Evaluation of a System for Transcutaneous Long-Term Capnometry

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Abstract

Background: The measurement of CO₂ partial pressure (P_{CO₂}) is of great importance. Former systems of transcutaneous capnometry combining the measurement of oxygen partial pressure (P_{O₂}) and P_{CO₂} had their limitations due to skin irritations caused by the heating-up of the sensor and a short application time of 4 h. Objectives: To evaluate for the first time combined monitoring of transcutaneous P_{CO₂} (tcP_{CO₂}) and oxygen saturation applying a lower temperature (sensor temperature 42 °C) and a new sensor technology in healthy individuals during sleep. Methods: Twenty-nine healthy individuals [12 males, age 35.2 ± 17.0 years, body height: 170.2 ± 12.0 cm (mean ± SD), weight: 76.3 ± 15.8 kg, body mass index 26.5 ± 5.4] were monitored for more than 6 h at night with the TOSCA 500 instrument (Radiometer, Basel, Switzerland). tcP_{CO₂} was continuously monitored and its correlation with selective measured capillary P_{CO₂} values (P_{capCO₂}) was monitored at 0.00 and 4.00 h. Results: At 0.00 h, P_{capCO₂} was 37.1 ± 5.1 mm Hg and tcP_{CO₂} was 43.4 ± 6.6 mm Hg (p < 0.001). At 4.00 h, P_{capCO₂} was 37.0 ± 5.6 mm Hg and tcP_{CO₂} was 43.5 ± 5.4 mm Hg (p < 0.001).

P_{capCO₂} and tcP_{CO₂} were positively and significantly correlated (0.00 h: r = 0.5, p < 0.02 and 4.00 h: r = 0.72 and p < 0.001) at both time points. In the course of the night, there was no significant drift in the tcP_{CO₂} values. Conclusion: The investigated system enables stable measurement of tcP_{CO₂} without relevant drift in healthy individuals and does not require recalibration. tcP_{CO₂} is highly suitable as a measure of P_{capCO₂} because the two parameters are highly correlated and there is no inconvenience to the patient.

Introduction

The determination of CO₂ partial pressure (P_{CO₂}) in blood is of great importance as a measure of ventilation in various fields of medicine [1–6]. CO₂ measurement is also gaining increasing importance in the diagnosis and therapy of the obesity hypoventilation syndrome, sleep-related respiratory disturbances and chronic respiratory insufficiency [7–11], where it serves to determine whether ventilation is insufficient already at rest or only under physical stress or during sleep. Thus, it can be helpful in weaning patients on long-term ventilation if the introduction of noninvasive or invasive ventilation or its monitoring is indicated.

Key Words
Capnometry · Transcutaneous carbon dioxide · Oxygen saturation · Sleep-related breathing disturbances · Obesity hypoventilation · Chronic respiratory insufficiency
CO₂ can be measured in arterial or arterialized blood samples, in expired air and transcutaneously [12–14]. Disadvantages of invasive CO₂ measurement are precisely its invasiveness, its painfulness, the costs involved, and the sleep impairment caused by hyperemization and puncture if the measurements are done during the night. The quality of the results depends on the carefulness of the measurement (insufficient hyperemization time, squeezing of the tissue, air trapped in the sample). If the CO₂ value is measured at night, it may be affected by sleep disruption and the related hyperventilation. Measurements of expired CO₂ in ventilated patients are strongly affected by artifacts [12, 13] and the inhomogeneity of pulmonary ventilation.

tcPCO₂ measurements are based on the principle of the permeability of body tissues and skin to CO₂. Additional heating of the tissues increases the arterial perfusion of the skin, thus intensifying the gas exchange between capillary blood and the skin. tcPCO₂ measurements are thus not direct measurements of the arterial PCO₂ (PaCO₂): they measure the epidermal CO₂ content below the measuring site, which correlates with PaCO₂.

Thus, a distinction has to be made between PaCO₂, capillary PCO₂ (PcapCO₂) and tcPCO₂. Hyperemization of the skin by pharmaceuticals or heat leads to vasodilation, which decreases the difference between PaCO₂ and PcapCO₂. However, there is an additional difference between PcapCO₂ and tcPCO₂ due to the production of CO₂ by the skin cells themselves, which influences the measurement of tcPCO₂ (metabolic constant). The metabolic constant depends on skin age and thickness and is estimated at 5 mm Hg. In addition, heat also increases the metabolism of poorly oxygenated skin layers (anaerobic factor). These two factors lead to an increase in tcPCO₂ compared to PcapCO₂ [15–17].

