ACUTE EFFECTS OF PASSIVE SMOKING ON PERIPHERAL VASCULAR FUNCTION- A PROSPECTIVE STUDY AT TERTIARY CARE HOSPITAL FROM CENTRAL INDIA.

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ABSTRACT

Disease risk due to smoking is not limited to smokers only. Passive smoking, exposure to environmental tobacco smoke, is associated with adverse health effects, and it increases the risk of several diseases. This paper summarizes the cardiovascular effects of tobacco smoke and the current data on the effects of environmental tobacco smoke on the development of cardiovascular disease. According to the results of epidemiologic and experimental studies, environmental tobacco smoke has marked harmful effects on the cardiovascular system. It is estimated that it increases the risk of an acute event of coronary heart disease by 25-35%. Even though the number of studies conducted in the work environment is small, there is no reason to assume that the cardiovascular effects of environmental tobacco smoke differ markedly between the home and the workplace. Firm and timely actions are needed to protect people from exposure to environmental tobacco smoke, both in occupational and other environments. Environmental tobacco smoke (ETS) acutely affects peripheral and coronary vascular tone. Whether ETS exerts specific deleterious effects on aortic wave reflection through nicotine exposure, whether they persist after ETS cessation, and whether the smoke environment impairs microvascular function and increases asymmetrical dimethyl-arginine levels are not known. We tested these hypotheses in a randomized, crossover study design in 12 healthy male nonsmokers. The effects of 1 hour of exposure to ETS, as compared with a nontobacco smoke and normal air, on augmentation index corrected for heart rate and skin microvascular hyperemia to local heating were examined. Augmentation index increased both during (P=0.01) and after (P<0.01) the ETS sessi Environmental tobacco smoke (ETS) has been associated with cardiovascular mortality. Pathophysiologic pathways leading from ETS exposure to cardiopulmonary disease are still being explored. Reduced cardiac autonomic function, as measured by heart rate variability (HRV), has been associated with cardiac vulnerability and may represent an important pathophysiologic mechanism linking ETS and risk of cardiac mortality. In this study we evaluated acute ETS exposure in a commercial airport with changes in HRV in 17 adult nonsmokers. We conducted ambulatory electrocardiographic (ECG) monitoring for 8-hr periods while participants alternated 2 hr in nonsmoking and smoking areas. Nicotine and respirable suspended particle concentrations and participants' blood oxygen saturation were also monitored. We calculated time and frequency domain measures of HRV for periods in and out of the smoking area, and we evaluated associations with ETS using comparative statistics and regression modeling. ETS exposure was negatively associated with all measures of HRV. During exposure periods, we observed an average decrement of approximately 12% in the standard deviation of all normal-to-normal heart beat intervals (an estimate of overall HRV). ETS exposures were not associated with mean heart rate or blood oxygen saturation. Altered cardiac autonomic function, assessed by decrements in HRV, is associated with acute exposure to ETS and may be part of the pathophysiologic mechanisms linking ETS exposure and increased cardiac vulnerabilit. Nicotine levels after the exposure were related to the peak rise in augmentation index (r=0.84; P<0.01), denoting a predominant role of nicotine in ETS vascular effects. This was confirmed in a second set of experiments (n=14), where the sublingual administration of nicotine was associated with an acute impairment in wave reflection as compared with placebo (P=0.001). Both ETS and nontobacco smokes increased plasma asymmetrical dimethyl-arginine levels (P<0.001), but only ETS reduced the late rise in skin blood flow in response to heating (P=0.03). In conclusion, passive smoking specifically increases aortic wave reflection through a nicotine-dependent pathway and impairs microvascular function, even after the end of the exposure. However, both tobacco and nontobacco passive smoking inhalation increase plasma asymmetrical dimethyl-arginine levels.

