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Comparison of Transcutaneous and Arterial Blood Gas Analyses in Patients with Sepsis and Septic Shock

Sepsisli ve Septik Şoklu Hastalarda Transkutanöz ve Arter Kan Gazı Analizlerinin Karşılaştırılması

Received/Geliş Tarihi : 01.11.2019
Accepted/Kabul Tarihi : 17.05.2020

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Turkish Journal of Intensive Care published by Galenos
Publishing House.

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ABSTRACT Objective: This study aims to compare the effectiveness of non-invasive pressure of transcutaneous CO₂ (PtcCO₂) and O₂ (PtcO₂) analyzers versus conventional blood gas sampling in patients with sepsis and septic shock.

Materials and Methods: Sepsis patients without a need for inotrope support (sepsis) were prospectively enrolled to group 1 (n=50), whereas group 2 (n=50) was composed of patients needing inotropes (septic shock). Demographic data, laboratory tests, Acute Physiology and Chronic Health Evaluation-II (APACHE-II) and Sequential Organ Failure Assessment (SOFA) scores, standard monitoring data, data of blood gas analysis (pH, PaCO₂, PaO₂, and SaO₂), and transcutaneous CO₂ and O₂ were collected at the first, second, third, and fourth hours.

Results: No significant difference was noted between the groups in terms of demographic parameters, baseline white blood cell, hematocrit, baseline heart rate, central venous pressure, respiratory rate, and positive end-expiratory pressure values. Group 2 had significantly higher serum urea and creatinine levels and lower albumin levels and mean arterial pressure, whereas group 1 had significantly lower APACHE-II and SOFA scores and peak inspiratory pressure and FiO₂.

No significant difference was noted between the PtcCO₂ and PaCO₂ values in group 1, whereas the PtcCO₂ values of group 2 were significantly lower than PaCO₂.

PtcO₂ and PaO₂ values were significantly lower in group 1, whereas PtcO₂ vs PaO₂ values were significantly lower in group 2. A strong correlation was noted between arterial and transcutaneous CO₂ and O₂ values in both the groups.

Conclusion: PtcCO₂ assessment may be an alternative method in patients with sepsis but not in septic shock. PtcO₂ measurement may not be a reliable method for patients with sepsis and septic shock.

Keywords: Sepsis, septic shock, ICU, transcutaneous CO₂, transcutaneous O₂, arterial blood gas analysis

ÖZ Amaç: Sepsisli ve septik şoklu hastalarda non-invaziv transkutanöz parsiyel CO₂ (PtcCO₂) ve O₂ (PtcO₂) basıncı analizörlerinin etkinliğini geleneksel kan arter kan gazı analizi ile karşılaştırmayı amaçladık.

Gereç ve Yöntem: Sepsis 3 tanı kriterlerine göre "sepsis" tanısı alan hastalar grup 1'e (n=50), "septik şok" tanısı alan hastalar grup 2'ye (n=50) ayrıldı. Demografik veriler, laboratuvar testleri, Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi-II (APACHE-II) ve Ardışık Organ Yetersizliği Değerlendirme (SOFA) skorları, 1., 2., 3., ve 4. saatlerdeki standart monitorizasyon verileri, kan gazı analizi verileri (pH, PaCO₂, PaO₂, SaO₂) ve transkutanöz CO₂ ve O₂ değerleri kaydedildi.

Bulgular: Gruplar arasında demografik parametreler, başlangıç beyaz küre, hematokrit, kalp hızı, santral venöz basınç, solunum sayısı ve pozitif ekspirasyon-sonu basınç değerleri açısından anlamlı bir fark bulunamadı. Grup 2'de serum üre ve kreatinin seviyeleri belirgin olarak yüksekken, albümin seviyeleri, ortalama arteriyel basınç daha düşüktü. APACHE-II ve SOFA skorları, tepe inspiratuar basınç ve FiO₂ grup 1'de belirgin olarak düşüktü.

