ORIGINAL ARTICLE

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Association Between Near Infrared Spectroscopy (NIRS) and Normobaric and Hyperbaric Oxygen Treatment in Acute Carbon Monoxide Poisoning

ABSTRACT

Objective: Carbon monoxide (CO) is the main cause of death and morbidity associated with poisoning in developed countries. The most important mortality and morbidity cause of CO poisoning is cerebral hypoxia. Near infrared spectroscopy (NIRS) is a useful method for assessing brain oxygenation. In this study, we aimed to evaluate the brain oxygenation of CO poisoning patients with NIRS and to investigate its benefits in patients follow up and treatment.

Methods: The study was conducted as a single-center, prospective clinical trial with 33 patients who were diagnosed by measuring blood carboxyhemoglobin (CO-Hb) level or referred from other hospitals diagnosed with CO poisoning. Patients were divided into two groups as normobaric oxygen therapy (NBOT) group and hyperbaric oxygen therapy (HBOT) group according to the treatment method applied.

Results: Although average cerebral saturation (ScO2) levels after treatment were higher in the NBOT group than before treatment, no statistically significant difference was found except the left frontal ScO2 values. In HBOT group, there was no difference between ScO2 values before and after treatment sessions.

Conclusions: Our study concluded that NIRS may be useful in assessing brain oxygenation in CO poisoned patients, but not in determining the HBOT start-up, and not in monitoring the effectiveness of HBOT.

Keywords: Carbon Monoxide Poisoning, Hyperbaric Oxygen Therapy, Near-Infrared Spectroscopy, Normobaric Oxygen Therapy

Akut Karbonmonoksit Zehirlenmesinde Near Infrared Spectroskopy (NIRS) ile Normobarik ve Hiperbarik Oksijen Tedavisi Arasındaki İlişki

ÖZET

Amaç: Karbonmonoksit (CO) gelişmiş ülkelerde zehirlenme ile ilişkili ölüm ve morbiditenin ana nedenidir. CO zehirlenmesinin en önemli mortalite ve morbidite nedeni serebral hipoksidir. Near infrared spectroscopy (NIRS) beyin oksijenizasyonunu değerlendirmede kullanışlı bir yöntemdir. Bu çalışma ile CO zehirlenmelerinde hastaların beyin oksijenizasyonunu NIRS ile değerlendirerek, hastaların takip ve tedavisindeki faydalarını araştırmayı amaçladık.

Gereç ve Yöntem: Araştırma tek merkezli, prospektif klinik çalışma olarak, Ekim 2013 - Nisan 2014 tarihleri arasında, tanısı kan karboksihemoglobin (CO-Hb) düzeyi bakılarak veya CO zehirlenmesi tanısı ile diğer hastanelerden sevkli gelen 33 hasta ile yapıldı. Hastalar uygulanan tedavi yöntemine göre normobarik oksijen tedavisi (NBOT) grubu ve hiperbarik oksijen tedavisi (HBOT) grubu olarak 2 gruba ayrıldı.

Bulgular: NBOT grubunda tedavi sonrası ortalama serebral satürasyonu (ScO2) düzeyleri tedavi öncesine göre daha yüksek tespit edilmesine rağmen, sol frontal ScO2 değerleri dışında istatistiki olarak anlamlılık tespit edilmedi. HBOT grubunda ise tedavi öncesi ve tedavi seansları sonrası ScO2 değerleri arasında farklılık tespit edilmedi.

Sonuç: Çalışmamızda CO zehirlenmeli hastalarda NIRS'ın beyin oksijenizasyonunu değerlendirmede faydalı olabileceği fakat HBOT başlama kararı vermede ve HBOT'nin etkinliğini izlemede faydalı olmadığı sonucuna varılmıştır.

Anahtar Kelimeler: Karbonmonoksit Zehirlenmesi, Hiperbarik Oksijen Tedavisi, Near İnfrared Spektroskopi, Normobarik Oksijen Tedavisi

INTRODUCTION

Carbon monoxide (CO) is the main cause of death and morbidity associated with poisoning in developed countries and is responsible for more than half of the deadly poisonings in many countries (1). CO is a colorless and odorless gas resulting from the inadequate burning of carbon. When CO intoxication is suspected, the level of carboxyhemoglobin (CO-Hb) is measured and high CO-Hb levels indicate CO exposure and support the diagnose (2).

The most important cause of mortality and morbidity CO poisoning is cerebral hypoxia. In recent years, it is pointed out that a noninvasive method, Near infrared spectroscopy (NIRS), has been used to assess brain oxygenation. NIRS is a device that measures cerebral saturation (ScO2) by measuring the levels of oxy and deoxyhemoglobin in the brain with the help of infrared light technology and two sensors from the frontal area. NIRS is based on the principle of transmission and absorption when passing near-infrared light (7600-1000 nm) through tissue. The absorption of near infrared light is proportional to the concentration of copper in the hemoglobin, iron and cytochrome a3. Since oxygenated and deoxygenated hemoglobin has different absorption spectra, oxygen can be detected (3). There are also many studies showing that tissue oxygenation can also be used for evaluation (4). However, the number of studies in the literature about the use of carbon monoxide poisoning is very few.

