Interactions between exhaled CO, smoking status and nicotine dependency in a sample of Turkish adolescents

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The aim of this study was to show the interactions between nicotine dependency, exhaled carbon monoxide (CO) and smoking status including environmental passive tobacco smoke exposure in a sample of Turkish adolescents. This study was a cross-sectional research conducted among high school students of Erzurum province (n=536). The level of exhaled CO of all participants who accepted to participate in the study was measured by Microbio CO Analyzer (Microbio Med). Nicotine dependency was measured by a six-item version of the Fagerstrom Tolerance Questionnaire. Mean age of the adolescents was 17.0±1.6 (median: 17) and 77.1% were male. Of the study population, 30.2% and 11.4% of the students were regular and occasional smokers, respectively. Non-smokers who were exposed to environmental tobacco smoke had significantly (p<0.01) higher exhaled CO levels (2.8±2.6 ppm) than not-exposed non- smokers (1.8±1.9 ppm). Only 8.6% of adolescents who reported themselves to be a regular smoker had 7 ppm and higher exhaled CO. There was a statistically significant and positive correlation between exhaled CO levels and nicotine dependency after controlling for environmental tobacco smoke exposure and cigarettes per day (partial correlation, r=0.334, p=0.004). Exhaled CO can be used as a predictor of smoking status and environmental tobacco smoke exposure and an indicator of nicotine dependency in adolescents.

Key words: exhaled CO, smoking status, nicotine dependency, environmental tobacco smoke exposure, adolescents.

Cigarette smoking is the single most preventable cause of morbidity and mortality, causing five million deaths worldwide each year. A systematic study of biological, behavioral, and environmental factors is necessary to identify specific patterns of increased disease risks among various subgroups of smokers[1].

Exhaled carbon monoxide (CO) is a biological indicator to assess smoking status[2-4]. It was recently used as an indicator to monitor follow-up smoking cessation programs[5-8]. Exhaled CO is also considered as a biomarker of some pulmonary diseases like asthma, chronic obstructive pulmonary disease, primary ciliary dyskinesia, cystic fibrosis and bronchiectasia[7-9]. It is suggested that exposure to CO can induce myocardial ischemia in subjects with coronary artery disease[10].

Exhaled CO level provides an easy, immediate way of assessing a subject's smoking status. It can also be used to show the impact of active smoking and environmental tobacco smoke exposure on nicotine dependency[11].

Many of the studies including measurement of CO were done in adult patients or in patients having specific diseases, whereas few of the studies involved patients of adolescent age. The aim of this study was to show the associations between nicotine dependency, exhaled CO and smoking status, including environmental passive tobacco smoke exposure, in adolescents.

Material and Methods

Design and sample size

This study was a cross-sectional research for the high school students in one province (Erzurum, Turkey). The number of high school students in Erzurum urban city center was 10140 according to the Regional Directorate of Education. The number of the sample that represents the provincial city center was determined as 536 students with an alpha set of 0.05 using a statistical formula[12]. The subjects were chosen randomly from four official high schools (Şukrupaşa, Erzurum, Cumhuriyet and Atatürk high schools, 134 students from each school). High schools were chosen from four different sites of the urban city center. For each school, three different classes from each grade (classes from grades 9, 10 and 11) were chosen randomly by toll drawn to achieve randomization to avoid selection bias. All students in the determined classes were included in the study. The lists of each class were obtained from the directorate of each school. In each class, the first student to be included in the study was determined by toll drawn, and student selection was continued using random number table until the number of students targeted was reached.

Subjects

All students with no known diagnosed chronic obstructive pulmonary disease, asthma, or coronary arterial disease were accepted as subjects for the study.

Procedures

The level of exhaled CO of all participants who accepted to participate in the study was measured by Microbio CO Analyzer (Microbio Med). After this measurement, a structured questionnaire was completed by trained public health residents via face to face interview. The questionnaire included two sections. The first included questions regarding sociodemographic factors, the current smoking status of the participants, their parents and friends, exposure to environmental tobacco smoke at home and during leisure time, and daily cigarette consumption number. The second section of the questionnaire was Modified Fagerstrom Tolerance Questionnaire (mFTQ).

