

Are perioperative near-infrared spectroscopy values correlated with clinical and biochemical parameters in cyanotic and acyanotic infants following corrective cardiac surgery?

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Abstract

Background: Near-infrared spectroscopy (NIRS) is a useful non-invasive tool for monitoring infants undergoing cardiac surgery. In this study, we aimed to determine the NIRS values in cyanotic and acyanotic patients who underwent corrective cardiac surgery for congenital heart diseases.

Methods: Thirty consecutive infants who were operated on with the diagnosis of ventricular septal defect (n=15) and tetralogy of Fallot (n=15) were evaluated retrospectively. A definitive repair of the underlying cardiac pathology was achieved in all cases. A total of six measurements of cerebral and renal NIRS were performed at different stages of the perioperative period. The laboratory data, mean urine output and serum lactate levels were evaluated along with NIRS values in each group.

Results: The NIRS values differ in both groups, even after the corrective surgical procedure is performed. The recovery of renal NIRS values is delayed in the cyanotic patients.

Conclusion: Even though definitive surgical repair is performed in cyanotic infants, recovery of the renal vasculature may be delayed by up to two days, which is suggestive of a vulnerable period for renal dysfunction.

Keywords

near-infrared spectroscopy; tetralogy of Fallot; ventricular septal defect; pediatric cardiac surgery; renal circulation

Introduction

Near-infrared spectroscopy (NIRS) is a non-invasive method for the assessment of regional oxygen supply and demand in different tissue beds. The different measurements obtained from different parts of the body provide the determination of adequacy of local organ perfusion.¹ Acute kidney injury is a consequence of systemic inflammation, ischemia, emboli and low cardiac output states.² The newborn period has some unique properties when the immaturity of the renal system is considered, especially, the vascular resistance is high in the newborn and infantile periods.³ Although the estimation of renal function is possible by the determination of several parameters in children and adolescents with cyanotic and acyanotic congenital heart diseases, data about the infancy period are limited.⁴ Cerebral blood flow and oxygen supply may be preserved in low cardiac output states due to the effective

autoregulation mechanisms in the brain and, therefore, different measurements from different body parts is important when using NIRS monitoring.⁵ Although

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Presented at the 64th International Congress of the European Society for Cardiovascular and Endovascular Surgery (ESCVS), March 26-29, 2015, Istanbul, Turkey.

cardiopulmonary bypass (CPB) is not considered as a major determinant of neurological impairment following cardiac surgery, perfusion is a modifiable factor that enhances the quality of cerebral protection.^{6,7}

In this study, we aimed to determine the relationship between the perioperative NIRS values (cerebral, renal) and the clinical and biochemical parameters of renal function in two groups of patients with the diagnosis of cyanotic and acyanotic congenital heart diseases. The question was whether the clinical effects of preoperative renal and cerebral perfusion with deoxygenated blood in the cyanotic patients were promptly relieved and NIRS values, as well as clinical parameters of renal dysfunction, became equivalent in both groups following corrective cardiac surgery in infants.

Patients and Methods

A retrospective analysis of the perioperative NIRS data of 30 consecutive infants who were operated on for isolated ventricular septal defect (VSD) or tetralogy of Fallot (TOF) were evaluated following the approval of the institutional ethical committee. All of the patients were operated on in the infancy period (range 2 to 12 months). Group I were acyanotic infants with isolated VSD (n=15) whereas Group II were cyanotic patients with TOF (n=15). Patients with a palliative surgical treatment instead of a definitive repair were excluded. Preoperative renal dysfunction and emergency surgical interventions were other criteria for exclusion. The common target for surgical intervention was determined as an unobstructed biventricular outflow without any residual shunts at atrial and ventricular levels. All the patients received low to moderate doses of positive inotropic support.

