Anatolian Journal of Emergency Medicine 2018;1(1); 1-4

ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA MAKALESİ

# Comparing Noninvasive Pulse CO-Oximeter vs Blood Gas Analysis in Emergency Department Patients with Carbon Monoxide Poisoning

*Karbonmonoksit Zehirlenmesi ile Acil Servise Başvuran Hastalarda Noninvaziv Nabız CO-oksimetre ile Kan Gazı Analizinin Karşılaştırılması*

Sinan KAYA[1], Mehtap BULUT[2], Behçet VARIŞLI[3], Yalçın KATI[4], Ulaş KARAOĞLU[2]

## ABSTRACT

**Introduction:** In order to diagnose carbon monoxide (CO) poisoning, clinical suspicion, a reliable history, and the detection of high level of carboxyhemoglobin (COHb) in blood gas analysis are required. The purpose of this study is to compare noninvasive pulse CO-oximetry versus blood gas analysis (BGA) in emergency department (ED) patients with CO poisoning.

**Methods**: From the patients, who were 18 years of age or over, presenting with suspicion of CO poisoning and who were eligible for inclusion in the study, arterial/venous blood gas samples were collected and SpCO was measured by pulse CO-oximetry and recorded by the time of ED visit. Sensitivity and specificity percentages, positive and negative predictive values were determined with ROC analysis. Bland-Altman analysis was used to assess the agreement between two measurement methods.

**Results**: The study was carried out prospectively on 213 patients in total, 133 (62%) of whom were female with a mean age of 38 ± 15. The limits of agreement were -6.5 to 9.9% COHb (bias 1.7%, precision 4.1%). Cut off value in CO measurement was 23, sensitivity was 97.2%, specificity was 80.4%, NPV was 96.6%, and PPV was 83%. Concordance coefficient value (0.868) between BGA, and pulse CO-oximetry was found out to be significantly high.

**Conclusion:** When pulse CO-oximetry is compared with BGA, it appears to diagnose CO poisoning rapidly and accurately and therefore, it may be used both in pre-hospital period and EDs as a screening test for CO poisoning.

**Keywords:** Carbon monoxide (CO) poisoning; noninvasive pulse CO-oximetry; blood gas analysis; emergency department

## ÖZET

**Giriş:** Karbon monoksit (CO) zehirlenmesinin tanısı için klinik şüphe, güvenilir bir anamnez ve kan gazında yüksek karboksihemoglobin (COHb) düzeyinin saptanması gereklidir. Bu çalışmada CO zehirlenmesi ile acil servise başvuran hastalarda noninvaziv nabız CO-oksimetre ile kan gazı analizinin karşılaştırılması amaçlanmıştır.

**Metot:** CO zehirlenmesi şüphesi olan ve çalışmaya dahil edilmeye uygun 18 yaş ve üzeri hastalarda, acil servis başvurusu esnasında arteriyel/venöz kan gazı örnekleri alınmış ve nabız CO-oksimetre ile SpCO düzeyleri ölçülmüştür. ROC analizi yapılarak sensitivite, spesifite, negatif prediktif değer (NPD) ve pozitif prediktif değer (PPD) saptanmıştır. İki ölçüm metodu arasındaki uyumu değerlendirmek için Bland-Altman analizi kullanılmıştır.

**Bulgular:** Çalışma toplam 213 hasta üzerinde prospektif olarak yapılmıştır. Hastaların 133'ü (%62) kadın olup ortalama yaş 38 ± 15'tir. Uyum sınırları -6.5 ila 9,9% COHb'dir (bias %1,7, kesinlik %4,1). CO ölçümü için sınır değeri 23, sensitivite %97,2, spesifite %80,4, NPD %96,6, PPD %83 olarak hesaplanmıştır. Kan gazı analizi ile nabız CO-oksimetre arasındaki uyum katsayısı değeri (0,868) anlamlı ölçüde yüksek bulunmuştur.

**Sonuç:** Nabız CO-oksimetre, kan gazı ile karşılaştırıldığında CO zehirlenmesinde hızlı ve hassas bir biçimde tanı koymaktadır ve hem hastane öncesi dönemde hem de acil servislerde CO zehirlenmesi için bir tarama testi olarak kullanılabilir.

