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ACUTE SYMPTOM RESPONSES TO PASSIVE CIGARETTE SMOKE IN ASTHMATIC AND NONASTHMATIC INDIVIDUALS

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Acute 65-min responses to passive cigarette smoke were tested in 24 healthy nonasthmatic nonsmokers and 16 asthmatic nonsmokers, using an environmental chamber. Each subject was exposed to air (sham), and machine-generated cigarette smoke containing 17 ppm and 31 ppm carbon monoxide (CO). Nonasthmatic subjects exercised intermittently (mean respiratory minute volume ($\dot{V}_E$) of 44 l/min during each of two 15-min exercise bouts); asthmatic subjects remained at rest. After completion of the exposure, subjects made a 0-5 rating of the severity of symptoms, as well as rating the overall severity of exposure on a 0 to 100 scale. Both symptoms and exposure severity rating were significantly related to CO concentrations. Ratings for a given smoke exposure tended to be higher for asthmatic than for nonasthmatic subjects. Overall exposure severity rating was significantly ($p < 0.05$) related to seven symptom scores for the asthmatics and three for the nonasthmatic subjects. Although the non-asthmatic subjects were exercising intermittently, and thus received a higher effective dose, (as confirmed by CO uptake), the asthmatic subjects appeared to be more adversely affected by the smoke exposures.

INTRODUCTION

Cigarette smoke remains an annoying and potentially hazardous constituent of indoor air. Symptoms reported during passive cigarette smoke exposure include unpleasant odour, eye irritation and lachrymation, nasal irritation, nasal stuffiness and rhinorrhoea, shortness of breath, sore/dry throat, cough, tightness in the chest, wheezing, dizziness and nausea (1-3), with associated small impairments of pulmonary function (2-4).

In previous 2-hr chamber studies (2), we have exposed nonasthmatic nonsmokers to two concentrations of machine-generated cigarette smoke (mean ambient CO 20 and 31 ppm). During each exposure, subjects exercised intermittently (four 15-min periods separated by 15-min rest periods), generating a mean exercise $\dot{V}_E$ of 31 l/min.

We have now repeated this study, but at an increased workrate, simulating conditions potentially encountered by a waiter or waitress in a poorly ventilated bar occupied by a large number of smokers (2). When the hyperventilation of exercise was combined with "moderate" or "heavy" cigarette smoke concentrations, the nonasthmatic subjects were exposed to the most adverse conditions that could be expected. Shephard et. al (2) also exposed subjects to high concentrations of cigarette smoke, but different subjects were exposed to each of two smoke concentrations, making it difficult to test for dose-response relationships. In the present study, each subject was exposed on three separate occasions, to room air alone (sham), to moderate and to heavy smoke concentrations, according to a randomized complete block design. We also tested the response of resting asthmatic subjects to the same smoke concentrations.

METHODS

Subjects included 24 nonasthmatic adults (12 males and 12 females) and 16 asthmatics (8 males and 8 females), all current nonsmokers. Ages ranged from 18 to 34 years among the nonasthmatics, and from 19 to 63 years among the asthmatic subjects. The asthmatic individuals were free of acute symptoms, and continued normal medication during the study, although no additional medication was provided during exposures. Physical characteristics and baseline pulmonary function data are given in Table 1.

There were four laboratory visits. The first (visit 1) was for clinical screening and to obtain baseline data. During visits 2, 3 and 4, subjects sat alone for 65-min in a 14.6 m^3 exposure chamber filled with room air to which had been added cigarette smoke in a high concentration ("heavy smoke", 31 ppm CO), a lower concentration ("moderate smoke", 17 ppm CO), or room air ("sham"), according to a design where six permutations of the three treatments were equally represented. Cigarette smoke was generated by a smoking machine enclosed in a mixing box, outside the exposure chamber, but visible to the subjects. During sham exposure, the cigarettes were "smoked", but the smoke was diverted away from the exposure chamber. Exposure conditions and methods of measuring smoke constituents have been described previously (4). Asthmatic individuals sat at rest throughout the 65-min exposures. Nonasthmatic subjects exercised intermittently on a cycle ergometer for two 15-min periods (initiated after 8 and 38 min of exposure). The average $\dot{V}_E$ during exercise was 43.6 l/min BTPS. When not exercising, the nonasthmatic subjects sat at rest.

In an attempt to create a single blind situation, subjects were shown a similar bank of burning cigarettes during all three exposures. It was obvious that there was little smoke in the chamber during the sham experiment, but any difference in the density of the "smoke cloud" between the moderate and heavy exposure conditions was not immediately apparent to the subjects.

