Near-infrared monitoring of myocardial oxygenation during intermittent warm blood cardioplegia

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Abstract

Objective: This study was performed to examine the ability of near-infrared spectroscopy to monitor tissue oxygenation in the cardioplegically arrested heart and to assess myocardial oxygen metabolism during intermittent warm blood cardioplegia.

Methods: Using a three-wavelength near-infrared spectroscopy, we continuously measured myocardial tissue oxygen saturation and the tissue hemoglobin concentration during intermittent warm blood cardioplegia. Under normothermic cardiopulmonary bypass, 20 dogs received three 5-min periods of antegrade warm blood cardioplegia, interrupted by three 10-min episodes of ischemia in group 1 \( n = 7 \), three 15-min episodes of ischemia in group 2 \( n = 6 \), or three 20-min episodes of ischemia in group 3 \( n = 7 \).

Results: Myocardial oxygen saturation during beating and ventricular fibrillation was 80 ± 1 and 59 ± 1%, respectively. Myocardial oxygen saturation rapidly increased to 82 ± 1% at blood cardioplegic infusion and decreased to 58 ± 1% 3 min after cardioplegic interruption. The time required to reach the peak oxygen saturation level decreased significantly at the second and third infusions compared to the first infusion in group 1, whereas the time increased significantly at the third infusion in groups 2 and 3. The slower rate of increase in oxygen saturation suggested reduced coronary vasodilator reserve due to microvascular abnormalities. Reperfusion ventricular fibrillation occurred in none of group 1, one of group 2, and three of group 3.

Conclusions: Near-infrared spectroscopy is a useful method of continuously monitoring myocardial oxygenation and ischemia during warm heart surgery. Episodes of ischemia longer than 10 min during warm blood cardioplegia resulted in less-than-optimal myocardial preservation and should be avoided. © 1997 Elsevier Science B.V.

Keywords: Cardioplegia; Myocardial oxygenation; Myocardial ischemia; Near-infrared spectroscopy

1. Introduction

Continuous warm blood cardioplegia has been introduced as an alternative technique for achieving myocardial protection, avoiding myocardial ischemia and the subsequent reperfusion injury, and eliminating the adverse effects of hypothermia [12,22]. Intermittent warm blood cardioplegia has recently been proposed as an effective method of achieving myocardial protection and a better surgical field [1,9,15,20]. Although the effects of regional warm ischemia on the beating heart have been investigated [11,21], the effects of global ischemia on myocardial oxygen metabolism during warm blood cardioplegic arrest have not been fully clarified. To avoid myocardial damage due to warm ischemia, the monitoring of changes in myocardial oxygenation during cardioplegic arrest would be beneficial.

Near-infrared (NIR) light passes through biological tissue with relative ease and is absorbed significantly by oxygenated and deoxygenated tissue hemoglobin [5]. These molecular species have distinctly different absorption spectra in the NIR region, and therefore changes in the tissue concentration of each molecule can be calculated based on changes in absorption at various wavelengths [3,5,14,18,24]. NIR spectroscopy
provides a new technology capable of the continuous monitoring of changes in tissue oxygenation and has been used experimentally in the beating heart [18, 19]. A three-wavelength NIR spectroscopy has recently been developed to quantify tissue oxygen saturation and the tissue hemoglobin concentration [17, 26]. This apparatus allows the continuous and nondestructive monitoring of changes in tissue oxygenation.

The present study was undertaken to examine the ability of three-wavelength NIR spectroscopy to monitor myocardial tissue oxygenation in the cardiopically arrested heart and to investigate myocardial oxygen metabolism during intermittent warm blood cardioplegia in the canine heart.

2. Material and methods

Twenty adult mongrel dogs weighing 10–15 kg were studied. The animals were anesthetized with an intramuscular administration of ketamine hydrochloride (20 mg/kg) and intravenous sodium pentobarbital (30 mg/kg), and were mechanically ventilated with a volume respirator. Dogs received humane care in compliance with the ‘Principles of Laboratory Animal Care’ (National Society for Medical Research) and the ‘Guide for the Care and Use of Laboratory Animals’ (National Academy of Science, NIH publication 85-23, revised 1985). Cardiopulmonary bypass was equipped with a membrane oxygenator and a centrifugal pump. During cardiopulmonary bypass, the flow rate was kept at 80 ml/kg, the mean arterial pressure was kept at 60–70 mmHg, and the systemic temperature was maintained at 37°C. Blood cardioplegia consisted of blood mixed 4:1 with either high- or low-potassium cardioplegic solution. One liter of cardioplegic solution contained 1.2 ml of 7% sodium bicarbonate for a pH of 7.5. The blood cardioplegia had a hematocrit of 20% and was warmed at 37°C. Blood cardioplegia consisted of blood mixed 4:1 with either high- or low-potassium cardioplegic solution. One liter of cardioplegic solution contained 1.2 ml of 7% sodium bicarbonate for a pH of 7.5. The blood cardioplegia had a hematocrit of 20% and was warmed at 37°C.