INTRODUCTION

Cardiovascular diseases (CVDs) refer to disorders which can affect the heart and blood vessels and have been proven as the most common cause of death all around the world[1,2] The conditions are so serious that that they are responsible for 50 and 25% mortality rate in developed and developing countries, respectively[1,2,3] Unhealthy dietary behaviors and obesity, physical inactivity, overconsumption of alcoholic beverages, and smoking are known as the major risk factors for CVDs[2] among which cigarette smoking has been known as the most conspicuous factor for CVD deaths as well as an annual premature deaths[5,6,7,8] Over the last decades, research has also expanded in the area of passive smoking (PS) and its effects on aspects of human health[8,9] According to WHO, PS (also known as second-hand, tobacco smoking) refers to the involuntary inhalation of smoke from cigarettes or other tobacco products smoked by others[10,11] Several lines of research have been conducted with a focus on passive smoking(PS)and its impact on various aspects of Cardiovascular deaths(CVDs)[12,13,14,15] They have indicated its association with coronary artery disease among individuals (non-smokers) who had lived with a smoker[16,17;18] It has also been evidenced that PS could increase the risk of coronary heart disease by 70–80%[12,13] Furthermore, meta-analytic evidence highlighted the association between PS and a minor increase in the risk of coronary heart disease[13] while this finding was not obtained in another case–control study[14,15] Since the association between PS and CVD has not yet been fully clarified, this study was performed. The first objective of this meta-analysis was to evaluate the association between the incidence of CVDs and PS, and the second objective was to determine whether the PS is associated with increased mortality rate due to CVD. Exposure to environmental tobacco smoke (ETS) has een recgnized recently as a strong contributor to cardiovascular mortality, accounting for >50 000 deaths annually in the United States.[1] In recent years, extensive research has elucidated many aspects of the long-term ETS-related adverse effects on the cardiovascular system.[1] However, the use of normal air inhalation as a control limits the interpretation of the physiopathological processes underlying the acute cardiovascular toxicity of ETS[4,14] Whether lung irritation and/or the stress provoked by smoke inhalation generate a nonspecific cardiovascular reaction[5] and whether this can explain the effect of ETS[19,20,21,22,23] are not known. We, therefore, decided to test the hypothesis that the vascular effects of ETS cannot simply be ascribed to a nonspecific reaction to smoke. This would provide further clear-cut evidence that ETS exerts specific deleterious cardiovascular effects beyond those of smoke pollution. To further prove the specificity of the toxic effects of ETS, our second new hypothesis was that the deleterious vascular effects of ETS would be related to the rise in plasma nicotine levels. The above-mentioned studies[2–4] did not determine plasma nicotine. The role of nicotine in the changes in aortic wave reflection to

ETS[24,25,26,27] can be suspected from the established sympathoexcitatory effects of nicotine in active smokers[6] but has not been demonstrated previously to our knowledge. Third, previous human studies on the acute effects of passive smoking have considered only the cardiovascular response during the acute smoke exposure[28,29,30,31,32] However, ETS exposure is an intermittent phenomenon, and it is unknown whether the acute deleterious effects of ETS persist after the smoke exposure.[33,34,35] We tested the new hypothesis that the negative effects of ETS persist during periods where subjects again breathe normal air. This would reveal that the toxicity of ETS exposure is underestimated when only the duration of the acute exposure is taken into account. Fourth, the effects of ETS and nontobacco smoke on microvascular function are unknown in humans. Because ETS exposure induces endothelial dysfunction of large conductance arteries,[7,8] we also assessed the effects of ETS on microvascular function by evaluating the skin hyperemic response to heating.Finally, several in vitro studies have emphasized the adverse effects of chronic cigarette smoke exposure on endothelial NO bioavailability, particularly through a competitive inhibition of NO synthase by asymmetrical dimethyl-arginine (ADMA).[6,9,10] Effects of nontobacco smoke on ADMA levels are unknown and were compared with those of ETS in our study.[36,37,38]