Grup 1'de PtcCO₂ ve PaCO₂ değerleri açısından belirgin bir fark bulunamadı. Grup 2'deki PtcCO₂ değerleri PaCO₂ ile karşılaştırıldığında belirgin olarak düşüktü. Grup 1'de PaO₂ değerleri ile karşılaştırıldığında PtcO₂ belirgin olarak düşüktü. Grup 2'de PaO₂ ile karşılaştırıldığında PtcO₂ değerleri belirgin olarak düşüktü. Her iki grupta da arter ve transkutanöz CO₂ ve O₂ değerleri arasında güçlü bir korelasyon mevcuttu.

Sonuç: PtcCO₂'nin değerlendirilmesi septik şoklu hastalarda olmasa da sepsisli hastalarda alternatif bir yöntem olabilir. PtcO₂ ölçümleri her iki gruptaki hastalarda da güvenilir bir yöntem olarak görülmemiştir.

Anahtar Kelimeler: Sepsis, septik şok, YBÜ, transkutanöz CO₂, transkutanöz O₂, arter kan gazı analizi

Introduction

Sepsis is one of the leading causes of mortality and morbidity and has great clinical importance in general intensive care units (ICUs) in adults. Microcirculatory perfusion fails due to various mechanisms related to sepsis, which impairs measurement and assessment of peripheral oxygen saturation (SpO_2). Analysis of arterial blood samples is known as "gold standard" method to evaluate systemic oxygenation in septic patients (1,2).

However, the method used in routine clinical practice is invasive, expensive, painful and time-consuming. Manufacturers are also willing to introduce advanced non-invasive oxygenation monitoring devices and techniques. Nevertheless, the accuracies of these novel devices in different clinical situations are debated and have not been extensively studied.

To our knowledge this is one of the pioneering prospective studies in the literature comparing the transcutaneous O_2 and CO_2 analysis versus arterial blood gas analysis in septic patients in ICU. The aim of the study is to compare the effectiveness of non-invasive pressure of transcutaneous CO_2 (Ptc CO_2) and O_2 (Ptc O_2) analyzers versus conventional blood gas sampling in patients with sepsis and septic shock.

Materials and Methods

Approval of the study has been obtained from the Clinical Research Ethics Committee of the Gaziantep University (decision no: 249, date: 20.12.2011). A hundred patients, who have been admitted to the ICU with a diagnosis of sepsis or septic shock, were enrolled to the study. All the patients and/or their relatives were informed verbally and also written consent were obtained.

Patients, who are under 18 years old or have body mass indices (BMI) >35 or <18 kg/m^2 , were excluded from the study. Patients diagnosed with sepsis were divided into two study groups. Sepsis patients without a need for inotrope support (sepsis) were enrolled to group 1 ($n=50$), and group 2 ($n=50$) was composed of sepsis patients with a need for inotropes (septic shock). Diagnosis of sepsis and septic shock were made according to classical criteria (3).

Demographic data of the patients (including age, gender, BMI), baseline white blood cell (WBC) count, hematocrit (Hct), serum urea, creatinine, albumin levels, Acute Physiology and Chronic Health Evaluation-II (APACHE-II) and

Sequential Organ Failure Assessment (SOFA) scores were recorded.

Heart rate, mean arterial pressure (MAP), central venous pressure (CVP), oxygen saturation (SaO_2), respiratory rate, peak inspiratory pressure (PIP), positive end-expiratory pressure (PEEP), fraction of inspired oxygen (FiO_2) values were also simultaneously recorded.

Body temperature was continuously monitored and recorded.

Radial artery was cannulated for blood gas analysis and procedure lasted for approximately 5 minutes. Blood samples for blood gas analysis were collected at the 1st, 2nd, 3rd, and 4th hours and pH, Pa CO_2 , Pa O_2 , SaO_2 were analysed with Cobas b 121TM (Mennheim, Germany).

