia remains unchanged. The rewarming process during CPB and continuous hypotension while anesthesia is maintained pose the highest risk for cerebral hypoxia, regardless of appropriate arterial oxygen saturation (SaO_2). Regional cerebral oxygen saturation ($rScO_2$) is most likely to detect conditions associated with cerebral hypoxia. Cerebral desaturation may require aggressive management; however, peripheral arterial oxygen saturation (SpO_2), mean arterial pressure (MAP), or central venous oxygen saturation (CvO_2) cannot predict it. To maintain normal $rScO_2$ (>60%), interventions can include adjustments in cerebral oxygen consumption (central temperature, anesthesia depth), SpO_2, MAP, vasoactive drugs, and volume administration. It has been reported that BIS values also increase during the rewarming phase, possibly reflecting higher levels of consciousness. Thus, in combination with NIRS, BIS plays a crucial role in detecting cerebral ischemia during cardiac surgery in children.[12]

The primary aim of our study is to identify which variables are more sensitive to cerebral ischemia in pediatric patients undergoing cardiac surgery when cerebral perfusion is monitored by combining BIS and NIRS. Our primary hypothesis is that combined NIRS and BIS monitoring in pediatric cardiac surgeries provides valuable data for cerebral perfusion. Our secondary hypothesis is that changes in central venous saturation, central venous pressure (CVP), lactate, MAP, and temperature during CPB may also show changes in NIRS and BIS values, and correlations among these parameters may be observed.[13]

Materials and Methods

This single-center, prospective study was conducted in our hospital from March 01, 2024, to July 01, 2024. Pediatric patients under 18-years-old with congenital heart disease undergoing cardiac surgery were examined. Patients with preoperative neurological comorbidities, syndromic conditions, or cyanotic features were excluded from the study. Participants who filled out the survey forms incompletely, gave up participating in the study, and could not be reached were excluded from the study. A total of 50 cases (28 males, 22 females) were included.

When our patients were routinely brought into the operating room, monitoring with electrocardiography, non-invasive blood pressure, and pulse oximetry was performed, followed by the administration of induction drugs. For induction, 0.1 mg/kg midazolam, 1 μg/kg fentanyl, 1 mg/kg ketamine, and 0.6 mg/kg rocuronium bromide were administered. Immediately afterward, 30 mg/kg intravenous cefazolin and 3 mg/kg methylprednisolone were routinely administered. After intubation, pediatric cardiac anesthesia specialists placed central venous catheters and arterial cannulas. Routine monitoring continued during surgery, including invasive arterial blood pressure, CVP, end-tidal carbon dioxide, BIS (BIS, Covidien, USA), cerebral and somatic (renal) NIRS (INVOS 5100C cerebral/somatic oximeter monitors, Medtronic, Minneapolis, MN), and esophageal temperature. A pre-prepared study form was filled out during each surgery. This form recorded demographic characteristics, preoperative clinical status, echocardiographic information, CPB duration, and cerebral and renal oxygen saturation (rSO_2-NIRS), $CvSO_2$, BIS, hematocrit (Htc), temperature, MAP, lactate, CVP, and saturation (SpO_2) at 6 intraoperative time points. These 6 time points were T1 (entry), T2 (immediately after entering the pump), T3 (deepest temperature on pump), T4 (after rewarming on pump), T5 (end of operation), and T6 (admission to intensive care).

The CPB circuit was prepared with priming solutions containing blood. After circulation stabilized on CPB, midazolam, and rocuronium were administered through the CPB circuit. When the CPB duration was prolonged, the same drugs were added every hour. Mild to moderate hypothermia was used. Anesthesia maintenance continued with sevoflurane after CPB. Analgesia was provided with 10 mg/kg paracetamol and 0.05 mg/kg morphine, and all patients were extubated in the operating room with 3–5 mg/kg intravenous sugammadex administered at the end of surgery. Patients were transferred to the intensive care unit (ICU) with nasal oxygen support.

