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SMOKING AND CARDIOVASCULAR RISK: IMPACT OF CHRONIC EXPOSURE TO NICOTINE

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Abstract: Smoking remains one of the main modifiable risk factors for cardiovascular disease and is responsible for significant global morbidity and mortality. In recent years, the rise of electronic vaporization devices, such as electronic cigarettes (ENDS), has raised concerns about their potential adverse effects on the cardiovascular system. This literature review aimed to analyze the impacts of chronic exposure to nicotine, from both combustible cigarettes and electronic devices, on cardiovascular parameters. We included studies published in the last five years, indexed in PubMed, which addressed aspects such as endothelial function, vascular inflammation, oxidative stress and hemodynamic alterations. The findings indicate that acute and chronic exposure to nicotine, including through ENDS, promotes increases in blood pressure and heart rate, increased arterial stiffness and endothelial dysfunction, mechanisms associated with sympathetic activation, oxidative stress and reduced nitric oxide bioavailability. Although ENDS present a potentially lower cardiovascular risk than traditional cigarettes, their deleterious effects are evident, especially among regular users. Thus, the data reinforces the need for stricter regulation and prevention strategies that include both smoking cessation and the reduction of harm related to emerging electronic devices.

Keywords: Smoking; Cardiovascular risk; Electronic cigarette; Nicotine; Endothelial dysfunction; Oxidative stress; Vaporization.

INTRODUCTION

Smoking is one of the main risk factors for cardiovascular disease (CVD) and is widely recognized for its deleterious impact on endothelial function, vascular inflammation and oxidative stress, accounting for up to 30% of CVD deaths. (BENOWITZ; LIAKONI, 2022) In recent years, there has been an exponential growth in the use of e-cigarettes and vaporizing devices, especially among young people and adults, largely due to the misconception that they represent a safer alternative to traditional cigarettes. (ROSE et al., 2023), 2023) However, chronic exposure to nicotine through these devices has raised concerns about their effects on the cardiovascular system, since they not only contain nicotine, but also a variety of potentially harmful substances, including carcinogenic compounds and inflammatory toxins. (FRIED; GARDNER, 2020) Regardless of the presence of nicotine, many constituents of ENDS products, including flavoring additives, hygroscopic carriers such as propylene glycol and glycerol, and metals (from the heating coil), have been shown to induce cardiopulmonary toxicity in animal and in vitro studies. (JASON J. ROSE 2023)

Nicotine, the main active compound in tobacco, is a volatile alkaloid with a pyrrolidine structure, isolated in its pure form in 1928 by Posselt and Reiman. In the case of cigarettes, the smoke has an acidic character (pH 5.5), which means that nicotine remains predominantly in its non-protonated form, efficiently favoring its uptake in the pulmonary alveoli. As pulmonary absorption is very rapid, the plasma concentration of nicotine increases progressively, reaching a maximum value within 10 minutes. Nicotine is poorly bound to plasma proteins and is rapidly and widely distributed to the body's organs and tissues, subsequently being excreted in the urine (OGA; CAMARGO; BATISTUZZO, 2021).

The emergence of lung diseases associated with the use of e-cigarettes, culminating in more than 2,800 hospitalizations in the United States in 2019, reinforces the need for in-depth research into the cardiovascular risks of these products. (ROSE et al., 2023) Currently, all e-cigarettes are regulated as tobacco products, without the obligation of pre-market safety studies in humans and animals, which compromises the understanding of long-term adverse effects. (SHAHANDEH; CHOWDHARY; MIDDLEKAUFF, 2021) Recent data indicate that heated tobacco products, such as IQOS, despite emitting reduced levels of chemical substances compared to conventional cigarettes, also promote significant changes in heart rate, blood pressure and endothelial function, showing potential cardiovascular risk. (FRIED; GARDNER, 2020)

In addition, studies show that exposure to nicotine through vaporization is associated with neurohumoral activation, oxidative stress, systemic inflammation and endothelial dysfunction, all factors that contribute to atherogenesis and an increased risk of cardiovascular disease. The growing popularity of cannabis vaporization, whose cardiovascular risks have yet to be fully elucidated, represents a further public health concern, especially when associated with the use of smuggled products, which may contain highly harmful additives (FRIED; GARDNER, 2020).

