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The measurement of exhaled carbon monoxide in healthy smokers and non-smokers

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Summary The measurement of exhaled carbon monoxide (CO) level may provide an immediate, non-invasive method of assessing smoking status. The aims of this study were to use a portable CO monitor to compare the exhaled CO levels in established smokers and non-smokers.

The exhaled CO levels were measured in 322 subjects (243 healthy smokers, 55 healthy non-smokers, 24 passive smokers) who applied to healthy stand during the spring student activity of Fırat University in Elazıǧ. Exhaled CO concentration was measured using the EC50 Smokerlyser.

The mean exhaled CO level was 17.13 ± 8.50 parts per million (ppm) for healthy smokers and 3.61 ± 2.15 ppm for healthy non-smokers, and 5.20 ± 3.38 ppm for passive smokers. There were significant positive correlation between CO levels and daily cigarette consumption, and CO levels and duration of smoking in healthy smokers ($r = +0.550$, $P < 0.001$, $r = +0.265$, $P < 0.001$, respectively. Spearman's test). When smokers and non-smokers were looked at as a whole, a cutoff of 6.5 ppm had a sensitivity of 90% and specificity of 83%.

In conclusion, exhaled CO level provides an easy, an immediate way of assessing a subject's smoking status.

Introduction

For a long time now, it has been known that smoking is associated both etiologically and prostognically with numerous diseases of the respiratory system. However, despite this knowledge, many subjects continue to smoke.[1] Smoking habits of patients are clinically important, for example as a risk factor or as a reason for failure to respond to treatment,[2] and it enables appropriate antismoking advice to be given. It has been reported that the use of carbon monoxide (CO) monitor to demonstrate an immediate and potentially harmful consequence of smoking increased further the number who complied with advice to quit.[3]

CO may play a role in pathophysiology of airway diseases.[4] CO has been recovered in exhaled air from normal subjects and at higher levels from the exhaled air of patients with asthma.[4] Significantly lower CO concentrations have been reported in exhaled air from asthmatic patients receiving glucocorticoid treatment than from asthmatic patients not receiving this therapy.[4] In contrast, in a study by Zetterquist et al.[5] it was reported that the levels of CO in the exhaled air of the subjects with asthma, allergic rhinitis or cystic fibrosis were not significantly increased. Levels of CO in exhaled air has been widely used as indication of smoking cessation.[4,6,7]

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The measurement of exhaled CO level may provide an immediate, non-invasive method of assessing smoking status, although other sources of pollution including exhausts gases causes elevations in the fractional concentrations of CO in expired air.[1,5] Furthermore, the development of relatively inexpensive portable CO monitors enables breath CO levels to be assessed in a wide variety of clinical settings.[1] In practice, measuring the concentration of CO in the exhaled air, is non-invasive, cheap, quick, portable, and does not require special technical background.[8,9]

The aim of this study was to compare the breath CO levels in established smokers and non-smokers and to investigate factors that may affect breath CO levels by measuring exhaled CO levels.

Methods

Three hundred and twenty-two subjects who visited the student health club desk during the spring student activity of Fırat University in Elazığ were included the study. The subjects were informed of the purpose of the Smokerlyser and were reassured that the results were confidential in order to encourage accurate reporting of smoking habits. Background information about their health, age, gender, smoking habits, occupational state and passive smoke was obtained. Questions about smoking history were the same for healthy current smokers and passive smokers. An active smoker was defined as a person who currently smoked at least one cigarette a day. Healthy smokers was described as follows: all of the healthy current-smokers subjects had normal clinical evaluation (no respiratory symptoms) or minimal respiratory symptoms (these symptoms varied from isolated symptoms; cough, sputum production, dyspnea after strenuous activity). They were detected only by means of clinical questioning, and were commonly considered to be normal among smokers.[10] Passive smoking was defined as they had never smoked cigarettes or had stopped smoking for at least 10 years before the date of the interview and were not current smokers of pipes, cigars, or cigarillos. Exposure to environmental tobacco smoke (ETS) was ascertained using data derived from the same questions asked to the subjects. A person was deemed to have been exposed to ETS if a household member had regularly smoked cigarettes in their presence or if a co-worker smoked in the same indoor room in their presence for more than one year during the past 10 years.[11]

Finally, all subjects were asked to provide one breath into Smokerlyser because of a previous study has been reported the first reading to be significantly higher than the second as described below.[1]

Breath CO monitoring

Exhaled CO concentration was measured using the EC50 Smokerlyser (Bedfont Instruments; Kent, UK). Bedfont EC50 analyser is reported to correlate closely with blood carboxyhaemoglobin concentration in smokers and in non-smokers, and it is an inexpensive, portable CO monitor that has previously been shown to be effective.[9,12] Prior to the start of the study, the analyser was calibrated with a mixture of 50 ppm CO in air.[8] The Smokerlyser measures breath CO levels in parts per million (ppm) based on the conversion of CO to carbon dioxide (CO_2) over a catalytically active electrode.[1]

The measurement of exhaled CO was done at students health club desk which was placed in an open air at University exhibition field. To standardize the breath being analyzed by the Smokerlyser, the subjects are asked to exhale completely, inhale fully, and then hold their breath for 15 s before exhaling rapidly into disposable mouthpiece. Ambient CO levels were recorded before each breath.