After the ascending aorta was cross-clamped, 500 ml of high-potassium blood cardioplegia solution was infused antegradely in 5 min through an aortic root cannula using a cardioplegia infusion set (BCD Advanced System, Shiley, Irvine, USA). Thereafter, 500 ml of low-potassium blood cardioplegia was used for repeat infusions. Twenty dogs received three 5-min periods of warm blood cardioplegia, interrupted by three 10-min episodes of ischemia in group 1 (n = 7), three 15-min episodes of ischemia in group 2 (n = 6) or three 20-min episodes of ischemia in group 3 (n = 7) (Fig. 1). Then the aortic cross-clamp was removed and the heart resumed beating or was defibrillated, if necessary. All animals were able to be weaned from cardiopulmonary bypass without inotropic agents after 30 min of reperfusion.

Myocardial tissue oxygenation and the tissue hemoglobin concentration were measured by three-wavelength NIR spectroscopy (PSA-IIIN, Biomedical Science, Kanazawa, Japan). The principle of the technique is as follows. The iron-porphyrin moieties of oxygenated and deoxygenated hemoglobin have absorption peaks at NIR wavelengths (700–1000 nm) that readily penetrate intact tissue [5]. The relationship between the concentration of a chromophore and the intensity of light transmitted through a solution are expressed, in accordance with the Beer-Lambert law, as shown below.

\[
- \log(I/I_o) = A
\]

\[
A = \varepsilon \cdot C \cdot D
\]

where \( I \) is the intensity of the transmitted light at a given wavelength, \( I_o \) is the intensity of incident light, \( A \) is light absorption, \( C \) is the concentration of a solute, \( \varepsilon \) is the extinction coefficient of the solute, and \( D \) is the pathlength that light is transmitted through the solution. When the light is transmitted in a homogeneous tissue, this law is valid [3,14,17–19,24]. NIR light is diffusely scattered by the tissue. It is hypothesized that the heart is nearly homogeneous and the intensity of reflected light obtained from the heart surface is almost the same as that of transmitted light in the same distance. Since oxygenated hemoglobin and oxygenated myoglobin each have essentially identical NIR absorption spectra, hemoglobin plus myoglobin (Hb) are added together. When an incident light of a specified wavelength is absorbed by Hb in myocardial tissue, Eq. (1a) can be expressed as follows:

\[
A = \varepsilon_a \cdot C_a \cdot d + \varepsilon_b \cdot C_b \cdot d + A_t
\]

where \( \varepsilon_a \) and \( C_a \) are the extinction coefficient and the concentration of oxygenated Hb, \( \varepsilon_b \) and \( C_b \) are the extinction coefficient and the concentration of deoxygenated Hb, respectively, \( d \) is the mean optical pathlength in the tissue, and \( A_t \) is the light attenuation of bloodless tissue. Since the light attenuation of bloodless...
tissue is relatively independent of wavelength in the NIR range, differences among the light attenuation at three wavelengths ($\lambda_1$, $\lambda_2$ and $\lambda_3$) can be neglected. Since the extinction coefficients of oxygenated and deoxygenated Hb at each wavelength are known values [18], and light absorption at wavelengths $\lambda_1$, $\lambda_2$ and $\lambda_3$ can be measured by spectroscopy, $C_{a\cdot d}$ and $C_{b\cdot d}$ can be calculated. $C_{a\cdot d}$ plus $C_{b\cdot d}$ corresponds to the total Hb concentration, and $C_{a\cdot d}$ divided by $C_{a\cdot d}$ plus $C_{b\cdot d}$ corresponds to tissue oxygen saturation (SO$_2$). Since the total amount of myoglobin does not change significantly during brief ischemia and reperfusion, adding the signals of oxygenated Hb and deoxygenated Hb cancels out changes in myoglobin saturation, allowing measurement of the relative changes in the tissue hemoglobin concentration [5,18]. Since most hemoglobin is located in capacitant vessels, changes in tissue SO$_2$ are most sensitive to changes in the capillary and venous oxygen content.

