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The Acute Effect of Exercise Test on Exhaled Carbon Monoxide Rate

Egzersiz Testinin Ekshale Karbon Monoksit Oranı Üzerindeki Akut Etkisi

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ABSTRACT Objective: The aim of this study is to analyze the acute effect of exercise on the rate of exhaled carbon monoxide (CO) in healty young smokers. **Material and Methods:** Twenty four male smokers were included in the study. Pulmonary functions of the participants were evaluated by spirometer forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), FEV_1/FVC, peak flow rate (PEF) and forced expiratory flow at 25 to 75% of FVC (FEF 25%-75%). Exercise testing was performed by using bicycle ergometer. Maximal load, maximum oxygen uptake (VO_2max), rest and maximal heart rate were recorded. CO levels before and after the test were mesured with portable breath CO monitor. CO levels and changes were assessed and compared on the exercise test day and rest day (without exercise test). **Results:** 25% of the participants have dyspnea, 20.8% have cough and 50% have sputum complaints. The results of the pulmonary function test and exercise test of young healthy smokers are as follows: % FEV1=89.7±9.9, % FEV1/FVC=87.4±8.2, % PEF=77.4±9.5, mean rest heart rate=94.8±9.8 bpm, mean maximal heart rate=170.3±9.7 bpm and mean VO_2max=30.9±6.5 mL/min/kg. There is a statistically significant difference between the first and the second CO values of the participants measured on both days (p<0.001). There is a significant difference between the mean change of CO on the exercise test day and rest day (p<0.001). **Conclusion:** Our results show that smoking causes respiratory symptoms, impaired cardiopulmonary responses to exercise and increased CO level and exercise increases to the exhaled CO rate in young and healthy male.

Keywords: Smokers; carbon monoxide; exercise; pulmonary function

ÖZET Amaç: Bu çalışmanın amacı, sigara içen genç sağlıklı bireylerde egzersizin ekshale karbon monoksit (CO) oranı üzerindeki akut etkisinin araştırılmasıdır. **Gereç ve Yöntemler:** Çalışmaya sigara içen 24 erkek birey dâhil edildi. Katılımcıların solunum fonksiyonları spirometri birinci sn zorlu ekspirasyon volümü [forced expiratory volume in one second (FEV1)], zorlu vital kapasite [forced vital capacity (FVC)], FEV_1/FVC, tepe akım hızı [peak flow rate (PEF)], FVC'nin %25 ile 75'inde zorlu ekspiratuar akış (FEF %25-75) ile değerlendirildi. Egzersiz testi bisiklet ergometresi kullanılarak yapıldı ve test sırasında maksimum yük, maksimum oksijen tüketimi (VO_2max), istirahat ve maksimum kalp hızı değerleri kaydedildi. Bireylerin CO düzeyleri egzersiz testi öncesi ve sonrası portatif CO cihazı ile ölçüldü. CO düzeyleri ve değişiklikler egzersiz testinin yapıldığı gün ve (egzersiz testinin yapılmadığı) istirahat gününde değerlendirildi ve karşılaştırıldı. **Bulgular:** Katılımcıların %25'inde dispne, %20,8'inde öksürük ve %50'sinde balgam şikâyeti bulunmaktadır. Katılımcıların solunum fonksiyon testi ve egzersiz testi sonuçları şöyledir: % FEV_1=89,7±9,9, % FEV_1/FVC=87,4±8,2, % PEF=77,4±9,5, ortalama istirahat kalp hızı=94,8±9,8, ortalama maksimum kalp hızı=170,3±9,7 ve ortalama VO_2max=30,9±6,5 mL/min/kg. Katılımcıların her 2 gün ölçülen 1. ve 2. CO değerleri arasında istatistiksel olarak anlamlı bir fark vardır (p<0.001). Egzersiz testi yapılarak değerlendirilen CO değişimi ile egzersiz testi yapılmadan değerlendirilen CO değişimi arasında istatistiksel olarak anlamlı bir fark vardır (p<0.001). **Sonuç:** Bu çalışmaya katılan genç ve sağlıklı erkeklerde sigara tüketimi solunumsal semptomlara, egzersize verilen kardiyopulmoner yanıtların bozulmasına ve CO seviyesinin artmasına neden olmuştur. Bu bireylerde atılan CO miktarının egzersizle birlikte daha fazla olduğu görülmüştür.

