

ORIGINAL ARTICLES

Passive smoking and expired carbon monoxide concentrations in healthy and asthmatic children

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SUMMARY

Background: carbon monoxide (CO) in expired air has been reported to be an indirect measurement for the quantity of passive smoking. Since endogen CO is produced in inflammatory processes and inflammation is the main pathogenetic mechanism of asthma, it was aimed to investigate the relationship between the intensity of passive smoking and CO concentration in expired air of healthy and asthmatic children.

Methods and Results: the study was performed in the outpatient pediatrics clinics and day care centers. Knowledge about indoor smoking habits were obtained from parents. The exhaled CO concentrations were measured by a portable device in 235 healthy (mean age, 4.4 ± 2.3 years) and 54 asthmatic (mean age, 4.5 ± 1.7 years) children. Children with no smoking parents had the lowest exhaled CO concentrations. Significant relationships were found between the number of smoking cigarettes in the house and exhaled CO concentrations in both healthy ($p = 0.003$) and asthmatic ($p = 0.01$) children. Carbon monoxide concentrations were higher in asthmatic children than healthy ones (mean \pm SD, 1.32 ± 1.50 ppm and 0.86 ± 1.35 ppm, respectively, $p = 0.028$) if their parental smoking habits were not taken into account. Asthmatic children of non-smoking parents had higher CO concentrations than healthy subjects of non-smoking parents (1.05 ± 1.55 ppm vs 0.37 ± 0.53 ppm, $p = 0.01$). On the other hand, asthmatic children who has no smoking parents and did not receive inhaled steroids had significantly higher CO concentrations (1.75 ± 1.45 ppm) than those who received steroids (0.58 ± 0.65 ppm, $p = 0.024$).

Conclusions: exhaled CO can be used as an indicator of passive smoking in children. Higher expired CO of asthmatic children may reflect inflammation of the lung in asthma.

Key words: Carbon monoxide. Passive smoking. Children. Asthma. Corticosteroids.

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INTRODUCTION

In order to detect the magnitude of passive smoking, parental questionnaires have been used extensively. Epidemiological studies on respiratory effect of passive smoking in children suggested urinary cotinine excretion for determining the intensity of exposure to tobacco smoke (1-4). In some other studies, carbon monoxide in expired air has been reported to be an indirect measurement for the quantity of passive smoking and CO poisoning (5, 6). Since measurement of cotinine excretion is expensive and require more sophisticated laboratory work-up, measurement of carbon monoxide in expired air may be an alternative to estimate magnitude of environmental tobacco smoke especially for nonaffluent countries and for epidemiological studies. However, CO is produced *in vivo* in many tissues of the body by an enzyme called Heme oxygenase-1 (7). Heme oxygenase is present in the pulmonary vascular endothelium (8) and alveolar macrophages (9) and is upregulated by the oxidative stress (9) and inflammatory cytokines (10). On the basis of the fact that there is an inflammatory process in the pathogenesis of asthma, we examined whether asthmatic children produced more CO than do healthy children, besides investigating the relationship between CO in expired air and the intensity of passive smoking determined by a parental questionnaire in healthy and asthmatic children.

MATERIAL AND METHODS

This study of cross-sectional design was performed in 235 healthy children in day care centers, nursery schools and primary schools in summer months that there was no air pollution and no need to heat with stove. All 54 asthmatic children followed up at Pediatric outpatient clinics of Dicle University Hospital included in the study had mild persistent to moderate asthma (before admission; > 2 attack per week, night symptoms > 2 a month or > 1 a week, FEV1 > 60% of predicted). Thirty of them were being treated with inhaled corticosteroids (budesonid 200-400 µg/day, twice a day) at least for the last 4 weeks prior to the CO measurements, but the rest 24 asthmatics were admitted to the hospital with acute asthma attack and CO measurements were performed after 2 weeks of attack while patients were receiving only β_2 agonists. They did not receive inhaled steroids during CO measurements, but after 1-2 months, 9 of them could not be controlled with beta-agonists and we had to treat them with corticosteroids. Thus 15 patients in non-steroid group had less severe asthma symptoms and 9 of them had similar asthma severity compared to the steroid-received group. All of the asthmatic children were included in the study provided that they were at symptom-free intervals at least for the 2 weeks during their routine follow-up and they did not have any symptoms of infection. Knowledge about parental smoking habits at home was obtained from parents using a questionnaire and an informed consent was taken. In addition to questions about parental smoking habits and how many cigarettes they smoked in house daily, some questions were added to the questionnaire to clarify whether children had doctor-diagnosed asthma, wheezing attacks or recent upper respiratory infections. According to answers, children with the past and current history of asthma, wheezing or recent upper respiratory infections were excluded from the healthy group. We have taken the smoking habits of parents for the last 6 months into account. All children were examined by the same physician, including lung auscultation. Carbon monoxide in expired air was measured by using MicroCO Meter (Micro Medical, England). Time of measurement was 08⁰⁰ and 09⁰⁰ hours a.m. in healthy children and in the asthmatic group with no steroid therapy, and 2-3 hours after receiving inhaled steroids in the steroid receiving asthmatic group. The device is based on electrochemical fuel cell, which works through the reaction of carbon monoxide with an electrolyte at one electrode, and oxygen at the other. This reaction generates an electrical current