Our aim in this study is to evaluate patients' brain oxygenation in CO poisonings with NIRS in the early period, noninvasively and at the bedside and to investigate the benefits of follow up and treatment of patients.

MATERIAL AND METHODS

Study Population: The study was conducted as a single center, prospective clinical study. After receiving the local ethics committee approval (Ethics Committee No: 2013/45), a total of 33 patients over 18 years of age who attended emergency service during the 6-month period from October 2013 to April 2014, and were diagnosed by measuring CO-Hb levels in their blood or referred from other hospitals with CO poisoning diagnosis, were included in the study. Patients with the acute ischemic disease such as acute ischemic cerebrovascular disease, acute peripheral arterial occlusion, acute mesenteric ischemia, patients with advanced stage liver and heart failure story, patients with arrest, patients who refused to participate in the study, were excluded from the study. Patients were divided into 2 groups as normobaric oxygen therapy (NBOT) group (27 patients) and hyperbaric oxygen therapy (HBOT) group (6 patients). Statistical analysis was calculated separately among the groups and the results of both groups were compared with each other.

All of the patients demographic informations, major complaints, vital signs (heart rate, systolic and diastolic blood pressures, respiratory rate), duration of exposure to CO and Glasgow Coma Scale (GCS) were recorded in the study form at the time of admission. Electrocardiography (ECG) of patients were assessed and ECG changes were recorded. Samples were taken to evaluate the laboratory findings. In addition, CO-Hb levels were measured at the time of application and at the end of the treatment period with blood gas taken from the venous blood. The results were recorded in the study form.

Treatment Protocol: All patients received 100% NBOT as the first treatment. HBOT was administered in the presence of specific conditions such as confusion / consciousness change, seizures, coma, focal neurological deficit, presence of evidence of acute myocardial ischemia, pregnancies with CO-Hb levels above 15%. NBOT duration was determined by checking blood CO-Hb values intermittently, and the treatment was terminated when the blood level of CO-Hb <5%. HBOT was administered to a total of 6 patients, of whom 2 had GCS: 8 and had entubation, 2 patients had GCS: 11, and 2 patients had high cardiac enzymes. In addition to a 2-hour single session after the diagnosis, HBOT was applied to the patients by hospitalization a total of 3 sessions were performed 1 session per day.

Cerebral Oximetry Measurement: Cerebral saturation levels were measured by NIRS using an INVOS 5100c device (Somanetics, Troy, MI, USA). Cerebral saturation (ScO2) measurements were performed at the time of both groups patients' initial admission of the emergency department, and when the blood COHb level was normalized in the NBOT group, and as for the group that was given HBOT after each session. Measurements were made by sticking the NIRS probes two-sided to the frontal region provided that the probes were 1 centimeter (cm) above the eyebrows and the 3 cm away from each other, and the average values were recorded for 10 minutes.

Statistical Analysis: SPSS (Statistical Package for Social Sciences for Windows v.17.0) program was used for the statistical analysis of the study. Whether the data were appropriate for normal distribution was determined using the Shapiro-Wilk test. In the NBOT group, Paired Samples T-Test was used for statistical analysis of pre- and post-treatment values. Repeated measures of ANOVA test was used for statistical analysis of pre-treatment and post-treatment sessions values in the HBOT group. Mann Whitney U test was used for statistical analysis between laboratory values and Independent Samples Test was used for comparing ScO2 before and after treatment between the two groups. Pearson Correlation Test

was used for correlation analysis. The significance level of the results was accepted as $p < 0.05$.

RESULTS

A total of 33 patients, 27 patients who were given NBOT and 6 patients who were given HBOT, were included in the study. Patients in the NBOT group were discharged to emergency services at the end of treatment. Patients in the HBOT group were hospitalized after the first emergency HBOT administration and taken to daily HBOT sessions. No mortality was observed in any patient during follow-up.

Demographic and clinical characteristics of all the patients included in the study were shown in Table 1 and laboratory findings in Table 2. From cardiac biomarkers, Troponin and Myoglobin of patients in the HBOT group were significantly higher than compared to the NBOT group ($p = 0.009$, $p = 0.011$, respectively). Although there was a statistically significant difference between the pre-treatment COHb values and the post-treatment COHb values in the NBOT group, no significant difference was found in the HBOT group ($p < 0.001$, $p = 0.117$, respectively).