**Anahtar Kelimeler:** Karbon monoksit (CO) zehirlenmesi; noninvaziv nabız CO-oksimetre; kan gazı analizi; acil servis

[1] Department of Emergency Medicine, Muş Şifa Hospital, Muş, Turkey
[2] Department of Emergency Medicine, İstanbul Medipol University Faculty of Medicine, İstanbul, Turkey.
[3] Final International University İFU Eğitim Kurumları Limited, Girne, KKTC
[4] Department of Emergency Medicine, Bursa İnegöl State Hospital, Bursa, Turkey
**Corresponding Author:** Mehtap Bulut, MD, Department of Emergency Medicine, İstanbul Medipol University Faculty of Medicine, İstanbul 34214, Turkey. **Phone:** +90 505 716 3665 **E-mail:** mbulut94@yahoo.com

## Introduction

Carbon monoxide (CO) is a colorless, odorless, and tasteless gas that is present if carbon-based agents burn incompletely. Acute CO poisoning is a leading type of poisoning which might cause death due to its early and late period effects.(1) CO poisoning, which has an increasing frequency especially during cold winter months in Turkey, is still an important community health problem both in Turkey and in the world.(1-3) Official data from the United States indicate approximately 20.000 exposures and 459 deaths per year, including only non-fire related and unintentional cases.(4, 5) Large registry trials, however, show much higher numbers than those officially reported, with approximately 50.000 visits per year to emergency departments (EDs) alone, representing 0.05% of all patients.(6) In Turkey CO poisoning has been reported to represent 31% of all poisonings causing death, which is also the most common cause.(3)

Symptoms of CO poisoning are nonspecific, ranging from mild headache, nausea, confusion, and dizziness to end-organ injury such as myocardial infarction, stroke, and death. Diagnosis is therefore difficult and relies on clinical suspicion and confirmation by measurement of carboxyhemoglobin (COHb), using either arterial or venous blood gas (BG) analysis (4,7). However, blood gas analyzers are not ubiquitously available. As a result, many victims of CO poisoning might be overlooked and misdiagnosed (7).

In 2005, a device was manufactured for noninvasive bedside measurement of blood carboxyhemoglobin level (Rad-57 signal extraction pulse CO-oximeter, Masimo Corporation, Irvine, CA). This is a FDA (Food and Drug Administration) approved pulse CO-oximetry device for noninvasive bedside measurement which can give results within 30 seconds without requiring arterial or venous blood gas sampling. This kind of device may enable quick diagnosis and the start of treatment in busy EDs as soon as possible. The use of the device not only by hospital EDs but also by ambulance crew will enable the cases with suspicion of CO poisoning to be taken to the most appropriate hospital during pre-hospital period in a shorter time. There have been few published studies thus far on comparison between the COHb values measured by that recent device and BG analysis in patients presenting to the ED while other studies were carried out in laboratories, hyperbaric centers, and burn centersc(7,8). We aimed to compare noninvasive pulse CO-oximeter with blood gas carboxyhemoglobin measurement in ED patients with suspected CO poisoning.

## Materials and Method

This research was carried out prospectively at Bursa Şevket Yılmaz Training and Research Hospital emergency medicine department following the approval of Ethics Committee (no: 2012/16/2). The province of Bursa is located in south Marmara region of Turkey and is subjected to severe southwester especially during winter-fall season. Therefore, during these periods CO poisoning is highly experienced in our city. Our hospital is a tertiary TRH admitting nearly 45.000 ED patients per month (total ED admissions in 2013 is 540.000 patients).

The patients who were 18 years of age or over, presenting to adult ED with suspicion of CO poisoning between November 2012 and April 2013 were included in the study. Patients were excluded if they were younger than 18, if they were dead on arrival (DOA), if they were transferred from another center, if informed consent could not be obtained, and if the patients did not have the suspicion/history of CO poisoning. Diagnosis of CO poisoning included presentation with a history compatible with exposure, symptoms typical of the syndrome, and demonstration of an elevated blood COHb level. All patients included in this study were managed as usual for CO poisoning: physical examination, electrocardiography and typical laboratory tests were conducted. Blood pressure, pulse rate, respiratory rate, temperature, and Glasgow Coma Scale (GCS) were recorded at the time of admission. After initial examination of patients, arterial/venous blood samples were collected simultaneously for measuring COHb levels and finger-tip measurement was performed non-invasively with a Rad-57Pulse CO-oximeter for measuring SpCO. SpCO is defined as COHb level that is noninvasively measured via pulse CO-oximeter. The Rad-57 Pulse CO-oximeter was used as stated in the Masimo Rainbow® SET® operator's manual. Collected blood samples were analyzed by an arterial blood gas analyser (ABL700 series analyser, Radiometer America, Copenhagen, DK).