proportional to CO concentration (5). Children were asked to expire through the device and the best value was recorded after three attempts. Measurements of CO in 23 healthy and 5 younger asthmatic children were done by lack of adequate cooperation and those children were excluded from the study. Asthma diagnosis was established by using asthma criteria of American Thoracic Society (11). None of the asthmatics and healthy children was active smoker.

Statistical analysis: results are expressed as mean \pm Standard deviation (SD). Due to skewed distribution of CO values non-parametric Kruskal-Wallis one-way ANOVA and Mann-Whitney U tests were performed for comparison of data belonging to different groups. Spearman correlation analysis was performed to assess the relationship between the number of cigarettes smoked by parents per day and CO concentrations of children. Chi-square test was used to test differences between parental smoking habits of healthy and asthmatic children. P value less than 0.05 was accepted as significant.

RESULTS

The mean age of healthy subjects was 4.4 ± 2.3 years (3-10 yrs) and asthmatic children was 4.5 ± 1.7 years. Male to female ratio was 1.4:1 for healthy children and 1.8:1 for asthmatics. Parental smoking habits of healthy and asthmatic children and their CO levels were shown in table I. Parental smoking habits of asthmatic children were similar to the healthy subjects (37.0% vs 33.6% non-smokers and 63.0% vs 66.4% smokers). When parental smoking habits were not taken into consideration, the CO concentration (mean \pm SD) of asthmatics (1.32 ± 1.50 ppm) was higher than those of healthy children (0.86 ± 1.35 ppm, $p = 0.028$).

In comparison of asthmatic and healthy children of non-smoker parents, higher CO concentrations were found in asthmatic children than in healthy subjects (1.05 ± 1.55 ppm vs 0.37 ± 0.53 ppm, $p = 0.01$). Asthmatic children whose parents smoke 1-5 and 6-10 cigarettes per day had also higher CO concentrations compared to healthy children with similar parental smoking habits ($p = 0.03$, $p = 0.03$). There was no difference in CO levels between asthmatic and healthy children whose parents smoke 11 or over cigarettes per day at home ($p > 0.05$) (table I).

Children, whose neither parents were smoker, had lowest exhaled CO concentrations. The mean CO levels of children whose mother or father smoke alone or both parents smoke were similar ($p > 0.05$) (table I).

Table I

Influence of contact with smokers on carbon monoxide in expired air of healthy and asthmatic children (mean \pm SD)

	Healthy children (n = 235)		Asthmatics (n = 54)		Significance	
	* n (%)	** CO (ppm)	* n (%)	** CO (ppm)	* P	** P
Amount smoked in the home (cigarettes per day)						
Zero	79 (33.6)	0.37 ± 0.53	20 (37.0)	1.05 ± 1.55	NS	0.01
1-5	22 (9.4)	0.41 ± 0.33	11 (20.4)	0.77 ± 0.59		0.03
6-10	63 (26.8)	0.87 ± 1.05	13 (24.1)	1.68 ± 1.75		0.03
11-20	64 (27.2)	1.49 ± 1.60	10 (18.5)	2.02 ± 2.25		NS
>20	7 (3.0)	1.75 ± 2.31	—	—		—
Parental smoking in the home						
None	79 (33.6)	0.37 ± 0.53	20 (37.0)	1.05 ± 1.55	NS	0.01
Father alone	24 (10.3)	0.94 ± 1.14	9 (16.7)	1.04 ± 0.73		NS
Mother alone	37 (15.7)	1.10 ± 1.19	11 (20.4)	1.25 ± 0.96		NS
Both parents	95 (40.4)	1.18 ± 1.45	14 (25.9)	1.93 ± 2.42		NS
Contact with smokers other than parents						
Yes	128 (54.4)	0.92 ± 1.47	23 (42.6)	1.42 ± 1.52	NS	NS
No	107 (45.6)	0.79 ± 1.14	31 (57.4)	1.25 ± 1.40		NS

NS: not significant, CO: carbon monoxide, * P: difference between parental smoking habits, according to Chi-square test; ** P: difference between healthy and asthmatic children at each row according to Mann-Whitney U test.