MATERIALS AND METHODS

Twenty-five healthy male subjects with normal physical examination who were on no medication were enrolled in the study. All were nonsmokers, and they were not regularly exposed to ETS. The ethical committee approved the study protocol, and informed written consent was obtained from each subject.During 3 sessions at 1-week intervals, 11 healthy male subjects (mean age: 24.6±3 years; body mass index: 22.5±2.1 kg/m^2) were randomly exposed for 1 hour to sidestream tobacco smoke, sidestream nontobacco smoke, and normal air. We used a randomized, single-blinded, placebo-controlled, crossover study design with identical air particle densities during ETS and nontobacco smoke exposure. All of the measurements were performed in a quiet room with the subject resting, but not sleeping, in the supine position under carefully standardized conditions. All of the subjects abstained from meals, alcohol, and coffee beverages for 12 hours before each study period. Subjects were excluded from the experiment if they had used nonsteroidal antiinflammatory drugs for ≥3 days before each visit. After a resting period of 20 minutes, subjects were exposed to the tested smoke or air for 1 hour. We used sidestream smoke from commercial cigarettes (Lucky-Strike; nicotine: 0.8 mg; tar: 10.0 mg) for tobacco smoke and herbal cigarettes (NTB, Arkopharma; nicotine: 5.0 μg; tar: 3.0 mg) for nontobacco smoke. Standardized smoke exposure conditions were achieved by placing a hermetic Plexiglas box of 0.1 m^3 over the head of the subject. For the duration of the experiment, the box was ventilated by a motorized system composed of 2 separate

tubes (input and output) ensuring a constant airflow through the box. Subjects breathed through a low-resistance mouthpiece with a nose clip to ensure exclusive mouth breathing. Expired gases were brought out of the box through a nonrebreathing valve. Eyes were protected by glasses that were delicately placed on the eyes to avoid any pressure to the ocular globes. A total of 6 cigarettes were lit in the input tube, 1 every 10 minutes for 1 hour, to allow a progressive infusion of the sidestream smoke inside the box. During the normal air session, the same protocol was applied with a simulation of a lighting cigarette every 10 min*l*To assess the role played by nicotine in aortic wave reflection changes produced by passive smoking, a separate group of 14 male healthy subjects (mean age: 24±1 years; body mass index: 24±0.5 kg/m^2) were randomly exposed to a 2-mg nicotine sublingual tablet (Nicorette microtab, nicotine betadex, Pfizer) or to a placebo tablet, using a randomized, double-blind crossover study design. Similar experimental conditions than those of the passive smoke protocol were applied Aortic wave reflection was assessed noninvasively in all of the subjects at baseline, at 10-minute intervals during the 60 minutes of smoke exposure, and 20 minutes after smoke cessation, using a fully automated and validated, commercially available system (Sphygmo Cor, Atcor Medical). This technique has been described in detail previously.[11] The augmentation index (AIx; 100× augmentation pressure/pulse pressure) represents the pressure boost that is induced by the return of the reflected waves to the aorta, expressed as a percentage of the pulse pressure. Higher values of AIx indicate an earlier return of the reflected wave to the aorta, either because of decreased aortic compliance or because of increased peripheral resistance. The aortic pressure waveform depends on the ventricular ejection time, which is proportionally associated with cardiac cycle duration.[12] Consequently, the change in AIx may be masked or overestimated when there are concomitant alterations in HR. This is why all of the AIx presented in the article are corrected for HR according to the linear relationship established by Wilkinson et al,[13] namely, that for every 10-bpm increase in HR, AIx decreases by 4%. Two consecutive AIx measurements were performed at each time interval, and their mean value was calculated. A third measurement was performed, according to the Task Force III recommendations for user procedures, if the first 2 measures differed by >3%.[14] The aortic pulse transit time, defined as the time of reflection from the foot of the pressure wave to the shoulder of the first systolic peak, was also evaluated. All of the measurements were made by the same observer (D.A).Skin blood flow measurement was performed using a laser Doppler flowmeter (PeriFlux PF4001 and 5000, Perimed). The blood flow response to local heating, normalized for beat-to-beat mean blood pressure (BP), was measured with a specific module (PeriTemp System, Perimed) before and after exposure to ETS. A 3-minute recording under resting conditions preceded all of the skin blood flow reactivity tests. The probe used for