Ptc O_2 and Ptc CO_2 were measured with Transcutaneous Combi M4 (TCM4)TM (Radiometer®, Copenhagen, Denmark) and were recorded simultaneously with the arterial blood sampling. Device was calibrated before inserting the transcutaneous blood gas probe in every patient. If unexpected alterations of recorded values were noticed, bio calibration was repeated. Conventionally, temperature of the electrode of TCM4TM was set to 43 °C. The electrode of the TCM4TM was put on a hairless area of the forearm using a sticky fixation ring (E 5260/E 5280: Fixation ring 904-891; 30 mm; Radiometer Medical ApS, Denmark) at the opposite side of the arm that arterial blood samples were obtained. A few beads of electrolyte solution (Electrolyte solution, Radiometer Medical ApS, Denmark) were dropped to establish a contact between the electrode and the skin. The localization of the electrodes remained constant during the study.

Inotropic indices of the patients in group 2 were calculated according to the following formula depending on the vasoactive drug(s) used: Inotropic index = Dopamine* + Dobutamine* + (100x Epinephrine*) + (100x Norepinephrine*) + (15x Milrinone*) (4). (* $\mu g/kg/min$ infusion rate)

Statistical Analysis

The normality of distribution of continuous variables was tested by Kolmogorov-Smirnov test. Student's t-test was used for comparison of two independent groups of variables with a normal distribution and Mann-Whitney U test was used when the distribution was not normal. Paired t-test was utilized for comparison of two dependent groups of variables with normal distribution and Wilcoxon test was preferred when the distribution was not normal. The chi-square test

was used to assess relation between categorical variables and Pearson correlation coefficient was utilized for assessing relation between continuous variables. Descriptive statistic parameters were presented as frequency, percentage (%) and mean \pm standard deviation. Statistical analysis was performed with SPSS for Windows version 11.5[®] and a p-value <0.05 was accepted as statistically significant.

Results

A hundred patients were enrolled to the study. Female to male ratios of group 1 and 2 were 24/26 and 25/25, respectively ($p=0.841$). Mean age of the patients in group 1 and 2 were 53.72 ± 20.39 and 54.18 ± 20.26 , respectively ($p=0.911$). Also, BMI values of the patients in group 1 and 2 were 25.55 ± 3.15 kg/m² and 25.05 ± 3.10 kg/m², respectively ($p=0.423$).

There was no significant difference between groups in terms of baseline WBC ($19062\pm 13913/\text{mm}^3$ vs $19492\pm 9573/\text{mm}^3$; $p=0.857$) and Hct ($30.94\pm 5.77\%$ vs $31.66\pm 6.40\%$; $p=0.556$). Serum urea (80.16 ± 49.75 mg/dL vs 122.54 ± 71.89 mg/dL; $p=0.003$) and creatinine (1.42 ± 1.32 mg/dL vs 2.38 ± 1.70 mg/dL; $p=0.001$) levels were significantly higher, whereas albumin levels (2.94 ± 0.47 g/dL vs 2.68 ± 0.49 g/dL; $p=0.008$) were lower in group 2. APACHE-II (28.26 ± 4.84 vs 33.94 ± 5.20 ; $p=0.001$) and SOFA (8.02 ± 2.13 vs 10.64 ± 2.53 ; $p=0.001$) scores were significantly lower in group 1.

Baseline heart rate (114.78 ± 29.84 bpm vs 120.90 ± 24.47 bpm; $p=0.265$) and CVP (3.96 ± 2.81 cmH₂O vs 3.32 ± 2.97 cmH₂O; $p=0.272$) values were not significantly different between the groups. Baseline MAP was significantly decreased in group 2 compared with group 1 (96.94 ± 22.18 mmHg vs 76.36 ± 17.49 mmHg; $p=0.001$).

There was no significant difference between groups in terms of body temperature (37.12 ± 1.03 °C vs 37.09 ± 1.42 °C; $p=0.806$).

Comparison of baseline respiratory rate ($20.98\pm 6.98/\text{min}$ vs $21.24\pm 5.79/\text{min}$; $p=0.840$) and PEEP (6.30 ± 1.79 cmH₂O vs 6.76 ± 2.03 cmH₂O; $p=0.231$) values was not statistically different between two groups. However, baseline PIP (15.34 ± 5.03 cmH₂O vs 18.64 ± 5.73 cmH₂O; $p=0.003$) and FiO₂ (0.502 ± 0.19 vs 0.625 ± 0.21 ; $p=0.003$) values were significantly decreased in group 1.

