Effect of limb cooling on peripheral and global oxygen consumption in neonates

I A-A Hassan, Y A Wickramasinghe, S A Spencer

Aim: To evaluate peripheral oxygen consumption (VO₂) measurements using near infrared spectroscopy (NIRS) with arterial occlusion in healthy term neonates by studying the effect of limb cooling on peripheral and global VO₂.

Subjects and methods: Twenty two healthy term neonates were studied. Peripheral VO₂ was measured by NIRS using arterial occlusion and measurement of the oxyhaemoglobin (HbO₂) decrement slope. Global VO₂ was measured by open circuit calorimetry. Global and peripheral VO₂ was measured in each neonate before and after limb cooling.

Results: In 10 neonates, a fall in forearm temperature of 2.2°C (mild cooling) decreased forearm VO₂ by 19.6% (p < 0.01). Global VO₂ did not change. In 12 neonates, a fall in forearm temperature of 4°C (moderate cooling) decreased forearm VO₂ by 34.7% (p < 0.01). Global VO₂ increased by 17.6% (p < 0.05).

Conclusions: The NIRS arterial occlusion method is able to measure changes in peripheral VO₂ induced by limb cooling. The changes are more pronounced with moderate limb cooling when a concomitant rise in global VO₂ is observed. Change in peripheral temperature must be taken into consideration in the interpretation of peripheral VO₂ measurements in neonates.

Methods

Subjects

Healthy term infants during the first few days of life were recruited on the postnatal wards of North Staffordshire Hospital. None were receiving medication or supplemental oxygen. A pragmatic approach was taken to sample size, with this set as a minimum of 10 successful studies, as no data were available to perform statistical power calculations.

Consent

The study and the information leaflet given to parents were approved by North Staffordshire research ethics committee. Parental written informed consent was obtained before the study.

Measurements

Peripheral VO₂

Peripheral VO₂ was measured using NIRS and arterial occlusion as previously described and illustrated. In brief, NIRS can be used to monitor changes in concentrations of oxygenated haemoglobin (HbO₂) and total haemoglobin (HbT). When arterial occlusion is performed, there is an abrupt decrease in HbO₂ which is entirely due to oxygen utilisation, provided that no blood enters or leaves the limb. Thus peripheral VO₂ can be calculated by measurement of the slope of HbO₂ decrement provided that HbT does not change. Not every occlusion is satisfactory; movement in

Abbreviations: VO₂, oxygen consumption; NIRS, near infrared spectroscopy; HbO₂, oxygenated haemoglobin; HbT, total haemoglobin; CI, confidence interval
particular may cause problems. Therefore in our previous work, criteria were defined for accepting an occlusion as suitable for further analysis. Only occlusions meeting these predefined criteria\(^{10}\) have been included in the results. For an occlusion to pass, there has to be an abrupt decrease in HbO\(_2\) and increase in Hb immediately after the occlusion. The HbT trace also has to remain stable, with a maximum permitted change of < 10% of the change in HbO\(_2\). The coefficient of variation for the measurement V\(_O_2\) is 6.6%.

NIRS units

The basic uncorrected units for HbO\(_2\) are mM.cm. V\(_O_2\) is calculated using the rate of change of HbO\(_2\) signal during arterial occlusion and is expressed as mM M\(_O_2\).cm/min. By taking into account the molecular ratio of Hb to O\(_2\), which is 1:4, V\(_O_2\) can be expressed as mM M\(_O_2\).cm/min. These units have been used for the interpretation of our results. However, in this paper we use mM.cm to show that the value has not been divided by the path length correction factor, which is assumed to be a constant 3.59. For a distance of 3 cm between probes, the conversion factor is 100/(3.59 \times 3), which is 9.3. Thus µmol O\(_2\)/100 ml/min = 9.3 \times mM M\(_O_2\).cm/min. (The convention in NIRS is to use mM.cm to show that the value has not been divided by the path length correction factor.)

Global VO\(_2\)

This was measured using open circuit calorimetry (Morgan Ltd, Gillingham, Kent, UK).\(^{11}\) The technique was modified to use a facemask rather than an incubator for gas collection.\(^{12}\)

Briefly described, the infant’s expired air was continuously drawn through a face mask (cushion flex infant mask; Intra-surgical, Wokingham, Berkshire, UK) held in front of the infant’s mouth and at a constant flow rate of 2–3 litres/min. Room air was also continuously sampled and the oxygen concentration of both the mixed expired air and room air was measured continuously by open circuit calorimetry.

