Effect of cardiopulmonary bypass on cortical cerebral oxygenation during coronary artery bypass grafting

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Abstract

Objective: To investigate the changes in cerebral oxygenation during coronary artery bypass grafting (CABG) with normothermic cardiopulmonary bypass (CPB) using near infrared spectroscopy.

Methods: Measurement of cerebral cortical oxygenation changes included concentration of deoxygenated haemoglobin [HHb], oxygenated haemoglobin [O2Hb], changes in the redox status of the cytochrome c oxidase [Cyt-Ox], cerebral saturation as expressed by the tissue oxygenation index (TOI), and cerebral blood volume (CBV) as expressed by tissue haemoglobin index (THI). Measurements were performed in 19 consecutive patients undergoing normothermic (34–36 °C) CPB. Data were recorded at 0.5s intervals and averaged into 30 s epochs. Data analysis was carried at baseline, 1, 20, and 40 min after start of CPB, at rewarming, on weaning from CPB, and at closing of chest. Results: There were no in-hospital death, neurological deficits, or myocardial infarcts. Compared to baseline, during the entire CPB duration, there was a marked reduction in [O2Hb] and CBV which reached their worst level 40 min after initiation of CPB (from \(23.03 \pm 5.1\) to \(29.25 \pm 7.20\) mmol/l for [O2Hb], and a 24% reduction for CBV (both \(P < 0.0001\))). The deterioration in [O2Hb] was recovered by the end of surgery, while the changes in CBV persisted. No significant changes occurred with respect to [HHb], [Cyt-Ox], and TOI. Conclusions: Conventional CABG is responsible for deterioration in [O2Hb], and CBV, which peak at 40–60 min following initiation of CPB. The changes in [O2Hb] are reversible whereas the reduction of CBV persists to the end of the surgery. This suggests a transient impairment in the autoregulatory mechanisms controlling cerebral blood flow following discontinuation of cardiopulmonary bypass.

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Keywords: Near infrared spectroscopy; Cerebral oxygenation; Coronary artery bypass grafting; Cardiopulmonary bypass

1. Introduction

The reported incidence of neurological abnormalities after coronary artery bypass grafting (CABG) ranges from 0.4 to nearly 80%, depending on how the deficit is defined and selection of study population [1,2]. There are a number of difficulties in assessing and quantifying minor cerebral injury post cardiac surgery and a number of methods have been employed, although their reliability and validity remains debatable [3,4].

Near infrared spectroscopy (NIRS) allows real time, non-invasive measurement of cerebral tissue oxygenation indices and compares well with the previously established invasive method of jugular venous bulb oxygenation (SjvO2) measurement [5]. It permits monitoring of several markers of cerebral cortical oxygenation including concentration of deoxygenated haemoglobin [HHb], oxygenated haemoglobin [O2Hb], changes in the redox status of the cytochrome c oxidase [Cyt-Ox], cerebral saturation as expressed by the tissue oxygenation index (TOI), and changes in tissue haemoglobin index (THI). In the absence of hemodilution, changes in THI should reflect changes in cerebral blood volume (CBV) [6,7].

This technique is being increasingly used by vascular surgeons to monitor cerebral cortical oxygenation during carotid endarterectomy [8].

Aim of this study is to use NIRS technology to assess changes in cortical cerebral oxygenation during conventional coronary surgery with normothermic cardiopulmonary bypass (CPB).
2. Materials and methods

2.1. Patient selection

Eligibility for surgery was based on the medical history and a recent coronary angiogram. Exclusion criteria included history of head trauma or stroke causing, significant active neurologological disease, a history of neurosurgery, severe or symptomatic carotid artery disease, left ventricular ejection fraction (EF) of less than 40%, recent myocardial infarction (<1 month), re-operation, and need of concomitant valve surgery. The study was approved by the United Bristol Healthcare Trust Ethics Committee and all patients gave informed consent.

2.2. Anaesthetic, CPB and surgical management

A standardised anaesthetic technique was used for all patients. Induction of anaesthesia was carried out with Midazolam 0–3 mg, Fentanyl 10–15 μg/kg, Propofol 0–1.5 mg/kg and neuromuscular blockade achieved with Pancuronium 0.15 mg/kg. Anaesthesia was maintained using 0–1.5 mg/kg and neuromuscular blockade achieved with Midazolam 0–3 mg, Fentanyl 10–15 μg/kg, Propofol 3–5 mg/kg per h from the prebypass period and propofol 3–5 mg/kg per h from the onset of bypass. The patients were ventilated to achieve normocapnia with air and oxygen (FiO₂; 45–50%) avoiding the onset of bypass. The patients were ventilated to achieve normocapnia with air and oxygen (FiO₂; 45–50%) avoiding the use of positive end expiratory pressure.