For the simultaneous determination of oxygen saturation, tcPCO₂ and heart rate, a system is now available that works with reduced heating of the skin (sensor temperature 42 °C) and is able to measure over longer periods of time without recalibration [19–21]. The system has been used in neonatological intensive care and in adult patients with acute respiratory or cardiac failure or during cardiopulmonary exercise testing [8, 22–24]. The examinations consistently show a good correlation between PaCO₂ and tcPCO₂ with a mean difference of 3 mm Hg. The system causes fewer artifacts and is easy to apply, in particular in intensive care. However, it has not been validated yet in healthy individuals, in particular over several hours. The objective of our study was thus to examine (1) how tcPCO₂ values correlated with PcapCO₂ values, and (2) whether there was a drift of the tcPCO₂ values over night if the apparatus was not recalibrated.

**Methodology**

**Patients**

Twenty-nine healthy individuals, 12 males and 17 females, participated in the study. Only patients over 18 years who did not have heart diseases, diseases of the respiratory system or of the hematopoietic system were included. Anamnestic evidence of dyspnea at rest or during exercise, sleep-related breathing disturbances or thoracic pain were exclusion criteria. Pregnant women were not allowed to participate. The study was carried out in compliance with the Ethics Commission of the University of Witten/Herdecke. The participants gave their written consent.

**Design**

Measurements were made during a sleep phase of at least 6 h in a hospital room. A capillary blood gas analysis after hyperemization of the earlobe was made at two time points during the night (0.00 and 4.00 h). The samples were analyzed immediately (Ecosys II™, Eschweiler, Kiel, Germany). Transcutaneous long-term capnometry was carried out during the whole night. The tcPCO₂ value was read at 23.30, 0.00 and 0.30 h as well as at 3.30, 4.00 and 4.30 h. Additional measurements of tcPCO₂ 30 min before and after each capillary blood gas analysis served to find changes in the PCO₂ value caused by capillary sampling. The measurements at two different time points during the night served to detect a drift in tcPCO₂ compared to PcapCO₂.

No in vivo calibration was carried out before the beginning of the measurement nor was the system recalibrated during the night.

**Long Term Capnometry**

The study was carried out using the TOSCA 500 system (Radiometer, Basel, Switzerland). A combined electrode to determine heart rate, oxygen saturation and tcPCO₂ is fixed on the earlobe (fig. 1). The pH value is measured via a pH glass electrode and an Ag/AgCl electrode is used as reference. The sensor is coated with a hydrophilic membrane permeable to gas. A hydrophilic space above the sensor surface contains the electrolyte solution.

From the skin, the CO₂ diffuses into the electrolyte solution in the spacer through a membrane permeable to gas. The pH value is the primary measuring parameter. The skin is heated via a sensor (sensor temperature 42 °C) that causes local hyperemia and increases the supply of arterial blood to the dermal capillary bed, thus improving CO₂ diffusion.

Calibration was carried out at the beginning of the measurement with a known CO₂ concentration. In the system, the pH value is converted into PCO₂, which is proportional to the logarithm of the change in PCO₂. The displayed PCO₂ value is estimated according to the following equation based on the data of Severinghaus [17]:

\[
P_{\text{CO}_2} = \frac{(\text{t}c\text{PCO}_2 - 5 \text{ mm Hg})/10^{0.019(T-37)}}{11554} 
\]

where T is the temperature in degrees centigrade, PaCO₂ = the estimated arterial value displayed on the screen after temperature
correction, tc\(\text{PCO}_2\), the transtcutaneously measured value at sensor temperature (42 °C) before temperature correction.

The term \(10^{0.019(T-37)}\) is the compensation of the anaerobic factor attributed to the increased CO\(_2\) production in skin layers with an anaerobic metabolism. The subtraction of 5 mm Hg is meant to compensate the metabolic constant accounted for by the increased CO\(_2\) production of the epidermal cells.

The technical data of the sensor are as follows: diameter 15 mm, height 8 mm, weight 3 g, P\(\text{CO}_2\) range 1–200 mm Hg, in vitro response time (10–90%) \(\leq 50\) s, in vitro drift \(<0.5\%/\text{h}\), resolution: 1 mm Hg.

Oxygen saturation was determined with an integrated pulse oximeter using two wavelengths (658 and 880 nm) to differentiate between oxygenized and deoxygenized blood. The measurement is made with the sensor, using red and infrared light-emitting diodes that send light through the earlobe to the photo diode. Oxygen saturation range: 0–100%, accuracy (70–100%) \(\pm 3\) digits, resolution: 1%. The perfusion index (0.02–9.99 and 10.0–20.0%) is a relative assessment of the pulse strength at the monitoring site. The perfusion index is defined as the ratio of the amplitudes of the pulsatile (AC) and the nonpulsatile (DC) infrared signals expressed in percent. The perfusion index is a relative number and varies from patient to patient. A low value indicates weak pulse strength and might indicate insufficient perfusion at the measurement site [25]. The heating power reference describes the energy needed to achieve the defined sensor temperature. It allows local perfusion to be estimated (fig. 2).