There was no difference between CO concentrations of boys and girls with Mann-Whitney U test ($p > 0.05$). Age was not a predictor for exhaled CO concentration with Spearman's correlation analysis ($p > 0.05$).

Significant relationship between the number of smoking cigarettes in the house per day and exhaled

CO concentrations were found in healthy ($r = 0.35$, $p = 0.003$) and in asthmatic children ($r = 0.44$, $p = 0.01$) with Spearman's correlation analysis (table II).

Asthmatic children who did not receive corticosteroids ($n = 24$) had higher CO concentrations (1.78 ± 1.53 ppm) than healthy children (0.86 ± 1.77 ppm, $p = 0.022$), and steroid-treated asthmatic patients (0.96 ± 0.95 ppm, $p = 0.02$), whereas asthmatic children who received inhaled corticosteroids ($n = 30$) had similar CO concentrations in comparison with healthy children ($p > 0.05$) (table III).

In order to eliminate the effect of passive smoking on the CO concentrations of asthmatics, we compared asthmatic children of non-smoker parents either treated or not treated with inhaled corticosteroids (budesonid, 200-400 μ g per day). Thus, we found significantly higher CO levels in children who did not receive steroids (1.75 ± 1.45 ppm) than those who did (0.58 ± 0.65 ppm) ($p = 0.024$) (table III).

DISCUSSION

In this study, we compared data about passive smoking obtained from parental questionnaire and CO in expired air measured by a portable device.

Table II

Carbon monoxide levels according to gender and age in healthy children

	n (%)	CO (ppm) (mean ± SD)	p
Gender			
Boys	124 (52.8)	0.84 ± 1.47	NS*
Girls	111 (47.2)	0.87 ± 1.26	
Age of child (Years)			
3-4	74 (31.5)	0.89 ± 0.77	NS* **
5-6	62 (26.3)	0.75 ± 0.71	
7-8	57 (24.3)	0.86 ± 1.96	
9-10	42 (17.9)	1.00 ± 2.40	
Total	235 (100)	0.86 ± 1.35	

NS: not significant, * according to Mann-Whitney U test, ** according to Kruskal-Wallis test.

Table III

Exhaled carbon monoxide concentrations (mean \pm SD) of asthmatic children who has taken or not inhaled steroids, according to parental smoking habits

Parental smoking habits	n	Steroid group CO (ppm)	n	Non-steroid group CO (ppm)	Significance p
Number of daily smoked cigarettes					
Non-smoker	12	0.58 \pm 0.65	8	1.75 \pm 1.45	0.024
1-5	6	0.57 \pm 0.77	5	1.02 \pm 1.05	NS
6-10	5	1.41 \pm 1.15	8	1.85 \pm 1.51	NS
11-20	7	1.64 \pm 1.95	3	2.92 \pm 2.05	NS
>20	—	—	—	—	—
Total	30	0.96 \pm 0.95	24	1.78 \pm 1.53	0.02

We found significant relationship between concentrations of CO measured in expired air and intensity of exposure to tobacco smoke (ETS) assessed by parental questionnaire. Children having parental smoking are often exposed to higher levels of ETS. In the study of Irvine, et al (1) many children of 501 families were exposed to high levels of environmental tobacco smoke and their cotinine levels were heavily dependent upon to the parental smoking. Since parents of asthmatic children usually learn the detrimental effects of cigarette smoking on their children's health, they reduce the amount of indoor smoking near their children (12). This may be an important factor that prevented the excessive levels of exhaled CO in asthmatic children.