*Statistical analysis*

Statistical analysis of the data was performed through SPSS 15.0 software program (SPSS Inc., Chicago, Illinois, USA). Descriptive statistical methods (frequency, percentage, mean, standard deviation) were also employed for assessments. In order for the comparison of quantitative data paired samples t-test was used for within-group comparison. Concordance Correlation Coefficient and Pearson Correlation Coefficient were determined for concordance of the method. The method described by Bland-Altman was used to assess agreement between measurement by CO-oximeter (SpCO) and by blood gas analysis (COHb). The mean difference (bias or accuracy, d) as a metric for the systematic measurement error, the SD of the differences (precisions, s), and the limits of agreement (d ± 1.96s) as metrics for scatter were calculated (7). Cut off values for both were established by ROC analysis and thus sensitivity and specificity percentages, positive and negative predictive values were determined in accordance with that analysis. The findings were evaluated at 95 percent confidence interval (CI) considering significance level as $p<0.05$.

## Results

Although 351 patients were included in the study at the beginning, 138 of them were excluded as their blood gas analysis could not be made due to breakdown of blood gas device in our hospital time to time. Therefore, total 213 patients (133 female (62%), 80 males (37%)) were eligible for the study. The mean age of the patients was 38 ± 15 (17-88). The most common source of CO poisoning was coal stove (152 patients, 71%). 211 (99%) of the patients came to hospital from home. The most frequent symptom of the patients presenting with CO poisoning was headache (65%). Vital signs and GCS scores of the poisoned patients were determined as follows: mean of systolic arterial pressure (SAP) 118 ± 17 mmHg, mean of diastolic arterial pressure (DAP) 71 ± 10 mmHg, mean of pulse 90 ± 16 bpm, mean of respiratory rate (RR) 16 ± 2, mean of temperature 36.5 ± 0.3 °C, mean of GCS 14.9 ± 0.271 (Table1).

**Table 1** Baseline characteristics of study population (n=213)

| Variables | Subgroups | Values |
|---|---|---|
| Sex, n (%) | Female | 133 (62.4) |
| | Male | 80 (37.6) |
| Age, mean ± SD, (range), years | | 38.11 ±15.68 (17-88) |
| Source of CO, n (%) | Coal stove | 152 (71.3) |
| | Natural gas | 32 (15) |
| | Water heater | 26 (12.2) |
| | Exposure to fire | 3 (1.5) |
| Place of CO poisoning, n (%) | At home | 211 (99.1) |
| | At work | 2 (0.9) |
| Transport to the hospital, n (%) | 112 ambulance | 118 (55.4) |
| | Personal car | 76 (35.7) |
| | By walk | 19 (8.9) |
| Chief complaints, n (%) | Headache | 139 (65.2) |
| | Nausea | 118 (55.3) |
| | Vertigo | 81 (38) |
| | Malaise | 50 (23) |
| Vital signs, mean ± SD, (range) | SAP (mmHg) | 118.1 ± 17.3 (80-200) |
| | DAP (mmHg) | 71.5 ± 10.2 (50-100) |
| | Pulse (beats/min) | 90.06 ± 16.8 (36-140) |
| | Respiratory rate (breaths/min) | 16.5 ± 2.2 (12-26) |
| | Temperature (°C) | 36.5 ± 0.3 (35.9-39.3) |
| | GCS | 14.9 ± 0.2 (12-15) |

SAP: Systolic arterial pressure; DAP: Diastolic arterial pressure; GCS: Glasgow Coma Scale.

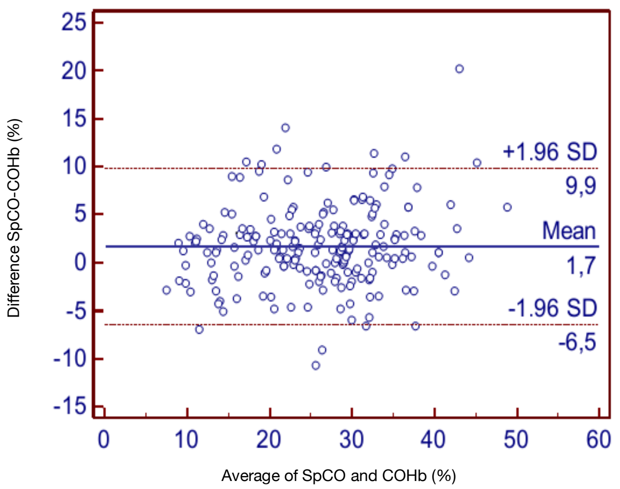


**Figure 1.** Bland-Altman diagrams comparing CO-oximetry (SpCO) with blood gas analysis (COHb). d denotes the bias (mean SpCO to COHb), s denotes the precision (SD of the differences between SpCO and COHb). Dotted lines represent the limits of agreement for SpCO (d±1.96).

