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ORIGINAL ARTICLE

Remote second-hand tobacco exposure in flight attendants is associated with systemic but not pulmonary hypertension

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Abstract

Background: *Second-hand tobacco smoke has been associated with cardiopulmonary dysfunction. We sought to examine the residual effects of remote second-hand smoke exposure on resting and exercise cardiopulmonary hemodynamics. We hypothesized that remote second-hand smoke exposure results in persistent cardiopulmonary hemodynamic abnormalities.*

Methods: *Participants were non-smoking flight attendants who worked in airline cabins prior to the in-flight tobacco ban. Participants underwent clinical evaluations and completed smoke exposure questionnaires. We used Doppler echocardiography to measure pulmonary artery systolic pressure (PASP) and pulmonary vascular resistance (PVR) at rest and during supine bicycle ergometer exercise, using the validated formula $TRV/VTI_{RVOT} \times 10 + 0.16$, where VTI_{RVOT} is the velocity time integral at the right ventricular outflow tract and TRV is the tricuspid regurgitation velocity. The group was divided into quartiles according to the degree of smoke exposure. Analysis of variance was used to determine the differences in hemodynamic outcomes.*

Results: *Seventy-nine flight attendants were included in our analysis. Baseline characteristics among participants in each quartile of smoke exposure were similar except for history of systemic hypertension, which was more prevalent in the highest quartile. Peak exercise PASP rose to the same degree in all test groups (mean PASP 44 mm Hg, p = 0.25), and PVR increased by approximately 27% in all quartiles. There was no significant difference in pulmonary artery systolic pressure or pulmonary vascular resistance among quartiles of smoke exposure.*

Conclusions: *We found that remote heavy second-hand smoke exposure from in-flight tobacco is associated with systemic hypertension but does not have demonstrable pulmonary hemodynamic consequences.* (Cardiol J 2008; 15: 338–343)

Key words: second-hand smoke, echocardiography, exercise physiology, pulmonary artery pressure

Introduction

Acute and chronic exposure to second-hand tobacco smoke has been associated with cardiopulmonary dysfunction including impaired endothelial function, coronary artery disease and abnormal pulmonary function [1–6]. However, some studies have failed to show significant cardiopulmonary effects of second-hand smoke exposure after adjusting for potential confounding variables [7, 9]. While studies using bicycle ergometry have demonstrated normal cardiopulmonary hemodynamics in normal individuals and athletes and abnormal hemodynamics in patients with chronic pulmonary diseases, cardiac transplant, systemic lupus erythematosus and adults with congenital heart diseases [10–13], no study has examined cardiopulmonary hemodynamics in relation to remote second-hand smoke exposure.

Long-term residual effects of such exposure are important because of concerns about the substantial numbers of individuals with a history of this exposure. Among the populations most heavily exposed to second-hand smoke were flight attendants, who spent as much as 1000 hours per year on commercial aircraft in contact with significant second-hand smoke in a small, enclosed environment. Since the smoking ban on domestic commercial flights in 1990 and on international flights in 1996, residual effects of remote in-flight tobacco exposure have not been systematically examined. The Flight Attendant Medical Research Institute (FAMRI) was created to study the health effects of second-hand smoke. While studies have shown that former smokers have a persistent decrease in exercise capacity compared with non-smokers [14], the effects of remote second-hand smoke exposure on cardiopulmonary function is unknown.

Therefore, we sought to examine the effects of remote second-hand smoke exposure on residual baseline or exercise cardiopulmonary hemodynamics. We hypothesized that remote in-flight second-hand smoke exposure results in persistent abnormalities in cardiopulmonary hemodynamics in proportion to the degree of exposure.