Symptoms were assessed by a questionnaire immediately after each exposure and included: unpleasant odour, nausea, cough, sputum/phlegm, eye irritation, tightness in the chest, shortness of breath, dizziness, wheezing, nasal discharge, nasal stuffiness, headache, fatigue, sore/dry throat, soreness or

awareness of soreness (muscle, substernal or other) and other symptoms, which although not part of the list, were noted by the subject. Subjects were asked to report the presence and severity of each symptom using a categorical scale, in which : 0 represented no symptoms, 1-trace, 2-minimal, 3-moderate, 4-severe, and 5-incapacitating. Subjects were also asked to assess the overall severity of their exposure, on a scale of 0-100, in which: 0 represented no perceived exposure, and 100 an incapacitating exposure.

Statistical methods have been described previously (4). Analyses were run separately for each subject group. All models included each subject's identification code as a factor; thus relationships identified were between exposures, within subjects, taking into account events within each subject. Covariance analysis tested the relationship between CO concentration and (1) individual symptoms and (2) the exposure severity rating. Additional estimates of smoke exposure were based on an oxygen rebreathe estimate of the increment in blood carboxyhaemoglobin over the exposures, and an estimated CO dose (chamber CO concentration x V_E x exposure duration). Multiple regression analysis was employed to identify the symptom variables that best predicted the pollution rating. The initial analysis included all 17 symptoms, and the analysis was repeated including only symptom variables with p values less than 0.50. The final multiple regression model included symptoms identified from the second analysis with p values of less than 0.20.

RESULTS

Table 2 relates two estimates of smoke exposure, (CO concentration and CO dose), to the perceived exposure severity. The CO concentrations for asthmatic and nonasthmatic subjects were matched to within 1% for the moderate and 5% for the heavy smoke concentrations. However, the CO dose for the nonasthmatics was more than double that of the asthmatics. Nevertheless, the mean exposure rating was no greater for the nonasthmatics.

Both subject groups showed significant exposure-response relationships between chamber CO concentration and various complaints/symptoms, including unpleasant odour, eye irritation, sore/dry throat, nasal discharge and stuffiness, cough, and the overall exposure severity rating. With the exception of sore/dry throat, symptom ratings for a given smoke exposure were higher for the asthmatic than for the nonasthmatic subjects.

The final models for the multiple regression analyses are shown in Table 3. Eight symptoms were included in the final model for asthmatic subjects and five for nonasthmatics. For the asthmatic subjects, seven symptoms were significant ($p < 0.05$), while only three symptoms were significant for nonasthmatic subjects. Three symptoms were common to both groups: nasal discharge, unpleasant odour and headache, and only headache for nonasthmatics was not significant ($p=0.07$). Both headache and sputum/phlegm were statistically significant for asthmatic subjects, but had negative regression coefficients. All other symptoms had positive regression coefficients.

The model r^2 from the covariate analysis with exposure rating vs mean chamber CO concentration (not shown), although highly significant ($p < 0.0001$), was lower for both asthmatics (0.80) and nonasthmatics (0.84) compared to the 8-symptom model for asthmatics ($r^2=0.93$) and the 5-symptom model for nonasthmatics ($r^2=0.93$). When the calculated CO dose replaced CO concentration, the p value was unaltered, but the model r^2 was reduced, for both subject groups. Finally, when the rebreathe carboxyhaemoglobin increment replaced the CO dose, the p value was again unaltered, but the model r^2 was further reduced, for both subject groups.

DISCUSSION

Although smoke concentrations were essentially the same, and the nonasthmatic subjects received double the effective dose because they were exercising, the asthmatic subjects reported being more adversely affected. The multiple regression model showed seven significant symptoms for asthmatics, compared to three for nonasthmatic subjects. Furthermore, the mean exposure severity rating and ten of the symptom ratings were higher for the asthmatic compared to the nonasthmatic subjects. For the heavy smoke condition, the mean exposure rating for nonasthmatics was 71, compared with 75 for asthmatic subjects, on the 0-100 scale.

In the multiple regression analysis, nasal discharge and unpleasant odour were the only significant variables common to both subject groups. These were also among the main complaints in previous passive smoke studies (2,3). Reported wheezing in asthmatic subjects, as in our previous study (3), was a significant variable in the multiple regression analysis. Eye irritation was significant for asthmatic but not for nonasthmatic subjects, although when unpleasant odour was removed from the 5-symptom model for nonasthmatics, eye irritation became significant. This apparent anomaly for nonasthmatic subjects reflects the high correlation between eye irritation and unpleasant odour ($r=0.78$). The negative regression coefficients for headache and sputum/phlegm in asthmatic subjects suggests that those who reported a high overall exposure rating also reported a low rating for these two symptoms. However, the mean ratings for these symptoms with smoke exposure, was 1 or less, indicating that these findings are likely a random occurrence, associated with the number of significant coefficients accepted.