The pH values of patients in group 1 were significantly higher than group 2 at the baseline (7.41 ± 0.08 vs 7.34 ± 0.15 , $p=0.005$), 1st hour (7.41 ± 0.07 vs 7.34 ± 0.15 , $p=0.004$), 2nd

hour (7.41 ± 0.07 vs 7.34 ± 0.14 , $p=0.004$), 3rd hour (7.41 ± 0.07 vs 7.34 ± 0.14 , $p=0.004$) and 4th hour (7.40 ± 0.07 vs 7.34 ± 0.14 , $p=0.003$).

There was no significant difference between PtcCO₂ and PaCO₂ values analyzed simultaneously at baseline, 1st, 2nd, 3rd and 4th hours in group 1 (Table 1).

PtcCO₂ values of group 2 were significantly lower when compared with PaCO₂ at baseline, 1st, 2nd, 3rd and 4th hours (Table 2).

PtcO₂ versus PaO₂ values were significantly lower in group 1 at baseline, 1st, 2nd, 3rd and 4th hours (Table 3).

PtcO₂ vs PaO₂ values were significantly lower in group 2 at baseline, 1st, 2nd, 3rd and 4th hours (Table 4).

There was a statistically strong positive correlation between arterial and transcutaneous CO₂ values in group 1

Table 1. PtcCO₂ and PaCO₂ values of patients in group 1

Time	PtcCO ₂ (mean \pm SD)	PaCO ₂ (mean \pm SD)	p
Baseline	37.26 \pm 6.55	37.66 \pm 6.72	0.072
1 st hour	37.10 \pm 6.11	37.60 \pm 6.24	0.231
2 nd hour	36.86 \pm 6.11	37.03 \pm 6.42	0.332
3 rd hour	37.12 \pm 5.96	37.12 \pm 6.07	0.967
4 th hour	37.12 \pm 5.94	37.10 \pm 5.99	0.881

SD: standard deviation

Table 2. PtcCO₂ and PaCO₂ values analyzed in group 2

Time	PtcCO ₂ (mean \pm SD)	PaCO ₂ (mean \pm SD)	p
Baseline	34.64 \pm 7.19*	39.00 \pm 7.12	0.001
1 st hour	34.76 \pm 7.01*	39.04 \pm 7.00	0.001
2 nd hour	34.66 \pm 6.89*	38.89 \pm 6.79	0.001
3 rd hour	34.58 \pm 7.16*	38.96 \pm 7.22	0.001
4 th hour	34.44 \pm 7.08*	38.92 \pm 6.91	0.001

*Significant difference between PtcCO₂ and PaCO₂ values $p<0.05$. SD: standard deviation

Table 3. PtcO₂ and PaO₂ values in group 1

Time	PtcO ₂ (mean \pm SD)	PaO ₂ (mean \pm SD)	p
Baseline	66.16 \pm 14.68*	82.87 \pm 18.26	0.001
1 st hour	70.20 \pm 16.58*	86.65 \pm 19.60	0.001
2 nd hour	71.58 \pm 14.59*	88.13 \pm 20.63	0.001
3 rd hour	72.04 \pm 13.05*	87.96 \pm 18.19	0.001
4 th hour	71.46 \pm 12.90*	87.01 \pm 17.06	0.001

*Significant difference between PtcO₂ and PaO₂ values $p<0.05$. SD: standard deviation

at the baseline ($r=0.972, p=0.001$), 1st ($r=0.971, p=0.001$), 2nd ($r=0.982, p=0.001$), 3rd ($r=0.986, p=0.001$) and 4th ($r=0.988, p=0.001$) hours. There was a statistically similar strong positive correlation between arterial and transcutaneous CO₂ values in group 2 at the baseline ($r=0.983, p=0.001$), 1st ($r=0.976, p=0.001$), 2nd ($r=0.981, p=0.001$), 3rd ($r=0.981, p=0.001$) and 4th ($r=0.982, p=0.001$) hours. Correlation between PtcCO₂ ve PaCO₂ alterations in group 1 and group 2 are shown on Figure 1.