Global VO\(_2\) was calculated using the formula:

\[
V_{O_2} = Q \left[ F_{IO_2} - F_{EO_2} \right]
\]

where Q = flow through the system, F\(_{IO_2}\) = fractional concentration of oxygen in inspired air (room air), and F\(_{EO_2}\) = fractional concentration of oxygen in expired air (infant’s expired air). Global VO\(_2\) results were expressed as ml O\(_2\)/kg/min.

Skin temperature

Forearm and abdominal skin temperatures were measured with a digital thermometer (Libra Medical), which had previously been calibrated against a mercury in glass thermometer. The skin probe was placed on the dorsal aspect of the forearm opposite the NIRS optode holders. A second temperature probe placed on the upper abdomen continuously measured abdominal skin temperature.

Protocol

The same researcher performed measurements on all neonates. They were all carried out at the same time of day (11 am), 1–1.5 hours after a feed and in the same environment (postnatal ward). The neonate was placed fully clothed in his/her cot. Clothing was then partially removed for the purpose of placing temperature probes and NIRS probes in position, and to place an appropriately sized neonatal blood pressure cuff around the upper arm. The distance between the transmitting and receiving optical probes was 3 cm. When the baby had settled, the measurements were started.

Initial measurements of global VO\(_2\), forearm and abdominal skin temperatures, and up to three successful measurements of forearm VO\(_2\) were performed on each neonate. In 10 neonates, the forearm was then cooled by exposure of the forearm to room air for 15–20 minutes (mild limb cooling). In the other 12 neonates, the forearm was cooled by the application of cotton wool soaked in tepid water (moderate limb cooling). All the measurements were then repeated up to three times. The distance between the transmitting and receiving optical probes was 3 cm.

Data analysis

The results of global and peripheral VO\(_2\) and skin temperatures for all subjects are presented as means with 95% confidence intervals (95% CI). Where more than one successful measurement of peripheral VO\(_2\) was obtained in a subject, before or after the intervention, then the mean value was used. Paired \(t\) tests (before and after) were used to determine the significance of observed changes. The level of significance was set at 0.05.

RESULTS

Twenty two neonates were included and completed the whole study.

Mild limb cooling

Subjects

Table 1 gives the details of the 10 neonates studied.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Details of neonates studied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number in study group</td>
<td>Mild cooling</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>38 (3)</td>
</tr>
<tr>
<td>Mode of delivery</td>
<td>CS, 3, VD 7</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>3.5 (2.7–4.0)</td>
</tr>
<tr>
<td>Postnatal age (days)</td>
<td>2 (1–6)</td>
</tr>
<tr>
<td>F:M</td>
<td>6:4</td>
</tr>
</tbody>
</table>

Values are mean (SD) or median (range).

CS, Caesarean section; VD, vaginal delivery; F, female; M, male.

Intra-surgical, CS, Caesarean section; VD, vaginal delivery; F, female; M, male.

CS, Caesarean section; VD, vaginal delivery; F, female; M, male.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Results of mild limb cooling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forearm skin temperature (°C)</td>
<td>Before</td>
</tr>
<tr>
<td>95% CI</td>
<td>33</td>
</tr>
<tr>
<td>31.4 to 34.6</td>
<td>29.3 to 32.3</td>
</tr>
<tr>
<td>Abdominal skin temperature (°C)</td>
<td>Before</td>
</tr>
<tr>
<td>95% CI</td>
<td>36.8</td>
</tr>
<tr>
<td>36.2 to 37.4</td>
<td>36.6 to 37.4</td>
</tr>
<tr>
<td>Peripheral VO(_2), [mM O(_2).cm/min]</td>
<td>Before</td>
</tr>
<tr>
<td>95% CI</td>
<td>1.38</td>
</tr>
<tr>
<td>1.10 to 1.66</td>
<td>0.87 to 1.35</td>
</tr>
<tr>
<td>Global VO(_2), [ml/kg/min]</td>
<td>Before</td>
</tr>
<tr>
<td>95% CI</td>
<td>9.95</td>
</tr>
<tr>
<td>8.91 to 10.99</td>
<td>7.82 to 11.9</td>
</tr>
</tbody>
</table>

Results are means with 95% confidence intervals (CI).
Temperature and \( \text{VO}_2 \)
The mean (SD) room temperature was 28.5 (1.7)\(^\circ\)C throughout the studies. Table 2 shows the results of mild limb cooling; they can be summarised as follows.
- Mild limb cooling led to a mean fall in peripheral skin temperature of just over 2\(^\circ\)C.
- Abdominal skin temperature did not change significantly.
- There was a highly significant fall in peripheral \( \text{VO}_2 \).
- There was no significant change in global \( \text{VO}_2 \).

