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Endothelial dysfunction in passive smokers

Abstract

Nowadays, there is no doubt that exposure to passive smoking, whatever it may be approached to be studied – and there are a lot of study approaches: clinical, biological, metabolic, epidemiologic, statistic and so on, that recognize different pathogenetic mechanisms of damage- leads to only one final result that is a reversibly functional harm of the heart and blood vessels following acute exposure, and pathologic alterations that become, in the long run, irreversible lesions of the above target organs after chronic exposure. The harm of the heart and blood vessels from passive smoking is the result of either an isolated action or combined action of some toxics contaminated indoor air by tobacco products, primarily nicotine and carbon monoxide. Among the different types of vessel damage caused by acute exposure to passive smoking, there is evidence that endothelial dysfunction, characterized by impaired endothelium-dependent vasodilation as a result of reduced nitric oxide (NO) production, is the earlier alteration to appear, although, initially, is transient but repeatable.

Keywords: passive smoking, endothelial dysfunction, nicotine, carbon monoxide, thiocyanate

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Introduction

Nowadays, there is no doubt that exposure to passive smoking leads to well-defined results which are a reversible andfunctional harm of the heart and blood vessels following acute exposure, as well as pathologic alterations that become, in the long run, irreversible lesions of these structures after chronic exposure.[1–26] Therefore, the American Heart Association has included passive smoking among the major risk factors for heart disease in both adults and children.[6] No country is free from passive smoking problem, which plagues developing and developed countries alike, although with different results due to different lifestyles and diffusion of antismoking campaigns. Passive smoking influences negatively the health of both adults and children, particularly following chronic exposure, even if this occurs irregularly but prolonged in time.

Characteristics of passive smoke

Chemically, environmental tobacco smoke is probably the main pollutant of indoor air acting in different places: workplaces, public buildings in some countries, business offices, and home. The chemical mixture of passive smoking able to damage the heart and blood vessels consists of three main components diffused and dispersed in three phases defined as sidestream smoke, mainstream smoke, andvapor phase. Sidestream smoke contains the greatest concentration of tobacco chemicals since it is unfiltered by the cigarette filter due to the fact that they do not pass into this device. Nicotine in the gaseous phase, and therefore easily spreading, and carbon monoxide is particularly present in sidestream phase. The mainstream smoke contains prevailingly nicotine in a particulate phase. Mainstream smoke is inhaled and exhaled particularly by the smokers making stronger the action of active smoking on themselves. Finally, vapor phase is constituted by those cigarette components in different mixture concentrations–nicotine, carbon monoxide andthiocyanates- that diffuse through the cigarette paper into the environment.[7] Table 1 describes the main composition of passive smoking.

Exposure to passive smoking is currently defined either as an exposure to sidestream smoke from burning cigarettes or as an exposure to mainstream smoke. Both sidestream smoke and mainstream smoke contain those toxic substances-in a large number–which lead to cardiovascular damage due to the fact that the pollutants stagnate in the environment even after the consumption of cigarettes smoked, and spread out surrounding environment by their gaseous phase. Usually, the particles of sidestream smoke are smaller than those of mainstream smoke so that they can be inhaled more deeply into the lungs.[8] From this way, harmful components of passive smoking reach blood flow and target organs including heart and artery vessels.

Table 1 Passive smoking composition

Sidestream smoke	Nicotine and Carbon Monoxide
Mainstream smoke	Particulate nicotine
Vaporphase	Nicotine, Carbon Monoxide, Thiocyanate

The harm of the heart and blood vessels from passive smoking is the result of either an isolated action or the combined action of particularly some active pollutants derived from burning tobacco. Burned tobacco contains over 4,000 chemicals.[9] The majority of these pollutants has carcinogenic and/or negative effects on the heart and blood vessels in humans and animals. Passive smoking damages the cardiovascular system by biochemical pollutants which act as a major risk factor. With regard to endothelium, there is evidence that nicotine and carbon monoxide mainly play their adverse effects, the first during acute exposure and the latter in those subjects exposed chronically.