the heating test was placed on the antecubital region of the left forearm and heated to 44°C for 20 minutes to allow maximal vasodilatation. All of the subjects underwent continuous ECG recording throughout the study. Finger BP was also measured by a beat-to-beat hemodynamic monitoring system (Finometer Pro, FMS). HR, finger BP, and blood flow response to local heating were recorded online on a computer with a Powerlab data acquisition system (AD Instruments) for subsequent analysis. Carboxyhemoglobin levels were measured at baseline and after the smoke exposure (COoximeter IL682, Instrumentation Laboratory). Nicotine and ADMA plasma levels were assessed by an independent laboratory (Advanced Technology Corp, University Hospital Centre of Liege), using a liquid chromatographic method coupled with tandem mass spectrometry. Because our subjects were not usually exposed to passive smoking, nicotine was determined only at the end of the tobacco and nontobacco sessions, whereas ADMA levels were measured both before and after the smoke exposure in each session. These dosages were not performed in 1 subject because of difficult venous access Particulate exposure was measured in real time with a portable instrument (MetOne Aerocet 531) placed inside the box during the experimental session. This particulate counter provides estimates of 4 usual categories of particulate matter (PM) size (PM 1.0, PM 2.5, PM 7.5, and PM 10.0).All of the measurements were analyzed in a blinded fashion. Systolic and diastolic BP, HR, AIx corrected for HR, and transit time are expressed as absolute unit changes from baseline values. Skin blood flow values during the heating laser Doppler test were analyzed by the Powerlab data acquisition system. The mean values for every minute during the test were calculated and expressed as the percentages of the maximal vasodilatation observed during each session. Thereafter, the response to heating stimulation was quantified as the absolute unit change of every minute from baseline skin blood flow values.

Statistical Analysis
Data are expressed as means±SEMs. Baseline hemodynamic parameters and carboxyhemoglobin levels in tobacco smoke, nontobacco smoke, and normal air sessions were compared using a 1-way ANOVA (SPSS Windows 13.0). A 2-way repeated-measures ANOVA was used to detect significant changes in variables over time between the experimental sessions and separately during and after the 3 exposures, after applying a Bonferroni correction for multiple comparisons. A 2-way repeated-measures ANOVA was also used to detect changes in skin blood flow during the heating provocation test performed before and after the 3 experimental sessions. Smoke particle concentrations and serum nicotine levels were compared using a Student's paired *t* test. Carboxyhemoglobin and ADMA changes after the smoke exposure were compared using a 2-way repeated-measures ANOVA (time×smoke interaction). The relation among serum nicotine levels, AIx corrected for HR, and skin blood flow heating test

changes was assessed using Pearson's correlation coefficient. Significance was assumed at *P*<0.05.

RESULTS
Baseline Characteristics
There were no differences in all of the baseline hemodynamic parameters or in carboxyhemoglobin levels among the 3 sessions (Table 1).

Table 1. Baseline Parameters				
Parameters	**Tobacco Smoke, Mean±SEM**	**Nontobacco Smoke, Mean±SEM**	**Normal Air, Mean±SEM**	***P***
SBP indicates systolic BP; DBP, diastolic BP; AIx, AIx corrected for heart rate; NS, nonsignificant.				
Peripheral SBP, mm Hg	107±2	104±4	104±4	NS
Peripheral DBP, mm Hg	61±1	57±3	58±2	NS
Mean BP, mm Hg	73±1	70±3	70±2	NS
HR, bpm	56±1	57±2	57±2	NS
Central SBP, mm Hg	89±1	86±3	86±3	NS
Central DBP, mm Hg	61±1	57±3	58±2	NS
AIx, %	−14±2	−13±2	−13±1	NS
Transit time, ms	172±4	166±5	172±5	NS
Carboxyhemoglobin, %	1.3±0.1	1.3±0.1	1.5±0.1	NS

Smoke Exposure
All of the subjects were exposed equally to smoke during the tobacco and nontobacco smoke sessions, as assessed by smoke particle concentrations. The carboxyhemoglobin levels reached after 60 minutes of nontobacco smoke exposure were slightly higher than with tobacco smoke (*P*<0.05; **Table 2**).