The NIR spectroscopy probe (PSP-15R, Biomedical Science), specially designed for the heart, was attached to the anterior surface of the right ventricle, avoiding epicardial fat. This probe contains three light-emitting diodes as light sources and three pairs of silicone photodiodes to detect the intensity of reflected light. The light-emitting diodes delivered NIR light at the three wavelengths ($\lambda_1 = 700$ nm, $\lambda_2 = 730$ nm, $\lambda_3 = 770$ nm), eliminating the spectral interferences by cytochrome aa$_3$. The distance between the light-emitting diode and the photodiode and the distance between the paired photodiodes were each set at 2.5 mm. Thus, optical information from a myocardial tissue depth of 2.5–5.0 mm was obtained.

Cumulative data are expressed as the mean ± standard error of the mean. Statistical analysis was performed with Student’s t-test and analysis of variance and Scheffe’s F-test to detect significant (P < 0.05) differences between measured variables.

3. Results

The serial changes in myocardial tissue SO$_2$ and the Hb concentration in group 1 are shown in Fig. 2. Myocardial SO$_2$ and Hb during induced ventricular fibrillation were 59 ± 1% and 473 ± 12 mm·g/l, respectively. Increases in myocardial SO$_2$ and Hb began 20 s after the induction of cardioplegia, achieving electromechanical arrest, and they coincided with cardioplegic administration at subsequent cardioplegic infusions. Myocardial SO$_2$ and Hb increased rapidly and reached the same plateau level (82 ± 1%, 661 ± 22 mm·g/l) at each blood cardioplegic infusion. The decreases in myocardial SO$_2$ and Hb coincided well with each interruption of cardioplegia. They dropped gradually and reached the same levels (58 ± 1%, 446 ± 11 mm·g/l, respectively) within 3 min of each cardioplegic interruption. After aortic clamp release, the myocardial SO$_2$ and Hb returned to 80 ± 1% and 641 ± 21 mm·g/l, respectively, and the hearts beat spontaneously.

The serial changes in myocardial SO$_2$ and Hb in groups 2 and 3 also coincided with the infusion and interruption of cardioplegia (Fig. 3). Although myocardial SO$_2$ increased rapidly in group 1 at each cardioplegic infusion, it increased slowly at the second and third cardioplegic infusions in groups 2 and 3. The time required to reach the peak SO$_2$ level at the second and third cardioplegic infusions was significantly less than that required at the first cardioplegic infusion in group 1, but in groups 2 and 3 the time increased at the second and third cardioplegic infusions (Table 1). The time required to reach the peak Hb level correlated well with the time to the peak SO$_2$ level. The decrease in myocardial SO$_2$ reached a plateau in each of the three groups within 3 min after discontinuing cardioplegia.

Electromechanical activity occurred spontaneously in two dogs of group 3 but in none of groups 1 or 2 during interruption of cardioplegia. Reperfusion ventricular fibrillation requiring defibrillation occurred after aortic clamp release, in one dog of group 2 and three of group 3, but in none of group 1.

4. Discussion

This study reports the first application of NIR spectroscopy in cardioplegically arrested hearts. The results

Fig. 3. Changes in myocardial tissue oxygen saturation (SO₂) during the first (A), second (B) and third (C) infusions and interruptions of warm blood cardioplegic solution. VF, ventricular fibrillation; XCL, aortic cross-clamp; WBC, warm blood cardioplegia.

demonstrate that myocardial tissue SO₂ and the Hb concentration were sensitive to the changes caused by infusion and interruption of warm blood cardioplegic solution, and that NIR monitoring is a useful method of assessing myocardial tissue oxygen metabolism in warm heart surgery. Tissue pH is a reliable metabolic indicator of the magnitude of ischemic injury [6], and nicotinamide adenine dinucleotide (reduced form) fluorescence is sensitive to changes in myocardial metabolism [4]. Nuclear magnetic resonance spectroscopy has been employed for studying the changes in myocardial energy metabolites [23], but at present this is not practical for use in the operating room. For the safe practice of using warm blood cardioplegia in a continuous or intermittent fashion, the monitoring of cardioplegic delivery and efficacy is needed in the clinical setting. It is difficult to predict the time point beyond which myocardial metabolism shifts towards anaerobic patterns in a given patient with coronary artery disease or myocardial hypertrophy. NIR spectroscopy is a sensitive and valuable method of monitoring tissue oxygen metabolism. NIR spectroscopy for monitoring tissue oxygenation status has been reported in the brain [14,23], heart [18,19], skeletal muscle [3] and kidney [24]. In the present study, the use of three-wavelength NIR allowed a quantitative measure of oxygenated and deoxygenated Hb, and therefore provided a quantification of tissue SO₂ and the Hb concentration. NIR monitoring of the heart may be beneficial in detecting inappropriate cardioplegic delivery due to coronary artery stenosis or aortic insufficiency during antegrade infusion or the dislodging of a coronary sinus catheter during retrograde infusion.