2.3. Surgical technique

A standard bypass circuit was used consisting of PVC tubing, a Monolyth hollow fibre membrane oxygenator and a 40-μm arterial line filter (Sorin Biomedica Cardio, Saluggia, Italy), and a Stockert roller pump (Stockert Instrumente GmbH, Germany). Priming of the circuit was carried out with 1000 ml of Hartmans’ solution, 500 ml of Gelofusine (B Braun Medical Ltd, Switzerland), 6000 IU of heparin, 7 ml of 10% calcium gluconate and 0.5 g/kg of mannitol. Initial heparinisation was carried out with 300 IU/kg of heparin to achieve an activated clotting time (ACT) above 480 s during CPB. Bypass was commenced with partial side-clamping. Metaraminol and phentolamine was used to maintain mean arterial pressure (MAP) between 50 and 100 mmHg and alpha stat pH management was followed. Systemic temperature was maintained between 34 and 36 °C with nasopharyngeal monitoring. Prior to discontinuing CPB, rewarming to 37 °C was carried out. Following weaning from CPB, 3 mg/kg protamine was given to reverse the effects of heparin.

2.4. NIRS principles

Near infrared light in the wavelength range between 700 and 1000 nm penetrates biological tissue and bone quite well, which makes transcranial measurements through the intact skull and scalp feasible [10]. The technique of NIRS relies on the application of a modified Lambert–Beer law for the calculation of changes in the concentration of tissue chromophores from measured variations in attenuation of light, which depends on scattering and absorption of the investigated medium [10,11]. Changes in concentration of a number of chromophores can be computed simultaneously from the changes in attenuation at a number of wavelengths using a least square regression algorithm incorporating the relevant extinction coefficients for each wavelength and chromophore [12].

Changes of cerebral cortical oxygenation measurable with NIRS include concentration of deoxygenated haemoglobin [HHb], oxygenated haemoglobin [O₂Hb], changes in the redox status of the cytochrome c oxidase [Cyt-Ox], a putative parameter for cellular oxygenation [13], cerebral saturation as expressed by the TOI, which is the ratio of oxygenated to total tissue haemoglobin, and changes in THI. The latter represents the total amount of haemoglobin in the tissue under investigation. This has two components, the concentration of haemoglobin in blood and the volume of blood in the brain. In the absence of hemodilution, changes in THI should reflect changes in CBV [6,7]. Changes in CBV from baseline can be calculated using the equation

$$ΔCBV = ΔHbT × 0.89/Hb,$$

where HbT is the sum of [O₂Hb] and [HHb] and Hb is the blood haemoglobin concentration, which was measured serially according to the time points for NIRS monitoring.

2.5. NIRS monitoring

Monitoring commenced at chest incision and continued until the end of surgery. Data were recorded at 0.5-s intervals and averaged into 30-s epochs. Data analysis was carried at baseline, 1, 20, 40, and 60 min after start of CPB, on weaning from CPB, and at closing of the chest.

Changes in [O₂Hb], [HHb], [Cyt-Ox], (TOI) and (THI) were recorded using a NIRO 300 near infrared spectroscope (Hamamatsu Photonics KK, Hamamatsu City, Japan). The NIR light transmitting optode and the light detector were located in the right frontal region just below the hairline avoiding the temporalis muscle and midline sinuses. An interoptode spacing of 5 cm was used and the optode and detectors were secured with a double-sided adhesive dressing and a Coban self-adherent wrap (3M Health Care Inc., USA). The optodes were then shielded from ambient
light. A pathlength factor of 6.0 was used to correct for the multiple light scattering effects of biological tissues [14]. A personal computer with NIRO 3000L software was connected to the system to download data.

2.6. Haemodynamic monitoring

Blood pressure (systolic, diastolic and mean), heart rate, central venous pressure (CVP) and arterial saturation were monitored using a Marquette patient monitoring system (Solar 8000 Patient Monitor, Marquette Medical Systems, Milwaukee, USA). Parameters were recorded at baseline, at the onset of CPB, and 20, 40, and 60 min of CPB duration, at the end of CPB, and at closure of the chest.

2.7. Statistical analysis

Results are expressed as means ± standard deviation (SD) unless otherwise stated. Changes in [O$_2$Hb], [HHb], [Cyt-Ox], (TOI) and (THI) with time were analyzed using a repeated measures analysis of variance design with post-hoc Tukey testing using SAS 8.1, SAS Inc., Cary NC. A difference of more than 6.8 μmol/l between deoxy and oxyhaemoglobin was regarded as suggestive of cerebral ischemia [14]. A P-value of less than 0.05 was considered a statistically significant difference. All analyses were performed using SAS release 8.1 (SAS Institute, Cary, NC, USA).