### Moderate limb cooling

#### Subjects
Table 1 gives details of the 12 neonates studied.

#### Temperature and \( \text{VO}_2 \)
The mean room temperature was 28.5 (1.7)\(^\circ\)C throughout the studies. Table 3 gives the results of mild limb cooling; they can be summarised as follows.
- Moderate limb cooling led to a mean fall in peripheral skin temperature of 4\(^\circ\)C.
- Abdominal skin temperature did not change significantly.
- There was a highly significant fall in peripheral \( \text{VO}_2 \).
- There was a significant increase in global \( \text{VO}_2 \).

### DISCUSSION
These studies show that, subject to the selection criteria stated in the measurement section, arterial occlusion and NIRS detects the expected fall in oxygen uptake resulting from limb cooling. The effect is more pronounced when the decrease in limb temperature is greater. Mild limb cooling does not appear to represent a sufficient cold stress to significantly increase global metabolic rate. This is in line with previous studies in which a fall of 1.5\(^\circ\)C was found to cause sleep disturbance but no increase in global \( \text{VO}_2 \). \(^{11}\)

Mild limb cooling on the other hand did elicit a global response, even though abdominal skin temperature was not significantly affected. This response may have been elicited as a result of sympathetic stimulation from the application of tepid water, which is not only a cold stimulus but may also cause mild discomfort. Alternatively, the heat loss from the limb may have been sufficient to cause the neonate to move out of the thermal neutral zone, so that an increase in global metabolic rate was required to maintain body temperature. The rise in global metabolic rate did not counteract the effect of peripheral cooling; further studies are required to determine whether peripheral \( \text{VO}_2 \) measurement is sensitive to change in global metabolic rate.

In this study, data are presented using the same units as in our previous study. No assumptions on differential path length factor are required, therefore comparisons between babies are valid. Others have assumed that differential path length is near enough a constant to allow comparisons between babies using a venous occlusion technique. \(^{12}\) Our own work comparing venous and arterial methods suggests a poor correlation, with values about 50% higher using the venous technique. \(^{12}\) In normotensive sick preterm infants, the mean \( \text{VO}_2 \) has been reported as 23.9 \( \mu\text{mol} / 100 \text{ml} / \text{min} \) using the venous technique. \(^{13}\) The mean value obtained in healthy term infants before limb cooling translates to 12.8 and 9.4 \( \mu\text{mol} / 100 \text{ml} / \text{min} \) for the mild and moderate limb cooling studies respectively. Clearly, healthy term and sick preterm babies are not comparable. Unfortunately comparable data on healthy term infants are not available, apart from our previous validation work. \(^{13}\) In this study the results for arterial occlusion translates to 10.4 \( \mu\text{mol} / 100 \text{ml} / \text{min} \) and for venous occlusion translates to 14.8 \( \mu\text{mol} / 100 \text{ml} / \text{min} \).

The findings of this study have two important implications. Firstly, they lend support to the hypothesis that changes in peripheral \( \text{VO}_2 \) can be assessed using this method. Unfortunately there is no ideal non-invasive method available, with which NIRS occlusion techniques can be validated. Therefore indirect evidence is the best that can be obtained.

Secondly, if this technique is to be used to assess the need for circulatory support, this study shows the importance of monitoring peripheral temperature. It has to be recognised that reduced peripheral perfusion may cause a fall in skin temperature, which may make the results harder to interpret. \(^{19}\) However, vasomotor response to cooling is less developed in the preterm infant, \(^{16}\) especially in the very small sick infant. Thus interpretation of results may be straightforward in this group, particularly in the controlled environment of a humidified incubator.

### Conclusion
NIRS with arterial occlusion can be used to monitor peripheral \( \text{VO}_2 \). This measurement is very sensitive to changes in limb temperature in term infants.

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### REFERENCES