The perioperative regional cerebral and renal oxygen saturation were continuously monitored by a NIRS sensor (INVOS™-5100 C, Medtronic Inc., Minneapolis, MI, USA). A total of six measurements for both cerebral NIRS (c-NIRS) and renal NIRS (r-NIRS) were performed at different stages of the perioperative period; I: before induction of the anesthesia, II: at the time of cross-clamping, III: following the termination of cardiopulmonary bypass, IV: at the 4th, V: 24th and VI: 48th postoperative hours. The laboratory data which were evaluated together with the total urine output at the 24th postoperative hour included serum creatinine and lactate levels.

Surgical technique and cardiopulmonary bypass

Following the induction of anesthesia and endotracheal intubation, a midline sternotomy was performed in all

cases. Intravenous heparin was administered in order to achieve an activated clotting time >480 seconds. The ascending aorta and the superior and inferior vena cavae were cannulated with an 8-10 Fr aortic cannula and 12-14 Fr venous cannulae (DLP, Medtronic Inc.), respectively. All the cases were operated under CPB and aortic cross-clamping at moderate to low hypothermia. The CPB circuit was primed with heparinized fresh blood and the hematocrit level was maintained between 28% and 35% during CPB. Pulsatile perfusion was implemented with a pulsatile roller pump (Maquet HL20, Hirrlingen, Germany) and a Capiiox Baby RX05 hollow-fiber membrane oxygenator (Terumo Corp., Tokyo, Japan) in both groups. Pulsatile flow was used in all cases in which the base flow rate, start time and stop time were 10%, 20% and 80%, respectively. The mean arterial pressure was maintained at 40 mmHg during CPB. Myocardial management was achieved with intermittent cold (4°C) blood cardioplegia. Weaning from CPB was commenced at a rectal temperature of 36.7°C. Ultrafiltration (Hemofilter 6S, Hospal, Lyon, France) was implemented in all cases at the rewarming phase until the end of the termination of CPB, with a blood flow through the arterial line to the filter at a rate of 10-15 mL/kg/min.⁸

The surgical technique included complete correction of the underlying cardiac pathology in both groups. In Group I, the VSDs were closed using interrupted polypropylene sutures, with the autologous pericardial patch treated with glutaraldehyde. All the patients had isolated VSDs, but six cases had patent foramen ovale that were concomitantly closed. In Group II, the patients with TOF underwent total correction with VSD closure and enlargement of the right ventricular outflow tract (RVOT) stenosis. Transannular patch enlargement was implemented in nine of the cases, whereas a subannular patch with preservation of the pulmonary valve was implemented in six cases. We did not encounter any significant residual shunts or impairments in ventricle function in our patients in the postoperative echocardiographic evaluation.

Statistical analysis

Results were analyzed with the Statistical Package for the Social Sciences (SPSS) version 17.0 (SPSS Inc., Chicago, IL, USA). Comparisons between the groups were performed with the 'Mann-Whitney U Test' whereas the 'Wilcoxon Signed Rank Test' was used for the statistical analysis in the groups for comparison of preoperative and postoperative values. The lactate values (I to VI) in the groups were compared with the 'Friedman test' and the determination of the group that was leading to the statistically significant difference was performed with 'Bonferoni-adjusted Wilcoxon Signed

Table 1. The demographic properties, hematocrit changes, cardiopulmonary bypass and aortic cross-clamp times of the patients are presented.

Groups	Age (months)	Weight (kg)	Δ Hct	X-clamp time (min)	CPB time (min)
Group I	6.3 \pm 3.7	6 \pm 2.1	4.5 \pm 3.6	48.6 \pm 10.4	77.3 \pm 21.1
Group II	6.8 \pm 3.1	6 \pm 2.2	8.7 \pm 3.8	86.9 \pm 23.8	126.3 \pm 23.7
p	ns	ns	0.026	0.0001	0.0001

Δ Hct: hematocrit change, X-clamp: aortic cross-clamp, CPB: cardiopulmonary bypass, ns: non-significant.

Rank Test' ($p < 0.01$). Statistically significant difference was determined with a p-value lower than 0.05.

