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Review

Effects of Involuntary Smoking and Vaping on the Cardiovascular System

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Abstract:

In deaths and diseases attributed to tobacco smoke cardiovascular events exceed cancer and respiratory diseases. Second hand smoke (SHS) promotes the development of arteriosclerosis and can also trigger acute changes of endothelial function and of blood coagulability. Indoor smoking bans reduced coronary syndrome and myocardial infarction 10-20% within one year and were followed by sustainable decreases of stroke and diabetes. With a smoke-free hospitality industry people recognized tobacco smoke as an air pollutant, smoking in public was denormalized and social acceptance of smoking in front of children and pregnant women decreased also in homes and in cars. Combined effects with ambient air pollution are proven for active smoking and suspected for SHS. Contamination with third hand smoke (THS, "cold smoke") persists for months in homes and cars, creating secondary pollutants that in some cases are more toxic (e.g., tobacco-specific nitrosamines). Remnants found in air, dust, and on surfaces (carpets, wallpapers, upholstery, soft toys) were associated with their metabolites in saliva and urine of children and with elevated levels of nicotine on hands and cotinine in urine of nonsmokers residing in homes previously occupied by smokers. In animal experiments effects of THS were found on thrombogenesis, insulin resistance through oxidative stress, on the developing immune system, lipid metabolism and alterations in liver, lung, skin and behavior. Much less is known about health effects for bystanders from the aerosols exhaled during "vaping" of e-cigarettes, but nicotine and other toxins from e-cigarettes are certainly a hazard, which should be prevented by the use of dermal and oral nicotine products, which are safer for nicotine replacement and without risk for bystanders.

Keywords: second-hand smoke; cardiovascular disease; third-hand smoke; passive vaping; electronic cigarettes; heated tobacco; water pipe; myocardial infarction; stroke; diabetes

1. Introduction

Cardiovascular deaths from tobacco use and secondhand smoke (SHS) exceed deaths from cancer and respiratory diseases attributed to tobacco smoke [1-3]. But many smokers are still unaware of the link between tobacco smoke and cardiovascular diseases (CVD), e.g. stroke [4], even in countries like China where many strokes from smoking in men and from SHS in women occur [1,5,6]. Information on links between tobacco use or exposure on heart attacks, stroke, peripheral vascular disease and impotence is still news for many people and even medical doctors sometimes doubt that SHS causes CVD, because they occur less frequently than in active smokers.

2. Burden of CVD from SHS

Worldwide, 40% of children, 33% of male non-smokers, and 35% of female non-smokers were exposed to second-hand smoke in 2004 [7], This exposure was estimated to have caused 379 000 deaths from ischemic heart disease and a total of 603 000 premature deaths, 47% of which occurred

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in women, 28% in children, and 26% in men. Disability adjusted life years (DALYs) lost because of exposure to SHS amounted to 10.9 million, of which 61% were in children. The largest disease burdens in adults (2 836 000) were from ischemic heart disease [7] Prospective cohort studies showed high risks of SHS for coronary heart disease [8] and stroke [9], without evidence of a threshold [10]. Especially at work places like bars or discotheques, where many smokers release SHS, substantial increases of acute coronary events were found [11,12]. The acute cardiovascular effects of SHS were attributed mainly to the ultrafine particles released from the burning end of cigarettes between puffs [11,13].