Measurements

The calibration of the analyzer was done before the beginning of the measurement of exhaled CO in adolescents. The measurements of exhaled CO were performed with Microbio CO Analyzer (Microbio Med). The Microbio CO Analyzer measures breath CO levels in parts per million (ppm) based on the conversion of CO to carbon dioxide (CO2) over a catalytically active electrode. We attempted to determine the optimal cut-off score in order to access optimal sensitivity and specificity. The measurement of 7 ppm and above was accepted to indicate regular smoking. Fagerstrom test scores less than 4, 5 and more than 6 were accepted to show low, moderate and high nicotine dependency, respectively. To standardize the breath being analyzed by the CO Analyzer, the subjects were asked to exhale completely, inhale fully, and then hold their breath for 15 seconds before exhaling rapidly into a disposable mouthpiece. The measurements and interviews were performed at the nurse's office of each high school. We performed exhaled CO measurement between 10-12 pm and we pre-accepted that the adolescents did not smoke during school time.

Questionnaire

The first section of the questionnaire included the questions regarding gender, age, the current smoking status of the participants, their parents and friends, exposure to environmental tobacco smoke at home and during leisure time, and daily cigarette consumption number. The current smoking status of the adolescents was expressed as regular smokers, occasional smokers and non-smokers. If a student reported smoking at least one cigarette per day, he/she was accepted as regular smoker. If a student expressed occasional smoking, he/she was accepted as occasional smoker. If a student stated that he/she was not a smoker, he/she was accepted as a non-smoker. The number of cigarettes consumed per day and onset age of smoking were recorded for each participant.

The environmental tobacco exposure was measured by two different questions for two different places where the students spent their out of school time (indoor exposure at the sites of leisure time activities and at home). If a student was exposed to environmental tobacco smoke at home or during indoor leisure time activities, he/she was accepted as an exposed subject. It was accepted that the students were not exposed to tobacco smoke at school. They were also asked how much time they generally spent at these two places per day. The current smoking status of their parents (maternal and paternal) was questioned. They were also asked if they had a close friend who was a regular smoker. Finally, in the first section of the questionnaire, they were asked if they wanted to or had tried to give up smoking.

The second section of the questionnaire was the mFTQ. The adolescent six-item version of the FTQ was developed and tested by Fagerstrom, Heatherton and Kozlowski[13] and it was adapted to Turkish and found reliable by Uysal et al.[13]. Responses ranged from 0 to 3 on two items and 0 to 1 on four items, yielding possible summed scores of 0 to 10. A score of 6 or above on the mFTQ was considered as indicative of high nicotine dependence.

Statistical Analysis

The normality test of Kolmogorov-Smirnov for CO measurements and Fagerstrom scores were performed. Spearman correlation analyses were used to evaluate the relationship between the exhaled CO levels – Fagerstrom scores - daily cigarette consumption – and duration of smoking in regular smokers. Mann-Whitney U test was used to find the determinants of nicotine dependency. The statistics were analyzed by SPSS 11.0 package program (SPSS, Inc, Chicago, IL, USA).

Ethical Issues

The study was approved by the Regional Directorate of Education and the Ethics Panel of Atatürk University. All of the adolescents were informed about the nature of the study and written informed consents from all participants were obtained.

Results

A total of 536 students participated in the study. Exhaled CO levels of all participants were determined.

Characteristics of the study population are shown in Table I. Mean age of the adolescents was 17.0±1.6 (median: 17), and 77.1% were male. Of the study population, 30.2% and 11.4% were regular and occasional smokers, respectively. Non-smokers accounted for 58.4% of the study population. Mean smoking duration of regular smokers was 3.6±0.2 years. Onset age of smoking of regular smokers was 13.9±2.7 (median: 15, range: 7-20). Daily cigarette consumption was 8.8±6.6 pieces for regular smokers. Of the regular smokers, 95.1 and 78.0% wanted and tried to give up smoking, respectively.

Table I. Characteristics of the Study Population, 2006

Characteristics	N	%*
Male gender	413	77.1
Age ≤18	462	86.2
Smoking status		
Non-smoker	313	58.4
Regular smoker	162	30.2
Occasional smoker	61	11.4
Age of onset		
≤10	22	13.8
11-15	90	56.6
>15	47	29.6
Passive exposure at home	274	51.1
Passive exposure in leisure time	298	55.6
Smoker father	299	55.9
Smoker mother	27	5.1
Smoker close friend	421	79.1
Nicotine dependency		
Low	121	22.6
Moderate	17	3.2
High	24	4.5

*% of all subjects.

