Quantification of the dermal vascular response to hyperbaric oxygen with laser-Doppler flowmetry

B. RATZENHOFER-KOMENDA, H. KOVAC, F. M. SMOLLE-JÜTTNER, G. B. FRIEHS, and G. SCHWARZ
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Ratzenhofer-Komenda B, Kovac H, Smolle-Jüttner FM, Friehs GB, Schwarz G. Quantification of the dermal vascular response to hyperbaric oxygen with laser-Doppler flowmetry. Undersea Hyper Med 1998; 25(4):223–227.—The vasoconstrictive response to hyperbaric oxygen (HBO₂) therapy was non-invasively quantified in eight healthy volunteers at 1.95 and 2.5 atm abs (197.5 and 253.2 kPa; multiphase chamber, air environment) by laser-Doppler flowmetry (LDF). The sensors for continuous measurement of microvascular perfusion (flux) and skin temperature were localized on the thenar eminence. Transcutaneous oxygen (tcPO₂) and carbon dioxide (tcPCO₂) tensions, blood pressure, heart rate, respiration rate, peripheral oxygen saturation, and temperature of the hyperbaric chamber were recorded at five conditions: 1) baseline—air breathing at 1.0 atm abs; 2) after 15 min of HBO₂ at 2.5 atm abs; 3) after 15 min of HBO₂ at 1.95 atm abs; 4) 1 min after decompression with oxygen breathing at 1.0 atm abs; and 5) after 15 min of breathing air at 1.0 atm abs. Flux decreased continuously at conditions 2 (76.5%), 3 (50.6%), and 4 (37% of baseline, P < 0.05; Tukey test). Skin temperature fell below baseline at conditions 2, 3, 4 (P < 0.01, Tukey test), and 5 (P < 0.05, Tukey test, P < 0.001, analysis of variance). Range of correlation between inspired gas PO₂ (PiO₂) and alteration of flux 0.91 to 0.72, median 0.41. Correlation between PiO₂ and tcPO₂, r = 0.98. Chamber temperature and tcPO₂ remained stable. HBO₂ reduced dermal microcirculation and temperature disproportionate to PiO₂. LDF is suitable for use under hyperbaric conditions.

hyperbaric oxygenation, laser-Doppler flowmetry, microcirculation monitoring, dermal blood flow, microvascular perfusion

Hyperbaric oxygen (HBO₂) is used in a wide range of clinical and experimental settings including carbon monoxide poisoning, gas embolism, acute blood loss anemia, necrotizing infections, and to improve angiogenesis in compromised wounds.

Several authors have observed that HBO₂ induces vasoconstriction in the skin (1,2). In which context this vascular condition may impair the cardiovascular performance, e.g., in septic patients, is not yet clear. There is not much experience with quantitating the vasoconstrictive response of the microcirculation to elevated ambient pressures.

Our study aimed to evaluate whether laser-Doppler flowmetry (LDF) can be used in a hyperbaric chamber and whether the response of the peripheral microcirculation to HBO₂ is uniform and reproducible in healthy volunteers.

PATIENTS AND METHODS

Eight volunteers (4 women, 4 men) were included in the study (25–62 yr, body weight 50–110 kg, preexperimental hematocrit 34.3–44.4 g · 100 ml⁻¹). The study was approved by the local ethics committee of the Medical Faculty of the University of Graz, Austria. Only subjects who passed the hyperbaric performance check entered the study. The hyperbaric performance check consists of a clinical examination of the heart and the lungs including chest x-ray, lung function testing, and inspection of the ears, nose, and throat by an otorhinolaryngologist. The subjects were non-smokers and were taking no medication. All participants gave informed consent. The ears were cleared before and during compression by swallowing or Valsalva’s maneuver.

Measurements were taken with the subjects in sitting position as follows:

 Flux, defined as the average speed of the red blood cells multiplied by their concentration in the sample volume, was measured on the thenar eminence with a laser-Doppler blood flow monitor (Moor Instruments Ltd., Millwey, Axminster, Devon, UK). In addition to the flux sensor there was a sensor for skin temperature measurement integrated into the probe.

Transcutaneous oxygen tension (tcPO₂) and carbon dioxide tension (tcPCO₂) (TINA, TCM3, Radiometer, Copenhagen, Denmark) were measured on the same extremity. The calibrated sensor for transcutaneous blood gas measurement was located on the medial part of the forearm proximal to the wrist. Additionally, heart rate and systolic, diastolic, and mean blood pressures were recorded on the opposite arm (Propaq bedside monitor, Physiocom, Vienna, Austria).
Pulse oximetry (\(\text{Sao}_2\)) values were taken from a fingertip distal to the flux sensor. Furthermore, the respiration rate and the temperature in the hyperbaric chamber were recorded.

