Day-to-day variability of transcutaneous oxygen tension in patients with diabetes mellitus and peripheral arterial occlusive disease

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Purpose: We evaluated the day-to-day variability of transcutaneous oxygen tension (tcPO2) in patients with diabetes mellitus and peripheral arterial occlusive disease who were at risk for chronic foot ulceration.

Methods: The tcPO2 was measured in the morning once daily for 3 consecutive days in 10 male patients with diabetes mellitus who were hospitalized. The mean age of the patients was 65 ± 13 years, and they had a mean duration of diabetes mellitus of 33 ± 6 years. The tcPO2 was measured at a reference point at the chest (I2 dx), the dorsum of the foot, and in the first intermetatarsal space. Measurements of tcPO2 in the first intermetatarsal space were performed before and during inhalation of 100% oxygen.

Results: The mean tcPO2 was higher (P < .001) at I2 dx (56 ± 10 mm Hg) than at the dorsum of the foot (25 ± 19 mm Hg) and first intermetatarsal space (27 ± 20 mm Hg). tcPO2 increased (P < .001) during inhalation of 100% oxygen, whereas the increase was severely reduced in three patients with tcPO2 less than 10 mm Hg at baseline. A reasonably good day-to-day variability of tcPO2 was seen; the linear relations between tcPO2 investigated on days 1, 2, and 3 were highly significant (P < .0001) at each measuring site, and no systematic differences were seen between the repeated measurements (analysis of variance; P = .13 to .85).

Conclusion: The results show an acceptable day-to-day variability of tcPO2, both at baseline and during oxygen inhalation, in patients with diabetes mellitus and peripheral arterial occlusive disease. (J Vasc Surg 2001;34:277-82.)
Examining procedure. Measurements of tcPO₂, systolic and diastolic arm blood pressures, and systolic toe blood pressure were performed on three consecutive days (days 1, 2, and 3) at the Microcirculatory Laboratory of Karolinska Hospital. The measurements were made in the morning after the patients had eaten a light breakfast and approximately 90 minutes after insulin injection. The patients were asked to refrain from smoking and drinking coffee for at least 2 hours before the examinations. No change in the medical treatment was made during the study period. tcPO₂ and peripheral blood pressure were measured with the patient in the supine position, after an acclimatization period of 20 minutes. The room temperature was kept between 22°C and 24°C. If the patient had foot ulceration, the foot with ulceration was chosen for the examinations.

Blood pressure measurement. Systolic and diastolic arm blood pressures (mm Hg) were measured by means of the Riva Rocci method. The systolic toe blood pressure was assessed by recording the pressure (mm Hg) with a miniature cuff (2 cm wide) placed around the base of the great toe, in which return of blood was shown by means of laser Doppler fluxmetry of the toe pulp when the cuff was slowly deflated from suprasystolic values. This method is highly correlated \((r = 0.985; \ P < .001)\) to pressure measurements with photoplethysmography.21

Transcutaneous oxygen tension. The tcPO₂ measurement was made with an electrochemical transducer (Oxykapnomonitor, SMK 363 Hellige, Freiburg im Breisgau, Germany). The monitor was calibrated against air and a zero solution, according to the manufacturer’s instructions. The measurement site was cleaned carefully with disinfection solution (chlorhexidin spirit), and the probe was attached to the skin with double-sided adhesive rings and contact liquid supplied by the manufacturer. To increase the permeability of the skin to oxygen molecules at the measuring site, we heated the transducer to 44°C with a built-in sensor heater. Hyperemic stabilization occurred within 20 minutes, and the tcPO₂ signal was continuously recorded on paper. A reference value was determined by placing the transducer on the chest at the right side in the subclavicular region \((I_2 dx)\). The transducer was then placed at the dorsum of the foot (over the dorsal pedal artery), and after a measurement was taken at this point, the transducer was moved to the first intermetatarsal space. The measured skin areas were marked with ink to ensure the same measuring site at each investigation. tcPO₂ in the first intermetatarsal space was measured before and during inhalation of 100% oxygen. The patients inhaled oxygen by breathing in a plastic hood supplied with oxygen for 15 to 20 minutes. After an inhalation period of 5 to 10 minutes, a tcPO₂ plateau was reached and was registered as the tcPO₂ level during inhalation of 100% oxygen. None of the tcPO₂ measurements were performed with direct contact with any foot ulceration.