In addition to the direct adverse effects of nicotine and its delivery vehicles, there is also an indirect impact of smoking on cardiovascular health, mediated by behavioral and metabolic factors. Individual smokers, including users of electronic devices, are more likely to adopt unhealthy lifestyle habits, such as a sedentary lifestyle, a high-fat diet and excessive alcohol consumption, which act synergistically in accelerating the atherosclerotic process. (MCCOY et al., 2022) In addition, nicotine modulates the release of catecholamines,

contributing to chronic sympathetic hyperactivity, with a consequent sustained rise in blood pressure and increased arterial stiffness - factors closely related to the development of major cardiovascular events, such as acute myocardial infarction and stroke. (SHAHANDEH; MIDDLEKAUFF, 2021) This evidence reinforces the need for integrated public health approaches that include not only the cessation of nicotine use, but also the modification of lifestyles, with a view to mitigating the multiple risk factors involved in the genesis of cardiovascular diseases.

Given this scenario, a comprehensive review of the cardiovascular effects of smoking and chronic exposure to nicotine is essential, considering both conventional cigarettes and emerging electronic devices. Understanding the underlying pathophysiological mechanisms and the potential impacts of these products is essential to support prevention, regulation and smoking cessation strategies, with a view to reducing cardiovascular morbidity and mortality attributable to chronic nicotine use (BENOWITZ; LIAKONI, 2022; FRIED; GARDNER, 2020; ROSE et al., 2023; SHAHANDEH; CHOWDHARY; MIDDLEKAUFF, 2021).

METHODOLOGY

The methodology adopted for this literature review followed strict criteria for selecting and analyzing studies in order to synthesize the most recent information on the impact of chronic exposure to nicotine on cardiovascular risk. Articles published in the last five years and indexed in the PubMed database were included, using the descriptors 'Tobacco' and 'Cardiovascular Risk'. The search process was carried out systematically in order to ensure the comprehensiveness and relevance of the information collected.

The inclusion criteria included original studies, systematic reviews and meta-analyses that addressed the effects of smoking and the use of electronic vaporizing devices on cardiovascular parameters such as endothelial function, vascular inflammation, oxidative stress, heart rate and blood pressure. Clinical trials, observational studies and experimental research with a robust methodology and appropriate design were prioritized.

Articles that did not meet the inclusion criteria were excluded, as were those that were not available on the PubMed database. Duplicate studies, publications in languages other than English or Portuguese and studies that did not specifically address the cardiovascular effects of smoking were also discarded. The selection of studies was carried out in two stages: initially, by analyzing the titles and abstracts, followed by a full reading of the eligible texts, ensuring the consistency and relevance of the information to the discussion of the topic.

RESULTS AND DISCUSSION

The findings of this review show that acute exposure to electronic nicotine delivery systems (ENDS) induces significant hemodynamic and vascular changes, with direct implications for cardiovascular risk. Short-term clinical studies show that the use of ENDS containing nicotine raises systolic and diastolic blood pressure, as well as increasing heart rate, patterns consistent with sympathetic hyperactivation and arterial stiffness. These changes are corroborated by cross-sectional analyses that have associated the use of ENDS with a higher prevalence of chest pain, palpitations, coronary artery disease and arrhythmias. Heart rate variability measurements reinforce this profile, with a reduction in parasympathetic modulation and an increase in sympathetic tone after acute exposure. In addition, impairment of peripheral endothelial function is observed, characterized by redu-

ced flow-mediated dilation and decreased nitric oxide bioavailability, mechanisms closely linked to atherogenesis. Imaging studies confirm reductions in blood velocity and vascular reactivity after ENDS use, suggesting early microvascular dysfunction (BENOWITZ; LIAKONI, 2022; ROSE et al., 2023).