3. Pathogenesis of CVD from SHS

Chronic inhalation of SHS contributes to development of CVD in healthy persons by oxidative stress and vascular inflammation, while acute effects of SHS are decisive for manifestation of CVD in risk groups [11,15]. Toxins distributed on the large surface of ultrafine particles inhaled with SHS elicit acute endothelial dysfunction with inactivation of nitric oxide (mediating vasodilatation), impairment of the viability of endothelial cells and reduction of the number and functional activity of circulating endothelial progenitor cells. In addition, platelets of non-smokers appear to be susceptible to pro-aggregatory changes with every passive smoke exposure. Apart from vasoconstriction and thrombus formation from sticky platelets, increased fibrinogen and other factors of blood coagulation the myocardial oxygen balance is further impaired by SHS-induced adrenergic stimulation and autonomic dysfunction with heart rhythm disturbances [11,15-17] and impairments of diastolic function [18]. Experiments in healthy men showed that a 30 minute exposure to SHS (e.g. the time of a meal) is sufficient for reduction of coronary flow velocity reserve [19] and sustained vascular injury characterized by mobilization of dysfunctional endothelial progenitor cells with blocked nitric oxide production and triggering of platelet aggregation in blood [15,16,20,21]. Chronic vascular effects of SHS start with endothelial dysfunction in children [22], arterial stiffness [23] and develop to thickening of intima-media [24] and atherosclerosis [25,26]. Combined effects of tobacco smoke with ambient air pollution have been detected [27], so that interactions have to be assumed also for SHS and ambient PM2.5. Complex interactions with nutrition are likely, especially in connection with diabetes. SHS is a risk factor for metabolic syndrome [28,29], glucose intolerance [30], insulin resistance and the development of type 2 diabetes mellitus [31]. A meta-analysis of 6 prospective cohort studies [32] concluded, that SHS increases the relative risk of new diabetes to 1.21 (95 % CI 1.07–1.38). Another meta-analysis on 7 prospective studies [31] found that the increase of the relative risk for developing type 2 diabetes from passive smoking was 1.33 (95% CI 1.20-1.46) and after adjustments for publication bias it was 1.27 (95%CI 1.16-1.40). After manifestation of diabetes vascular complications are increased by exposure to tobacco smoke.

4. Benefits of smoke-free legislation

Most at risk for acute effects of SHS like myocardial infarction or stroke are patients with preexisting coronary or cerebrovascular diseases, which in turn are promoted by chronic exposure to SHS. Since Sargent et al. [33] published reduced incidence of admissions for myocardial infarction associated with a public smoking ban, numerous studies confirmed, that enforcement of smoke-free laws rapidly reduces admissions for acute coronary syndrome [34-36] and also other cardiac and cerebrovascular diseases [37]. Smoke-free legislation is associated with a lower risk of hospitalization and death from CVD, significantly lower rates of hospital admissions or deaths from coronary events (relative risk, 0.85; 95%CI 0.82–0.88), other heart disease (relative risk, 0.61; 95%CI 0.44–0.85),and cerebrovascular accidents (relative risk, 0.84; 95%CI 0.75–0.94). More comprehensive laws were associated with larger changes in risk [37]. Indoor smoking bans reduced myocardial infarction up to 33-40% [33,38] and in most studies by 10-20%, in the first year mainly associated with the elimination of passive smoking and followed by sustainable decreases of coronary syndrome, myocardial infarction, stroke and incident diabetes also in ex-smokers [37,39-42]. With a smoke-free hospitality industry people recognized tobacco smoke as an air

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pollutant, smoking in public was denormalized and social acceptance of smoking in front of children and pregnant women decreased also in homes and in cars [43-47]. A meta-analysis came to the conclusion that public smoking bans (workplaces including the hospitality industry) reduced children's exposure to SHS at home by 28% [48]. Therefore it is not amazing that enforcement of smoke-free legislation was also followed by a 10% reduction in preterm birth and hospital admissions of children with asthma [49].

5. Dose-response relationships for SHS and CVD

Substantial and rapid reaction of the cardiovascular system (platelet and endothelial function, arterial stiffness, atherosclerosis, oxidative stress, inflammation, heart rate variability, energy metabolism, and increased infarct size) explains why SHS increases the risk of coronary heart disease by about 30% [50]. Cardiovascular risks have been underestimated in many studies by comparison of active smokers with non-smokers, of which a large part was exposed to SHS [51]. There is evidence of a strong, consistent and dose-dependent association between exposure to secondhand smoke and risk of myocardial infarction and stroke, suggestive of a causal relationship, with disproportionately high risk at low levels of exposure suggesting no safe lower limit of exposure for risk groups [10,11]. Chronic exposure of persons, which are healthy at begin of exposure, is associated with a continuous increase of risk of CVD. Already Whincup et al. [52] were able to show, that in male, light and heavy passive smokers, classified by serum cotinine at begin of follow up, major coronary heart disease increased by years of follow up. The increase in heavy passive smokers was comparable to the increase in light active smokers. In a European cohort a hazard ratio of 1.25 (95%CI 1.04-1.50) was calculated for passive smoking (verified in a subsample by plasma cotinine) per each additional hour/day of exposure [53]. A meta-analysis on health effects of SHS found a relative risk of 1.35 (95 % CI: 1.22-1.50) for stroke and 1.27 (95 % CI: 1.10-1.48) for ischemic heart disease [54]. The risks were higher in women. Flores et al. [55] proved that the premature mortality hazard of recalled and unconscious exposure to SHS is comparable and predicted by serum cotinine at begin of observation. There was a significant trend in years of life lost, adjusted for confounders, across cotinine categories both in non-smokers ($P < 0.0001$) and non-smokers reporting no SHS exposure ($P = 0.002$).