The forearm and hand were kept in a stable and comfortable position to avoid motion artifacts. The blood flow sensor was protected from light to keep off interferences with visible light. Oxygen was delivered via a non-re-breathing demand valve with an antibacterial filter (Oxidem 2000 demand valve, Dräger Corp., Lübeck, Germany); additional breathing through the nose was impeded by a nose clip (PCS-64019 nose clip, B&F Medical Products Inc., Toledo, OH).

All values were obtained at five conditions:

**Condition 1:** Baseline values were obtained at 1.0 atm abs (101.3 kPa) with breathing air [fraction of inspired oxygen (\(\text{Fi}_{\text{O}_2}\)) of 0.21]. After a period of adaptation to the environment the chamber was compressed to 2.5 atm abs with the volunteer breathing air (\(\text{Fi}_{\text{O}_2}\) of 0.21). The rate of compression was 0.2 atm abs \(\cdot\) min\(^{-1}\). After this, \(\text{O}_2\) breathing was begun producing a \(\text{Fi}_{\text{O}_2}\) of 1.0.

**Condition 2:** The second set of values was obtained after 15 min of \(\text{HBO}_2\) at 2.5 atm abs. The ambient pressure was then decreased to 1.95 atm abs at a \(\text{Fi}_{\text{O}_2}\) of 1.0.

**Condition 3:** The third set of values was obtained after 15 min of \(\text{HBO}_2\) at 1.95 atm abs. With the subjects continuing breathing \(\text{O}_2\), the chamber was then decompressed at a rate of 0.2 atm abs \(\cdot\) min\(^{-1}\) with an additional safety break of 3 min at 1.3 atm abs.

**Condition 4:** The fourth set of values was obtained 1 min after decompression on \(\text{O}_2\) at 1.0 atm abs. Oxygen breathing was then stopped and the subject switched over to air breathing.

**Condition 5:** The fifth set of values was obtained after 15 min of air breathing at 1.0 atm abs.

The graph of gas exposure vs. time and of the conditions previously described is shown in Fig. 1.

The hyperbaric protocol was based on the frequent clinical practice of using 2.5 atm abs for most clinical indications, except clostridial myonecrosis for which 3.0 atm abs is used (3). Decompression was performed according to the guidelines of the U.S. Navy (4). The hyperbaric chamber consists of two hyperbaric units each of which is equipped as a standard operating room (Wagner-Biro, A-8020 Graz, Austria).

As \(\text{O}_2\) toxicity with cerebral convulsions may occur with \(\text{O}_2\) breathing over 2 atm abs, the period of \(\text{O}_2\) exposure was limited to 15 min at 2.5 atm abs (corresponding to condition 2) followed by immediate decompression to 1.95 atm abs. Only the sensors for LDF and skin temperature were installed within the chamber. The signals were transmitted to outside monitors for safety reasons. A physician trained in diving medicine and a biomedical engineer accompanied each volunteer throughout the hyperbaric chamber.

**Principle of microvascular perfusion measurement:** The backscattered light collected on the surface of a photodetector induces a photocurrent that is amplified and processed by an analogue processor and then by a digital processor and delivers data such as flux, concentration, or speed of the red blood cells. The monitor contains stable solid laser diodes operating at a wavelength of 780 nm. Laser light is transmitted to the tissue surface and collected by an optic fiber cable that is enclosed in the probe with a thermistor for skin temperature measurement. The optic fiber consists of silica glass, numerical aperture 0.29, core diameter 200 \(\mu\)m, with the fibers in the probe 500 \(\mu\)m apart. The Doppler signal is processed at a bandwidth of 20–15 kHz, output signal constants being 0.1 s. Data are stored on line and displayed graphically or numerically.

**Statistical analysis:** Series of one-way repeated measures analysis of variance (ANOVA) were performed. In addition, post-hoc analyses (Tukey test) were performed, and correlations between inspired gas \(\text{PO}_2\) and flux and \(\text{tcPO}_2\) were calculated.