Mean exhaled CO level of the whole study group was 4.1±3.0 ppm (min=0, max=15, median=3). Mean exhaled CO levels of regular, occasional and non-smokers were 7.23±1.5, 4.0±2.1 and 2.5±2.4 ppm, respectively. The difference between non-smokers and regular smokers was statistically significant ($p<0.001$). Male subjects had higher exhaled CO levels ($p<0.001$).

Of the adolescents who declared themselves as non-smokers, 87.2% had exhaled CO levels under 7 ppm. Further, 92.0% of the subjects who declared themselves as regular smokers were found to have exhaled CO levels of 7 ppm or more. Although only 30.2% of the adolescents claimed to be a regular smoker, according to exhaled CO level, 37.3% of the study population were current smokers. Only 8.6% of adolescents who claimed to be a regular smoker had exhaled CO of 7 ppm and higher.

The mean exhaled CO levels of the adolescents who were exposed and not exposed to environmental tobacco smoke were 4.6±3.0 and 2.8±2.6 ppm, respectively ($p<0.01$). The exhaled CO levels of adolescents according to smoking status and environmental tobacco smoke exposure are shown in Figure 1. Non-smokers who were exposed to environmental tobacco smoke had statistically significantly ($p<0.01$) higher exhaled CO levels (mean exhaled CO for non-smokers but exposed subjects: 2.8±2.6 ppm) than not-exposed non-smokers (mean exhaled CO for non-smokers and not-exposed subjects: 1.8±1.9 ppm). Although the exhaled CO level of exposed regular smokers was found to be higher than of not-exposed regular smokers, the difference was not statistically significant ($p>0.05$). Mean daily environmental smoke exposure duration was 8.5±3.7 hours per day. There was no statistically significant difference between regular and non-smokers ($p>0.05$) for daily exposure duration. A statistically significant, positive correlation between exhaled CO level and daily environmental smoke exposure duration was found (Spearman correlation, $r=0.38$, $p=0.001$) for regular smokers. After controlling for daily cigarette consumption, the significance did not remain stable (partial correlation, $r=0.007$, $p>0.05$).

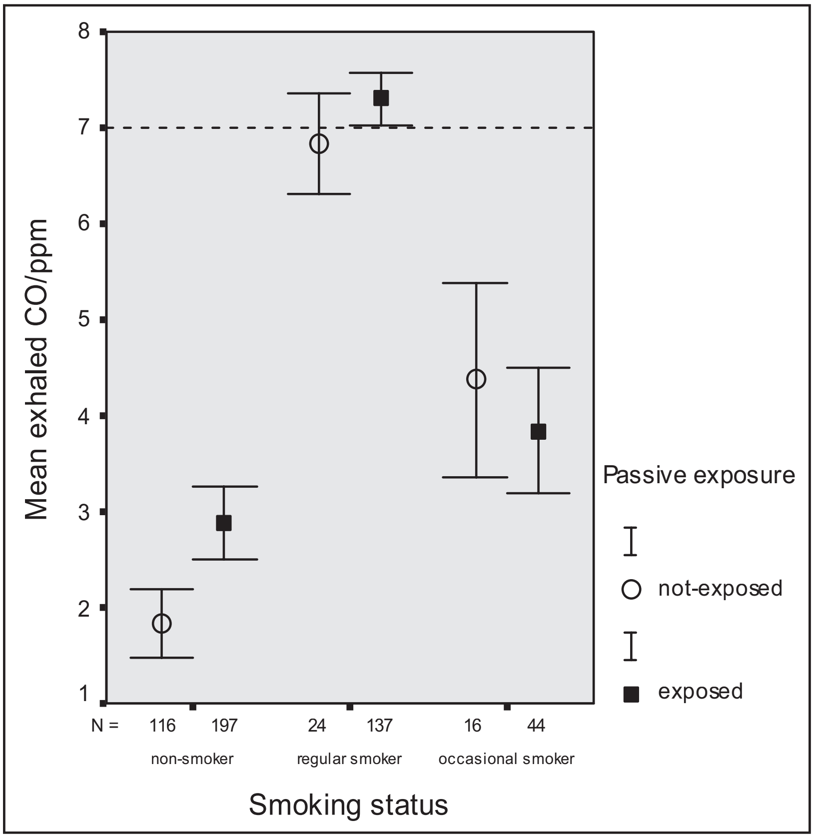

Fig. 1. Level of exhaled CO according to smoking status and environmental tobacco smoke exposure.