Correlation analysis of arterial and transcutaneous O₂ values in group 1 was performed and a statistically strong positive correlation was revealed at the baseline ($r=0.815, p=0.001$), 1st ($r=0.881, p=0.001$), 2nd ($r=0.890, p=0.001$), 3rd ($r=0.863, p=0.001$) and 4th ($r=0.882, p=0.001$) hours. A similar statistically strong positive correlation between arterial and transcutaneous O₂ values in group 2 was observed at the baseline ($r=0.826, p=0.001$), 1st ($r=0.827, p=0.001$), 2nd

($r=0.659, p=0.001$), 3rd ($r=0.838, p=0.001$) and 4th ($r=0.834, p=0.001$) hours. Correlation between PtcCO₂ ve PaCO₂ alterations in group 1 and group 2 are shown on Figure 2. Inotropic index was 25.54 ± 13.92 in group 2.

Discussion

Septic patients have compromised tissue perfusion due to microcirculatory disturbances. Impaired tissue microperfusion of patients with septic shock had been clearly shown in previous studies. In general, macro circulatory parameters are the main targets in order to optimize treatment of septic shock in early phase (5). However, persistent compromisation of tissue perfusion may occur in some patients due to microcirculatory disturbances. Although conventional blood gas sampling methods are considered as "gold standard", there is always place for a less invasive, painless, and timesaving "patient-friendly" alternatives. There are many papers implicating the cons of unnecessary blood draws with respect to not only anemia but also infection control and healthcare costs (6,7). Therefore the need for less invasive monitoring methods is evident.

In the English literature there are recent papers regarding comparison between non-invasive PtcO₂/PtcCO₂ monitoring and conventional blood gas sampling methods such as in neonatal and adult ICUs (8-10), but to the best of our

Time	PtcO ₂ (mean ± SD)	PaO ₂ (mean ± SD)	p
Baseline	64.53±17.12*	81.91±21.53	0.001
1 st hour	65.69±17.21*	81.77±20.35	0.001
2 nd hour	66.66±17.64*	80.64±22.67	0.001
3 rd hour	66.77±17.64*	81.56±19.76	0.001
4 th hour	66.47±17.65*	80.47±18.05	0.001

*Significant difference between PtcO₂ and PaO₂ values $p<0.05$. SD: standard deviation