**Statistics**

Descriptive statistics were computed according to the measurement scale of each variable. Exploratory comparisons between different time points and between different parameters were tentatively made at an \(\alpha\)-level of 5% using Wilcoxon’s matched-pair test. The Pearson product-moment correlation coefficient was measured to study the correlation between different parameters.

**Results**

The subjects were 35.2 ± 17.0 years old (range 18–73). Their body height was 170.2 ± 12.0 cm (145–192), their weight 76.3 ± 15.8 kg (50–121), their body mass index 26.5 ± 5.4 (18.6–40.4).

At 0.00 h, P\(\text{cap CO}_2\) was 37.1 ± 5.1 mm Hg and tc\(\text{PCO}_2\) was 43.4 ± 6.6 mm Hg (\(p < 0.001\)). At 4.00 h, P\(\text{cap CO}_2\) was 37.0 ± 5.6 mm Hg and tc\(\text{PCO}_2\) was 43.5 ± 5.4 mm Hg (\(p < 0.001\)). The difference was significant at both times and there was a significant positive correlation between P\(\text{cap CO}_2\) and tc\(\text{PCO}_2\) at both times (0.00 h: \(r = 0.5\), \(p < 0.02\) and 4.00 h: \(r = 0.72\) and \(p < 0.001\)) (fig. 3).

In order to detect interferences caused by blood sampling, tc\(\text{PCO}_2\) was recorded both before and after the puncture. The measured values of tc\(\text{PCO}_2\) at 23.30, 0.00 and 0.30 h as well as 3.30, 4.00 and 4.30 h corresponded very well with each other and did not show any statistical differences either (table 1).

In order to be able to recognize a drift of tc\(\text{PCO}_2\) during the night, tc\(\text{PCO}_2\) was read at two time points at an interval of 4 h and compared to the P\(\text{cap CO}_2\) values. There was no significant difference between the tc\(\text{PCO}_2\) values at both time points. Nor was there a significant difference between P\(\text{cap CO}_2\) at 0.00 and 4.00 h (table 1). Most of the individual differences in the values of tc\(\text{PCO}_2\) and P\(\text{cap CO}_2\) between 0.00 and 4.00 h were measured within a narrow range (fig. 4). The change in the measured values of P\(\text{cap CO}_2\) was \(0.0 \pm 4.9\) and of tc\(\text{PCO}_2\) \(-1.8 \pm 4.1\)
Fig. 2. Screen shot of long-term capnometry. The figure presents two 6-hour-measurements in healthy individuals. The lines represent (from top to bottom): 'SpO$_2$': oxygen saturation; 'Puls': heart rate; 'PcO$_2$': capnometry; 'HPWR': heating power reference; 'Sensortemperatur': temperature of the sensor; 'Perfusion': perfusion index. Both graphs show constant levels of tcPCO$_2$ and SpO$_2$. However, there are some short periods with sharp decreases of tcPCO$_2$ which are accompanied by variations in the perfusion index or heating power reference indicating artifacts.
Thus, there was no relevant drift of tcP CO 2 in the course of the night.

The mean oxygen saturation during the recording period was 97.4 ± 1.3% with a small range between the 5th and 95th percentile and a small portion of time below 90% (table 2).

**Discussion**

For the subjects in this study there was a very good correspondence between tcP CO 2 and Pcap CO 2 data. tcP CO 2 correlated significantly with Pcap CO 2. However, tcP CO 2 was about 5 mm Hg higher than Pcap CO 2. A relevant drift of tcP CO 2 during the night could not be proven. For healthy individuals, there is no relevant difference between the measurements before and after waking compared to the values during waking.

It is of particular clinical importance that a relevant deviation of tcP CO 2 over night did not occur. In prior applications of long-term capnometry, a drift of the CO 2 values during long-term measurement was found [26], which made re-calibration during the night necessary. The system examined in this study was technically improved to avoid this phenomenon (covering the sensor, different electrolyte composition). We carried out two
PcapCO₂ measurements during the night and compared them to tcPCO₂ in order to detect a drift of the transcutaneously measured value over time. There was no significant or clinically relevant difference between PcapCO₂ and tcPCO₂ at the same measuring site or between the two different measuring sites. Thus, a drift could not be found with the system tested in this study.