Statistical analysis

All statistical analyses were done using SPSS v10.0 software. Results were expressed as mean ± SD. ANOVA was used to compare all exhaled CO levels between groups and LSD test was used depending on sample distribution. A value of P less than 0.05 was considered significant. Spearman correlation analyses were used to evaluate the relationship between the exhaled CO levels-daily cigarette consumption, and CO levels-duration of smoking in healthy smokers.

Results

Exhaled CO was detectable in all subjects. Ambient air concentrations of CO were at 0–2 ppm level during the measurements.

Breath CO levels were assessed in a total of 322 subject; 243 of them was healthy smokers (224 men; 19 women; mean age 24.69 ± 5.89), 55 of them was healthy non-smokers (46 men; 9 women; mean age 22.30 ± 5.27) and 24 of them was passive smokers (21 men; 3 women; mean age 27.20 ± 9.15).

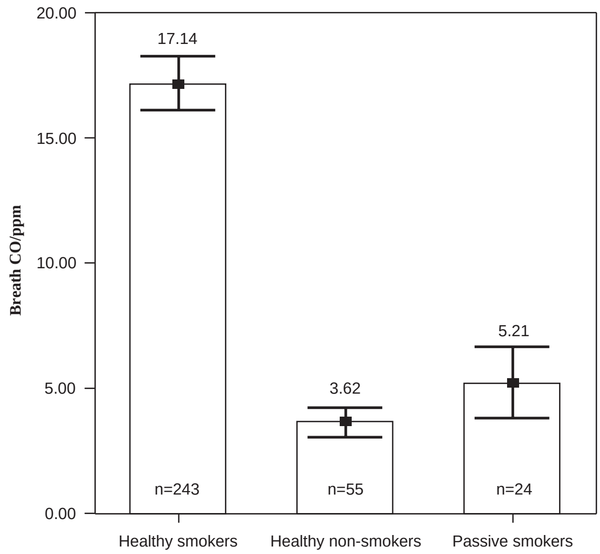

Figure 1 CO concentrations in exhaled air in healthy smokers ($n = 243$), healthy non-smokers ($n = 55$), and passive smokers ($n = 24$).

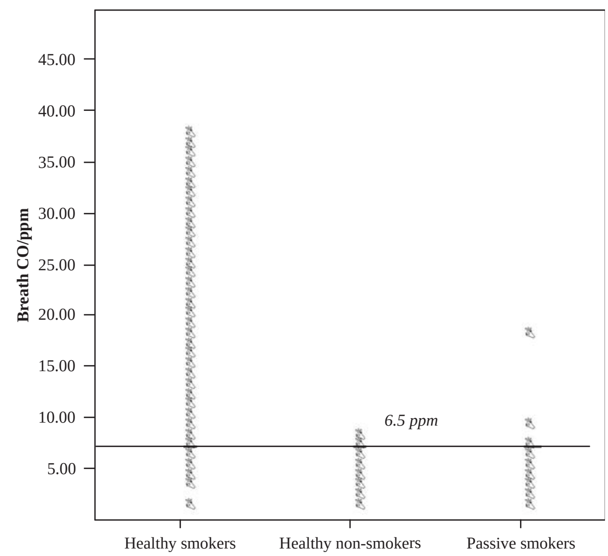

Figure 3 A cutoff level of CO in healthy smokers and non-smokers.

