Influence of external cardiac pacing on cerebral oxygenation measured by near-infrared spectroscopy in children after cardiac surgery

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Summary

Background: The brain of children in the early period after repair of congenital heart defects with cardiopulmonary bypass (CPB) may be more vulnerable to hemodynamic changes because of impaired cerebral autoregulation. During postoperative testing of the external temporary safety pacer, we performed desynchronizing ventricular pacing (VVI) while monitoring cerebral oxygenation using near-infrared spectroscopy (NIRS).

Methods: We prospectively investigated 11 children (6 girls, 5 boys). Mean age was 6.1 months (±3.8 months) and mean weight: 5.3 kg (±1.5 kg). We performed measurements at four study steps: baseline I, VVI pacing, baseline II and atrial pacing (AOO) to exclude effects of higher heart rate. We continuously measured the effects on hemodynamic and respiratory parameters as well as on cerebral tissue oxygenation index (TOI). Hemoglobin difference (HbD) was calculated as a parameter for cerebral blood flow (CBF).

Results: Ventricular pacing leads to a significant decrease in arterial blood pressure and central venous saturation accompanied by an immediate and significant decrease in TOI (63.3% ± 7.6% to 61.5% ± 8.4% [P < 0.05]) and HbD (0.51 ± 1.8 μmol·l⁻¹ to −2.9 ± 4.7 μmol·l⁻¹ [P < 0.05]).

Conclusion: Cardiac desynchronization after CPB seems to reduce CBF and cerebral oxygenation in children.

Keywords: cerebral oxygenation; near-infrared spectroscopy; children; ventricular pacing; cerebral pressure autoregulation

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**Introduction**

With the advances made in pediatric cardiac surgery and critical care medicine, neurological outcome has become an important issue in children with congenital heart defects (CHD).

Hemodynamic alterations with low cardiac output (CO) may have greater impact on cerebral perfusion after cardiopulmonary bypass (CPB) as cerebral pressure autoregulation (CPA) may be impaired (1). Situations with decreased CO, as they can appear in postoperative arrhythmia, can be simulated by desynchronizing atrial and ventricular contraction. During ventricular pacing (VVI), CO is decreased by about 10–20% because of the lack of the atrial ‘kick’ (2). However, little is known about the impact of cardiac desynchronization on cerebral oxygenation and blood flow.

Near-infrared spectroscopy (NIRS) provides a continuous, noninvasive method to measure regional cerebral oxygenation. Previous studies have shown that the difference between the measured oxygenated (O$_2$Hb) and deoxygenated hemoglobin (deoxyHb) reflects cerebral blood flow (CBF), whereas total hemoglobin (tHb) seems to be sensitive to changes in cerebral blood volume (CBV) (3–5).

To study the effects of hemodynamic changes on cerebral oxygenation we observed the NIRS changes during testing of external pacemakers in the early phase after cardiac surgery.

The purpose of our study was to evaluate the impact of cardiac desynchronization on cerebral oxygen and blood supply.

**Methods**

**Patients**

We prospectively studied 11 children (six girls, five boys) after elective surgical repair of CHD. The characteristics of the patients and the duration of CPB are shown in Table 1. The underlying diagnoses were ventricular septal defect (VSD) ($n=8$), tetralogy of Fallot ($n=2$) and complete atrio-ventricular septal defect ($n=1$). None of the patients had a significant right to left or left to right shunt that could have influenced the cerebral oxygenation.

None of the patients had deep hypothermic cardiac arrest or regional head perfusion during the operation on CPB. CPB was performed in all children using the pH-stat method.

The study was approved by the local ethics committee, and written informed consent was given by the parents.

**Near-infrared spectroscopy (NIRS)**

Near-infrared spectroscopy (NIRS) provides a continuous, noninvasive method to measure regional cerebral oxygenated (O$_2$Hb) and deoxygenated hemoglobin (deoxyHb) concentrations based on the different light absorption spectra of the two. As the sum of both, changes in total hemoglobin (tHb) content can be calculated.

We used the NIRO 300 (Hamamatsu Phototonics, Tokyo, Japan) as near-infrared spectroscope. The NIRO 300 uses laser-emitting diodes to generate light at four different wavelengths (775, 810, 847 and 919 nm). It employs the technique of spatially resolved spectroscopy (SRS) and uses multiple closely spaced detectors to measure light attenuation as a function of source – detector separation. This SRS method, which is described in detail by Matcher *et al.* (6) and Suzuki *et al.* (7), allows the measurement of an absolute value for tissue oxygenation index (TOI) (TOI = O$_2$Hb/tHb × 100). TOI seems to show a good correlation with central venous saturation (CVS) in stable conditions (8).