Anahtar Kelimeler: Sigara içicileri; karbon monoksit; egzersiz; pulmoner fonksiyon

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Cigarette smoking is considered as one of the most common and important causes of early death, mortality, and morbidity in many developed and industrial countries. Cancer risks, especially lung cancer and cardiopulmonary diseases are generally more common in smokers than non-smokers.[1,2] It is also stated that cigarette smoking is increasing especially in young people and it is ignored during this period due to the fact that the symptoms and effects are not severe. Cigarette contains countless bioactive chemical compounds such as carbon monoxide (CO), nicotine and particulate matter (tar) etc., associated with tobacco and this leads to the onset and acceleration of pathological diseases through an oxidative stress-free radical mechanism.[3,4]

Exhaled CO concentration is affected by normal and pathophysiological conditions such as lung inflammation, smoking, exercise and aging. It is reported that cigarette smoking increases both respiratory and blood CO levels.[5] Since CO has an affinity approximately 225 times than that of O_2 for hemoglobin (Hb), CO easier to combine than Hb. In healthy smokers, the amount of CO excreted is higher than that of healthy non-smokers, and the smoking status of the individual and the carboxyhemoglobin (COHb) levels in the individual are related.[6] Smoking affects not only the airways but also the lung parenchyma and pulmonary arteries and leads to irreversible obstruction.[7] Combined with cigarette consumption; nicotine increases myocardial oxygen demand and increased CO levels cause functional anemia. These effects also lead to hypertension, increased heart rate and decreased exercise tolerance.[8] Some studies suggest that long-term exercise may have the potential to diminish some of the negative effect of smoking and can be a useful aid to stop smoking.[9] However, little has been published about the acute effect of exercise on exhaled CO rate.[10] Therefore, in this study we aimed to analyze the acute effect of exercise on the rate of exhaled CO in healty young smokers.

MATERIAL AND METHODS

SUBJECTS

This cross-sectional study included 24 healthy male students who recruited from school of physical therapy and rehabilitation and smoker for at least 5 years between 2016 and 2019. The inclusion criteria were having at least 1/2 pack smoking per day for at least 5 years, being between the ages of 18-26 and male gender, absence of any pulmonary disease such as asthma, pneumonia, etc. and other disease (cardiac, musculoskeletal, neurological, etc.) was confirmed by a doctor, having normal body mass index (BMI), without regular exercise habits, volunteering to participate in the study. The exclusion criteria were failing to complete the tests.

STUDY DESIGN

After the first evaluation, CO levels were measured after 30 minutes the last cigarette smoked by the participants. Then, the pulmonary function tests of the participants were performed and they were taken to the exercise test. The test lasted about approximately 15-20 minute and CO levels were measured at the end of the test. The same subjects' CO levels were measured after 30 minutes of the last smoking the next day and at the same time. After this, the CO levels were measured again after waiting approximately 15-20 minutes (the time spent in the exercise test) before doing anything. CO levels and changes on the days with and without exercise testing were assessed and compared. Thus, the effect of the exercise on the excreted CO level was evaluated.

MEASURES

The demographic and clinical status were collected through face-to-face interviews. Age, weight, height, BMI, smoking history, respiratory symptoms (cough, sputum and dyspnea etc.) were recorded through medical history and physical examination. While the measurement of dyspnea severities of the participants were evaluated by using the Borg 0 to 10 category-ratio scale, whether there were cough and sputum complaints were evaluated subjectively.[11]

PULMONARY FUNCTIONS MEASUREMENT

Before starting the exercise test, pulmonary functions were evaluated. Pulmonary functions were assessed by spirometry. Forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), FEV_1/FVC, peak flow rate (PEF), forced expiratory flow at 25 to 75% of FVC (FEF 25%-75%) were measured in the sitting position according to the American Thoracic Society (ATS) / European Respiratory Society (ERS) criteria.[12]

EXERCISE TEST PERFORMANCE

Subjects exercised on the Jaeger brand bicycle ergometer with an ever-increasing loading. The first 3 minutes were cycled with no load. The next 3 minutes were continued with 20 watt loading. Then continued to load in 3-watt increments every 10 seconds until the maximum load was reached. After reaching the maximum load, 20 watts for 2 minutes and 10 watts were loaded for 2 minutes and the test was terminated with 1 minute no-load pedaling. The metabolic measurement system consisted of a face mask, a pneumotachograph, a mass-spectrometer and a personal computer. The maximum load and oxygen uptake values reached at the end of the test were recorded. Participants' heart rate and peripheral oxygen saturation were monitored throughout the test. Heart rate was monitored simultaneously with a 12-lead electrocardiography, using a standard chest lead throughout the measurement, to determine the end point of ramp exercise. The experimental room was controlled to maintain the temperature and air ventilation. All experiments were performed between 9.0 and 10.30 a.m. in the morning and all participants smoked for half an hour before the test.[13]