Kagawa et al. [27] described an ‘initial overshoot’ of tcPCO₂ in patients under general anesthesia and healthy individuals. tcPCO₂ was 5 mm Hg higher than the final value 8 ± 3 min after the beginning of the measurement. This can be avoided by initially increasing the heating of the skin. The temperature of the sensor examined increases automatically to 44°C during the first 20 min of monitoring and then readjusts to 42°C. This causes fast artefactization and stable tcPCO₂ values. In order to avoid the ambiguities of the initial phase, the measurements in our study were made at 0.00 and 4.00 h, when the system had already been operating for at least 2 h.

It was to be expected that the CO₂ values at night might be affected by waking the patient for the invasive blood gas analysis. It could be speculated that a possible hyperventilation at night might be compensated by waking the patient or that the waking and the alteration following hyperemiation of the earlobe and the painful puncture might cause hyperventilation. In order to take this factor into account, measurements of the tcPCO₂ values on the long-term capnometry system were not only carried out at the time of the blood sampling but also 30 min before and after the sampling time. These values turned out to be steady so that an influence by blood sampling could be excluded. So far, there are no comparable data from a collective of healthy individuals. In a prospective, open, nonrandomized study, Bernett-Buettiker et al. [24] examined 60 sick newborns 21 of whom were ventilated. They compared the tcPCO₂ with the PaCO₂ and PcapCO₂ values and found an average difference of 3.21 mm Hg between the arterially measured value and tcPCO₂. Compared to PcapCO₂, the difference was only 0.67 mm Hg. Senn et al. [8] compared the tcPCO₂ values of 18 adults with acute respiratory failure or decompensated heart insufficiency and those of 12 patients with obstructive sleep apnea syndrome. They found an average difference of 3 mm Hg. These data are in good agreement with the values measured in this study. The smaller difference between PcapCO₂ and tcPCO₂ in the neonatal collective compared to adults could be attributed to anatomical differences such as the much thinner skin.

Janssens et al. [21] published a study on the application of long-term (>8 h) capnometry in which they examined 28 patients under noninvasive ventilation most of whom were slightly hypercapnic. In agreement with our results on healthy individuals, those authors found a good correlation between PaCO₂ and tcPCO₂ using another system. A drift could not be proven in this study either. Janssens et al. [21] also showed a good correlation of data in a geriatric collective. No skin damage occurred and the measurements were well tolerated even with applications over 8 h [5].

Cuvelier et al. [23] studied 12 patients with chronic obstructive or restrictive lung diseases under invasive and noninvasive ventilation. The mean baseline PaCO₂ was 48.8 mm Hg. The authors compared PaCO₂ and tcPCO₂ during 40 min of spontaneous breathing and 40 min of ventilation. Both the absolute figures of PaCO₂ and tcPCO₂ at a PaCO₂ level <56 mm Hg and the changes in PaCO₂ and tcPCO₂ under ventilation correlated highly significantly. There are no studies on long-term capnometry on severely hypercapnic patients with the system presented here.

We did not use any in vivo correction in our study; however, the value displayed on the monitor can be adjusted to compensate for the difference with the PcapCO₂. However, this requires the difference between tcPCO₂ and PcapCO₂ to be constant. It was the objective of this study to evaluate the system with the current algorithm including the correction factors and no manual change was desired. Moreover, in the daily clinical routine, in vivo correction might affect the practicability as it increases the workload when using the system.

PcapCO₂ and tcPCO₂ showed a significant correlation at all measuring time points, with an average difference of 6.2–6.9 mm Hg. Including the correction factors, tcPCO₂ was thus systematically higher than PcapCO₂. In order to avoid misinterpretations in the daily clinical routine, the user has to be aware that tcPCO₂ exceeding PcapCO₂ by about 5 mm Hg should not be interpreted as hypercapnia. For a diagnosis of nocturnal hypventilation, for the indication of ventilation or for monitoring the effectiveness of ventilation, however, the evolution of tcPCO₂ during the night rather than its absolute value is decisive. These difficulties in interpretation can be avoided by in vivo calibration. However, this is still to be confirmed in prospective studies. Besides, there is hope that technical improvements will neutralize this difference.

Individual PcapCO₂ values measured differed relevantly from all other measurements in the same individual, making the values unlikely. Even if an adverse effect...
of blood gas sampling on the blood gas values could generally not be proven, such an adverse effect may occur in individual patients. In contrast to invasive CO₂ measurement, this phenomenon was not noticeable in transcutaneous measurements. Skin damage could not be observed with this system due to the low sensor temperature of 42°C. Bernet-Buettiker et al. [24] also underlined the simplicity of the method.

In summary, transcutaneous long-term capnometry with the technology investigated here correlated very well with the capillary values. A relevant drift of "CO₂ was not observed. The transcutaneously measured values are systematically higher than Pcap CO₂. This does not diminish the accuracy of the method. However, the user has to be aware of the difference in order to avoid misinterpretations.

References