The efficacy of warm blood cardioplegia has recently been investigated, but the number of published results of normothermic ischemia during cardioplegic interruption is limited [8–10,13]. The present study showed that NIR monitoring depicted myocardial oxygenation status during cardioplegic arrest in real time. Myocardial SO₂ dropped gradually and reached a stable plateau within 3 min of cardioplegic interruption. Landymore et al. [9] interrupted antegrade warm blood cardioplegia for single intervals of 1–10 min and found that oxygen debt occurred after 3.5 min of normothermic ischemia, which supports our result. In the present study, in contrast to the rapid increase in myocardial SO₂ and Hb at the second and third cardioplegic infusions in group 1, the rate of increase in myocardial SO₂ and Hb during subsequent cardioplegic infusions was slowed down in groups 2 and 3. These results suggested a reduced coronary vasodilation reserve, possibly due to ischemic/reperfusion damage of coronary endothelial cells [2,7]. Vaughan et al. also observed that the severity of ischemic injury was accompanied by a slower rate of increase in oxygenated and total hemoglobin during early reperfusion of the ischemic kidney [24]. The results of the present study also indicated that the total oxygen supply of the 5-min cardioplegic infusion after 15- and 20-min interruptions was less than that after the 10-min interruption. In addition, the electrocardiographic results showed that 15- and 20-min warm is-

Table 1
Time to the peak oxygen saturation level during cardioplegic infusion

<table>
<thead>
<tr>
<th>Groups</th>
<th>Infusion</th>
<th>First (s)</th>
<th>Second (s)</th>
<th>Third (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (n = 7)</td>
<td>66 ± 5</td>
<td>48 ± 3*</td>
<td>50 ± 2*</td>
<td></td>
</tr>
<tr>
<td>Group 2 (n = 6)</td>
<td>63 ± 5</td>
<td>73 ± 11</td>
<td>118 ± 13**</td>
<td></td>
</tr>
<tr>
<td>Group 3 (n = 7)</td>
<td>60 ± 5</td>
<td>88 ± 12</td>
<td>119 ± 13**</td>
<td></td>
</tr>
</tbody>
</table>

*P < 0.05 and **P < 0.01, compared to the time during the first cardioplegic infusion.
chemia in the cardioplegically arrested heart resulted in an increased incidence of reperfusion ventricular fibrillation after aortic clamp release. The slower rate of increase in myocardial SO2 and the Hb concentration during cardioplegic infusion may be a warning of less-than-optimal myocardial preservation. This should be avoided, but when this is observed it seems advisable to increase the volume of subsequent cardioplegic infusions and shorten the duration of cardioplegic interruption.

The safe duration of warm ischemia during intermittent warm blood cardioplegia is controversial. Landymore et al. [10] assessed systolic and diastolic function after 5, 10, and 15 min of ischemia during antegrade warm blood cardioplegia and 10 min of reperfusion, and found that systolic and diastolic functions were preserved after 10 min of warm ischemia but depressed after 15 min of warm ischemia. Misare et al. [12] reported that three 10- or 15-min interruptions of warm blood cardioplegia resulted in inadequate myocardial protection with depressed left ventricular contractile function [16]. Tian et al. [23] reported that six 10-min interruptions and six 5-min restorations of warm blood cardioplegia caused only mild and reversible changes in myocardial energy metabolites and intracellular pH, and that these changes were not cumulative. Lichtenstein et al. [13] reported that repeated interruption of warm blood cardioplegia was unlikely to cause adverse clinical results if single interruptions were less than 13 min, and they suggested that the longest single ischemic interval is more important than the cumulative ischemic time. Our present results suggested that ischemia of longer than 10 min during intermittent warm blood cardioplegia caused cumulative ischemic insult to the myocardium.

The limitations of NIR spectroscopy include light attenuation due to scattering events in tissue and reflection phenomena at tissue layer boundaries [14]. Coronary artery disease may create an inhomogeneity of the myocardium. As these optical events become predictable, the further refinement of NIR spectroscopy will be achieved. Epicardial fat obviously changes the NIR absorption and should therefore be avoided. Another limitation of NIR spectroscopy is that the optical pathlength in the myocardium is not determined, and the Hb concentration must therefore be expressed, multiplying by the pathlength factor. Assuming that the optical pathlength in the dog heart is the same as that of the rat brain, which is 4.34 times the interoptode distance [25], the Hb concentration in the cardioplegically arrested ischemic heart is calculated to be approximately 40 g/l.

NIR spectroscopy is a promising new method of monitoring myocardial tissue oxygenation and the hemoglobin concentration in the cardioplegically arrested heart. NIR monitoring of the heart may be beneficial during the clinical use of warm blood cardioplegia.

References