CARBON MONOXIDE MEASUREMENT

CO value of the patient was measured in a sitting position with the device called Breath Carbon Monoxide (Portable Bedfont Mini Smokerlyzer®). In exhaled CO value measurement, when the nose was closed with a latch, a deep inspiration was made and the breath was kept for 15 seconds, then expiratory into the device by means of a mouthpiece. The expiratory rate was adjusted according to a sound produced by the device (the operation was repeated when this sound did not emit when it was blown too fast or slowly). Three measurements were made before and after the exercise test and the rest day, the highest value was recorded.[14]

DATA ANALYSES

Sample size was calculated using G*Power (version 3.0.10) for medium effect size (d=0.5), 95% confidence interval and 80% power. Twenty four subjects were planned to be included in the study.

Data analysis was performed with IBM® SPSS® software (version 22.0). Descriptive statistics were summarized as frequencies and percentages for categorical variables. Continuous variables were presented as mean and standard deviation. Normality was verified by the Shapiro-Wilk test. The significance level was accepted as $p<0.05$. Paired sample t test was used to compare the repeated measurements of CO on both days. Significance between the CO changes of two days was measured by paired sample T test.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the Dokuz Eylül University Ethics Committe (Approval number: 2016/22-28, Date:05/08/2016) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Each study subject gave written informed consent to participation.

RESULTS

The study included 24 healthy male young people who have normal BMI value and not using any mediciation and didn't have any known health problems. The descriptive statistics of the participants were given in Table 1. The mean of pulmonary function test parameters of the participants were given in Table 2. The results of the pulmonary function test of young healthy smokers were as follows: % FEV_1=89.7±9.9, % FEV_1/FVC=87.4±8.2, % PEF=77.4±9.5. 25% of the participants had dyspnea and mean BORG scale score was 1.75±0.48, 20.8% had cough and 50% had

TABLE 1: Descriptive statistics of the participants.

Parameters	n	Mean (SD)	Minimum-Maximum
Age (years)	24	22.6±1.9	19.0-27.0
Height (cm)	24	178.5±5.3	165.0-190.0
Weight (kg)	24	75.6±8.03	55.0-99.0
BMI (kg/m^2)	24	23.3±3.5	18.9-26.8
Smoking (years)	24	7.2±2.5	5.0-15.0
Cigarette consumption (packet×years)	24	7.4±3.2	2.5-15.0

BMI= Body mass index; n= number; SD= standart deviation.

TABLE 2: Pulmonary function test parameters of participants.

Parameters	Mean (SD)	Minimum-Maximum
FVC (L/s) (%)	86.9±8.5	80.0-106.0
FEV1 (L/s) (%)	89.7±9.9	81.2-111.0
FEV1/FVC (L/s) (%)	87.4±8.2	80.9-99.7
PEF (L/s) (%)	77.4±9.5	72.0-117.0
FEF 25-75 (L/s) %	88.3±8,8	73.0-121.0
FEF 75 (L/s) %	82.5±9.8	62.0-120.0
FEF 50 (L/s) %	88.3±9.3	69.0-111.0
FEF 25 (L/s) %	106.4±7.7	80.0-129.0

FVC = Forced vital capacity; FEV1= forced expiratory volume in one second; PEF= peak expiratory flow; FEF 25%-75%= forced expiratory flow at 25 to 75% of FVC; FEF 75%= forced expiratory flow at 75% of FVC; FEF 50%= forced expiratory flow at 50% of FVC; FEF 25%= forced expiratory flow at 25% of FVC; SD=standart deviation.

TABLE 3: Cardiopulmonary exercise test results of all participants.

Parameters	Mean (SD)	Minimum-Maximum
Test time (min)	16.7±1.9	14.2-22.0
RER	1.1±0.08	1.9-1.2
VO_2max (ml.min-1.kg-)	30.9±6.5	17.3-44.6
$V'O_2$ (ml/min) %	70.6±9.1	48.0-100.0
MET (ml/kg/min)	8.8±1.8	5.0-12.7
VEmax (L/min)	85.7±9.3	50.0-91.0
Load max (watt)	181.2±13.5	130.0-240.0
Load max (watt) (%)	71.9±9.7	40.0-97.0
Resting HR (bpm)	94.8±9.8	78.0-110.0
HR max (bpm)	170.3±9.7	147.0-195.0
HR max (%) (bpm)	88.7±6.85	75.0-103.0

RER= Respiratory exchange ratio; VO_2max= Maximum oxygen uptake; MET= Metabolic equivalent; V_E= minute ventilation; HR= Heart rate; bpm= Beats per minute; SD= Standart deviation.