The smoking status of parents (both mother and father) was not found to be an indicator for exhaled CO level. If the subjects had a close friend who was a regular smoker, the level of exhaled CO of the adolescent was significantly higher than the adolescent with no smoker friend ($p<0.001$). There was a statistically significant positive but weak correlation between daily cigarette consumption number and exhaled CO level (Spearman correlation, $r=0.21$, $p<0.001$) for regular smokers. The correlation between daily cigarette consumption number was found to remain stable with an increasing coefficient after controlling for daily environmental tobacco smoke exposure duration (partial correlation, r=0.284, p<0.05).

Nicotine dependency

Exhaled CO levels of adolescents according to nicotine dependency are shown in Figure 2. Mean Fagerstrom test score of regular smokers (subjects who cited at least one cigarette consumption per day) was 3.1±2.0 (min=0, max=8, median=3). Due to Fagerstrom test, 4.5% and 14.8% of all adolescents and regular smokers had high nicotine dependency, respectively. Regular smokers who were exposed to environmental tobacco smoke had statistically significantly higher test scores (p<0.01) (score of exposed regular smokers: 3.3±2.0) compared with not-exposed subjects (score of not-exposed regular smokers: 2.0±1.5). The adolescents who were exposed to environmental tobacco smoke had higher nicotine dependency than of not-exposed adolescents, regardless of the level of nicotine dependency (Fig. 3). The adolescent who had a smoker mother had statistically significantly higher Fagerstrom scores (p<0.01). Gender, having a smoker father and having a smoker close friend were not found to be indicative for nicotine dependency.

There was a statistically significant, positive and moderate correlation between Fagerstrom scores and daily cigarette consumption number (Spearman correlation, r=0.238, p<0.01). After controlling for daily environmental tobacco smoke exposure duration, the significance of the correlation remained stable with an increasing coefficient (partial correlation, r=0.270, p<0.05).

There was also a significant and positive correlation between exhaled CO levels and Fagerstrom test scores (Spearman correlation, r=0.411, p<0.001). After controlling for daily cigarette consumption number and daily environmental tobacco smoke exposure duration, the correlation remained statistically significant, with an amount of decrease in correlation coefficient (partial correlation, r=0.334, p<0.01).

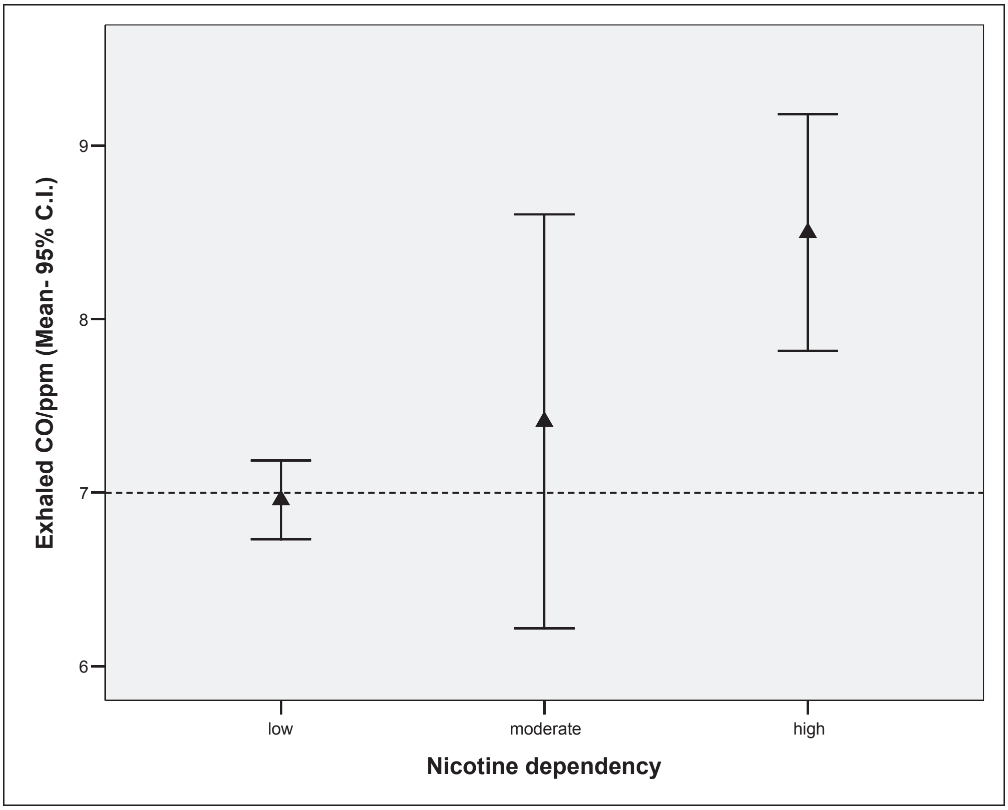

Fig. 2. Level of exhaled CO according to nicotine dependency.