Nicotine

Nicotine is one of the most important markers in assessing smoking habit and exposure to environmental tobacco smoke, particularly when its main metabolite Cotinine is dosed in the urine. Nicotine is metabolized to cotinine the liver. Both these compounds can cause heart and blood vessel alterations that are followed by failure of an effective vascular remodeling particularly after chronic exposure. The concentrations of these chemicals in individuals are a consequence of both active smoking and air pollution. Biochemical concentrations of nicotine and cotinine as well as other toxic substances permit to identify those individuals who are exposed to tobacco smoke, but provide poor reflection of smoking habits and level of cardiovascular damage.[27] Dosimetry of smoking constituents indicated that a

low nicotine delivery, as it is a concentration of less than 0.6 mg per cigarette, usually induces an active smoker to draw larger puff volumes (up to 55ml/puff), or to inhale more deeply, or to puff more frequently.[28] On the contrary, nonsmokers exposed involuntarily to environmental tobacco smoke have their harm depending from blood concentrations reached by smoking indoor pollutants. The main effects of nicotine on the endothelium are mediated by sympathetic nervous system stimulation, catecholamine release, primarily epinephrine, and association of these two mechanisms. Table 2 summarizes the main mechanisms by which nicotine influences endothelial dysfunction.

Table 2 Nicotine-mediated effects on endothelium

Sympathetic nervous system stimulation
Increased catecholamine release
Interaction between sympathetic nervous system and catecholamine

Carbon monoxide

Carbon monoxide is a gas quickly absorbed into the blood and then reducing blood capacity to carry oxygen to the whole body. Inhalation of carbon monoxide has the same effects on active or passive smokers, depending its effects from the concentrations reached into the blood.[2] Carbon monoxide toxicity is due primarily to its strong bond with hemoglobin that produces carboxyhemoglobin. However, also the direct effects of carbon monoxide- as poisonous gas–on the heart and blood vessels must be taken into account because of their potential toxicity. Since carbon monoxide is an extremely volatile gas, its potential toxicity is proportionally correlated with indoor cubic space, resulting, therefore, more harmful for individuals stayingat home and closed workplaces than that in open workplaces polluted by the gas. The affinity of hemoglobin for carbon monoxide is about 240 times than that of for oxygen, and carboxyhemoglobin levels in the blood are the close result of environmental tobacco smoke.

Biochemical monitoring of carbon monoxide inhalation from burning tobacco can be well measured by the dosage of carboxyhemoglobin before and after passive smoke exposure. Carboxyhemoglobin may be satisfactory measured.[29–32] in an arterial blood sample or, more easily, in a venous blood sample that must be collected in a closed container containing dry sodium heparin or disodium ethylene-diaminotetracetic acid (EDTA) as an anticoagulant. Blood samples may also be stored for several days prior to analysis in a dark, cold container (4°C) and then measured by spectrophotometric methods. The determination of exposure to carbon monoxide may be also conducted by measuring the gas in expired air. This determination may be useful, particularly in individuals undergone acute passive smoking exposure.[1]

In conclusion, carbon monoxide toxicity either following acute exposure or chronic exposure to environmental tobacco smoke is due particularly to tissue hypoxia that is a consequence of the much higher affinity for hemoglobin than that of oxygen. Therefore, the toxic effects of the gas on endothelium involve the endothelial cell layer with anatomical (structural) alterations following chronic exposure.

Thiocyanates

Thiocyanates are a group of chemical compounds that have toxic action on several body organs.[33–35] They inhibit mitochondrial ferricytochrome oxidase and other enzyme systems and hence block electron transport resulting in reduced oxidative metabolism and oxygen utilization, decreased ATP production and lactic acidosis. The impairment of respiratory cellular chain induces tissue hypoxia or worsens a pre-existing hypoxia. Burned tobacco commonly releases thiocyanates. People who smoke or undergo environmental tobacco smoke exposure may reach a mean level of thiocyanatesin the blood of about 0.4mcg/ml. These levels increase two to two times and half the concentrations measured for non-exposed individuals. There is evidence that thiocyanate is able to damage the endothelium following prolonged chronic exposure to passive smoking mainly increasing the degree of hypoxia resulting from the effects played by nicotine and, primarily carbon monoxide. The acute exposure to passive smoking is scarcely or not at all influenced by this substance.