3. Results

Patient demographic data are shown in Table 1. The study included 19 consecutive patients (15 male, mean age 60.9 ± 11.1 years) undergoing first time CABG. The mean number of grafts performed was 2.6 ± 0.8. The mean duration of NIRS measurement was 221 ± 27 min. All patients completed the study. There were no in-hospital death, neurological deficits or myocardial infarction. Post-operative complications included three (15.8%) atrial fibrillation, and two (10.5%) chest infections. Mean post-operative hospital stay was 5.8 ± 1.1 days. At a mean follow-up of 28 months (range from 14 to 35 months), all patients remain symptoms-free, with no late neurological complications. Haemodynamic parameters are reported in Table 2.

3.1. NIRS monitoring

Typical changes during surgery are shown in Fig. 1. Changes in haemodynamics and cortical cerebral oxygenation are reported in Table 2. Compared to baseline, during the entire CPB duration there was a marked reduction in [O$_2$Hb] and CBV as expressed by THI. The reduction begun 1 min after initiation of CPB and persisted throughout the entire operation with the worse levels reaching 40–60 min after onset of CPB. Particularly, [O$_2$Hb] declined from a baseline value of ~3.03 ± 5.1 to ~9.25 ± 7.20 μmol/l and to ~8.99 ± 7.49 μmol/l at 40 and 60 min, respectively (both P < 0.001), while CBV showed a similar 24% reduction at 40 and 60 min (both P < 0.0001). The deterioration in [O$_2$Hb] was recovered by the end of surgery, while the changes in CBV persisted. Compared to baseline, and throughout the study period there was also a reduction in [HHb], [Cyt-Ox], and TOI, however, these did not reach statistical significance.

4. Discussion

Over the last decade, NIRS technology has been used routinely by vascular surgeons during carotid endarterectomy to monitor cerebral cortical oxygenation [8]. More recently few cardiac surgery institutions have also shown interest in this technology due to its potential of allowing continuous monitoring of cortical cerebral oxygenation throughout surgery [15–19].

Our study has two main findings.

(i) Within 1 min since the onset of CPB, there were marked deteriorations of [O$_2$Hb], and CBV, with the worst level at 40 min since the onset of CPB.

(ii) At the end of the surgery [O$_2$Hb] fully recovered while the observed changes in CBV persisted.

The findings of the present study might be due to a number of factors including inflammatory activation, hemodilution, loss of pulsatile flow, cerebral hypoperfusion due to transient impairment of the auto-regulatory mechanisms of cerebral blood flow (CBF), and embolic phenomena. Inflammatory activation has been widely reported as a main detrimental effect of CPB [20].

Like others [5,15], we have found that the onset of CPB was associated with a significant reduction in [O$_2$Hb]. This could be due to the blood-free prime-induced hemodilution. These changes exceed previously established thresholds for
Table 2: Changes in hemodynamics and cerebral cortical oxygenation during CPB

<table>
<thead>
<tr>
<th>Time</th>
<th>Heart rate (beats/min)</th>
<th>MAP (mmHg)</th>
<th>CVP (mmHg)</th>
<th>Temperature (°C)</th>
<th>[Hb] (mmol/l)</th>
<th>[Cyt-Ox] (mmol/l)</th>
<th>[HHb] (mmol/l)</th>
<th>THI (%)</th>
<th>TOI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>77 ± 8.9</td>
<td>60 ± 12.0</td>
<td>4.2 ± 2.9</td>
<td>35.5 ± 0.3</td>
<td>0.95 ± 0.2</td>
<td>0.168 ± 0.05</td>
<td>0.62 ± 0.06</td>
<td>100</td>
<td>70.21</td>
</tr>
<tr>
<td>20 min</td>
<td>8.5 ± 0.5</td>
<td>4.2 ± 2.9</td>
<td>3.2 ± 1.7</td>
<td>35.5 ± 0.3</td>
<td>0.95 ± 0.2</td>
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<td>4.2 ± 2.9</td>
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<td>Off-CPB</td>
<td>9.5 ± 0.5</td>
<td>4.2 ± 2.9</td>
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<td>End of surgery</td>
<td>8.5 ± 0.5</td>
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Values are mean ± SD. *P < 0.05; **P < 0.01; ***P < 0.001 (compared with values at onset of bypass). Cyt-Ox, cytochrome oxidase; HHb, deoxyhaemoglobin; THI, normalized tissue haemoglobin index; O2Hb, oxyhaemoglobin; TOI, tissue oxygenation index.