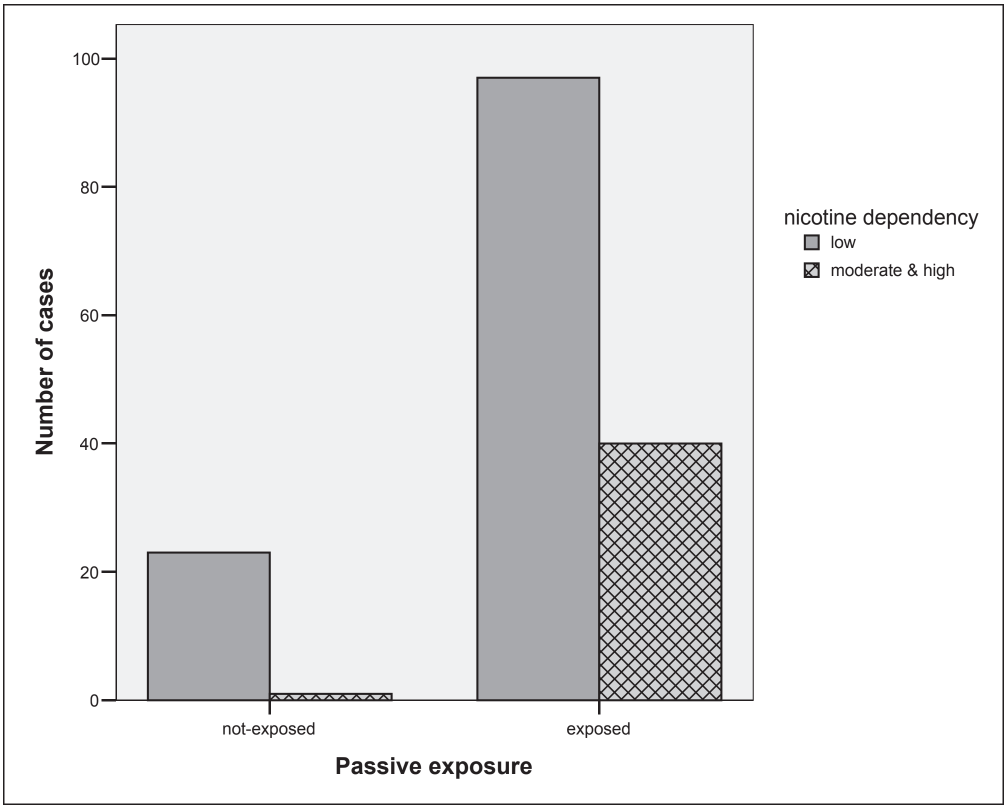

Fig. 3. Level of nicotine dependency according to environmental tobacco smoke exposure.

A statistically significant and positive correlation was found between lifetime smoking duration and nicotine dependency after controlling for daily cigarette consumption number and daily environmental tobacco smoke exposure duration (partial correlation, $r=0.264$, $p<0.05$).

Discussion

Our study population was a representative sample of high school students (n=536) in one province, with a median age of 17. This age group is an important and target group for further prevention. In this study, we aimed to find the determinants of nicotine dependency and the interactions between smoking status, environmental tobacco smoke exposure and exhaled CO.

With a comprehensive longitudinal study of Hublet et al.[14], which determined the smoking trends among adolescents in Canada and 10 European countries between 1990 and 2002, it was shown that 14.9% of adolescents were regular smokers in 2002. This study also showed that smoking increased to approximately 20% in developing countries of Europe like Latvia, Poland and Hungary. For developed countries like Canada and the United Kingdom, it was decreased to approximately 10% between 1990 and 2002. The lowest rate was 5.5% for Swedish adolescents. In Turkey, the Ministry of Health conducted a large survey among 15,957 adolescents and reported that one-third of adolescents had ever tried smoking and 10% were regular smokers[15]. In our study, we reported 30.2% for regular smoking. This rate was approximately three times higher than the regular smoking rate for the whole country. Erzurum is a province located in the east of Turkey and is one of the least developed parts of the country. Migration rate both in and out of the province is relatively high. Especially between adolescents and their parents, smoking may not be accepted as an unfavorable behavior. Various cultural effects may play a role in their addictive behaviors. Like Ertas[16] mentioned in his study, early prevention programs should be performed to decrease smoking rates, to prevent adolescents from starting to smoke, and to help them to quit by taking cultural differences into consideration.