Results

The patients in both groups were statistically identical when age, gender and bodyweight were considered. The mean age of the patients in Groups I and II were 6.3 \pm 3.7 and 6.8 \pm 3.1 months, respectively. The mean bodyweight of the patients in Groups I and II were 6.0 \pm 2.1 and 6.0 \pm 2.2 kg, respectively.

The preoperative oxygen saturation values were 94.6 \pm 14.3% and 81.9 \pm 5% for Groups I and II, respectively. The preoperative blood hematocrit level was 35.9 \pm 2.3% in Group I whereas it was 38.6 \pm 2.1% in Group II. When the postoperative hematocrit levels were considered, Group I had a hematocrit level of 31.4 \pm 2.3% whereas Group II had a hematocrit level of 29.9 \pm 2.3%. There was a statistically significant difference between preoperative and postoperative hematocrit levels when the two groups were compared. The hematocrit changes (Δ Hct), defined as the difference between the preoperative and postoperative hematocrit values in Group I and Group II, were 4.5 \pm 3.1% and 8.7 \pm 3.8%, respectively ($p = 0.026$). Table 1 presents the preoperative demographic properties and hematocrit changes of the patients as well as the CPB and aortic cross-clamp times.

Both the preoperative renal and cerebral NIRS values were statistically different between Groups I and II. Beginning at the induction of the anesthesia, there were significant differences between the two groups, according to the cerebral and renal NIRS values, continuing until the postoperative 48th hour. When the renal NIRS values were evaluated, the renal NIRS values were at the lowest level at stage II, which is the time of aortic cross-clamping. In both of the groups, the NIRS values began to rise at stage III, reaching a steady state at stage VI; they were statistically higher than at stage I ($p < 0.001$). When the cerebral NIRS values were evaluated, the lowest value was recorded in stage II in both groups. However, in Group I, there is a steep rise in stages III and IV; moreover, the basal level is reached at stage V, which is earlier than Group II ($p < 0.001$). In Group II, the rise in cerebral NIRS values began at the third stage and reached a level more than the basal values in stage VI ($p < 0.001$). The six

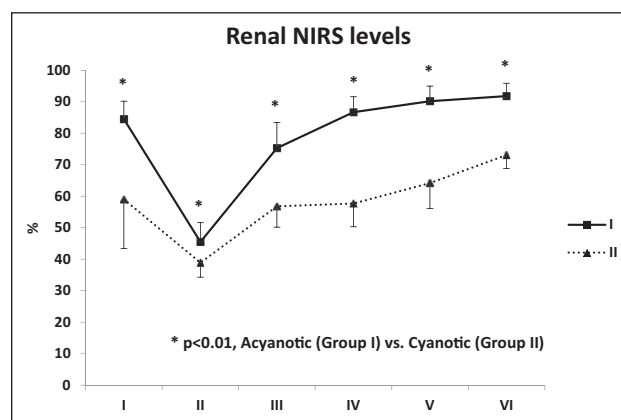


Figure 1. The renal NIRS levels in both groups at six different stages of measurement are demonstrated.

Stage I: before the induction of anesthesia, Stage II: after cross-clamping of the aorta, Stage III: after the termination of cardiopulmonary bypass, Stage IV: 4h post-CPB, Stage V: 24h post-CPB, Stage VI: 48h post-CPB.

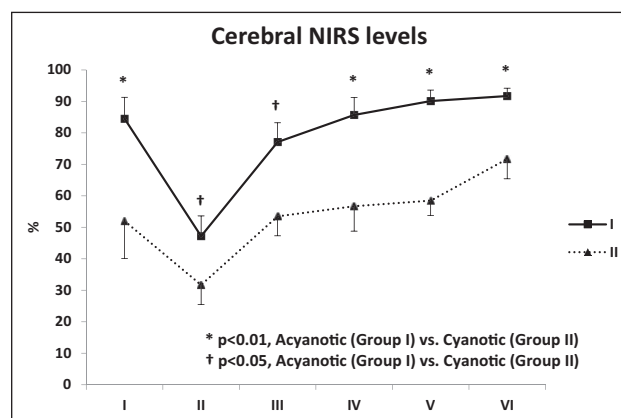


Figure 2. The cerebral NIRS levels in both groups at six different stages of measurement are demonstrated.