Estimate of exposure dose did not improve the predictive power of the model. Furthermore, the model with exposure rating vs symptoms had the highest r^2. Thus the subjective rating of exposure severity appeared to be an integrator of symptoms, related to exposure level or mean chamber CO concentration. The apparent increased severity of response in asthmatic subjects, specifically respiratory symptoms, may be due to the increased hyperreactivity characteristic of asthma.

TABLE 1 PHYSICAL CHARACTERISTICS AND BASELINE PULMONARY FUNCTION

Variable	NonAsthmatics	Asthmatics
Age (years)	25 ± 4	38 ± 15
Height (cm)	169.7 ± 8.7	169.2 ± 10.9
Body mass (kg)	62.8 ± 10.8	69.3 ± 13.1
FVC (l)	4.49 ± 0.95	4.10 ± 0.97
Percent predicted	103 ± 11	102 ± 13
FEV_1 (l)	3.82 ± 0.73	2.74 ± 0.84
Percent predicted	102 ± 12	81 ± 19
FEF_{50} (l/sec)	4.84 ± 1.02	2.44 ± 1.59
Percent predicted	114 ± 28	60 ± 35
FEF_{75} (l/sec)	2.40 ± 0.87	0.93 ± 0.65
Percent predicted	112 ± 36	47 ± 31

Data reported as the mean ± standard deviation for 24 non-asthmatics (12 males and 12 females) and 16 asthmatic subjects (8 males and 8 females). All pulmonary function values are corrected to BTPS. Percent predicted normal values according to: FVC (5), FEV_1 (6), FEF_{50}, and FEF_{75} (7).

TABLE 2 COMPARISON OF CO CONCENTRATION, CO DOSE & EXPOSURE RATING DURING SHAM, MODERATE & HEAVY SMOKE EXPOSURES

Exposure Condition	Exposure Estimate	NonAsthmatics (N=24)	Asthmatics (N=16)[a]
SHAM	CO (mg/m^3)	4.1 ± 1.4[b]	3.6 ± 1.0
	CO Dose (mg)	6.1 ± 2.1[b]	3.4 ± 1.1
	Exposure Rating	4 ± 1	13 ± 14
MODERATE	CO (mg/m^3)	19.8 ± 1.2	19.6 ± 1.0
	CO Dose (mg)	37.7 ± 13.1	18.4 ± 5.2
	Exposure Rating	45 ± 4	47 ± 27
HEAVY	CO (mg/m^3)	34.5 ± 2.1	36.2 ± 1.7[c]
	CO Dose (mg)	64.5 ± 18.2	27.0 ± 8.7[c]
	Exposure Rating	71 ± 5	75 ± 10

Data reported as the mean ± standard deviation. CO=mean CO conc. over 65-min exposure. CO mg/m^3 x 0.873=CO parts per million; CO mg/m^3 x 10^{-3}=CO mg/l. CO Dose=mean CO dose (mg), calculated as CO conc. (mg/l) x $\dot{V}_E$ (l/min) x 65-min. Exposure Rating=overall exposure severity rating (0-100 scale, in which 0=no perceived exposure, 100=incapacitating exposure). a N=15 subjects for heavy smoke. b N=23 subjects. c N=14 subjects.

TABLE 3 MULTIPLE REGRESSION ANALYSES RELATING OVERALL EXPOSURE RATING TO SYMPTOMS DURING SHAM, MODERATE AND HEAVY SMOKE EXPOSURES

Symptoms	Nonsthmatics		Asthmatics	
	Regression Coefficient[b]	P value[a]	Regression Coefficient[b]	P value[a]
Nasal discharge	3.8	0.02	7.3	0.003
Unpleasant odour	15.2	0.0001	7.6	0.008
Headache	5.2	0.07	-6.7	0.01
Eye irritation			4.7	0.04
Sore/dry throat			7.3	0.01
Sputum/phlegm			-17.7	0.0004
Wheezing			11.6	0.02
Fatigue			6.4	0.06
Cough	6.0	0.045		
Shortness of breath	4.1	0.12		
Intercept	2.3		21.73	
Subject[c]		0.052		0.045

Data reported for 16 asthmatics (47 exposures) and 24 non-asthmatic subjects (72 exposures). Multiple regression model includes only variables with $p < 0.2$. a P value associated with Student's t test of hypothesis that the partial regression coefficient is zero. b Model $r^2=0.93$ for both groups. c Subject's ID code, included as covariate. Exposure rating, 0-100 scale, as in Table 2. Symptom ratings, 0-5 scale.

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