Mean exhaled CO level of the whole study group was 4.1±3.0 ppm. Mean exhaled CO levels of regular, occasional and non-smokers were 7.23±1.5, 4.0±2.1 and 2.5±2.4 ppm, respectively. This was an expected result, but exhaled CO levels of adolescents were quite lower than of adults, which were studied before in Turkish young adults[2]. Exhaled CO levels can be used as an assessment tool to ascertain the accuracy of self statements regarding smoking status in adolescents[2-4]. In our study, we found a sensitivity of approximately 90% for accurate statements of smoking status. Environmental tobacco smoke exposure might play a role as a confounder in this issue. Therefore, passive smoke exposure is a very important issue in studies concerning smoking status and measurements like exhaled CO.

The determination of the level of passive smoke exposure is a serious problem. Generally, the questionnaires were done to ascertain the status of exposure. A moderate statistically significant correlation between daily tobacco smoke exposure duration and exhaled CO level was found (Spearman correlation, $r=0.38$, $p=0.001$). In our study, whether the student was a regular smoker or a non-smoker, the exposed subjects had higher exhaled CO levels (Fig. 3). Exhaled CO can be used as an assessment tool for environmental tobacco smoke exposure, as expressed in other studies[17,18]. The issue of environmental tobacco smoke exposure was the strongest part of our study compared to similar studies that investigated the association of measured exhaled CO and carboxyhemoglobin (COHb) and smoking status[3,9,19-21]. The only exception was determined for occasional smokers. This was probably due to a lack of regular behavior towards smoking and/or differences regarding environmental tobacco smoke exposure.

Like Gonzales et al.[22] and Deveci et al.[2], we also found a statistically significant correlation between the daily cigarette consumption number and exhaled CO level (Spearman correlation, $r=0.21$, $p=0.000$). It was found that the correlation with daily cigarette consumption number was found to remain stable with an increasing coefficient after controlling for daily environmental tobacco smoke exposure duration (partial correlation, $r=0.284$, $p=0.013$).

Mean exhaled CO for non-smokers but exposed subjects was higher than for not-exposed non-smokers. These levels were lower than determined for the non-smoker subjects of Deveci et al.[2] (healthy adults) but higher than reported by Zayasu[6] and Yamaya[7]. These differences may occur due to age and the study group. Environmental tobacco smoke exposure was also a determinant for non-smokers' exhaled CO. The place where the measurements were done might also be important.

Tobacco dependence (due to the presence of nicotine) has been noted among young smokers, with a New Zealand study estimating that one in every five 18-year-olds is dependent on tobacco, using modified DSM-III R (American Psychiatric Association) criteria[23]. This is similar to a prevalence rate of dependence of 20% found in a United States study of 21–30-year olds, and comparison with ages for uptake of regular smoking suggests that dependence develops rapidly among adolescent smokers[24]. The level of nicotine dependency was determined by Fagerstrom test in our study. According to Fagerstrom test, 14.8% of the adolescents who were regular smokers had high or very high level of nicotine dependency.

The adolescent who had a smoker mother had statistically significantly higher Fagerstrom scores ($p<0.01$). Like us, Blokland et al.[25] found that if an adolescent has a smoker parent, they were four times more likely to be a smoker. In accordance with Blokland et al., we found that maternal smoking was a significant determinant for adolescent nicotine dependency.

Different cut-off levels of exhaled CO (6, 6.5, 8, and 10 ppm) were used by different researchers[2,26-28]. We determined an optimal cut-off point as 7 ppm to flag smoking and measured a sensitivity of 92% and a specificity of 87.2% for self-report of current smoking. We considered this level as appropriate for public screening in Turkish adolescents, but this level should be tested in future with more studies.