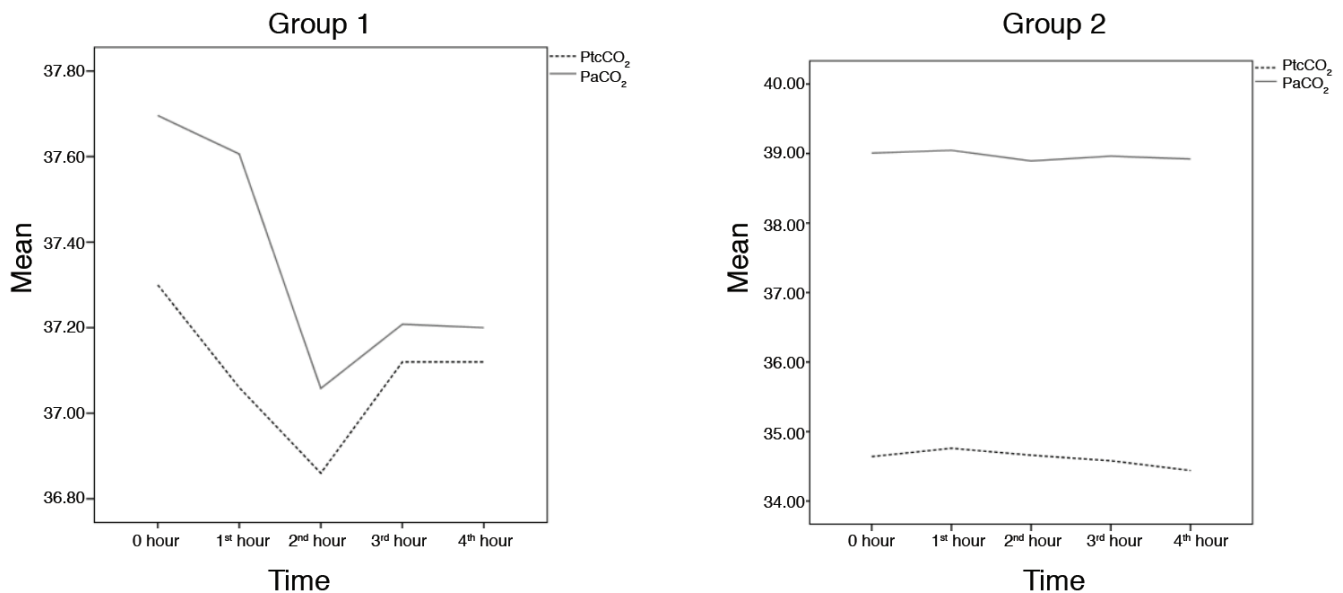


Figure 1. Correlation between PtcCO₂ and PaCO₂ alterations in group 1 and group 2

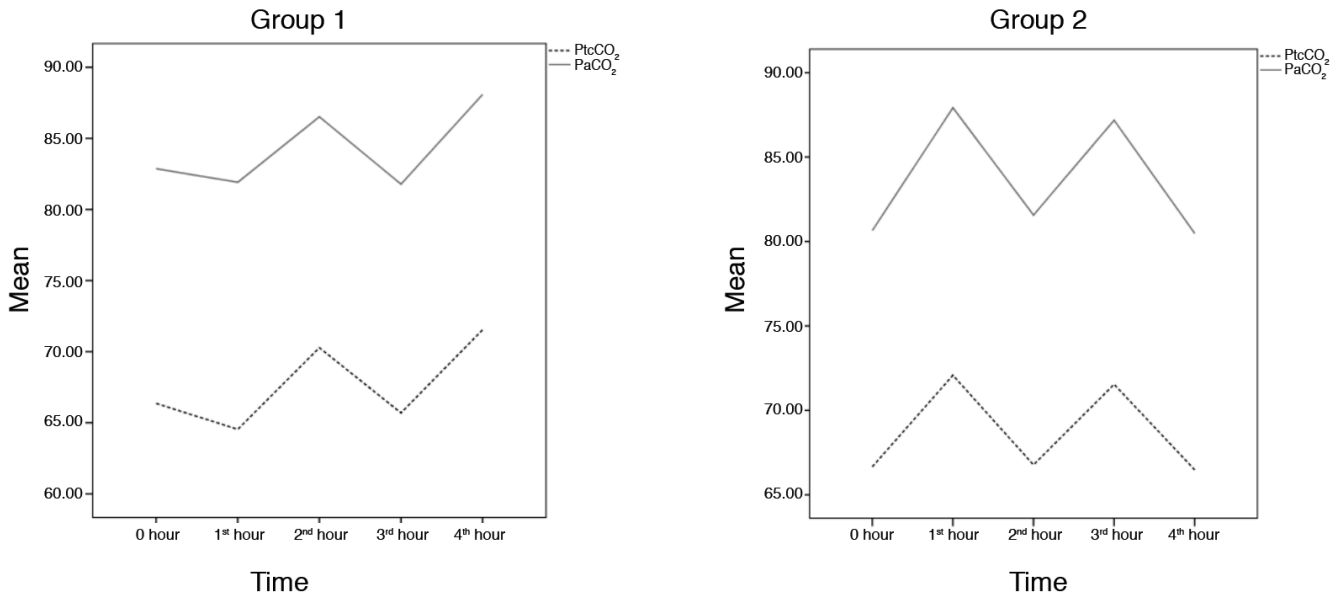


Figure 2. Correlation between PtcCO₂ and PaO₂ alterations in group 1 and group 2

knowledge this is the first prospective study comparing the transcutaneous O₂ and CO₂ analysis versus arterial blood gas analysis in a homogenous specific subgroup such as septic patients in ICU and also one of the largest sample size.