The emitter and receiver were fixed in a probe holder to ensure an interoptode distance of 40 mm and shielding prevented interference by external
light. The probe was placed on the forehead in the supraorbital region receiving reflected light from the frontal neocortex. This position is chosen to avoid signal disturbances and extracerebral contamination from the temporal muscle and the superior sagittal sinus. The NIRS probe is combined with the measuring unit, which is connected to the NIRO 300 display unit. NIRS values were recorded continuously and saved to disc with a sample rate of 1 s.

**Cardiac pacing**

During surgical repair of CHD, external pacer electrodes are placed on the epimyocardium of the ventricles as well as of the atria. As a result, cardiac pacing can be performed with an external pacemaker in the case of severe arrhythmia in the early postoperative stage. To ensure its functionality, the external pacemaker is tested in the intensive care unit (ICU). During this testing, atrial pacing (AOO) and ventricular demand pacing (VVI) with a frequency higher than the actual heart rate is performed. AOO pacing stimulates the atria and is then conducted to the ventricles via the natural atrioventricular conducting system, thus leading to synchronized contraction of the atria and the ventricles. VVI pacing is performed to test whether effective VVI is possible in the case of atrioventricular block. VVI pacing thus leads to faster contraction of the ventricles without effective and synchronized atrial filling. The lack of the atrial ‘kick’, as seen in atrial fibrillation, decreases CO by about 10–20% (2).

**Study design**

All children were intubated and ventilated mechanically. Sedation was maintained with continuous intravenous fentanyl (4–20 µg·kg⁻¹·h⁻¹) and midazolam (4–20 µg·kg⁻¹·min⁻¹). Continuous monitoring of heart rate, systemic arterial blood pressure of the radial or femoral artery, transcutaneous oxygen saturation (SaO₂) and central venous pressure was performed routinely after cardiac surgery. The study protocol was started 1–48 h after admission to the ICU with a mean time range after the end of CPB of 16.4 h (±10.5 h).

When children were in stable cardiorespiratory conditions, baseline values for NIRS parameters were recorded for 5 min (baseline I). After stable baseline values were reached, we performed 5 min of VVI pacing with a frequency 10% higher than the baseline sinus rhythm (VVI). A second baseline (baseline II) followed for 5 min. To evaluate whether changes in hemodynamics or cerebral oxygenation are attributed to a higher heart rate, another step with AOO pacing with the same frequency as the second step was performed. No changes in medication or ventilation were made during the study period.

At the end of each step a blood sample was taken from a central venous catheter which was placed in the right atrium. Blood gas analysis with measurement of CVS was performed using co-oxymetry (OSM3-Hemoxymeter; Radiometer, Copenhagen, Denmark). All hemodynamic parameters together with blood gas analysis and cerebral TOI were documented simultaneously.

**Statistics**

Mean values of the above-mentioned parameters over the 5 min of each step of the study were calculated. All data were analyzed using SPSS 10.0 for Windows. As data were not normally distributed, the Wilcoxon signed rank test was used to compare the deviations of the mean values of each step from its baseline during cardiac pacing. The data are presented as mean ± SD. P values <0.05 were considered to be significant.

**Results**

**Effects of cardiac pacing on cardiorespiratory parameters**

During VVI pacing, a significant decrease in systolic, diastolic and mean arterial pressure (MAP: \( P = 0.00 \)) from baseline was observed (Table 2); however, there was no significant change in central venous blood pressure (CVP: \( P = 0.47 \)) or transcutaneous arterial oxygen saturation (SaO₂: \( P = 0.75 \)). Central venous saturation decreased significantly after VVI pacing (CVS: \( P = 0.03 \)), but remained stable during AOO pacing (CVS: \( P = 1.0 \)). There were no significant changes in blood gas analysis parameters such as pHv, pO₂v or pCO₂v taken from the central venous line during the whole study. The changes in
arterial blood pressure and all the other hemodynamic parameters from baseline II caused by AOO pacing were not significant (Table 2).

**Effects of cardiac pacing on NIRS parameters**

A characteristic example of the original NIRS data collected during the study is shown in Figure 1.

Oxygenated hemoglobin and tHb showed a relative decline, whereas deoxyHb increased during VVI pacing. As a result, a significant decrease in HbD ($P = 0.02$) was calculated (Table 2). When VVI pacing was ended, the values tended to return to baseline values, and no further changes were observed during AOO pacing.

Cerebral TOI was significantly diminished during VVI pacing ($P = 0.03$) (Table 2). AOO pacing, however, did not cause any significant changes in cerebral TOI ($P = 0.76$).