Statistical analysis. Data of peripheral blood pressures are given as mean ± SD in Table I. The results of tcPO₂ are shown in Table II as mean ± SD, and the mean tcPO₂ for days 1 through 3 was determined. The difference in tcPO₂ between different measuring sites was investigated by means of the paired \(t\) test with the Bonferroni correction. The means of the systolic toe blood pressures and tcPO₂ values at the foot were calculated in each patient and plotted against each other in a scattergram, and the linear relation was determined (Fig 1). The repro-
ducibility was investigated by means of regression analyses and 1-factor analysis of variance with repeated measures, and the data are shown in Figs 2 and 3 and are given in the “Results” section. A P value less than .05 was considered to be significant. For each patient, the within SD (SDwithin) and mean were calculated for the three repeated measurements of tcPO2. The within SDs and means were then averaged for the patients. Mean and approximate 95% CIs for the within variation were given by means of these estimates as mean ± 2*SDwithin. These data are given in Table III.

RESULTS

Peripheral blood pressure. The toe/arm blood pressure index was less than 0.7 in all patients. Significant linear relations between the systolic toe blood pressures measured on days 1, 2, and 3 (r² = 0.89-0.93; P < .001) was shown by means of regression analysis, and no systematic difference (analysis of variance; P = .42) was seen between the repeated measurements.

Transcutaneous oxygen tension. The tcPO2 measured at the reference point (I₂ dx) was higher (P < .01) than that measured at the dorsum of the foot and in the first intermetatarsal space, whereas there was no significant difference (P = .489) between tcPO2 measured at the dorsum of the foot and that measured in the first intermetatarsal space. tcPO2 in the first intermetatarsal space increased (P < .001) significantly during inhalation of 100% oxygen, and the increase was more than 400% in seven patients (without oxygen, 37 ± 11 mm Hg; with oxygen, 243 ± 58 mm Hg). The tcPO2 level during inhalation of 100% oxygen was considerably lower (4-33 mm Hg) in three patients with severely reduced tcPO2 at baseline (< 10 mm Hg). No significant linear relation (r² = 0.06, P = .42) was seen between mean systolic toe blood pressure and mean tcPO2 at the foot (Fig 1).

Day-to-day variability of tcPO2. Highly significant linear relations were shown by means of regression analyses between tcPO2 determined on days 1, 2, and 3 at each measuring site: I₂ dx (r² = 0.73-0.98; P < .001); dorsum of foot (open circle), and in first intermetatarsal space before (dot) and during inhalation of 100% oxygen (solid box).

Table I. Systolic and diastolic arm blood pressure (mm Hg) and toe blood pressure (mm Hg) on three consecutive days (1, 2, and 3) in 10 patients with diabetes mellitus and PAOD

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm blood pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic (mm Hg)</td>
<td>135 ± 21</td>
<td>129 ± 16</td>
<td>130 ± 14</td>
</tr>
<tr>
<td>Diastolic (mm Hg)</td>
<td>78 ± 14</td>
<td>74 ± 12</td>
<td>75 ± 12</td>
</tr>
<tr>
<td>Toe blood pressure (mm Hg)</td>
<td>56 ± 44</td>
<td>53 ± 39</td>
<td>50 ± 38</td>
</tr>
<tr>
<td>Toe/arm blood pressure index</td>
<td>0.42 ± 0.33</td>
<td>0.40 ± 0.30</td>
<td>0.38 ± 0.29</td>
</tr>
</tbody>
</table>

The values are presented as mean ± SD.
were seen between the lowest and highest tcPO2 values at each measuring point (Fig 3).

Mean and approximate 95% CIs for the within variation of the tcPO2 measurements are shown in Table III. Although the CIs are formed for single new observations for the variables in Table III, the lengths of the intervals seem to be rather narrow, indicating a reasonably good day-to-day variability of tcPO2.

DISCUSSION

In this study, the day-to-day variability of tcPO2 was investigated in 10 patients with diabetes mellitus and PAOD. All patients were at high risk for chronic foot ulceration; 8 patients had chronic foot ulcers, and the other 2 patients had a history of chronic foot ulcers. The tcPO2 was measured in three different skin areas, the chest, the dorsum of the foot, and in the first intermetatarsal space.