**RESULTS**

The findings are summarized in Table 1. There was a significant decrease of the flux at conditions 2, 3, and 4 compared to the baseline value, but a return toward it at condition 5 (\(P < 0.05\), Tukey test; \(P < 0.001\), ANOVA).
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Table 1: Behavior of the microvascular perfusion, skin temperature, and vital signs in the hyper- and normobaric environment. Results of the measured parameters at five conditions

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Condition 1 1.0 ATA air breathing baseline</th>
<th>Condition 2 2.5 ATA HBO: 15 min</th>
<th>Condition 3 1.95 ATA HBO: 15 min</th>
<th>Condition 4 1.0 ATA oxygen breathing: 1 min</th>
<th>Condition 5 1.0 ATA air breathing: 15 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flux (% of baseline)</td>
<td>100.0 ± 0.0</td>
<td>76.5 ± 20.22 *</td>
<td>50.6 ± 10.2 *</td>
<td>37.0 ± 10.3 *</td>
<td>98.1 ± 24.5</td>
</tr>
<tr>
<td>Skin temperature (\degree C)</td>
<td>33.0 ± 0.4</td>
<td>30.0 ± 0.4 **</td>
<td>29.9 ± 0.6 **</td>
<td>29.5 ± 0.7 **</td>
<td>31.5 ± 0.7 *</td>
</tr>
<tr>
<td>tc\textsubscript{PO} \textsubscript{2} (mm Hg)</td>
<td>52.0 ± 4.8</td>
<td>946.0 ± 83.6 **</td>
<td>683.5 ± 77.2 **</td>
<td>286.0 ± 41.2 **</td>
<td>76.0 ± 5.8</td>
</tr>
<tr>
<td>tc\textsubscript{CO} \textsubscript{2} (mm Hg)</td>
<td>32.5 ± 2.9</td>
<td>28.5 ± 2.2</td>
<td>29.5 ± 2.0</td>
<td>30.0 ± 2.4</td>
<td>31.5 ± 1.9</td>
</tr>
<tr>
<td>BP systolic (mm Hg)</td>
<td>128.1 ± 7.2</td>
<td>133.2 ± 7.1</td>
<td>127.0 ± 6.1</td>
<td>132.4 ± 5.0</td>
<td>132.5 ± 7.1</td>
</tr>
<tr>
<td>BP diastolic (mm Hg)</td>
<td>81.7 ± 3.9</td>
<td>87.0 ± 3.5</td>
<td>83.0 ± 3.5</td>
<td>87.5 ± 3.1</td>
<td>89.3 ± 4.9</td>
</tr>
<tr>
<td>BP mean (mm Hg)</td>
<td>95.0 ± 6.7</td>
<td>99.4 ± 4.8</td>
<td>95.0 ± 3.7</td>
<td>98.1 ± 3.7</td>
<td>103.6 ± 5.3</td>
</tr>
<tr>
<td>Heart rate (1/min)</td>
<td>74.6 ± 3.0</td>
<td>66.8 ± 3.5</td>
<td>62.8 ± 4.1 **</td>
<td>66.3 ± 4.9</td>
<td>65.6 ± 3.5 **</td>
</tr>
<tr>
<td>Respiration rate (1/min)</td>
<td>16.9 ± 0.8</td>
<td>15.5 ± 1.7</td>
<td>16.1 ± 1.8</td>
<td>16.5 ± 1.5</td>
<td>15.4 ± 1.6</td>
</tr>
<tr>
<td>Sa\textsubscript{O} \textsubscript{2} (%)</td>
<td>98.0 ± 2.0</td>
<td>100.0 ± 0.0</td>
<td>100.0 ± 0.0</td>
<td>100.0 ± 0.0</td>
<td>99.9 ± 1.0</td>
</tr>
<tr>
<td>Chamber temperature (\degree C)</td>
<td>25.2 ± 0.2</td>
<td>25.2 ± 0.2</td>
<td>25.3 ± 0.3</td>
<td>25.1 ± 0.3</td>
<td>25.3 ± 0.3</td>
</tr>
</tbody>
</table>

Key: Flux, product of the average speed and concentration of moving red blood cells in the tissue sample volume; BP = blood pressure (mmHg); * = P < 0.05, ** = P = 0.01 (Tukey test).

*Numbers are given as mean values ± SEM, n = 8. Brackets indicate the conditions that significantly differ from the others.

Temperature declined significantly at conditions 2, 3, and 4 (P < 0.01, Tukey test) and increased until condition 5 (P < 0.05, Tukey test), which was still lower than baseline values (P < 0.001, ANOVA).

Transcutaneous oxygen tension changed proportional to the partial pressure of O\textsubscript{2} of the inspired gas (P\textsubscript{t}O\textsubscript{2}) (P < 0.001, ANOVA). The series of measurements differed significantly from each other with altered ambient pressure (P < 0.01, Tukey test). Correlation between P\textsubscript{t}O\textsubscript{2} and tc\textsubscript{PO} \textsubscript{2}, r = 0.98 ± 0.01. No change was observed at normobaric conditions 1 and 5.