The correlations between cerebral oxygen saturation (rSO_2-NIRS), $CvSO_2$, BIS, Htc, temperature, MAP, lactate, CVP, and saturation (SpO_2) values recorded in the case forms were statistically examined. Postoperative ICU stay duration, postoperative seizure history, short-term (within the first 3 months) postoperative neurological morbidities, and mortality were recorded and analyzed for these patients.

Before the study, every patient gave written informed permission. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Başakşehir Çam Sakura Hospital local ethics committee (January 17, 2024).

Statistical Analysis

The number cruncher statistical system 2007 software (Kaysville, Utah, USA) was used for statistical analyses. Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, maximum) were applied when evaluating study data. The conformity of quantitative data to a normal distribution was assessed using the Shapiro-Wilk test and graphical analyses. For the comparison of non-normally distributed quantitative variables between two groups, the Mann-Whitney U-test was employed. For the preoperative and postoperative evaluation of non-normally distributed variables, the Wilcoxon Signed Ranks test was used. The Pearson Chi-square test was applied for the comparison of qualitative data. Statistical significance was set at $p<0.05$.

Table 1. Demographic and clinical variables for patients

	Mean±SD	Median (min-max)
Age (months)	42.4±52.7	17 (3–204)
Weight (kg)	16.3±14.3	10.3 (4.2–65)
Height (cm)	91±30.8	83.5 (59–170)
CPB time (min)	96.1±34.8	88.5 (42–190)
Lowest temperature (°C)	31±1.8	32 (24–32)
Hematocrit during hypothermia (%)	29.1±3.9	29.5 (20–35)
ICU stay (days)	3.2±2	2 (1–11)
	n	**%**
Procedure		
VSD repair	15	30
Total repair of TOF	9	18
ASD repair	6	12
ASD+PAPVR repair	5	10
Aortic valve repair	4	8
Pulmonary valve repair	4	8
Arch reconstruction	3	6
Others	4	8
Postoperative neurological complications		
Seizure	1	2
Motor deficit	2	4
Mortality	0	0

SD: Standard deviation; CPB: Cardiopulmonary bypass; ICU: Intensive care unit; VSD: Ventricular septal defect; TOF: Tetralogy of fallot; ASD: Atrial septal defect; PAPVR: Partial anomalous pulmonary venous return.

Results

Our study was conducted from March 01, 2024, to July 01, 2024, involving a total of 50 pediatric cases in our hospital, of which 56% (n=28) were male and 44% (n=22) were female. The ages of the cases ranged from 6 to 200 months, with a mean age of 42.4±52.7 months.

Height measurements varied between 59 and 170 cm, with an average of 91±30.8 cm, while weight measurements ranged from 4.2 to 65 kg, averaging 16.3±14.3 kg. The average CPB duration was 96.1±34.8 min. The types of surgeries performed and all demographic and clinical data are presented in Table 1.

When examining the neurological status of the patients within 3 months postoperatively, it was noted that one patient experienced a seizure during the 1st week after surgery, which did not recur in subsequent days with the administration of antiepileptic medications. Additionally, two patients had slight

Table 2. Intraoperative variables (median [interquartile range (IQR)] [min-max])

Time	rSO_2 (%)	BIS	$CvSO_2$ (%)	Hct (%)	Temperature (°C)	MAP (mmHg)	CVP (mmHg)	SpO_2 (%)	Lactat
T1	62.5 (45–90)	55.5 (34–73)	76.2 (52.6–96.2)	34.5 (23–49.7)	36.4 (35–38)	65 (48–89)	9.5 (4–16)	100 (92–100)	1.1 (0.6–2.3)
T2	59 (35–90)	59.5 (37–73)	72.4 (24–97.8)	31.3 (23.3–41)	36.4 (11.2–38.5)	47 (30–70)	10 (3–19)	100 (90–100)	1.25 (0.6–3.9)
T3	55 (32–77)	56 (35-72)	78.6 (43–96.3)	29.5 (18.3–38)	32 (24.5–33)	50 (30–81)	8 (1–18)	100 (93–100)	1.6 (0.8–4.7)
T4	57.5 (37–90)	62 (40–80)	77.7 (39–95.1)	31.9 (25.5–42.8)	36.5 (35–37.5)	49 (32–70)	11 (1–18)	100 (89–100)	2.1 (1.4–6.1)
T5	66 (39–90)	61 (30–75)	77.2 (53.2–97.2)	34.6 (25.7–45.3)	36.6 (35.3–37.9)	54 (43–76)	11 (3–16)	100 (93–100)	2.2 (1.3–5.2)
T6	65 (39–90)	75 (44–90)	75.3 (58–95)	37.2 (27.4–49.5)	37.2 (36.3–38.5)	73 (50–110)	12 (4–22)	98 (88–100)	2.5 (1.1–8)