Exhaled CO was a biological indicator to assess smoking status and to evaluate nicotine dependence. Although questionnaires and scales like Fagerstrom Test for Nicotine Dependence or Nicotine Dependence Syndrome Scale were used, the validities of these scales were also tested and compared with biologic indicators like serum cotinine and exhaled CO. This study provides an evaluation of such a comparison in a sample of Turkish adolescents. Okuyemi et al.[29] performed such a study on

African American smokers to determine the relations between nicotine dependence scales and exhaled CO. They found that there was a significant correlation (r=0.19), which was lower than that shown for our study group (r=0.33), although we controlled the correlation for passive smoke exposure and cigarettes per day. Exhaled CO is an easy tool for finding the validities of such scales and determining their usefulness.

The main limitation of our study was the distribution of gender. Male students were prominent. Stratification of the sample according to gender might be more useful. The other limitation was the lack of multivariate statistical analysis (linear regression) because measurements of exhaled CO did not show normal distribution by Kolmogorov Smirnov test. Exhaled CO is known to be influenced by other factors like environmental pollution and occupational exposures[30]. The results presented in this study should be evaluated taking these factors into consideration. Further, exhaled CO was a biological indicator and it increased in exhaled air approximately 60% in an hours' time after smoking[31]. We performed exhaled CO measurement between 10-12 pm and we pre-accepted that the adolescents did not smoke while at school. We did not ask them if they smoked while at school on the day of measurement because the reliability of the self reports would also be questionable.

Other than exhaled CO, serum cotinine or saliva cotinine levels can be used as a gold standard. Etter et al.[32] reported a moderate correlation (r=0.45) between daily cigarette consumption number and saliva cotinine level, which was higher than we found for exhaled CO (r=0.21). However, sensitivity of saliva cotinine to assess smoking status (86.5%) was lower (92.0%) than we found for regular smoker adolescents. Okuyemi et al.[29] also showed a significant correlation between serum cotinine and exhaled CO levels (r=0.46). Serum, saliva or urine cotinine measurements have also been shown as useful predictors to assess nicotine dependence, but measurement of exhaled CO is a cheaper and much easier modality. As Turkey is a developing county, we have limited resources; therefore, our study provides useful and unique information for Turkish adolescents for further studies on nicotine dependence.

It has also been widely acknowledged that prevention of adolescent smoking rather than cessation has received the greatest attention in research endeavors, despite the fact that the majority of adolescent smokers have made at least one serious attempt to quit[23]. We determined that 95.1% and 78.0% of regular smokers wanted and tried to give up smoking, respectively. This age group is a target group for intervention and assessment studies.

We found that beginning age and therefore lifetime smoking duration was an important determinant of nicotine dependency. This finding also indicates the importance of early detection of nicotine dependency and prevention in adolescents and it reports that exhaled CO measurement may be an easier tool for intervention programs for Turkish adolescents.

In conclusion, our study has provided important results regarding the determinants of nicotine dependency and the associations between exhaled CO, smoking status and environmental tobacco smoke exposure in a sample of Turkish adolescents.

REFERENCES

1. Mustonen TK, Spencer SM, Hoskinson RA, et al. The influence of gender, race, and menthol content on tobacco exposure measures. Nicotine Tob Res 2005; 7: 581-590.
2. Deveci SE, Deveci F, Acik Y, et al. The measurement of exhaled carbon monoxide in healthy smokers and non-smokers. Respir Med 2004; 98: 551-556.
3. Middleton ET, Morice AH. Breath carbon monoxide as an indication of smoking habit. Chest 2000; 117: 758-763.
4. Zetterquist W, Marteus H, Johannesson M, et al. Exhaled carbon monoxide is not elevated in patients with asthma or cystic fibrosis. Eur Respir J 2002; 20: 92-99.
5. Hung J, Lin CH, Wang JD, et al. Exhaled carbon monoxide level as an indicator of cigarette consumption in a workplace cessation program in Taiwan. J Formos Med Assoc 2006; 105: 210-213.
6. Zayasu K, Sekizawa K, Okinaga S, et al. Increased carbon monoxide in exhaled air of asthmatic patients. Am J Respir Crit Care Med 1997; 156: 1140-1143.
7. Yamaya M, Hosoda M, Ishizuka S, et al. Relation between exhaled carbon monoxide levels and clinical severity of asthma. Clin Exp Allergy 2001; 31: 417-422.
8. Horvath I, Barnes PJ. Exhaled monoxides in asymptomatic atopic subjects. Clin Exp Allergy 1999; 29: 1276-1280.
9. Montuschi P, Kharitonov SA, Barnes PJ. Exhaled carbon monoxide and nitric oxide in COPD. Chest 2001; 120: 496-501.