Table 2: Effects of Smoke Exposure on Nicotine, Carboxyhemoglobin, and Particle Matter			
Parameters	**Tobacco Smoke, Mean±SEM**	**Nontobacco Smoke, Mean±SEM**	***P***
NS indicates nonsignificant.			
PM 1.0, μg/m^3	52±2	51±2	NS
PM 2.5, μg/m^3	300±19	270±33	NS
PM 7.5, μg/m^3	400±40	320±40	NS
PM 10.0, μg/m^3	400±40	320±40	NS
Carboxyhemoglobin, %	2.1±0.1	2.5±0.1	NS
Serum nicotine levels, ng/mL	3.1±0.4	0.3±0.1	<0.001

Plasmatic Nicotine and ADMA Levels
Both tobacco and nontobacco smokes increased plasmatic ADMA levels (Figure 1), respectively, from 0.67±0.01 to 1.12±0.1 μmol/L and from 0.68±0.01 to 1.16±0.1 μmol/L (time effect: *P*<0.001; time×smoke interaction: *P* value not significant).
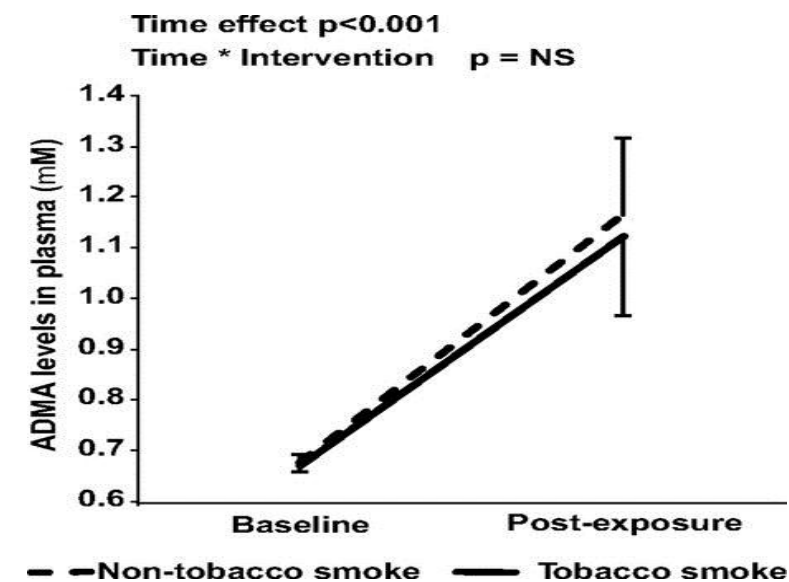

Figure 1: Effects of nontobacco smoke and tobacco smoke on ADMA.

Heart Rate
HR increased in the tobacco smoke session ($P<0.04$), reaching a peak level 50 minutes after exposure initiation. Moreover, HR values returned to baseline after the end of the smoke exposure. In the nontobacco session, no effects on HR were noted during or after smoke exposure. However, the interaction between the 2 sessions (tobacco versus nontobacco smoke) remained nonsignificant during and after the exposure (Figure S1, please see http://hyper.ahajournals.org).

Blood Pressure
Tobacco smoke had no effect on peripheral or aortic BP during or after the smoke exposure; similar observations were made during and after the nontobacco smoke exposure (Figure S1). The interaction between the 2 sessions (tobacco smoke versus nontobacco smoke) remained nonsignificant for systolic and diastolic BP at the periphery and at the aorta.