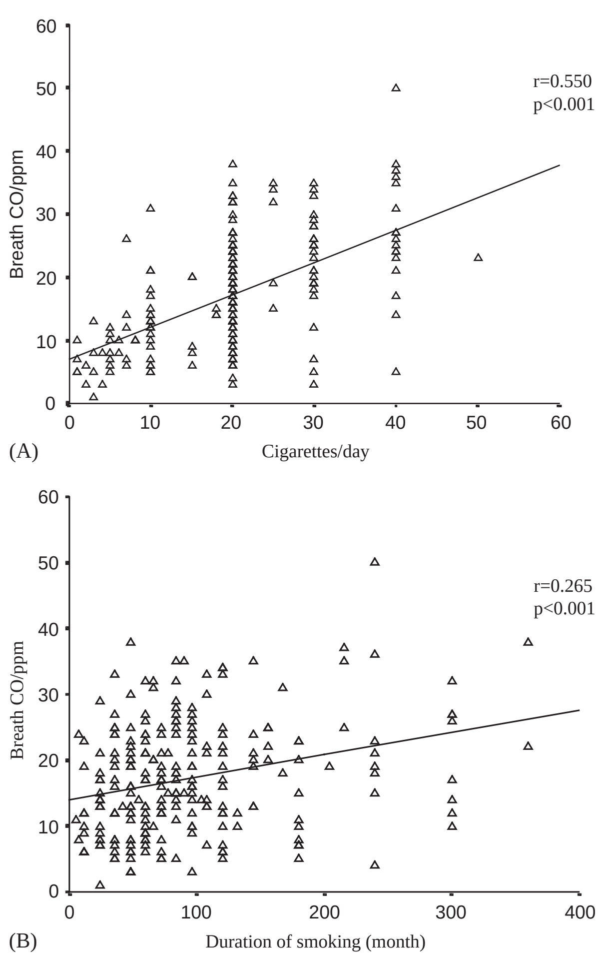

Figure 2 Correlation between exhaled CO levels and the number of cigarettes smoked in day (A), and exhaled CO levels and duration of smoking in healthy smokers (B).

For the smokers, the mean daily consumption of cigarettes was 19.79 ± 9.04 cigarettes/d and all of them reported that they had smoked on the day of testing.

The mean exhaled CO level was 17.13 ± 8.50 ppm for healthy smokers and 3.61 ± 2.15 ppm for healthy non-smokers, and 5.20 ± 3.38 ppm for passive smokers. The mean exhaled CO level was significantly higher in healthy smokers than healthy non-smokers ($P < 0.001$) and passive smokers ($P < 0.001$). The mean exhaled CO level was higher in passive smokers than healthy non-smokers but not significant ($P > 0.05$) (Fig. 1).

There was a significant positive correlation between CO levels and daily cigarette consumption, and CO levels and duration of smoking in healthy smokers ($r = +0.550$, $P < 0.001$; $r = +0.265$, $P < 0.001$, respectively. Spearman's test) (Figs. 2A and B).

A CO level of 6.5 ppm was taken as the cutoff between healthy smokers and non-smokers, as it gave the highest sensitivity and specificity. When smokers and non-smokers were looked at as a whole, a *cutoff* of 6.5 ppm had a sensitivity of 90% and specificity of 83% (ROC curve) (Fig. 3).

Discussion

There are several methods of assessing smoking status. Nicotine, cotinine, or thiocyanate levels in the plasma or urine may be used to indicate smoking status.[13] However, the blood tests are invasive and neither the blood nor the urine test provide an immediate assessment. The measurement of breath CO level may provide an immediate, non-invasive method of assessing smoking status.[1] This study supports that measuring breath CO levels provides an immediate, non-invasive, simple, and effective way of confirming a patients's smoking status.

Exhaled CO levels were higher in healthy smokers than in healthy non-smokers.[1,14] Also in our study, the exhaled CO level with the Smokerlyser was significantly higher in healthy smokers than healthy non-smokers and the values of exhaled CO in smoking and non-smoking subjects were similar to those of previous study.[1,14] There is a direct relationship between the smoking status of a given individual and the concentration of carboxyhaemoglobin (COHb) in their blood.[15,16] Exhaled CO reflects COHb accurately only if the lung acts as an effective tonometer, and exhaled CO is in dynamic equilibrium with COHb.[15] The measurement of exhaled CO is widely used to estimate COHb and, as such, to monitor the smoking habits of patients.[9,17,18] Considering that a COHb concentration $\geqslant 2\%$ is generally used in the clinical arena to separate smokers from non-smokers.[19] Our results shown that exhaled CO levels may be used to distinguish smokers from non-smokers as same as the others. Jarvis et al.[13] reported that CO measures as blood carboxyhaemoglobin or in expired as gave sensitivity and specifity of about 90% for distinguish smokers from non-smokers.

Our results shown that there was a significantly positive correlation between daily consumption of cigarettes and CO levels, and between duration of smoking and CO levels in healthy smokers. Likewise Gonzalez et al.[20] reported that CO in expired air correlated significantly with the number of smoked cigarettes. Smokers who develop chronic obstructive pulmonary disease, besides consuming a greater number of cigarettes, smoke them with a particular inhalation pattern (they inhale a greater volume of smoke and more deeply), thus permitting a higher quantity of oxidant substances.[21] Cunnington et al.[22] demonstrated that the mean breath CO concentrations increased in direct proportion to the number of cigarettes smoked.