**Discussion**

During our study, we observed a statistically significant fall in arterial blood pressure during VVI because of cardiac desynchronization, which, however, was not considered to be clinically relevant. NIRS monitoring showed a simultaneous decrease in cerebral TOI even if SaO$_2$ and CVP did not change significantly from baseline. We also observed a significant decrease in CVS measured after 5 min of VVI pacing.

To demonstrate that the observed changes are not caused by a higher heart rate during pacing, another step of AOO was carried out, without any significant changes.

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**Table 2**

Hemodynamics, venous blood gas analysis and near-infrared spectroscopy values presented as mean ± standard deviation for all four steps

<table>
<thead>
<tr>
<th></th>
<th>Baseline I</th>
<th>VVI Pacing</th>
<th>Baseline II</th>
<th>AOO Pacing</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (bpm)</td>
<td>$138.4 \pm 14.3$</td>
<td>$154.4 \pm 12.4^*$</td>
<td>$139.0 \pm 15.6$</td>
<td>$153.4 \pm 11.4^*$</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>$55.1 \pm 10.6$</td>
<td>$50.1 \pm 10.5^*$</td>
<td>$57.7 \pm 10.7$</td>
<td>$54.5 \pm 8.6$</td>
</tr>
<tr>
<td>CVP (mmHg)</td>
<td>$11.7 \pm 2.4$</td>
<td>$11.8 \pm 1.9$</td>
<td>$11.9 \pm 2.2$</td>
<td>$11.8 \pm 2.4$</td>
</tr>
<tr>
<td>SaO$_2$ (%)</td>
<td>$98.2 \pm 2.7$</td>
<td>$98.1 \pm 2.7$</td>
<td>$98.8 \pm 1.6$</td>
<td>$99.0 \pm 1.4$</td>
</tr>
<tr>
<td>pH ven.</td>
<td>$7.37 \pm 0.1$</td>
<td>$7.38 \pm 0.1$</td>
<td>$7.38 \pm 0.1$</td>
<td>$7.38 \pm 0.1$</td>
</tr>
<tr>
<td>pO$_2$ ven. (mmHg)</td>
<td>$37.2 \pm 6.7$</td>
<td>$36.2 \pm 7.3$</td>
<td>$34.9 \pm 6.6$</td>
<td>$35.1 \pm 7.8$</td>
</tr>
<tr>
<td>pCO$_2$ ven. (mmHg)</td>
<td>$47.9 \pm 7.4$</td>
<td>$47.7 \pm 7.3$</td>
<td>$47.3 \pm 6.5$</td>
<td>$46.5 \pm 7.5$</td>
</tr>
<tr>
<td>CVS (%)</td>
<td>$65.6 \pm 12.2$</td>
<td>$61.6 \pm 9.8^*$</td>
<td>$61.8 \pm 11.1$</td>
<td>$61.7 \pm 12.4$</td>
</tr>
<tr>
<td>TOI (%)</td>
<td>$63.3 \pm 7.6$</td>
<td>$61.5 \pm 8.4^*$</td>
<td>$63.6 \pm 7.4$</td>
<td>$63.6 \pm 7.6$</td>
</tr>
<tr>
<td>HbD ($\mu$mol/l$^{-1}$)</td>
<td>$0.51 \pm 1.8$</td>
<td>$-2.90 \pm 4.7^*$</td>
<td>$0.17 \pm 2.1$</td>
<td>$0.14 \pm 2.6$</td>
</tr>
</tbody>
</table>

*Deviation from baseline is significant for $P < 0.05$.

AOO, atrial pacing; CVP, central venous blood pressure; CVS, central venous saturation; HbD, Hemoglobin difference; MAP, mean arterial pressure; TOI, tissue oxygenation index; VVI, ventricular pacing.

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**Figure 1**

Original near-infrared spectroscopy data of a 3.9-month-old male baby after ventricular septal defect patch closure: The measurement shows the changes in total hemoglobin (cHb), deoxygenated hemoglobin (HHb), oxygenated hemoglobin (O$_2$Hb) and tissue oxygenation index (TOI) during the different steps of cardiac pacing: baseline values (BASE I + II) ventricular pacing (VVI), atrial pacing (AOO).
changes in hemodynamic or respiratory parameters or in cerebral oxygenation.

Oxygen supply and consumption in sedated and mechanically ventilated children should be stable, which is also reflected by the stable blood gas parameters and unchanged transcutaneous SaO$_2$ in our children. Therefore, we concluded that the decreased CVS is mainly caused by reduced CO because of the cardiac desynchronization. Reduced CBF is indicated by a significant increase in deoxygenated hemoglobin and a decrease in O$_2$Hb concentration (Figure 1). As a result, the hemoglobin difference (HbD) decreased significantly. In a neonatal piglet study it could be demonstrated that a decrease in HbD reflects a decrease in CBF (3–5).