Aortic Wave Reflection
AIx corrected for HR increased both during ($P=0.01$) and after ($P<0.01$) the tobacco smoke session but remained unchanged in the nontobacco smoke session. The interaction between the 2 sessions (tobacco versus nontobacco smoke) was significant for both exposure ($P=0.04$) and postexposure ($P=0.05$) periods (Figure 2).

The largest increases in serum nicotine levels after the exposure to tobacco smoke were related to the greatest increase in AIx ($r=+0.84$; $P<0.01$) observed 50 minutes after the initiation of ETS exposure (Figure S2). In the additional study, nicotine sublingual administration was associated with an increase in AIx corrected for HR ($P=0.001$) throughout the study (Figure S3).

Transit Time
Transit time decreased both during ($P=0.02$) and after ($P<0.01$) the tobacco smoke session, but remained unchanged in the nontobacco smoke session. The interaction between the tobacco and nontobacco smoke sessions was significant for both exposure ($P=0.02$) and postexposure ($P=0.01$) periods (Figure 2).

Heated Skin Blood Flow Reactivity
None of the interventions affected skin blood flow recorded in baseline conditions before the initiation of the heating protocol. Normal air and nontobacco smoke did not affect the early and late skin blood flow responses to heating (Figure 3). In contrast, the skin blood flow response to heating decreased after the tobacco smoke exposure ($P=0.02$) compared with the baseline response. This was because of a decrease in the late phase of the reaction after the smoke exposure ($P=0.03$), whereas the early phase of the reaction remained unchanged (Figure-3).
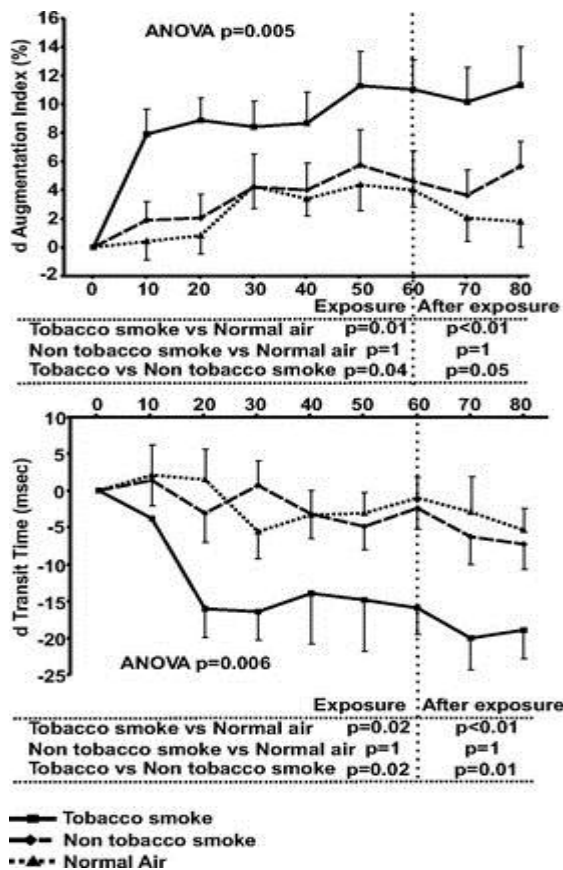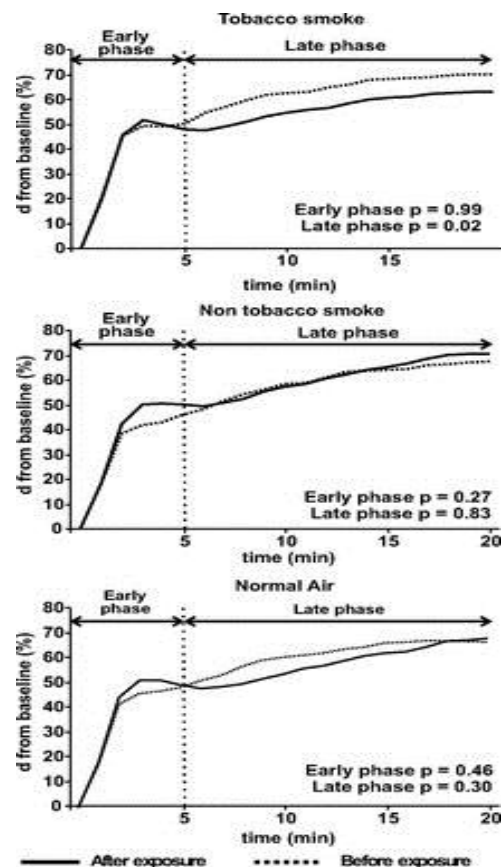