Methods

Participants

Participants were flight attendants recruited by the FAMRI clinic at the University of California, San Francisco, an outpatient clinic which performs cardiopulmonary evaluations in flight attendants exposed to second-hand smoke. The study was advertised through local newspapers, flight attendants'

union meetings, email distributions and announcements at airport symposia. Flight attendants were screened for initial eligibility based on established inclusion and exclusion criteria. Inclusion criteria were (1) second-hand smoke exposure ≥ 5 years while working as a flight attendant, and (2) the ability to perform supine bicycle ergometry. Exclusion criteria were (1) personal history of smoking, (2) history of clinically overt cardiac disease, including stable or unstable angina; coronary artery disease (defined as abnormal stress test, cardiac catheterization showing ≥ 70% coronary artery stenosis, history of revascularization, pathologic Q waves on EKG); congestive heart failure (defined as left ventricular ejection fraction < 55%; physical exam findings of coronary heart failure; symptomatic pulmonary oedema); moderate to severe valvular heart disease; and congenital heart disease; (3) history of clinically overt pulmonary disease, including asthma, recent-onset bronchitis, chronic interstitial lung disease, obstructive sleep apnea, collagen vascular disease requiring chronic steroid or immune modulating therapy and pulmonary hypertension; (4) history of significant second-hand smoke exposure at home; (5) physical inability to perform supine bicycle exercise testing, including: paralysis, weakness, amputation or symptomatic arthritis of the lower extremities, disabling back pain; and (6) inability to obtain adequate echocardiographic images due to technical reasons.

A total of 282 participants were screened, from which 130 participants were eligible and agreed to participate. From this sample, 20 participants were excluded after careful review of history and physical examination (6 for personal smoking history, 1 for severe resting hypertension, 4 for asthma, 6 for recent-onset bronchitis, 2 for collagen vascular disease, 1 for obstructive sleep apnea, and 1 for moderate aortic regurgitation). Supine bicycle ergometry was not performed on 24 participants due to patient availability and they were thus excluded. We also excluded 7 male participants since the majority of participants were female. These exclusions resulted in a sample of 79 female participants.

The study was approved by the institutional review board at the University of California, San Francisco.

Predictor variable:
Second-hand smoke exposure

The predictor variable, expressed as hour-years, is the degree of second-hand occupational smoke exposure based on a detailed questionnaire regarding in-flight smoke exposure. The question-

naire was stratified by decade and included number of years flown and number of hours per month flown.

Outcome variables:
Resting and exercise hemodynamics

We performed resting and stress echocardiograms using an Acuson Sequoia Ultrasound System (Mountain View, California) with a 3.5-MHz transducer. Before exercise, standard 2-dimensional parasternal short-axis, apical 2- and 4-chamber, and subcostal views obtained during breath-hold were planimetered using a computerized digitization system to determine end-systolic and end-diastolic left ventricular volume, left ventricular ejection fraction and left ventricular mass. Left ventricular ejection fraction was measured quantitatively using the 2-D echocardiography biplane method of discs [15, 16]. Left ventricular mass index was calculated based on the 2-D echocardiography truncated ellipse method [17]. In the parasternal short-axis view, pulse wave Doppler was used to determined the right ventricular outflow tract (RVOT) velocity time integral (VTI). In the apical 4-chamber view, continuous wave Doppler was used to determine the maximal tricuspid regurgitation velocity (TRV). Intravenous agitated saline (5 to 10 ml isotonic saline) was used in all participants to enhance the Doppler-derived tricuspid regurgitation jet. Left ventricular contrast was used to enhance 2-D echocardiographic images when deemed necessary by the supervising physician. The maximum tricuspid regurgitation gradient (in mm Hg) was estimated ($\Delta P = 4V^2$) by modification of the Bernoulli formula. Pulmonary artery systolic pressure (PASP) was computed as the sum of the tricuspid regurgitation gradient and right atrial pressure [13, 18]. Pulmonary vascular resistance (PVR) was calculated using the validated formula $TRV/VTI_{RVOT} \times 10 + 0.16$ [19].