Table 1. Baseline demographic and clinical characteristics of the NBOT and HBOT groups

Variables	**NBOT group** (n=27)	**HBOT group** (n=6)
Age; median (min,max)	36 (18-80)	19 (18-48)
Sex; n (M/F)	13/14	2/4
Hemodynamic charecters; median (min,max)		
▪ SBP (mmHg)	120 (70-180)	105 (95-160)
▪ DBP (mmHg)	70 (40-100)	67 (60-90)
▪ Heart rate (beats/min)	90 (64-130)	120 (100-140)
▪ Respiratory rate (breaths/min)	20 (16-30)	26 (12-40)
Symptoms; n(%)		
▪ Headache	13 (48.1)	
▪ Syncope	7 (25.9)	6 (100)
▪ Vomiting	4 (14.8)	
▪ Dizziness	2 (7.4)	
▪ Weakness	1 (3.7)	
Cause of exposure to CO poisoning; n(%)		
▪ Coal-fired stove	24 (88.9)	
▪ Hot water boiler	3 (11.1)	6 (100)
Length of exposure to CO; mean ± SD (h)	5.15 ± 0.76	7.67 ± 1.08
Glasgow Coma Score at admission; n(%)		
▪ 8		2 (33.3)
▪ 11		2 (33.3)
▪ 14	2 (7.4)	1 (16.7)
▪ 15	25 (92.6)	1 (16.7)
ECG findings at admission; n(%)		
▪ Normal	21 (77.8)	
▪ Sinusal taschycardia	6 (22.2)	6 (100)

y: year, M: male, F: female, SBP: systolic blood pressure, DBP: diastolic blood pressure, CO: carbon monoxide, ECG: electrocardiogram

In the NBOT group, there was no statistically significant difference in the right frontal ScO2 values before and after treatment while the left frontal ScO2 values were found to be statistically significantly higher after treatment ($p = 0.279$, $p = 0.017$, respectively). As for the HBOT group, there was no statistically significant difference between the values of the right frontal and left frontal ScO2 values before and after the treatment sessions. The ScO2 values before and after treatment in both groups are shown in Table 3.

The r and p values, which show the correlation between ScO2 values and CO-Hb values before and after treatment in both groups, are given in Table 4. In both groups, there was a negative correlation between the right and left ScO2 and CO-Hb values before and after treatment, but no statistical significance was determined.

Table 2. Laboratory findings of the sudy population

	NBOT group median (min,max)	**HBOT group** median (min,max)	**p value**
Blood gas values			
▪ Venos pH	7.37 (6.97-7.44)	7.37 (7.37-7.43)	0.266
▪ Venos pO2	20.4 (13-53)	34.65 (21-389)	0.285
▪ Venos PCO2	42 (27-54)	34 (23-38)	0.008
▪ sO2	60 (32-86)	66.5 (35-99)	0.2
▪ CO-Hb (Pre-treatment)	26 (5.6-41.5)	1.3 (0.8-8.6)	**<0.001** *
▪ CO-Hb (Post-treatment)	3.5 (1.1-5.6)	0.6 (0.5-1)[a]	0.117 **
Cardiac biomarkers			
▪ Troponin	0.002 (0-0.06)	3.415 (1.16-7.242)	**0.009**
▪ Myoglobin	25.2 (9.05-1000)	657.72 (67.62-1000)	**0.011**
▪ CK-MB	1.6 (0.05-76.56)	43.84 (4.07-127)	0.07
▪ AST	24 (9-58)	79 (16-216)	0.09

CO-Hb: Carboxihemoglobin, [a] after the first session of HBOT, *p value between CO-Hb (pre-treatment) and CO-Hb (post-treatment) in NBOT group, ** p value between CO-Hb (pre-treatment) and CO-Hb (post-treatment) in HBOT group

Table 3. Pre-treatment and post-treatment ScO2 values of the patients in the NBOT and HBOT groups

		Pre-treatment (mean ± SD)	**Post-treatment** (mean ± SD)	**p value**
NBOT group	Right frontal ScO2	66.07 ± 8.23	67.3 ± 7.18	0.279
	Left frontal ScO2	66.7 ± 8.68	69.22 ± 7.92	**0.017**
HBOT group	Right frontal ScO2	70.83 ± 13.1	72.83 ± 7.41[a]	0.665
			73.5 ± 9.83[b]	0.730
			69 ± 9.05[c]	0.619
			69.5 ± 6.89[d]	0.762
	Left frontal ScO2	69.5 ± 12.32	68.67 ± 11.53[a]	0.842
			74.33 ± 9.97[b]	0.496
			69 ± 10.29[c]	0.876
			70.83 ± 9.8[d]	0.634

[a] after the first session of HBOT, [b] after the second session of HBOT, [c] after the third session of HBOT, [d] after the fourth session of HBOT

DISCUSSION

Used to assess brain oxygenation during cardiovascular surgical operations, NIRS has been used in neonatology, neurology and emergency services to measure cerebral tissue oxygenation over the past decade (5). It can be used to show brain oxygenation, especially in cerebrovascular attacks (6). In this study, we too evaluated brain oxygenation with NIRS in patients diagnosed with CO poisoning, and for the first time in the literature, we investigated the relationship between HBOT and ScO2 values in CO poisoning.