The mean of COHb measurement by BG analysis was 26.6 ± 8.9% (min-max COHb: 6.1-53.2%). On the other hand, the mean of SpCO measurement by RAD-57 Pulse CO-oximeter was 24.9 ± 8.3% (min-max COHb: 8-46%). In terms of COHb values, the graphic of Bland-Altman method which was used for comparing the concordance/measurement values of BG and RAD-57 devices was displayed in Figure 1. In COHb measurement, bias was 1.7%, precision was 4.1%, and the limits of agreement were -6.5 to 9.9%. Concordance coefficient of COHb measurement values of BG and RAD-57 devices was 0.868 (95% CI 0.832 - 0.897) and it showed that the correlation between them is high. Pearson ρ correlation coefficient of BG and RAD-57 measurement values was found as 0.886.

In measurement, RAD-57 cut off value was 23. Accordingly, sensitivity of RAD-57 measurement compared to BG was 97.2% specificity was 80.4%, positive predictive value was (PPV) 83%, and negative predictive value was (NPV) 96.6%. Area under the curve, AUC= 0.948 ($p<0.0001$) was statistically significant (Figure 2).

## Discussion

Due to its effect on many systems and its non-specific symptoms, CO poisoning is difficult to diagnose (1,2,5). Invasive measurement of COHb by BG analysis is accepted as the standard diagnostic procedure in the diagnosis of CO poisoning (9,10). Yet, blood gas analyzers might not be available everywhere and anytime. One recent survey of acute care hospitals in the Pacific Northwest revealed that only 44% of the responding hospitals had the capacity to measure COHb levels (10,11). To the best of our knowledge, there has not been a study on this subject in our country but it can be said that in some of the hospitals within the borders of our province BG devices are not available. Besides, BG analysis can be a painful procedure requiring blood draw from the patient. A rapid and noninvasive method for measuring COHb levels accurately could offer numerous benefits, and a broad screening program could ideally detect previously unsuspected cases of poisonings presenting to the ED (11).

Methodologies and settings of the studies evaluating the performance of Rad-57 in current literature are variable (11). Those studies were carried out on healthy volunteers and selected small patient groups (12-16). Studies on non-selective and large group of patients do not exist. A study by Barker et al. is considered as the first study administered on human in which ten healthy volunteer subjects were subjected to CO such that the COHb level reached 15%. In this study they reported that when COHb level was at 0-15%interval, RAD-57 accurately detected it by ±%2 gap. Also, they stated that the device could be used both for COHb and methemoglobin measurements and Bland and Altman method comparison showed that bias and precision was -1.22% and ±2.2%, respectively. After all, they pointed out that clinical studies were needed to evaluate the performance of RAD-57 in patients with critical conditions and for higher COHb levels.(12) In their study with nine healthy subjects who were subjected to CO such that it raised the COHb to 10–14%, Zaouter et al. figured out that the Rad-57 provided a reading that was between −6% and 4% of the true COHb value for 95% of all samples (bias -0.8%, precision ±2.5%). Also, they determined that at COHb levels ≥10% to 14%, the Rad-57 CO-oximeter had a sensitivity of 54% and a specificity of 89%. They concluded that it was a rapid and non-invasive method for initial screening of the patients arriving to the ED with suspected CO poisoning and that when the readings of SpCO are ≥15% with Rad-57 a second screening with blood drawing should be performed.(17) In our study, the limits of agreement determined were-6.48 to 9.87% (bias 1.7%, precision 4.1%) for measurement. Cut off value in CO measurement was 23, sensitivity was 97.2%, specificity was 80.4%, NPV was 96.6%, and PPV was 83%.