A symptom-limited, graded exercise supine bicycle ergometry test was performed. A variable-load supine bicycle ergometer (Medical Positioning Inc. Q-Stress Echo Bed, Indianapolis, IN) was used for all testing with the ergometer table tilted to 20° (patient's left side down) to obtain the standard echocardiographic apical views. Patients pedalled at a constant speed, beginning at a workload of 10 W and increasing by 30 W every 3-min stage until reaching symptom-limiting fatigue. Heart rate, cuff blood pressure, pulse oximetry, segmental ventricular wall motion, right ventricular outflow tract velocity time integral and maximum tricuspid regurgitation velocity were recorded at rest, at each stage of exercise and after four minutes of recovery. Continuous 2-lead electrocardiogram and pulse oximetry were monitored throughout exercise. A single cardiologist (N.B.S.), blinded to clinical and laboratory information, evaluated all of the echocardiograms.

Resting and exercise pulmonary function tests

On the same day, complete resting and exercise pulmonary function testing (including diffusing capacity, ventilatory equivalents and oxygen consumption) were conducted, based on the methodology described previously [20–27]. Pulmonary function data will form the subject of another communication.

Other characteristics

Each participant completed an additional detailed questionnaire that included age, sex, medical history, medication history and occupation history. The questionnaire is available at www.tobacco.ucsf.edu. The level of functional capacity was assessed by the Duke Activity Status Index: a simple 12-item yes/no questionnaire which has been validated in various cardiopulmonary disease states [28–31]. Study personnel recorded current medications, height, weight and blood pressure.

Statistical analysis

Smoke exposure was classified into four quartiles, as lowest 25%, 25–50%, 50–75% and highest 75%. Analysis of variance was used to determine the differences in hemodynamic outcomes on the means for continuous variables and the proportions for dichotomous variables. We reported all data with 95% confidence intervals (CI). Analyses were performed using Statistical Analysis Software (Version 9, SAS Institute Inc, Cary, NC).

Results

Baseline characteristics among participants in each quartile of total smoke exposure are listed in Table 1. The mean age was 59 years and all participants were female. Compared with participants in the lower quartiles, those in the upper quartiles were more likely to have a history of hypertension. The upper quartiles of smoke exposure trended toward greater use of diuretics and hormone replacement therapy, although these were not statistically significant. The highest quartile of exposure had nearly 50% hormone replacement use. The upper quartiles of smoke exposure also trended toward higher Duke Activity Status Index, although this trend was not statistically significant. The mean resting PASP and PVR among all

Table 1. Baseline characteristics.

	Quartiles of total smoke exposure				p
	1st quartile (n = 19)	2nd quartile (n = 20)	3rd quartile (n = 19)	4th quartile (n = 21)	
Age (years)	56	57	58	60	0.29
History of hypertension (%)	5	5	26	33	0.03
History of diabetes (%)	5	5	5	0	0.78
History of hyperlipidemia (%)	32	25	42	33	0.74
History of sinus problem (%)	11	20	16	19	0.86
Duke activity index	12.6	14.5	15.2	15.3	0.07
Medication use:					
Beta-blockers (%)	0	0	0	0	NA
Diuretic (%)	0	0	11	19	0.06
Hormone replacement (%)	16	35	16	48	0.07
Vitamins (%)	53	65	58	48	0.73
Resting SBP [mm Hg]	125	119	133	127	0.17
Resting DBP [mm Hg]	70	72	73	70	0.82
Resting heart rate (bpm)	70	69	67	67	0.82
Left ventricular mass index [g/m^2]	73	72	75	67	0.36
Resting PASP [mm Hg]	21	19	22	21	0.20
Resting RVOT VTI [cm]	17.5	15.9	17.9	17.0	0.23
Resting PVR [Wood units]	1.5	1.5	1.5	1.5	0.93

SBP — systolic blood pressure; DBP — diastolic blood pressure; RVOT — right ventricular outflow tract; VTI — velocity time integral; PASP — pulmonary artery systolic pressure; PVR — pulmonary vascular resistance

participants were 21 mm Hg and 1.5 Wood units, respectively. There was no significant difference in resting blood pressure, heart rate, left ventricular mass index, PASP or PVR.

With exercise, there was no significant difference in blood pressure response, heart rate response or double product among the quartiles of exposure (Table 2). The intensity of exercise was adequate as judged by the achieved double product. The PASP at peak stress (mean 44 mm Hg among all participants) approximately doubled in all quartiles of exposure and did not differ statistically.

Table 2. Exercise data.