Any exposure to CO may occur in normal day-to-day life, due to environmental pollution, passive smoking, and occupational exposure, the most likely cause of high levels of exposure is smoking.[23] Another cause of high levels of CO exposure is occult CO poisoning, for example, due to a faulty automobile exhaust system or home heating system, although this is only likely to be responsible for a minority of cases of raised breath CO levels.[1] CO in expired air has been reported to be an indirect measurement for the quantity of passive smoking[24] and exhaled CO can be used as an indicator of indoor smoking.[25] In our study, the exhaled CO levels was 5.20 ppm in passive smokers. Laranjeira et al.[26] reported that exposure to environmental tobacco smoke is the most likely cause for the increase in CO levels among non-smoking waiters. In this study it is reported that pre-exposure exhaled CO level was 2.0 ppm and post-exposure exhaled CO level was 5.0 ppm. In our study, 9 of passive smokers ($n = 24$) were working in the university canteen which has indoor smoking place. Moreover, 15 of passive smokers were students and they explained that they usually spend their free time at this university canteen. As expected passive smokers had higher CO concentration than healthy non-smokers, but this elevation was not significant. In a previous studies, the mean exhaled CO concentrations was usually similar in healthy non-smokers. For example, exhaled CO levels were determined 1.5 ± 0.1 ppm in Zayasu et al.[4] study, 1.2 ± 0.9 ppm in Yamaya et al.[27] study and 1.2 ± 0.3 ppm in Yamaya et al.[6] study. In our study, the exhaled CO levels was 3.61 ppm in healthy non-smokers. These results were high compared with other studies results. This may be due to excessive environmental pollution, faulty automobile exhaust system, and home heating system in our city.

Our results shown that the optimal *cutoff* was 6.5 ppm, giving 90% sensitivity and 83% specificity. Similarly Middleton and Morice[1] reported that the optimal *cutoff* was 6 ppm (selectivity 96%, sensitivity 94%). Jarvis et al.[13] reported that the optimal *cutoff* was 8 ppm (sensitivity 90%, selectivity 89%), and Crowley et al.[28] also reported that a breath CO level >8 ppm was strongly associated with a self report of current smoking. When exhaled CO at 7 ppm or over differentiated "smokers" from "non-smokers", sensitivity was 93% and specificity was 95% for detecting smokers.[29] Likewise Hewat et al.[30] shown that exhaled CO levels were all below 7 ppm, within the normal range for non-smokers. Many studies using breath CO monitors have tended use 10 ppm as the *cutoff*.[31,32] In our study, when we take the *cutoff* was 10.5 ppm, giving 75% sensitivity and 98% specificity. This results suggest that 10.5 ppm is too high to be a *cutoff* for a screening test, as it will reduce its sensitivity.

Jarvis et al.[9] shown that the second breath CO level was significantly higher than the first. In contrast Middleton and Morice[1] reported that the first breath CO level was significantly higher than the second and they recommended that a single Smokerlyser assessment should usually be sufficient, provided that there is adequate technique. For this reason in present study exhaled CO levels were assessment with the first measurement.

In clinical practice, it would be important to ensure the Smokerlyser was calibrated regularly. This was not a problem in this study because of the measurements were done in 5 days at the open air near the student healthy club desk after the Smokerlyser calibrated. Moreover we think that exhaled CO level likely is not affected the ambient air because of the measurements were done at the open air.

In a previous study it was stated that exhaled CO may be affected by ambient CO and that this influence may be reduced by subtracting ambient CO from exhaled CO.[33] In contrast, Zetterquist et al.'s[5] study shown that ambient air did not affect the exhaled CO levels when subjects held their breath for 10 s. Since there seems to be no contribution of CO from the conducting airways it must have its origin from the alveoli. The increase in CO concentrations after breath-hold also supports this view. The inhaled CO concentration may affect the concentration gradient of CO over the alveolar membranes (and possibly in the airways), and should not be compensated for by direct subtraction. A standardised time of breath-hold of 15 s was used in all the experiments which should have been sufficient for equilibrium to take place.[5] Since we also ask to the subjects to hold their breath for 15 s we did not consider the impact of ambient air.

In conclusion, exhaled CO measurements may provide a non-invasive, sensitive, and immediate way of assessing a patient's smoking status. CO measurement will replace at some stage the usual question regarding the number of cigarettes consumed. Moreover exhaled CO level is recommended for evaluating the exposure of passive smoking. Determining of exhaled CO level >6.5 ppm strongly suggests that subject is a smoker.

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