The comparison with combustible cigarettes reveals important nuances. Although ENDS show lower magnitude of changes in ventricular repolarization and arterial stiffness compared to traditional cigarettes, acute exposure to both products raises pulse wave velocity to a comparable extent, indicating a similar impact on arterial stiffness. In addition, ENDS products have been shown to impair myocardial blood flow response to exercise, even without directly altering myocardial contraction or relaxation. In contrast, long-term users of ENDS showed greater arterial stiffness but similar endothelial function to non-smokers, suggesting that the vascular effects may persist even after cessation of use. Studies in smokers who switched to ENDS reported lower blood pressure and heart rate, as well as improvement in markers of vascular function, indicating relative benefits, although not without risks. (ROSE et al., 2023; SHAHANDEH; CHOWDHARY; MIDDLEKAUFF, 2021)

The results of this analysis highlight that acute exposure to nicotine via ENDS triggers adverse cardiovascular responses, including elevated blood pressure, tachycardia and arterial stiffness, mechanistically associated with sympathetic hyperactivation and endothelial dysfunction. These findings are consistent with the literature which points to nicotine as the main agent responsible for hemodynamic alterations, even in the absence of combustion. The reduction in the bioavailability of nitric oxide and the increase in oxidative stress following the use of ENDS suggest a pathophysiological pathway common to traditional smoking, albeit with less intensity. However, the magnitude of these effects varies according to the presence of nicotine in the e-liquid, reinforcing the central role of this substance in mediating cardiovascular damage (BENOWITZ; LIAKONI, 2022; ROSE et al., 2023).

In addition to the hemodynamic effects already discussed, recent evidence indicates that the aerosols generated by ENDS, even those free of nicotine, can induce structural and functional changes in the vascular endothelium, affecting the bioavailability of nitric oxide and promoting endothelial inflammation. The American Heart Association's scientific statement points out that components such as propylene glycol, glycerol and flavoring additives, often present in e-liquids, are associated with increased production of reactive oxygen species and mitochondrial oxidative damage, culminating in endothelial dysfunction and increased arterial stiffness. These effects are particularly worrying in chronic users and in vulnerable populations, such as adolescents and individuals with pre-existing cardiovascular diseases, suggesting that the risk associated with the use of ENDS is not limited to the presence of nicotine, but involves a complex interaction between multiple constituents of inhaled aerosols (ROSE et al., 2023).

In addition, studies show that the acute use of nicotine-containing ENDS leads to an increase in circulating biomarkers of oxidative stress, although to a lesser extent when compared to conventional smoking. Evidence indicates an increase in reactive oxygen species, activation of the NADPH oxidase pathway and increased expression of inflammatory cytokines after exposure to e-liquid aerosols. These effects are enhanced by flavoring additives such as cinnamaldehyde and vanillin, which induce mitochondrial dysfunction and reduce endogenous antioxidant capacity. Although the presence of nicotine is strongly

associated with these changes, there is also evidence that vehicles such as propylene glycol and glycerin contribute to the systemic inflammatory profile, even in nicotine-free products. These findings reinforce the hypothesis that the cardiovascular risk of ENDS is not limited to a single component, but results from the synergistic interaction between multiple constituents present in inhaled aerosols. (ROSE et al., 2023)

Despite the claims of harm reduction associated with heated smokeless tobacco (HNB) products, such as IQOS, the available clinical data is ambiguous. Although some inflammatory and lipid biomarkers show improvement compared to traditional smoking, studies show that HNB induce acute arterial stiffness, oxidative stress and endothelial dysfunction in a similar magnitude to that observed with combustible cigarettes. In addition, exposure to HNB aerosols in animal models and humans triggers cytotoxicity in bronchial epithelial cells and pulmonary inflammation, factors that can exacerbate cardiovascular comorbidities. These findings suggest that although the reduction of non-nicotinic toxicants in HNB is measurable, their cardiovascular effects remain clinically relevant and insufficiently mitigated (FRIED; GARDNER, 2020; SHAHANDEH; CHOWDHARY; MIDDLEKAUFF, 2021).

It is worth noting that nicotine is an agonist of the nicotinic acetylcholine receptor in the peripheral and central nervous system, i.e. it is related to the reinforcement systems, which contributes to the dependence of the individual who uses it and, consequently, their chronic exposure (OGA; CAMARGO; BATISTUZZO, 2021).

The transition from traditional cigarettes to ENDS or HNB may represent a harm reduction strategy for chronic smokers, as evidenced by the improvement in hemodynamic and inflammatory parameters in some studies. However, the persistence of vascular alterations and the induction of oxidative stress even with smokeless products highlight that no form of nicotine consumption is risk-free. The lack of long-term prospective data on cardiovascular events in ENDS and HNB users limits understanding of the cumulative impact of these products, especially in populations with greater vulnerability, such as the elderly or individuals with pre-existing comorbidities. In addition, the social normalization of electronic devices among young people may perpetuate nicotine dependence, delaying the cardiovascular benefits of total abstinence (BENOWITZ; LIAKONI, 2022; ROSE et al., 2023; SHAHANDEH; CHOWDHARY; MIDDLEKAUFF, 2021).