10. Wickramatillake HD, Gun RT, Ryan P. Carbon monoxide exposures in Australian workplaces could precipitate myocardial ischemia in smoking workers with coronary artery disease. Aust N Z J Public Health 1998; 22: 389-393.

11. Brimkulov NN, Vinnikov DV, Cholurova RA. Complex assessment of nicotine dependence using questionnaires and measurement of carbon oxide concentration in exhaled air. Ter Arkh 2004; 76: 53-58.

12. Tezcan S. Örnekleme. In: Tezcan S (ed). Epidemiyoloji. Ankara: Hacettepe Halk Sağlığı Vakfı, Yayın No: 92/1; 1992: 236-251.

13. Uysal MA, Kadakal F, Karşıdağ C, et al. Fagerstrom test for nicotine dependence: reliability in a Turkish sample and factor analysis. Tuberkuloz ve Toraks Dergisi 2004; 52: 115-121.

14. Hublet A, de Bacquer A, Valimaa P, et al. Smoking trends among adolescents from 1990 to 2002 in ten European countries and Canada. BMC Public Health 2006; 6: 280 (e-publication-single page).

15. Erguder T, Soydal T, Ugurlu M. Tobacco use among youth and related characteristics, Turkey. Soz Praventivmed 2006; 51: 91-98.

16. Ertas N. Factors associated with stages of cigarette smoking among Turkish youth. Eur J Public Health 2007; 17: 155-161.

17. Ece A, Gurkan F, Haspolat K, et al. Passive smoking and expired carbon monoxide in healthy and asthmatic children. Allergol Immunopathol 2000; 28: 255-260.

18. Gourgoulianis KI, Gogou E, Hamos V, et al. Indoor maternal smoking doubles adolescents' exhaled carbon monoxide. Acta Pediatr 2002; 91: 712-713.

19. Jarvis MJ, Belcher M, Vessey C, et al. Low cost carbon monoxide monitors in smoking assessment. Thorax 1986; 41: 886-887.

20. Rea JN, Tyrer PJ, Kasap HS, et al. Expired air carbon monoxide, smoking, and other variables. A community study. Br J Prev Soc Med 1973; 27: 114-120.

21. Vogt TM, Selvin S, Widdowson G, et al. Expired air carbon monoxide and serum thiocyanate as objective measures of cigarette exposure. Am J Public Health 1977; 67: 545-549.

22. Gonzalez Ruiz JM, Barrueco M, Cordovilla R, et al. Usefulness of CO measurement in expired air in the study of tobacco consumption by youths and adolescents. Rev Clin Esp 1998; 198: 440-442.

23. Stanton WR, Smith KM. A critique of evaluated adolescent smoking cessation programmes. J Adolesc 2002; 25: 427-438.

24. Breslau N, Kilbey M, Andreski P. Nicotine dependence, major depression and anxiety in young adults. Arch Gen Psychiatry 1991; 48: 1069-1074.

25. den Exter Blokland E, Engels R, Hale W. Lifetime parental smoking history and cessation and early adolescent smoking behavior. Prev Med 2004; 38: 359-368.

26. Crowley TJ, Andrews AE, Cheney J, et al. Carbon monoxide assessment of smoking in chronic obstructive pulmonary disease. Addict Behav 1989; 14: 493-502.

27. Nakayama T, Yamamoto A, Ichimura T, et al. An optimal cutoff point of expired-air carbon monoxide levels for detecting current smoking: in the case of a Japanese male population whose smoking prevalence was sixty percent. J Epidemiol 1998; 8: 140-145.

28. Jorenby DE, Smith SS, Fiore MC, et al. Varying nicotine patch dose and type of smoking cessation counseling. J Am Med Assoc 1995; 274: 1347-1352.

29. Okuyemi KS, Pulvers KM, Cox LS, et al. Nicotine dependence among African American light smokers: a comparison of three scales. Addict Behav 2007; 32: 1989-2002.

30. Antuni JD, Kharitonov SA, Hughes D, et al. Increase in exhaled carbon monoxide during exacerbations of cystic fibrosis. Thorax 2000; 55: 138-142.

31. Bacha ZA, Salameh P, Waked M. Saliva cotinine and exhaled CO levels in natural environment waterpipe smokers. Inhal Toxicol 2007; 19: 771-777.

32. Etter JF, Vu Duc T, Perneger TV. Saliva cotinine levels in smokers and non-smokers. Am J Epidemiol 2000; 151: 251-258.