Transcutaneous carbon dioxide tension values showed no statistically significant differences. Systolic, diastolic, and mean blood pressures remained stable throughout the study. Heart rate dropped significantly under altered conditions (P < 0.001, ANOVA). It decreased during HBO\textsubscript{2} and did not return to baseline values within 15 min of breathing air at 1.0 atm abs (P < 0.01, Tukey test). Respiration rate, Sa\textsubscript{O} \textsubscript{2}, and temperature within the chamber did not change significantly. Correlation coefficients between inspired gas Po\textsubscript{2} and percent change of flux ranged from -0.9 to 0.72 (median -0.41).

DISCUSSION

In 1959, Boerema et al. (5) showed that HBO\textsubscript{2} pressures could maintain sufficient tissue oxygenation even in the absence of hemoglobin because of the increased solubility of O\textsubscript{2} in the plasma at hyperbaric pressures. The amount of
O$_2$ dissolved in the plasma at 3 atm abs matches the O$_2$ consumption requirements under resting energy expenditure conditions. This finding was the rationale for further work in HBO$_2$ therapy and initiated a boom in hyperbaric chamber installation throughout the world.

At 2.5 atm abs, mean microvascular perfusion in the skin decreased to 76.5% of the baseline value and still continued decreasing when HBO$_2$ was continued at 1.95 atm abs. The nadir of reduction of the microvascular perfusion was measured after decompression to 1.0 atm abs with the subjects breathing pure O$_2$. However, measurements revealed baseline conditions of skin perfusion after 15 min of breathing air at 1.0 atm abs after decompression.

For minimizing the influence of ambient temperature on the vascular tone, alterations of temperature during compression and decompression were avoided. To counteract these temperature changes, compression and decompression were prolonged during our investigation so that the air conditioning in the chamber could compensate for them and keep ambient temperature stable. Alterations of skin surface temperature occurred after a short delay and proportionally to the flux, except at condition 5 when it still lay below baseline. As the chamber temperature was constant throughout the study, the decrease of the flux was not related to the ambient temperature but most likely to the vasoconstriction. Thus, the decline of skin surface temperature may reflect the vasoconstrictive state of the dermal vasculature.

The reduction of microvascular perfusion to 50.6% of the baseline value during HBO$_2$ at 1.95 atm abs was about twice as high as that reported by Hammarlund et al. (6) whose studies were performed at 2.0 atm abs. These authors measured microvascular perfusion at the fingertip and at the dorsum of the hand at 1.0 and 2.0 atm abs at a F$_{\text{O}_2}$ of 1.0. Their data suggested dose-dependent vasoconstriction.

In our study, the correlation between the tcPO$_2$ tension and the percent change of flux did not confirm a dose-dependency on the oxygen tension. Nevertheless, our HBO$_2$ therapy protocol started at 2.5 atm abs and then dropped to 1.95 atm abs so that residual tissue O$_2$ release possibly caused a delayed response to the stimulus of HBO$_2$. Wells and coworkers (7) showed that arterial Po$_2$ dropped to normal within 2 min after returning to sea level from 2.0 atm abs. But mass spectrometry analysis of muscle Po$_2$ took more than 180 min to return to normal; moreover, subcutaneous tissue took more than 4 h to return to normal. The impact of the duration of HBO$_2$ should be evaluated in further studies.

Hyperbaric oxygen slows heart rate, and animal studies have confirmed that cardiac output is reduced during exposure to pure O$_2$ at elevated ambient pressures. The increased amount of O$_2$ dissolved in the plasma under hyperbaric conditions augments the O$_2$ content in the arterial blood so that cardiac output can decline while maintaining its O$_2$ transport capacity (8).

In 1993, Bergø (9) studied the effects of HBO$_2$ on the cardiovascular system in rats at 1–5 atm abs and found effects similar to those observed in humans.

Laser-Doppler flowmetry is suitable for noninvasive bedside monitoring of skin perfusion under hyperbaric conditions (10). However, standardized criteria of evaluation and analysis procedures remain to be elaborated. The graphic data display shows the trend of the skin perfusion over the measuring period and reflects changes better than absolute values (11). Most publications have measured microvascular perfusion with tetrapolar or integral rheography or with labeled microspheres (1,12). These techniques are invasive and require more observation and work than LDF, which may easily be introduced into clinical practice.

In summary, cutaneous perfusion is reduced and local skin temperature declines in response to HBO$_2$ exposure. LDF is an appropriate method for noninvasive measurement of the local microcirculation under hyperbaric conditions. Further investigations will elucidate the interactions between O$_2$ tension, flux, and duration of HBO$_2$.

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