In summary, although ENDS and HNB have different toxicity profiles to traditional cigarettes, their acute and chronic cardiovascular effects reinforce the need for caution when promoting these products as safe alternatives. Even though the Food and Drugs Administration (FDA) has the authority to regulate the manufacture, marketing, distribution and sale of tobacco products, it faces challenges due to continuous innovation in the tobacco market, such as the emergence of new vaporization products. These challenges are exacerbated by gaps in regulation that allow the tobacco industry to continue selling many products that are easily accessible to children and young adults (ROSE et al., 2023), making it necessary to strengthen public policies that prioritize complete smoking cessation, coupled with educational efforts that elucidate the residual risks associated with chronic nicotine exposure, regardless of the route of administration. Longitudinal studies are urgently needed to elucidate the temporal relationship between ENDS/HNB use and clinical outcomes such as myocardial infarction and stroke (BENOWITZ; LIAKONI, 2022; ROSE et al., 2023; SHAHANDEH; CHOWDHARY; MIDDLEKAUFF, 2021).

CONCLUSION

This review shows that, although electronic nicotine delivery devices (ENDS) and heated tobacco products (HNB) have different toxicity profiles and, in certain respects, are attenuated compared to conventional cigarettes, the adverse effects on the cardiovascular system remain substantial and clinically relevant. Acute and chronic exposure to nicotine - regardless of the route of administration - is associated with endothelial dysfunction, increased arterial stiffness, sympathetic hyperactivity and intensified oxidative stress, pathophysiological mechanisms directly implicated in the genesis and progression of cardiovascular diseases.

Furthermore, the constituents present in the aerosols of these devices, such as hygroscopic solvents, flavorings and metals from the heating elements, have significant toxic potential, even in the absence of nicotine, contributing to vascular inflammation and functional impairment of the endothelium. These findings corroborate the notion that cardiovascular risk is not restricted to nicotine alone, but results from a complex synergy between multiple chemical components.

Considering the exponential growth in the use of these products, especially among young people, it is imperative to strengthen public policies aimed at strict regulation, restricting access and implementing educational and preventive strategies. The dissemination of the idea that ENDS and HNB are safe alternatives to traditional smoking lacks robust scientific support, especially given the scarcity of longitudinal studies evaluating their long-term cardiovascular effects.

Thus, there is a need for interdisciplinary actions that promote comprehensive cessation of nicotine use, combined with the formulation of guidelines based on up-to-date and contextualized scientific evidence. In addition, conducting prospective research, with rigorous methodological designs, is essential to elucidate the clinical outcomes resulting from chronic exposure to these products, thus supporting more effective regulatory decisions and tobacco control strategies that prioritize the preservation of collective cardiovascular health.

REFERENCES

BENOWITZ, N. L.; LIAKONI, E. Tobacco use disorder and cardiovascular health. **Addiction**, v. 117, n. 4, p. 1128–1138, abr. 2022.

FRIED, N. D.; GARDNER, J. D. Heat-not-burn tobacco products: an emerging threat to cardiovascular health. **American Journal of Physiology-Heart and Circulatory Physiology**, v. 319, n. 6, p. H1234–H1239, 1 dez. 2020.

OGA, Seizi; CAMARGO, Márcia Maria de Almeida; BATISTUZZO, José Antonio de Oliveira. **Fundamentos de toxicologia**. 5. ed. São Paulo: Atheneu, c2021. 848 p. ISBN 978-65-5586-216-4.

ROSE, J. J. et al. Cardiopulmonary Impact of Electronic Cigarettes and Vaping Products: A Scientific Statement From the American Heart Association. **Circulation**, v. 148, n. 8, p. 703–728, 22 ago. 2023.

SHAHANDEH, N.; CHOWDHARY, H.; MIDDLEKAUFF, H. R. Vaping and cardiac disease. **Heart**, v. 107, n. 19, p. 1530–1535, out. 2021.