rSO_2: Cerebral oxygen saturation; BIS: Bispectral index; $CVSO_2$: Central venous O_2 saturation; Hct: Hematocrit; MAP: Mean arterial pressure; CVP: Central venous pressure; SpO_2: Peripheral oxygen saturation.

motor function impairment in one arm, which completely resolved within weeks. At the end of the 3 months, no permanent neurological damage was observed in any of the patients.

The cases had an average ICU stay of 3.2±2 days. Upon reviewing the final status, it was found that there were no fatalities among the patients.

Patients were closely monitored throughout the surgery with continuous monitoring. Necessary interventions were made in response to sudden changes in NIRS and BIS values. Central venous saturation, Htc, temperature, MAP, CVP, SpO_2, and lactate levels were monitored and efforts were made to maintain stability through appropriate interventions. The variables monitored at 6 different time intervals are summarized in Table 2 and Figure 1.

Discussion

In our study, it has been observed that monitoring cerebral oxygenation with NIRS and BIS in pediatric cardiac surgeries provides significant insights for pediatric patients. To successfully perform open-heart surgery in pediatric patients, systemic and cerebral perfusion must be maintained within safe limits.[13] Blood pressure alone may not be a suitable indicator of systemic perfusion.[14] NIRS provides continuous monitoring of cerebral perfusion, detecting microcirculation even during CPB circulation, and studies have reported that continuous NIRS monitoring can diagnose silent ischemic conditions in the brain and thus prevent ischemic complications.[7] This is a non-invasive assessment of regional oxygen supply-demand balance. In a study by Mittnacht NIRS was reported to be a reliable indicator of tissue perfusion.[15] Therefore, in our patients, NIRS values were closely monitored during CPB and throughout the surgery, and prompt and appropriate interventions were applied for values that decreased by more than 10%, aiming to maintain a stable trend. In our study, NIRS values recorded at all times did not fall below an average of 55%, and the values at 6 different times showed a stable trend between 55% and 65%.

Studies have associated NIRS values with postoperative neurocognitive disorders and neurological comorbidities.[13] Moreover, a decrease in NIRS value serves as an important early warning sign for the clinician.[16] A study on pediatric patients undergoing