6. SHS effects in children and unborn

The younger the child the more vulnerable it seems to be, especially for SHS effects on brain and lungs, but also CVD [56,57]. Recently a meta-analysis on parental smoking and the risk of congenital heart defects concluded, that maternal active smoking was significantly associated with risk of atrial septal defect and right ventricular outflow tract obstruction and that also maternal passive smoking as well as paternal smoking increased the risk of congenital heart defects in offspring [58]. Many effects of prenatal exposure to tobacco smoke are related to nicotine [59], with adverse perinatal outcomes associated to placental syndromes [60] and direct toxic effects on arteries supplying the fetus [61,62] and his heart [63,64]. Prenatal exposure to constituents of tobacco smoke can also have long lasting effects on children and only few epidemiological studies were able to disentangle them from effects of postnatal exposure [65,66].

7. Third hand smoke (THS, "cold smoke")

SHS leaves accumulating contaminants on surfaces like carpets, wallpapers, upholstery, blankets or soft toys and these remnants endanger in particular children by oral, dermal and inhalation uptake from house dust, etc.. Even parents omitting SHS nevertheless bring toxins and carcinogens to indoor spaces and to their children by clothes, hair, skin and breath, but the highest contamination is found on surfaces of rooms used for smoking. From these surfaces toxins are released back into the air and by aging and chemical transformations more toxic pollutants are formed, e.g. residual nicotine from tobacco smoke sorbed to indoor surfaces reacts with ambient nitrous acid to form carcinogenic nitrosamines [67-69]. Animal experiments demonstrated numerous effects of THS:

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hyperactivity, persistent changes in the immune and hematopoietic system, lung cancer, liver damage, increased thrombogenesis, and metabolic effects, including elevated triglycerides, increased LDL, decreased HDL, and insulin resistance through oxidative stress [69-72].

8. Cardiovascular risks of passive exposure to emissions of water pipe, heated tobacco and electronic cigarettes

Water pipe (shisha) produces similar risks for bystanders as tobacco cigarettes, but concentrations of carbon monoxide and heavy metals are higher in SHS from shisha. Depending on intensity and duration of passive exposure similar CVDs could develop as proven for active consumption, while acute cardiovascular effects on risk groups are expected mainly from fine particulate matter, carbon monoxide and nicotine [73-75]. Animal experiments showed hypercoagulability, inflammation, as well as systemic and cardiac oxidative stress [76].

Heated tobacco products (HTPs) are marketed as less dangerous than conventional cigarettes because of less products of pyrolysis, however, biomarkers of potential cardiovascular harm did not support this claim [77]. HTPs impair vascular endothelial function measured by arterial flow-mediated dilatation in rats to the same extent as by cigarette smoke [78]. An advantage of electronic devices over conventional cigarettes is that SHS is only produced when the user exhales the aerosols and not continuously like in conventional smoking released from the burning end of cigarettes between puffs. The doses calculated for SHS uptake from electronic devices were significantly lower, below 1.6×108particles/kg bodyweight, than those due to combustion devices, but dosimetry estimates were 50% to 110% higher for HTPs than for e-cigarettes [79].

Electronic cigarettes (ecigs) have been called “wolf in sheep’s clothing”, because they serve as a gateway drug for youth, prolong nicotine addiction and the ritual in smokers who would otherwise be willing to quit and keep up the handling and use of cigarettes in public [80]. Exposure of bystanders to products of pyrolysis are lower than in passive smoking, but exposure to nicotine is similar and particles in the aerosol are smaller [81-84]. Aerosols exhaled during vaping are less persistent than SHS, nevertheless they are carriers for toxins, which they adsorb on their large surface and transport them into the depth of the lung, where clearance is less efficient [80]. Contamination of neighboring rooms was found [85] and it has to be assumed that also passive vaping increases cardiovascular risks, which were found for active vaping [86, 87]. Though exposure to nano-particles is not as high as in passive exposure to heated tobacco, the combination of ultrafine particles with nicotine and other toxins has to be regarded as cardiovascular risk, which is avoidable [88]. For smoking cessation dermal and oral nicotine products from pharmacies are safer for nicotine replacement and do not contaminate the breathing air of bystanders [80].

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