	Quartiles of total smoke exposure				p
	1st quartile (n = 19)	2nd quartile (n = 20)	3rd quartile (n = 19)	4th quartile (n = 21)	
Peak SBP [mm Hg]	182	176	183	186	0.44
Peak DBP [mm Hg]	91	92	86	84	0.07
Peak heart rate [bpm]	153	154	150	148	0.37
Exercise duration [s]	918	865	848	843	0.46
Double product (HR × SBP)	27873	27067	27484	27455	0.93
Peak PASP [mm Hg]	46	42	44	46	0.25
ΔPASP [mm Hg]	25	23	22	25	0.69
Peak RVOT VTI [cm]	19.5	18.6	21.9	19.6	0.61
Peak PVR [Wood units]	1.9	1.9	1.9	1.9	0.85
ΔPVR [Wood units]	0.4	0.4	0.4	0.4	0.93
Wall motion abnormality	0	0	0	0	NA

SBP — systolic blood pressure; DBP — diastolic blood pressure; HR — heart rate; RVOT — right ventricular outflow tract; VTI — velocity time integral; PASP — pulmonary artery systolic pressure; PVR — pulmonary vascular resistance; NA — not available

The PVR at peak stress (mean 1.9 Wood units among all participants) increased by approximately 27% in all quartiles without statistical difference. There was no evidence of stress-induced ST-segment depression or segmental wall motion abnormality on echocardiography in any participant.

Discussion

We found that the degree of remote heavy second-hand smoke exposure from in-flight tobacco is associated with treated systemic hypertension but does not have demonstrable residual pulmonary or systemic hemodynamic consequences. Previous studies have not found an association of chronic passive smoke exposure with hypertension [4, 32]. While acute second-hand smoke exposure can cause hypertension through increased norepinepherine, epinephrine, endothelin-1, carboxyhemoglobin and other cigarette constituents [4, 33–37], our population was remotely exposed. Thus chronically altered vascular reactivity from remote chronic intense smoke exposure may have been mechanistically related to the increased prevalence of systemic hypertension. However, since smoke exposure was associated with flight time, factors such as time spent at high altitude, circadian rhythm disturbance and emotional stress may be contributory.

Baseline and exercise PASP in our study population are similar to historic controls [13, 38, 39]. Similarly, baseline PVR in our patient population is within the normal range [40]. Furthermore, the response of PVR to exercise is similar to that of conditioned athletes [39]. These findings suggest that in-flight smoke exposure either had no significant cardiopulmonary effects or may have had cardiopulmonary effects that have since dissipated. These findings are reassuring in that they imply a potential for cardiopulmonary recovery after exposure has stopped.

We believe that the unique features of this study include its large sample size and its focus on the association of significant remote second-hand smoke exposure on resting and exercise cardiopulmonary hemodynamics. Nonetheless, several limitations must be considered when interpreting these results. First, our participants were former or current flight attendants recruited from the FAMRI clinic, an outpatient clinic specifically targeted to the health care issues of flight attendants exposed to second-hand smoke. These participants were health conscious, which may have resulted in sampling bias. However, despite this potential bias toward a positive finding, we did not find any significant cardiopulmonary hemodynamic differences among the four quartiles of exposure. Conversely, remote passive smoke could have caused severe impairment such as early sequele of advanced chronic obstructive pulmonary disease or death, favouring a negative finding. In addition, people who participate in clinical studies are generally healthier than the average population. Second, flight hours and perceived intensity of smoke are by self-report, which can result in reporting bias. A previous study has shown consistent self over-reporting of flight time when compared with company records [41]. Third, second-hand smoke exposure may be associated with cardiopulmonary damage not detected by hemodynamic measurements. Finally, our participants were exclusively female flight attendants, and our results may not be applicable to men.

Conclusions

We found that the degree of remote heavy second-hand smoke exposure from in-flight tobacco is associated with a history of systemic hypertension but does not have demonstrable pulmonary or systemic hemodynamic consequences or inducible ischemia. Whether this lack of association is due to a lack of causal relationship or recovery from prior impairment merits further study.

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