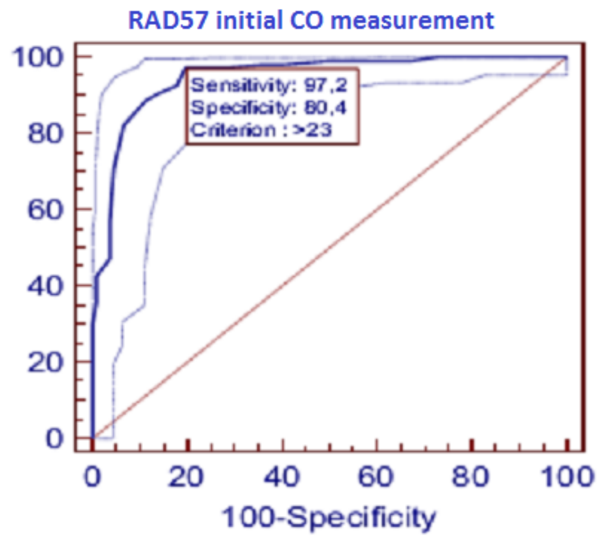


**Figure 2.** Receiver operating charateristics (ROC) curve analysis. Sensitivity and specificity graphic according to Carboxyhemoglobin measurement by RAD-57 pulse-CO oximetry

Touger et al. compared RAD-57 pulse CO-oximeter with blood gas COHb measurement on 120 CO toxicity patients presenting to ED and found out that median COHb level was 2.3%, median SpCO was 3.0, bias was 1.4%, and the limits of agreement were -11.6 to 14.4% with a precision of 6.6%.Since the range exceeded the value of ±5%, they concluded that RAD-57 measurement may not be used interchangeably with blood gas measurement.(8) In our study, mean COHb level was 26.68 ± 8.9%, mean SpCO was 24.98± 8.3%. For the measurement, bias was 1.7% and limits of agreement were -6.48 to 9.8%. 213 patients were included in this study but bias values were very close to those detected by Touger et al. and also our limits of agreement values were better in comparison to those of their study. Also, they determined that at COHb levels ≥15%, the Rad-57 CO-oximeter had a sensitivity of 54% and a specificity of 89%. In a study by Suner et al. with a sample of 64 patients, a bias of-4.2%, limits of agreement were-16to 7.5%, which was interpreted as “good agreement”. In the same study, the sensitivity and specificity of SpCO using venous COHb as the gold standard were 94% and 54%, respectively (13). In another study, both RAD-57 and blood gas COHb measurements were performed on 1578 ED patients, without considering the patient complaints, and CO poisoning was identified in 17 of those patients. A bias of 2.32%, a precision of 4.01% and, the limits of agreement of those 17 patients were -5.7 to 10.37%. In conclusion, the authors reported that pulse CO-oximetry was found to measure COHb with an acceptable bias and precision. The authors stated that through this device, the patients with occult CO poisoning could be detected among those who presenting to the ED (10). In our study, the limits of agreement were -6.48 to 9.87% (bias 1.7%, precision 4.1%). Cutoff value for CO measurement was 23, sensitivity was 97.2%, specificity was 80.4%, NPV was 96.6%, PPV was 83%. In another study administered in France by Coulange et al., during the 7-month study period, pulse CO-oximetry was measured on twelve non-smoker adult/child patients admitted to ED for suspected CO poisoning (14). Analysis by the Bland and Altman procedure suggested good alignment with a slight bias of -1.5%. Coulange et al. stated that CO-oximetry was cost-effective and more reliable than conventional laboratory techniques and it could be useful before and after arrival at the ED for all patients. When our bias, precision and, limits of agreement were compared with the results of other studies, it might be said that they are relatively more favorable. The device manufacturer cites unpublished validation data supporting accuracy of 3% (1 SD of differences) in the range of 1% to 40% carboxyhemoglobin (8,13,18).

Another study carried out with 49 patients presenting to hyperbaric center with CO poisoning revealed that when a reading of SpCO more than 20% was read by the RAD-57 CO-oximeter, the sensitivity was 77.8%, the specificity was 90.3%, while PPV was 82.4% and NPV was 87.5%. The study concluded that RAD-57 pulse CO-oximeter determined SpCO level accurately (19). In our study, when cutoff value was 23, the sensitivity, specificity, PPV, and NPV were 97.2%, 80.4%,83%, 96.6%, respectively. The values of COHb measurement in our study display resemblance especially with the study results of Kot et al. This might stem from the closeness of mean SpCO values both in our study (24.98± 8.3% (8-46%) and in Kot et al.'s study (17.6±11.3% (1-46%). In our opinion, the reason of different study results mentioned above might be because of different study groups (volunteer healthy subjects and patients) and different COHb levels.