Figure 2: Changes in AIx corrected for heart rate and transit time during and after the 3 experimental sessions. Values are expressed as means±SEMs.

Figure 3: Skin blood flow response to local heating before and after the exposure according to the experimental session.

DISCUSSION

The main new findings of our study are as follows: (1) ETS exposure induces an acute increase in central wave reflection and a decrease in skin microvascular dilatation, when compared with nontobacco smoke; (2) increased central wave reflection is linked to the levels of nicotine achieved with ETS; (3) these modifications persist ≤20 minutes after ETS cessation; and (4) smoke inhalation, regardless to the tobacco content, is followed by a plasmatic increase in ADMA. Hence, large and small arterial vascular functions are altered by acute exposure to tobacco smoke. Hemodynamic changes provoked by ETS are the result of a primary nicotinic toxic mechanism acting on the vascular tree and are not mediated by a sensory stimulation or a stressful reaction to the smoke itself. In addition, our study suggests that the toxicity of ETS is markedly underestimated when only the direct exposure time is taken into account.The Role of NicotineIn a previous study, 1 hour of ETS exposure acutely increased AIx by 16%.[2] However, this reaction could be interpreted as the sum of 3 different effects: a placebo effect, a cardiovascular response secondary to sensory stimulation and stress by smoke, and a specific effect of the tobacco smoke on vascular function.[5,15,16] In contrast, our results demonstrate that ETS exposure produces a marked change in the aortic waveform through a primary toxicity induced by tobacco on the vascular tree. Enhanced arterial wave reflection, because of a change in peripheral vascular reflection site, and/or augmented pulse wave velocity can generate an increase in AIx. Although pulse wave velocity was not measured directly, the aortic pulse transit time, which has been used as a surrogate marker of pulse wave velocity[17] was decreased by tobacco smoke. This finding suggests that the intensified arterial wave reflection in the aorta could be explained by a reduction in vessel compliance after ETS exposure. In patients with coronary artery disease, invasive measurements of the aortic pressure-diameter loop have demonstrated that 4 minutes of ETS exposure were able to decrease aortic distensibility[4] Our results are in accordance with this finding and suggest that changes in the aortic waveform in response to passive smoke are favored by active stiffening of the aorta. However, concomitant changes in aortic wave reflection resulting from an increased peripheral vascular tone, as reported previously in active smokers[18] may also have played a role. Previously, short-term ETS exposure (15 minutes) did not interfere with forearm vascular resistance measured by plethysmography[19] However, this segmental analysis of vascular resistance cannot rule out a systemic arteriolar vasoconstriction after a more prolonged ETS exposure and larger increases in plasma nicotine. Further studies are required to characterize the possible differential effects of impaired arterial compliance and early reflection site in the rise with ETS.The comparison of the vascular response to passive smoking of a real cigarette and an herbal cigarette reveals a more toxic effect of the tobacco smoke. At first glance, the main toxic difference between the 2 smokes may reside in the nicotine content