Stage I: before the induction of anesthesia, Stage II: after cross-clamping of the aorta, Stage III: after the termination of cardiopulmonary bypass, Stage IV: 4h post-CPB, Stage V: 24h post-CPB, Stage VI: 48h post-CPB.

stage (I to VI) measurements for c-NIRS and r-NIRS are presented Figure 1 and Figure 2, respectively.

Serum lactate levels (mmol/L) were similar in both groups at stages I and II. After stage III, serum lactate levels were significantly higher in Group II until the postoperative 48th hour (stage VI) when the difference

Table 2. Six-stage serum lactate levels (mmol/L) in both groups.

Groups	I	II	III	IV	V	VI
I	0.6 ± 0.7	0.8 ± 0.9	5.8 ± 4.8	5.7 ± 3.6	1.6 ± 0.3	1.0 ± 0.6
II	1 ± 0.7	1.2 ± 0.9	9.4 ± 4.8	9.0 ± 3.8	6.0 ± 0.5	1.6 ± 0.5
p	ns	ns	0.026	0.021	0.0018	ns

Stage I: before the induction of anesthesia, Stage II: after cross-clamping of the aorta, Stage III: after the termination of cardiopulmonary bypass, Stage IV: 4h post-CPB, Stage V: 24h post-CPB, Stage VI: 48h post-CPB.

Table 3. Perioperative and postoperative serum creatinine levels, mean urine output and peritoneal dialysis in patients in both groups.

Groups	Preop. Cr	Postop. Cr	MUO mL/kg/day	PD (n/total) day(s)
I	0.1 ± 0.06	0.5 ± 0.1	93.3 ± 50.4	3/15 (2.66 days)
II	0.1 ± 0.05	0.7 ± 0.1	108.6 ± 50.5	9/15 (4.33 days)
p	ns	ns	ns	0.0012

MUO: mean urine output, PD: peritoneal dialysis, Cr: creatinine.

became insignificant between the two groups again. The six stage (I to VI) measurements for lactate levels are presented in Table 2.

All the patients had normal serum creatinine levels at the preoperative evaluation. The mean urine output (MUO) at the postoperative 24th hour was 93.3 ± 50.4 mL/kg/day and 108.6 ± 50.5 mL/kg/day (p = 0.18) for Groups I and II, respectively. Preoperative and postoperative 24th hour serum creatinine levels (mg/dL) were similar for both of the groups (p>0.05). Peritoneal dialysis was performed in three patients in Group I (2.66 days/patient) and in nine patients in Group II (4.33 days/patient). (Table 3). Any permanent renal dysfunction was not encountered in either group at the time of discharge.

Discussion

Intraoperative and postoperative management of the adverse events related to low cardiac output in infants undergoing congenital heart surgery is an essential component of successful treatment. Conventional monitoring for the detection of tissue hypoxia is provided with mixed venous oxygen saturation and serum lactate levels.⁹ However, mixed venous oxygen saturation may not yield accurate results in patients with cyanotic congenital heart defects. Although serum lactate is a reliable marker of tissue oxygen delivery and cellular perfusion, it does not provide real-time monitoring of the patient.