TABLE 4: Comparison of rate of exhaled CO changes in participants.

	Mean (SD)	p_1 value	%	p_2 value
CO_1 (ppm)	20.7 ±5.2	<0.001*	3.9±0.8	<0.001*
CO_2 (ppm)	15.6 ±4.4		3.1±0.6	
CO_3 (ppm)	19.8 ±5.2	<0.001*	3.7±0.8	<0.001*
CO_4 (ppm)	17.3 ±4.9		3.4±0.7	
Δ CO on the day of exercise test	4.6 ±1.5	<0.001*	0.7±0.2	<0.001*
Δ CO on the day of rest	1.7 ±0.8		0.2±0.1	

ppm= Parts per million; CO_1= carbon monoxide level before exercise test; CO_2= carbon monoxide level after exercise test; CO_3= first measured carbon monoxide level at rest day; CO_4= carbon monoxide level measured on the day of rest after waiting for the loading time (exercise test) after CO_3 measurement; Δ CO on the day of exercise test= carbon monoxide change on the day of exercise test (CO_1-CO_2); Δ CO on the day of rest= carbon monoxide change on the day of rest, which didn't exercise test (CO_3-CO_4); SD=Standart Deviation; *= p<0.05, Min=minimum, Max=maximum, p_1 value =the difference between the two CO (ppm) values given in the row, p_2 value= the difference between the two CO% values given in the row.

sputum complaints. The mean of cardiopulmonary parameters of the participants were given in Table 3. The results of the cardiopulmonary tests were as follows: mean VO_2max=30.9±6.5 mL/min/kg, mean rest heart rate=94.8±9.8 bpm and mean maximal heart rate=170.3±9.7 bpm. As 4 people had leg fatigue and 5 people reached maximal heart rate early, the exercise tests of these subjects were completed before the expected time. However, all participants completed exercise tests without having any problem.

Measured CO values were high on both days [exercise test day first measurement of CO=20.7±5.2 ppm and rest day first measurement of CO=19.8±5.2 ppm]. There was a significant decrease in the CO values measured before and after the exercise test ($p<0.001$). There was also a significant decrease in CO measurements on the day of rest where the exercise test was not performed ($p<0.001$). However, when the last CO measurement results of both days were examined; the end of exercise CO value was lower. There was a significant difference between the mean change of CO on the exercise test day and on the day of rest ($p<0.001$). The amount of exhaled CO in the exercise test was higher than the rest day when the exercise test was not performed (Table 4).

DISCUSSION

In this study, we evaulated acute effect of exercise on the rate of exhaled CO in healthy and young smokers. Results showed that the amount of exhaled CO was higher on the day of the exercise test according to the day of the rest in the same subjects. That is, the amount of CO exhaled with exercise was greater. In our study, although it was shown that pulmonary functions measured by spirometry were not affected in young and healthy smokers, the presence of respiratory symptoms was observed due to smoking. There were negative effects on cardiopulmonary responses to exercise, such as increased heart rate during rest and exercise and decreased VO_2 max value although they were young individuals and had no known cardiopulmonary disorders.

The average COHb levels of smokers were between 3.9 and 4.1 %. COHb level was significantly lower in non-smokers than 1.3%.[6] In our study, COHb level measured in smokers were consistent with the other studies. Increased COHb shifts the oxygen dissociation curve to the left, thereby reducing oxygen release to the tissue. Since there is less Hb binding site for O_2, there is also a decrease in the transmission of O_2 to working muscles. This combination of low O_2 loading, low O_2 transmission and degraded extraction leads to a reduction in the VO_2max at high work rates.[15,16] Kouba et al. showed that the VO_2max value of smokers (35.7±0.9) during exercise was lower than the VO_2max of healthy individuals (39.0±0.7).[8] Although the individuals in our study were younger, there was a decrease in VO_2 max due to the increased CO amount similar to this study. However, Horvath et al. showed that VO_2max was not changed until CO levels exceeded 4.3% and a linear decrease occurred in VO_2max with increasing COHb levels.[17] In our study, although COHb level was below 4.3% there was a decrease in VO_2max. Waiting 30 minutes after smoking a cigarette, we measured the COHb level, so we think that COHb does not exceed this value. Arnow and et al. concluded in their study that due to increased COHb levels, exercise time and maximum oxygen consumption decreased, which could impair exercise performance. The mean age of the 10 healthy subjects in this study was 50.7±3.8 years, and the amount of CO was 3.9±0.4 %.[18] Although the mean age of the participants in our study was lower than in this study, the amounts of CO and deterioration in cardiac responses to exercise were similar. It is thought that exercise capacity may decrease rapidly in these individuals due to cigarette consumption and may cause more serious hemodynamic responses in later ages.