of tobacco smoke.[6] Indeed, it is widely accepted that nicotine has pleiotropic actions that could affect vasomotor regulation[19] Our results reveal a significant relationship between the changes in aortic waveform and the nicotine levels reached in plasma after 1 hour of tobacco smoke exposure (Figure S2). This relationship was confirmed in our second protocol demonstrating an acute impairment in arterial wave reflection produced by a pure nicotinic stimulus. This finding provides novel information regarding the role played by nicotine in the smoke-related vascular damage. However, the exact mechanisms responsible for the nicotine-induced rise in arterial wave reflection, the effect of the aortic hemodynamic changes on myocardial perfusion, and the possibility of tolerance development after chronic exposure to nicotine require further investigation.An important contribution of our study also resides in the demonstration that nontobacco smoke increases plasmatic ADMA levels, a competitive inhibitor of NO synthase. This occurred to a similar extent as with tobacco smoke. Usually the most common mechanism leading to accumulation of ADMA involves impaired metabolism by dimethylarginine dimethylaminohydrolase, an enzyme extremely sensitive to oxidative stress. Thus, we hypothesized that the free radical exposure, arising from identical particulate exposure of both smokes[20] produces the same inhibition of dimethylarginine dimethylaminohydrolase activity and generates the same degree of competitive inhibition of NO synthase. We believe that these results further add to the escalating evidence that exposure to polluted air is associated with short-term adverse cardiovascular effects.[22] Increased ADMA levels in our study, not reported previously in vivo, as well as with nontobacco smoke, provide a further indication on how air pollution may elicit cardiovascular events. Contrary to tobacco smoke, nontobacco smoke exposure produced no significant change in arterial waveform and skin blood flow, suggesting a key role of the nicotine content of smoke, at least in acute conditions. Despite this "relative" safety, herbal cigarette smoke increased plasmatic ADMA levels and exposed the subject to the same level of particle matter as ETS. Even if a previous study did not identify acute sympathetic or peripheral vascular effects of carbon monoxide,[23] carboxyhemoglobin increase from nontobacco smoke exposure has some detrimental effect on myocardial blood flow[24,25,26,27,28] For these reasons, we believe that herbal smoke cannot be considered as a safe cardiovascular smoke, especially because the role of fine particle matter[27,28,29,30.33] in the endothelial toxicity of cigarette smoke and air pollutants[34] remains unclear. Microvascular Effect of ETS exposure has immediate effects on endothelium-dependent vasodilatation of large arteries but our study also reveals an impairment of vascular reactivity in small-size vessels. Many studies have established the physiological substrate of skin thermal hyperimia Local heating evoked an initial vasodilatation followed by a plateau, which is ≈70% mediated by NO[31,32,33] However, even if the role of

endothelium-derived NO is predominant, endothelium-dependent hyperpolarizing factors are also involved in this reaction[28,29,33] Consequently, the microvascular impairment occurring after 1 hour of ETS exposure may be interpreted as a decrease in endothelium-dependent hyperpolarizing factor and/or endothelium-derived NO bioavailability. This will require further studies to better identify the mechanisms involved in the microvascular endothelial impairment observed with ETS. Moreover, only tobacco smoke impaired microvascular function in the presence of an increase in plasmatic ADMA. This paradox could be explained by a specific ability of tobacco smoke to decrease endothelial production of endothelium-dependent hyperpolarizing factor and/or NO, because nicotine can directly impair NO synthase expression,[6] whereas acrolein can increase endogenous reactive oxygen species produced by NADPH activation[29,33]

CONCLUSION

Passive smoking specifically increases aortic wave reflection through a nicotine-dependent pathway and impairs microvascular function, even after the end of the exposure. However, both tobacco and nontobacco passive smoking inhalation increase plasma asymmetrical dimethyl-arginine levels Our findings indicated that exposure to PS is significantly associated with increased risk of CVD incidence and mortality and is a public health hazard which should be minimized. General population need to be aware of this association and avoid exposure to PS. Better assessment of the patient's disease risk should be facilitated; advice should be given on target smoke avoidance; and counseling should be provided to household contacts regarding tobacco cessation. Also, countries must have a legal obligation to implement effective legislation and guidelines on the protection from exposure to second-hand smoke to provide protection from exposure to tobacco smoke in indoor workplaces, public transport, indoor public places, and, as appropriate, other public places.

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