There are three major results arising from this study. First, there was no significant difference between the values of PtcCO₂ and PaCO₂ in patients with sepsis. There was a strong positive correlation between PtcCO₂ and PaCO₂ values (Figure 1). These findings may support to use PtcCO₂ monitoring as an acceptable alternative method.

Second, PtcCO₂ values of group 2 were significantly lower than PaCO₂ values (p<0.05) and there was a strong positive correlation between the values indeed. This finding is not surprising because abolished peripheral microcirculation is a part of the septic shock pathophysiology itself. Hypo perfusion states like shock and/or acidosis may present decreased values of PtcO₂ and PtcCO₂ and vasoactive drug administration may also result in decreased PtcO₂ and PtcCO₂ (11-14).

Recent TCM™ devices with the help of selection of a sensor place near the carotid artery have led to improved correlation between PaO₂ and PtcO₂ measurements (15-18). Studies regarding placement of the sensor site on the distal part of an extremity have reported lower readings, due to vasoconstriction limiting blood flow (19-21). Other studies have shown that choosing a sensor area in chest,

infraclavicular area or ear is accompanied with more reliable results (22,23). In this present study, the sensor was placed in the forearm, which can be accepted relatively a distal part of the extremity, and therefore might have contributed to the lower reading of PtcCO₂ values in patients with septic shock. Although we demonstrated strong positive correlation between simultaneously obtained PtcCO₂ and PaCO₂ values, this may be accepted as a limitation of the study. This unexpected finding of our study also emphasizes the importance of correct selection of sensor electrode placement, especially when the pathophysiology of septic shock is considered.

Third, simultaneously measured values of PtcO₂ were significantly lower than PaO₂ and there were strong positive correlations in both study groups. This finding is consistent with the literature. The more the skin is warmed to highest tolerable temperature, the more increase takes place in the capillary blood flow. In order to reach the greatest increased blood flow, the highest tolerable temperature is reported as 45 °C, when the surface blood PtcO₂ rises to approximately PaO₂ (24). There is a generally accepted rule for safety as limiting the electrode temperature at 43 °C up to four hours, although suggested monitoring method for detection of PtcCO₂ and PtcO₂ is to increase the skin temperature up to 45 °C to arterialize capillary blood flow (25,26). However, higher electrode temperatures may generate the risk of skin

burning. In our study, we limited the electrode temperature at 43 °C for safety, which is appropriate for detecting PtcCO₂, but not for PtcO₂. Our concerns regarding safety instead of increasing the temperature of the electrodes for more accurate measurements seems to be another dilemma when interpreting our results.

Another explanation for the lower detected values of PtcO₂ in both groups may be impaired macro and microcirculation, which is similar to PtcCO₂.

Conclusion

In summary, transcutaneous monitoring of CO₂ may be a charming, less-invasive, time-consuming and reliable alternative method in patients with sepsis. The effectiveness and safety of this method in patients with septic shock is questionable. Transcutaneous monitoring of O₂ may not be a reliable and feasible method for patients with sepsis and septic shock. The need for further large scaled studies is evident to confirm the safety, effectiveness and optimization of these recent techniques of transcutaneous CO₂ and O₂ monitoring.

Ethics

Ethics Committee Approval: Approval of the study has been obtained from the Clinical Research Ethics Committee of the Gaziantep University (decision no: 249, date: 20.12.2011).

Informed Consent: All the patients and/or their relatives were informed verbally and also written consent were obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: R.S., B.K.U., Concept: R.S., B.K.U., S.G., Design: R.S., S.G., Data Collection and Process: R.S., S.G., P.T., Analysis or Interpretation: B.K.U., S.G., Literature Search: B.K.U., P.T., Writing: B.K.U.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: Financial support was received from Gaziantep University Rectorate Scientific Research Projects Department for this study (project no: TF12.33).

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