The effect of ETS as measured by the number of cigarettes smoked by parents, are likely to be different between cold climate countries and other cultures in which exposure is effectively reduced because the lack of tight sealing in homes increases ventilation rates. Questionnaires are generally used to measure the history of exposure to ETS but total exposure can be difficult to estimate from questionnaire because parents may change their smoking habits after the development of symptoms in their child (13). Our region is in South eastern Anatolia with a hot climate that only in four months a year people need indoor heating and there is no industrial factories. We carried out this study in spring and summer months and we can suggest that the effect of air pollution on children was minimal. Passive smoking is responsible for respiratory morbidity in children (14, 15). Some studies have failed to show a causal effect of passive smoking on incidence of asthma and demonstrated increased morbidity among asthmatic children (16). In most of these studies passive smoking exposure of the population was ascertained by questionnaires (17,

18). In one study a correlation was found between exposure to ETS and the child's carboxy hemoglobin (COHb) determined by direct measurement of capillary blood COHb levels (6). In the study of Rylander, et al (19) exposure to ETS was estimated from urinary cotinine measurement in children with wheezing bronchitis and control subjects. They found that ETS is an important risk factor for wheezing bronchitis and a single urinary cotinine measurement offer no major advantages to questionnaire data for assessment of long-term exposure to ETS (19).

Our results indicated higher exhaled CO concentrations in asthmatic children who did not receive inhaled corticosteroids in comparison with healthy subjects and asthmatic children who received inhaled steroids. These high levels of exhaled CO concentration may reflect inflammation of the lung. In asthmatic inflammation many cytokines are involved, including interleukin-1, interleukin-6 and tumour necrosis factor which can upregulate heme oxygenase-1 activity in human tissues (10). The normal CO concentration in expired air of asthmatic children who received corticosteroids suggest that inhaled corticosteroids downregulate heme oxygenase-1 activities through reduction of inflammatory cytokines. In the study of Zayasu, et al (20) increased exhaled CO concentrations were found in adult asthmatic patients not receiving corticosteroids compared to control subjects. Our study have shown similar results in children.

In conclusion, our results indicate that measurement of CO in expired air may be a reliable index for exposure to tobacco smoke in healthy children as well as a useful non-invasive marker of airway inflammation in asthmatics, since exhaled CO were found to be increased in asthmatic children and decreased with inhaled steroids.

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RESUMEN

Antecedentes: se ha comunicado que el monóxido de carbono (CO) en aire espirado es una medición cuantitativa indirecta de la inhalación pasiva de humo de tabaco. Como se produce CO endógeno en procesos inflamatorios y la inflamación es el principal mecanismo patógeno del asma, propusimos investigar la relación entre la inhalación pasiva de humo de tabaco y la concentración de CO en el aire espirado por niños sanos y asmáticos.

Métodos y resultados: el estudio se realizó en clínicas ambulatorias de pediatría y guarderías infantiles. Se obtuvo información de los padres acerca del hábito de fumar en el domicilio. Las concentraciones de CO exhalado se midieron con un dispositivo portátil en 236 niños sanos (edad media $4,4 \pm 2,3$ años) y 53 niños asmáticos (edad media $4,5 \pm 1,7$ años). Los niños cuyos padres no fumaban tuvieron las menores concentraciones de CO exhalado. Se encontró una relación significativa entre el número de personas que vivían en casa y fumaban y las concentraciones de CO exhalado en niños sanos ($p = 0,03$) y asmáticos ($p = 0,01$). Las concentraciones de monóxido de carbono fueron más elevadas en los niños asmáticos que en los sanos (media \pm DE, $1,32 \pm 1,50$ ppm y $0,86 \pm 1,35$ ppm, respectivamente, $p = 0,028$), independientemente del hecho de fumar o no los padres. Los hijos asmáticos de padres no fumadores tuvieron concentraciones más elevadas de CO que los hijos sanos de padres no fumadores ($1,05 \pm 1,55$ ppm vs $0,37 \pm 0,53$ ppm, $p = 0,01$). Por otro lado, los niños asmáticos cuyos padres no fumaban y que no utilizaban esteroides inhalados tuvieron concentraciones de CO significativamente mayores ($1,75 \pm 1,45$ ppm) que los que utilizaban esteroides ($0,58 \pm 0,65$ ppm, $p = 0,024$).

Conclusiones: el CO exhalado puede utilizarse como un indicador de la inhalación pasiva de humo de tabaco en niños. Las mayores concentraciones de CO espirado en niños asmáticos pueden reflejar inflamación pulmonar producida por el asma.

Palabras clave: Monóxido de carbono. Inhalación pasiva de humo de tabaco. Niños. Asma. Corticoides.

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