The measurement of tcPO2 reflects the amount of oxygen available in skin microcirculation during local hyperemia and is dependent on both central and local factors. The central factors may be systolic arterial blood pressure and arterial oxygen content, which are influenced by such factors as heart failure and respiratory diseases, whereas the local factors, such as local blood flow, local oxygen consumption, and diffusion, are influenced by such factors as angiopathy, infection, edema, and skin thickness. tcPO2 in patients with diabetes mellitus is generally somewhat lower than in age-matched control subjects who do not have diabetes mellitus, even in patients with a short duration of diabetes mellitus and without macrovascular complications.5-7 In patients with PAOD, tcPO2 can be very low or close to 0, and it has been suggested that these findings do not necessarily mean total skin anoxia, but rather that the amount of oxygen molecules available at the skin surface is too low for consumption by the electrode.9,22 The metabolic demand of skin tissue is low, and skin tissue can sometimes survive despite severely impaired blood circulation. However, tcPO2 levels less than 10 mm Hg are most often associated with a bad outcome, such as impaired ulcer healing, amputation, or both.9,15

The results of the current study are in line with other investigations showing a reduced tcPO2 at the foot level in patients with diabetes mellitus and PAOD,8,9 which indicates that oxygen delivery to the skin is mainly a flow-related phenomenon. Franzek et al9 investigated tcPO2 in healthy subjects and in patients with PAOD. In the healthy subjects, tcPO2 varied between 40 and 70 mm Hg at the chest level and between 30 and 70 mm Hg at the foot. In the patients with PAOD, tcPO2 at the chest level was between 30 and 80 mm Hg, whereas tcPO2 at the foot varied considerably (0-70 mm Hg). In the current study, three patients showed very low tcPO2 at baseline (< 10 mm Hg), and the responses during inhalation of 100% oxygen were also severely reduced (4-33 mm Hg) as compared with those in the other patients (170-330 mm Hg). These findings indicate an extremely impaired skin
microcirculation,8,9,14 a suggestion strengthened because two of these patients went on to have a major amputation within 7 weeks. The reasons for amputation were symptoms of critical ischemia and not acute infection. The third patient had undergone vascular reconstruction 5 weeks earlier and had a slight foot edema, which may explain the severely reduced tcPO2.23 However, this patient underwent a major amputation 12 months later. In contrast to the microcirculatory findings, toe blood pressure indicated critical limb ischemia in only one of these three patients (ie, a systolic toe blood pressure ≤ 30 mm Hg).24 However, two other patients had severely low toe blood pressures, whereas the tcPO2 levels were between 30 and 50 mm Hg (Fig 1), and none of these patients went on to have an amputation within the first year. Furthermore, the current study showed no significant relation between macrocirculation and microcirculation (Fig 1). This discrepancy between macrovascular and microvascular findings is in agreement with the results of an earlier study by our group,15 which also indicated that tcPO2 is a better predictor for outcome of chronic foot ulcers than toe blood pressure. A combination of peripheral blood pressure measurements and skin microcirculatory investigations, such as systolic toe blood pressure and tcPO2, may provide better assessment of the prognosis than one parameter alone.25,26 The reproducibility of systolic toe blood pressure measurements, with laser Doppler fluxmetry as the means of detection, was also investigated in this study, and a good agreement was demonstrated between the repeated investigations (Table 1).

The tcPO2 was measured in two adjacent skin areas at the foot because the disturbances in skin microcirculation may have a patchy distribution.20,27 The results showed no significant differences in tcPO2 between these two measuring points (Table II; P = .489), which may be because these skin areas are mainly supplied with blood from the same artery, the dorsal pedal artery.

This study shows a good day-to-day variability for tcPO2 measured at the chest, the dorsum of the foot, and in the first intermetatarsal space both before and during inhalation of 100% oxygen (Figs 2 and 3). These results are in line with a study by Rooke and Osmundson,18 who reported a “relatively” good agreement of the tcPO2 measurements when repeated 24 and 48 hours later. Lukkari-Rautiarinen et al28 investigated the day-to-day variability of tcPO2 in patients with “advanced distal ischemia of the lower limb” and found a coefficient of variation of 37%, which was reduced to 31% when patients with tcPO2 less than 10 mm Hg were excluded. To eliminate the problem with patients with very low tcPO2 values, we have chosen not to report the reproducibility with the coefficient of variation. The reason for the good reproducibility in this study is most probably that we investigated a homogenous group of hospitalized patients and the investigations were performed in a very standardized way (same time of the day, same time after medication). No significant difference in reproducibility of tcPO2 was seen between the different measuring sites, but the reproducibility may be somewhat better in the first intermetatarsal space when measured without oxygen inhalation.

In summary, this study shows an acceptable day-to-day variability for measurement of tcPO2, both at baseline and during oxygen inhalation, in patients with diabetes mellitus and PAOD who are at high risk for chronic foot ulceration.

REFERENCES


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