Near-infrared spectroscopy measures the equilibrium of oxyhemoglobin and deoxyhemoglobin in a mixture of veins, arteries and capillaries, with the application of the 'Beer-Lambert' law for the measurement of the concentration of a substance according to its absorption of

light.¹⁰ However, there are some limitations with NIRS monitoring, such as a lack of precise contribution of various vascular beds, the size of the area explored and a lack of a direct reference against which to correlate values.^{11,12}

In our study, we primarily aimed to evaluate the NIRS values following a corrective cardiac repair, which, theoretically, provides oxygenated blood supply to renal and cerebral beds, both in cyanotic and acyanotic patients. Our first observation was the lack of appearance of the effects of oxygenated blood perfusion to renal and cerebral beds, where cerebral and renal measurements were concerned. After complete surgical repair in the cyanotic group, the renal and cerebral NIRS measurements were still lower than the acyanotic group, which was statistically significant until the postoperative 48th hour. The serum lactate levels were significantly lower in the acyanotic group in the first postoperative 24 hours; however, the levels on the second day were statistically insignificant when both groups were compared. The postoperative 24th hour serum creatinine levels and mean urine output were statistically insignificant, as well. In our experience, early prophylactic peritoneal dialysis provides an effective electrolyte balance and input-output volume balance in patients undergoing cardiac surgery.¹³ Therefore, we performed peritoneal dialysis in both groups, 20% in Group I and 60% in Group II. Although a statistically significant difference is demonstrated between the two groups with regard to the implementation of peritoneal dialysis, we perform peritoneal dialysis more liberally in cyanotic patients and we do not attribute this difference to any NIRS measurement.

During cardiac surgery, the effect of hemoglobin levels on NIRS monitoring is inevitable.¹⁴ The hematocrit

changes in Groups I and II were statistically significant; however, its effect on the postoperative NIRS values of the cyanotic patients is multifactorial. We did not encounter high hematocrit levels in order to use blood-free prime in cyanotic patients, which was probably related to low ages at the time of the corrective cardiac surgery. Although the kidneys and brains of the patients in both groups, theoretically, should begin to receive oxygenated blood at the termination of CPB, there was a statistically significant difference in the cerebral and renal NIRS values in both cyanotic and acyanotic patients. The renal NIRS surge of the cyanotic and acyanotic patients suggests that the renal perfusion of these patients becomes similar at least 2 days after surgery. Therefore, this postoperative period should be optimally managed in terms of renal perfusion and urine output in cyanotic infants.

Our previous experience correlated the renal resistive index values with the cerebral and renal NIRS measurements as well as clinical outcomes in infants with an age of less than 3 months, all of whom were in the high-risk group according to the 'Aristotle Basic Complexity Risk Stratification' score. A renal resistive index value greater than 0.8 was found to be associated with lower postoperative mean urine output and significantly higher lactate levels as well as a significantly higher postoperative intensive care unit and hospital stay of the patients.¹⁵

Herein, we would like to clarify one issue about our study design. We did not aim to directly relate the NIRS values with renal or cerebral malperfusion in two pathophysiologically different patient populations. To the best of our knowledge, the NIRS surges in cyanotic and acyanotic infants have not been reported in the literature with regard to the hypothesis that both patients should have similar hemoglobin-oxygenation dynamics following the definitive repair of the underlying congenital heart disease without further ongoing intracardiac shunts. The major limitation of our study is the different CPB and aortic cross-clamping times, as well as the preoperative hemoglobin values which may directly affect the renal perfusion in the postoperative period. However, mean urine output and postoperative serum creatinine levels were similar in both groups, which may suggest effective renal protection in both groups. Our findings suggest that serum lactate levels become statistically similar in the 48th postoperative hour; however, cerebral and renal NIRS values still remain low in cyanotic patients. In our opinion, since these infants are candidates for early definitive surgical treatment of right to left shunts, persistently high levels of hematocrit and its adverse effects on microvasculature is not the only culprit for delayed recovery of the vascular bed in kidneys.

Our study suggests that the postoperative period, including the first 48 hours, is a vulnerable period for renal function with regard to NIRS measurements in infants undergoing cardiac surgery. Although serum lactate levels and cerebral NIRS values become normal at the end of the second day, renal NIRS values still remain low. However, if an effective mean urine output is provided, the renal NIRS values demonstrate signs of recovery two days after the operation.

Declaration of Conflicting Interest

The authors declare that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

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