In conclusion, RAD-57 pulse CO-oximeter device may be used both in pre-hospital period and EDs as a screening test. In high-volume urban EDs like our ED, rapid and accurate diagnosis will ease treatment and follow-up of the patients with CO poisoning. However, when existing studies (the accuracy, precision, and limits of agreement of SpCO measured by the RAD-57, as compared to actual COHb levels) are examined, it has been seen that very different methodologies and results are available (11). For this reason, further multi-centered and prospective studies with larger number of patients examining the accuracy and reliability of RAD-57 pulse CO-oximeter in measuring COHb levels are in need.

## Acknowledgements

Statistical data analysis of this research has been done by Fatih SONTAY from Bilgi Eğitim Danışmanlık, İstanbul 34714 Turkey.

## Funding

None Declared

## References

1. Van Weter KW. Carbon Monoxide Poisoning. In: Tintinalli JE, Kelen GD, Stapczynski JS, editors. Tintinalli's Emergency Medicine 6th ed. New York: McGraw-Hill; 2004.p.1238–42.
2. Iqbal S, Law HZ, Clower JH, et al. Hospital burden of unintentional carbon monoxide poisoning in the United States, 2007. Am J Emerg Med 2012;30:657-64.
3. Besli G, Ergüven M, Karadoğan M,et al. Çocuklarda Karbon Monoksit Zehirlenmesi. Akademik Acil Tıp Dergisi 2010;9:26-30.
4. Centers for Disease Control and Prevention (CDC). Nonfatal, unintentional, non–fire-related carbon monoxide exposures-United States, 2004-2006. MMWR 2008;57:896-9.
5. Centers for Disease Control and Prevention (CDC). Carbon monoxide-related deaths-United States, 1999-2004. MMWR2007;56:1309-12.
6. Hampson NB, Weaver LK. Carbon monoxide poisoning: a new incidence for an old disease. Undersea Hyperb Med2007;34:163-8.
7. Roth D, Herkner H, Schreiber W,et al. Accuracy of Noninvasive Multiwave Pulse Oximetry Compared With Carboxyhemoglobin From Blood Gas Analysis in Unselected Emergency Department Patients. Ann Emerg Med 2011;58:74-9.
8. Touger M, Birnbaum A, Wang J, et al. Performance of the RAD-57 PulseCO-oximeter Compared With Standard Laboratory Carboxyhemoglobin Measurement. Ann Emerg Med 2010;56:382-8.
9. Prockop LD, Chichkova RI. Carbon monoxide intoxication: an updated review. Journal of the neurological sciences 2007;262(1):122-30.
10. Hampson NB, Scott KL, Zmaeff JL. Carboxyhemoglobin measurement by hospitals: implications for the diagnosis of carbon monoxide poisoning. J Emerg Med 2006;31:13-6.
11. Wilcox SR, Richards JB. Noninvasive carbon monoxide detection: insufficient evidence for broad clinical use. Respir Care 2013;58:376-9.
12. Barker SJ, Curry J, Redford D, et al. Measurement of carboxyhemoglobin and methemoglobin by pulse oximetry: a human volunteer study. Anesthesiology 2006;105:892-7.
13. Suner S, Partridge R, Sucov A, et al. Non-invasive pulse CO-oximetry screening in the emergency department identifies occult carbon monoxide toxicity. J Emerg Med 2008;34:441-50.
14. Coulange M, Barthelemy A, Hug F, et al. Reliability of new pulse CO-oximeter in victims of carbon monoxide poisoning. Undersea Hyperb Med 2008;35:107-11.
15. Piatkowski A, Ulrich D, Grieb G, et al. A new tool for the early diagnosis of carbon monoxide intoxication. Inhal Toxicol 2009;21:1144-7.
16. Mottram CD, Hanson LJ, Scanlon PD. Comparison of the Masimo Rad 57 pulse oximeter with SpCO technology against a laboratory CO-oximeter using arterial blood. Respir Care 2005;50:1471.
17. Zaouter C, Zavorsky GS. The measurement of carboxyhemoglobin and methemoglobin using a non-invasive pulse CO-oximeter. Respir Physiol Neurobiol 2012;182:88-92.
18. Chee KJ, Nilson D, Partridge R, et al. Finding needles in a haystack: a case series of carbon monoxide poisoning detected using new technology in the emergency department. Clin Toxicol (Phila) 2008;46:461-9.
19. Kot J, Sićko Z, Góralczyk P. Carbon monoxide pulse oximetry vs direct spectrophotometry for early detection of CO poisoning. Anestezjol Intens Ter 2008;40:75-8.