Rowel et al., reported that nicotine-induced elevations in circulating catecholamines and increased CO levels caused functional anemia leads to an increase in cardiac output by increasing both heart rate and stroke volüme.[19] However, some studies have suggested that smoking has an inhibitory effect on heart rate during maximal work loads exercise.[20] Our finding of an increased heart rate after smoking at rest and at the maximal work loads is in line with the findings most of the other studies.[21,22] Yasuda et al. examined the effect of exercise on exhaled CO and stated that the total amount of exhaled CO (Vco) increased a linear during exercise, but the fraction of CO (Fco) decreased, and after the cessation of exercise Vco and Fco returned to the pre-exercise level within several minutes, according to the changes of VO_2 and minute ventilation.[23] Vogel et al. showed that the COHb concentration (%) gradually decreased due to exercise intensity from 1.7 % at rest to 1.0% at maximal exercise. This decline indirectly indicates that COHb may be the main source of exhaled CO.[16] However, it is still unclear whether blood CO content can be provided into the exhaled gas. A number of recent studies have indicated that Fco decreases and Vco increases in general depending on the exercise intensity.[10,24] In our study, there was a significant difference between the amounts of the first and the second CO, measured on the day of the exercise and the day of rest. However, the difference between the amounts of CO exchanges measured in both days was statistically significant. In coherence with the literature, the amount of exhaled CO amount was greater on the exercise day. Yet, in our study, the Fco value was not measured from the measurement device but only the total exhaled CO amount was measured.

Cigarette smoking is associated with both obstructive and restrictive lung diseases. In our study, although the respiratory symptoms such as cough, sputum and dyspnea were observed, we found that the results of pulmonary function test measured by spirometer were not affected significantly and were within the normal limits stated in the literature. Many recent studies have shown that smokers with open airflow obstruction in the spirometer, similar to our study, have evidence of structural lung disease, which is called symptomatic smokers, and have an important symptom burden. Woodruff et al. reported that 50% of current or old smokers with preserved pulmonary function (FEV_1/FVC 0.70 and a FVC above the lower range normal range after bronchodilator use) had many respiratory symptoms.[25,26] It is reported in the literature that spirometry is not very sensitive for diagnosis, especially in early or mild diseases. In addition, the highest lung function achieved and basal lung function in many people is unknown and a significant reduction in lung function may be started before meeting the airflow obstruction criteria.[27] In addition to the reasons stated in other studies, we also think that our subjects' results of the pulmonary function tests were in the normal range due to the fact that the individuals in our study were young and therefore any notable yearly decrease in lung function was not seen. Similar to the decrease in PEF in our study and the presence of respiratory symptoms, Cooc et al. reported that low PEF was associated with chronic respiratory symptoms such as sputum, coughing and dyspnea.[28]

The present study has some limitations. Firstly, our study was a cross-sectional framework with a small sample size. Secondly, we didn't use laboratory markers and radiographic findings. Thirdly, there was no control group that included non-smoker individuals. Despite these limitations, we believe that the results of our study make an important contribution to the field in order to overcome the shortcomings in the literature. More studies are needed to be conducted with more participants including non-smoking control group.

CONCLUSION

We can conclude that smoking causes respiratory symptoms, impaired cardiopulmonary responses to exercise and increased CO level in young and healthy male. Furthermore, the essential point is that the amount of exhaled CO level is greater with exercise. According to our results, we recommend that especially young and healthy people should be informed about the harm of smoking and the importance of smoking cessation and the studies examining this issue should be increased. Additionally, with this study, young and healthy males should be encouraged to do exercise by creating an objective awareness of the effect of exercise on CO level in smokers.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

***Idea/Concept:** Hazal Yakut, Sevgi Özalevli, Oğuz Kılınç; **Design:**Hazal Yakut, Sevgi Özalevli, Oğuz Kılınç; **Control/Supervision:** Hazal Yakut, Sevgi Özalevli; **Data Collection and/or Processing:** Hazal Yakut; **Analysis and/or Interpretation:** Hazal Yakut, Sevgi Özalevli; **Literature Review:** Hazal Yakut; **Writing the Article:** Hazal Yakut, Sevgi Özalevli, Oğuz Kılınç; **Critical Review:** Hazal Yakut, Sevgi Özalevli; **References and Fundings:** Hazal Yakut, Sevgi Özalevli, Oğuz Kılınç; **Materials:** Hazal Yakut, Sevgi Özalevli, Oğuz Kılınç.*

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