The persistence of deranged levels of THI by the end of surgery could be due to changes in CBF. Whilst CBF is autoregulated before and after CPB, several factors appear to affect CBF during bypass including hemoglobin, temperature, pH, and PaCO2 [18]. Nollert et al. found these factors to determine at least 85% of all changes in cerebral oxygenation during moderate hypothermia (26 °C) [18]. Our finding suggest that after normothermic CPB, the re-establishment of the autoregulatory mechanisms of CBF might take time, affecting the full recovery of THI by the end of surgery.

A further explanation of our results could be the normothermia, a factor that would increase oxygen demand [5]. Our results are similar to those of Kadoi and colleagues [5] who reported a 5–8% reduction in regional cerebral oxygen saturation throughout normothermic (>35°) CPB, whereas values were stable during hypothermia (30°C). However, in the same study, they also used jugular venous oxygen saturation monitoring (SjvO2) which revealed that neither the cerebral desaturation time (duration when SjvO2 was less than 50%) nor the ratio of the cerebral desaturation time to the total CPB time ratio differ significantly between the two groups. The fact remains that the evidence in the literature on the effects of CPB temperature on neurological function remains controversial. Regragui and colleagues reported a worse neurological outcome during normothermic (37°C) bypass compared to moderately hypothermic (32°C) perfusion, while further cooling to 28 °C conferred additional benefits in terms of cognitive function [22]. Similar results were reported by Martin et al. [23]. However, others have reported a favourable outcome following normothermic CPB. Objective cognitive P300 auditory-evoked potential measurements have indicated cognitive impairment following hypothermic (32°C) bypass to be more pronounced than during normothermic (37°C) bypass [24]. Finally, McLean and colleagues were unable to cerebral ischemia [21], albeit thresholds derived without the confounding factor of acute hemodilution. However, if intracellular respiration is not disturbed and the oxygen supply to the brain can meet its metabolic demands, the redox state of cytochrome oxidase would be expected to be unchanged. This was indeed the case in our study where the observed changes in [Cyt-Ox] were minimal and did not reach statistical significance, indicating an adequate supply of oxygen at mitochondrial level. Of interest is that at the end of surgery, there was a full recover of [O2Hb] but only a partial recover of CBV. Interestingly, this recovery occurred following active re-warming to 37 °C, a factor that would increase oxygen demand, and previously has been associated with marked reduction in cytochrome oxidase redox state in patients who developed cerebral deficits [16]. However, this is also the period during which the heart restarts to eject and partial pulsatile flow is re-established. This partial recovery with the return of a more physiological flow profile has been observed before [17].

Note: Changes in haemodynamics and cerebral cortical oxygenation during CPB

Baseline Onset of CPB 20 min 40 min 60 min Off-CPB End of surgery

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demonstrate neuroprotective effects of moderate hypothermia as compared with normothermic CPB [25].

Despite the occurrence of marked cortical cerebral oxygenation changes, none of our patients suffered any major neurological events during the in-hospital stay. We did not perform assessment of subtle cerebral dysfunction, like assessment of cognitive function, because of the absence of unanimous consensus on the available methodology. However, we believe that this remains a major limitation of our study.

We have recently reported our findings on the use of NIRS during off-pump coronary surgery [20]. This study showed that grafting of the anterior wall on the beating heart is responsible for changes in cerebral cortical oxygenation, which persisted early after returning the heart to its natural position. Grafting of the lateral and posterior wall result in transient reversible changes. The study aimed to ascertain the impact of positioning and stabilisation of the heart to graft the three main coronaries. We concluded that Trendelenburg positioning and right lateral tilting of the operating table, performed during grafting of lateral and posterior wall, might have had a protective role in preventing cerebral cortical ischemia. A comparison of these findings with the present study we believe would be questionable due to the impossibility of identifying similar intraoperative times of observation. The only possible comparable time being the end of surgery, at closure of chest, but this recording was only carried out in the present study, while the NIRS monitoring in the off-pump study stopped 5 min following completion of the last anastomosis. Furthermore, it has been difficult to carry out a validating comparison with what is published in the literature due to potentially confounding variables arising from differences in study design and methodology used.

Finally, we think that the observations of the present study are only valid for elective patients undergoing coronary surgery, for whom a relatively short CPB duration was required. Therefore, they cannot be extended to high-risk patients with previous history of cerebro-vascular accident or to patients requiring a longer CPB time.

In conclusion, this study shows that conventional CABG is responsible for changes in [O2Hb], and CBV, which reach the worst level at 40–60 min following initiation of CPB. The changes in [O2Hb] are reversible whereas the reduction of CBV persists up to the end of surgery. Further studies are required to assess the clinical importance of these observations.

Acknowledgements

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References