Endothelium

The endothelium has long been viewed as an inert cellophane-like membrane that lines the circulatory system with its primary essential function being the maintenance of vessel wall permeability. Nowadays, following the findings Furchgott & Zawadski[36] there is evidence thatthe endothelium plays a pivotal role in regulating blood flow by secreting a large number of vasodilator and vasoconstrictor chemicals. When the endothelium is intact vasodilator function is prevailing as an effect of nitric oxide (NO) production. However, vasodilator response may change as a result of injuring stimuli of different type, including passive smoking. In this case, an altered response of endothelial cells may be observed with increased vasoconstriction responsible, among other things, of dysfunction, which may be initially transient followed by baseline function restoration, or, in time, able to trigger those pathologic mechanisms that lead to atherosclerosis. Therefore, endothelial dysfunction has been identified as "the door" of this vascular disease.

Mechanisms of endothelial dysfunction from passive smoking: Dysfunction of endothelial cells is probably the earliest event in the process of lesion formation, and, therefore, hence, the assessment of endothelial function may be a useful prognostic tool for artery disease. Heterogeneity of vascular dysfunction may be observed, although some vascular structures like coronary arteries, carotid and brachial arteries show alterations with a major rate. Thus, endothelial dysfunction may be reflected systemically, thereby allowing for a less invasive approach to the assessment of overall endothelial cell biocompatibility. When endothelium loses its integrity becomes thrombogenic as an effects of blood and inflammatory cell migration at the site of altered surface. This factor has to be considered the promoter and early event to induce pro-atherosclerotic mechanisms that precede structural atherosclerosis.

Exposure to environmental tobacco smoke is undoubtedly a strong factor of endothelial dysfunction following both acute and chronic exposure,[37] although different responses are the result of this factor. The alterations following acute exposure are, as aforesaid, trannsient, but repeatable with functional characteristics, particularly inherent to changes in vasodilator mechanisms. On the contrary, chronic exposure leads to the formation of an atherosclerotic plaque.[38] Nicotine and carbon monoxide, the two main compounds of tobacco smoke able to induce endothelial dysfunction,cause changes of different degree and type to vascular endothelium that, usually, are earlier than that caused by the other major cardiovascular risk factors. However, it is useful to emphasize again that the functional disorders of the endothelium caused by acute exposure to passive smoking are as early as smoking exposure starts as documented by several studies.[39–42] These findings reached similar conclusions with regard to the type of damage following acute exposure to passive smoking. Table 3 summarizes the

main endothelial alterations due to passive smoke exposure. Evidence indicates that chronic exposure to passive smoking causes an increase in arterial stiffness as an effect of repeated and prolonged endothelial dysfunction.[43–44] as experimentally documented in the aorta of men.

Table 3 Main endothelial alterations from passive smoke

Acute exposure	Chronic exposure
Impaired endothelium-dependent vasodilation	Atherosclerotic plaque formation
Reduced NO production	Increased arterial stiffness
Increased vasoconstrition	

Conclusion

In conclusion, the observations described show that exposure to environmental tobacco smoke triggers early and constant endothelial dysfunction either in the individuals, who suffer from a pre-existing cardiovascular disease or also in healthy subjects. These alterations, when prolonged in time, cause atherosclerotic lesions up to plaque formation and its complications. Because exposure to passive smoking is often associated with other major cardiovascular risk factors with almost similar effects on the endothelium, it is logical to assess that endothelial dysfunction from environmental smoking is the "door" of future development of atherosclerosis.

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None.

Conflicts of interest

Authors declare that there is no conflict of interest.

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