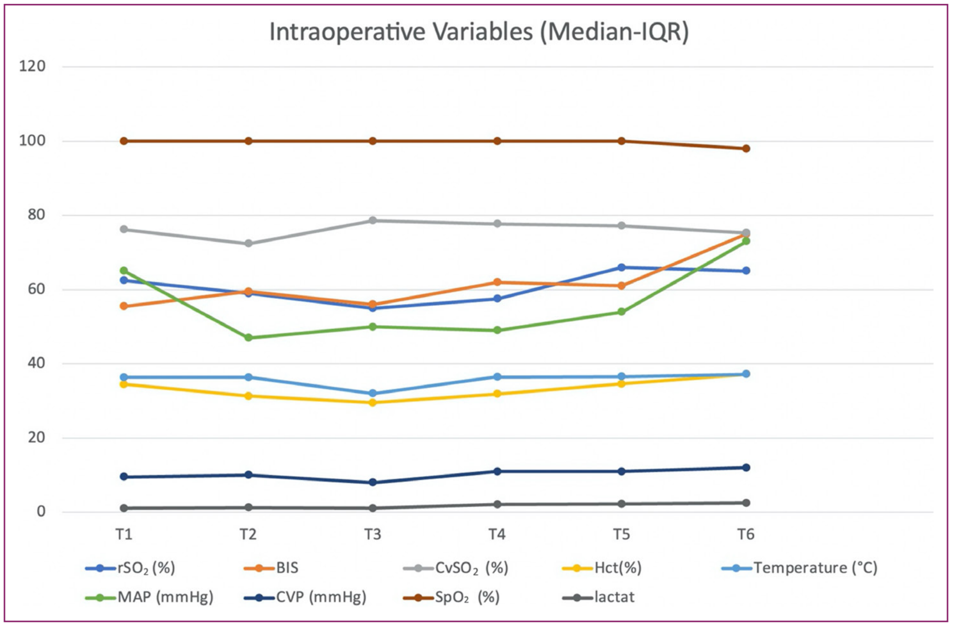

Figure 1. Intraoperative variables (median [ınterquartile range]).

rSO_2: Cerebral oxygen saturation; BIS: Bispectral index; $CVSO_2$: Central venous O_2 saturation; Hct: Hematocrit; MAP: Mean arterial pressure; CVP: Central venous pressure; SpO_2: Peripheral oxygen saturation.

cardiac catheterization associated significant decreases in NIRS values with hypoxic episodes and similar complications.[17] In our study, it was observed that cerebral ischemia could be prevented through the stable course of intraoperative NIRS values and rapid interventions, particularly in cases of decreases >10%. The absence of patients with persistent neurological comorbidity at the end of the 3rd postoperative month is associated with the stable maintenance of intraoperative monitoring values.

Although some studies have supported that the use of NIRS during cardiac surgery and CPB does not reduce mortality,[18] other studies have found a significant association between NIRS changes and mortality, even showing that as the rate of NIRS change increases, it is more significantly related to mortality.[14] No comment can be made in our study regarding the relationship between NIRS and mortality because no mortality was observed among our patients.

When acute EEG slowing due to cerebral ischemia occurs, a sudden and deep BIS decrease is observed, although the depth of anesthesia does not change. An increase in BIS values has also been reported during the rewarming phase.[10–12] In our study, as expected, an increase in BIS values was observed during rewarming (T4). Additionally, none of our patients experienced a sudden and deep BIS decrease, which supports the absence of cerebral ischemia and neurological comorbidity in our patients. Therefore, our study supports the use of BIS along with NIRS for detecting cerebral ischemia during cardiac surgery in children.

The rate of acute neurological complications after pediatric cardiac surgery has been found to vary in different studies. Avila-Alvarez et al. documented this rate as 4.2%, whereas Shahzad et al. reported it as 2.1%.[19,20] Although a meaningful statistic could not be conducted in our study due to the low number of patients with comorbidities, close examination of intraoperative values at all times for three patients with postoperative transient neurological complications showed that, unlike other patients, there was a significant decrease, albeit short-term, in Htc, MAP, and NIRS values at the time of pump initiation (T2). This suggests that NIRS, Htc, and MAP values at the start of CPB may be critical in terms of cerebral oxygenation. We believe that further studies with a higher number of neurological comorbidities and close examination of patients' intraoperative monitoring values are needed.

The most significant limitation of our study is the low number of patients who developed neurological comorbidities and the heterogeneous structure of the population resulting from the evaluation of pediatric patients with highly variable weights.

Conclusion

Our study results suggest that monitoring cerebral oxygenation through the combination of NIRS and BIS in pediatric cardiac surgeries may positively impact the neurological prognosis of pediatric patients. These non-invasive monitoring methods allow for early detection of cerebral hypoxia, enabling timely interventions with the potential to reduce postoperative neurological complications.

Future studies with larger sample groups may provide a more comprehensive evaluation of the long-term neurological outcomes, particularly regarding the monitoring of parameters such as Htc and MAP, which are sensitive to cerebral ischemia during CPB. In this context, the combined use of NIRS and BIS could be considered a standard monitoring approach in pediatric cardiac surgery.

Disclosures

Ethics Committee Approval: The study was approved by the Başakşehir Çam Sakura Hospital Clinical Research Ethics Committee (no: E-96317027-514.10-234539860, date: 17/01/2024).

Informed Consent: Informed consent was obtained from all participants.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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