Clinical findings suggesting cerebral hypoxia such as headache, nausea, dizziness, drowziness and syncope were observed in all patients with carbon monoxide intoxication. In our study, although statistically significant difference between pre-treatment CO-Hb values and CO-Hb values after treatment in the NBOT group was observed, no significant difference was found in the HBOT group. The reason for this was considered that the NBOT was started at the external center because all of the patients in the HBOT group were referred and that the CO-Hb levels initially observed in our emergency department were found to be incompatible low with the clinics.

HBOT is a proven method for the treatment of CO poisoning. In HBOT, the healing period of poisoning symptoms are shorter compared to NBOT, and mortality incidence and late neuropsychiatric findings are lower (7). The half-life of CO in the tissue is 3-4 hours, it is halved in 30-90 minutes with 100% oxygen, in 15-23 minutes with hyperbaric oxygen and 100% oxygen (8). Measurement of blood CO-Hb level in the presence of acute CO poisoning is a valuable method. But CO poisoning alone is not enough to make a decision to start HBOT. The low blood CO-Hb level of patients who were given HBOT in our study suggests that clinical findings are taken into account when making this decision. Recent studies indicate that serum cardiac troponin levels are indicative of cardiac injury in CO poisoning, and are an important predictor of HBOT start up (7, 9). In our study as well, cardiac biomarkers were

detected at higher levels in the HBOT group and they were effective when we decided to make HBOT.

Tichauer et al. measured the cerebral O2 saturation using NIRS after inducing hypoxia on newborn pigs and found that the NIRS measurements decreased with increasing hypoxia (10). Frish et al. used NIRS on 5 patients with cardiopulmonary resuscitation and noted that NIRS may be useful in assessing cerebral circulation (11). In Niemann et al. study evaluated how CO intoxication could best be reported with NIRS using two different NIRS devices, they detect ScO2 values significantly higher than normoxic status after CO exposure using the same INVOS-5100 NIRS device in our study (12). In the study conducted by Kalkan et al. again with INVOS-5100 NIRS device, the pre-treatment ScO2 levels were found to be low and the ScO2 levels after treatment were found to be significantly higher in CO intoxicated patients given NBOT in emergency services. (13). We also found in our study that similar to that of Kalkan et al, but in contrast to Niemann et al.'s study, the average ScO2 levels of patients treated with NBOT were higher than those of before treatment. In our study, however, only statistical significance was found between pre- and post-treatment values in left frontal ScO2 values in the NBOT group. As for the HBOT group, there was no statistical significance between ScO2 values after daily HBOT sessions except the first urgently given HBOT before both right and left frontal treatment. As a reason for the higher detection of the patients' average ScO2 levels at the time of arrival in the HBOT group compared to the NBOT group, it was considered that all patients in the HBOT group had been started by NBOT at the external center and that the blood CO-Hb levels were low at the time of arrival. We also found a correlation between the levels of blood CO-Hb and ScO2 values in our study results. With these findings, it can be deduced that the ScO2 values measured by NIRS in CO poisonings are significantly affected from the clinical findings of the patient whether it is normobaric or hyperbaric, the effect of given oxygen therapy and blood CO-Hb levels.

In CO poisonings, it is known that basal ganglia are mainly affected area in the brain (14, 15). It is difficult to determine the ScO2 values in the basal ganglia as NIRS measures the hemoglobin oxygen saturation in the whole tissue bed, which contains a mixture of brain tissue, arterial and venous blood. Therefore, we believe that the results of NIRS will not be reliable in order to determine the cerebral hypoxia that causes neurological findings in severe CO poisoning, to make the decision to start HBOT, and to monitor the efficacy of HBOT, according to our study results.

Limitations

The most important limitation of our study is the low number of patient populations. Another limitation is that NBOT is initiated when CO intoxicated patients were referred to ambulance or another center until reaching our hospital, which affected the outcome of our study, and we think that more significant results can be obtained from experimental studies. We could not compare the damage to the basal ganglia with the results of NIRS because all the patients included in our study could not underwent magnetic resonance imaging of the brain.

Conclusion

Based on findings from our study, we conclude that NIRS may be useful in assessing brain oxygenation in acute CO poisoning, and we think that it is not useful to determine HBOT start up in severe poisoning and to monitor the efficacy of HBOT. In addition, we found that ScO2 was affected not by clinical findings but by oxygen therapy and blood CO-Hb levels. In order to determine the relationship between HBOT and ScO2 values, more extensive studies are needed with larger number of patients.

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