We postulate, in our children, a constant rate of cerebral oxygen consumption and supply, and therefore a reduced CBF might result in a relatively higher extraction of oxygen from the blood during its passage through the brain. As a result, TOI as an integral measurement of arterio-capillary-venous oxygen saturation in the frontal neocortex decreased significantly.

Cerebral blood flow, however, should be maintained constant by CPA over a range of cerebral perfusion pressures despite an alteration in systemic blood pressure (9).

Within the range of the autoregulatory plateau, rises in blood pressure induce cerebral vasoconstriction, whereas a decrease in blood pressure will cause dilatation of the cerebral arteriolar vessels leading to diminished cerebrovascular resistance to keep the CBF constant (9). A recently published study evaluated the integrity of CPA in children after open-heart surgery by measuring NIRS-derived HbD and middle cerebral artery flow velocity by transcranial Doppler. In this study, two methods showed a high correlation (1). Bassan et al. suggested that concordance between the waveforms of MAP and HbD, as we observed in our children, is indicative of disturbed CPA. Also Morren et al. (10) examined the cerebrovascular autoregulation by NIRS in premature infants and concluded that concordance between HbD and MAP reflects impaired cerebral autoregulation.

Bassan et al. (1), however, found that hypercarbia and fluctuating MAP might predispose a patient to a disruption of CPA. As hypercarbia leads to cerebral vasodilatation of the resistance arterioles, CPA might become less efficient because of a reduced residual capacity for vasodilatation.

In our study there where no significant changes in carbon dioxide partial pressure which could explain the pressure passive changes of CBF. The changes in MAP we observed were statistically significant but still within clinical limits which can be considered hemodynamically irrelevant. Therefore, the fall in MAP should not exceed the autoregulatory plateau.

However, our study is limited by the fact that we did not measure CBF directly. We studied cerebral tissue oxygenation with NIRS, which gives information about the perfusion and oxygenation status of the smallest vessels and of the capillary bed in a small, defined part of the frontal neocortex. The cortical blood flow seems to be more vulnerable to changes in CBF so that HbD might be sensitive also for small changes in CBF. NIRS might reflect best the impact of changes in CBF on the smallest vessels, where minimal changes in diameter have the largest effect. In addition, we saw a decrease in tHb which indicates a reduction not only in CBF but also in CBV. We therefore believe that CPA in our children after cardiac surgery was affected.

We cannot differentiate whether the postulated alteration in CPA is caused by the CPB during cardiac surgery or is a result of the clinical conditions prior to cardiac surgery. All children were in clinically stable condition when admitted and the correction of CHD was elective. Therefore, we believe the impact of presurgery conditions on CPA not to be significant.

It should be mentioned that there was a rather large range of bypass times (34–308 min) in our study. It is possible that the longer the bypass runs the greater could be the inflammatory response and hence the greater the sequelae for cerebral vasculature and cerebral autoregulation. Unfortunately, splitting the group into long and short bypass times would not be statistically feasible because of the small sample size and the unequal distribution of the groups.

However, to evaluate the impact of prior CPB on impaired CPA a control group which was not operated on with CPB would be necessary, but such a group would be difficult to investigate because of the rarity of children with an internal pacemaker and the difficulty of examining awake children with a changing degree of cerebral activation.
A further limitation of our data must be mentioned: CVS declines significantly during VVI pacing but does not recover completely during the second baseline. This might indicate that the periods of 5 min were not long enough for the patients' physiology to have returned to equilibrium. The increase in TOI above CVS during AOO pacing (Table 2), with unchanged blood pressure, might suggest some degree of cerebral autoregulation.

In small children, invasive measurement of CO is more complicated than in adults and is highly invasive; therefore, CO was estimated only indirectly by CVS, which of course implies many pitfalls.

Our results are limited by a rather small sample size and a quite broad age range; however, we did not include any premature or newborn children as the maturation and vulnerability of the neonatal brain might have an impact.

Based on our observations we believe that cerebral oxygenation and CBF may be sensitive to cardiac desynchronization in children shortly after repair of CHD with CPB. Near-infrared spectroscopy might be useful in the early detection of cerebral desaturation and impaired CBF.

On the basis of our study and observations we would recommend strict synchronization of the atria and ventricles in children after CPB e.g. in the case of temporary or permanent atrioventricular block, junctional ectopic tachycardia or AV tachycardia. Effective resynchronization using external pacing or medical treatment improves not only CO but also cerebral oxygenation, even if the blood pressure is within normal ranges.

However, further studies with larger sample sizes are necessary to evaluate the correlation of low TOI and adverse neurological outcome in the postoperative course after repair of CHD.

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References


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