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SMOKING AS AN UNFAVORABLE LIFESTYLE FACTOR FOR THE PROGRESSION OF PRIMARY OPEN-ANGLE GLAUCOMA

Abstract. Introduction: Smoking remains a widely used and socially accepted psychoactive substance. According to a July 2024 national survey by the Bureau of National Statistics of Kazakhstan, 20.7% of the adult population are smokers–39.8% of men and 7.6% of women.Smoking is the leading preventable health risk and a major cause of premature death, associated with increased rates of cardiovascular, respiratory, gastrointestinal, endocrine diseases, and cancer.

Methods: This study is a literature review. Databases including PubMed, Scopus, Web of Science, and Springer were searched using the terms “smoking” and “primary open-angle glaucoma” for the period from 1990 to 2024. Duplicates were removed. The selected literature focused on the roles of microcirculation and neurodegeneration in glaucoma.

Results: Cigarette smoke contains over 7,000 chemicals, including 69 known carcinogens. Sidestream smoke, which constitutes 75% of total smoke, is more toxic than mainstream smoke and contributes to passive smoking.Smoking–both active and passive–causes mitochondrial dysfunction, oxidative stress, and systemic inflammation. It negatively affects the vascular endothelium and the nervous system, increas- ing neurotoxins like beta-amyloid and TNF- , while reducing protective factors like BDNF. These effects contribute to **primary open-angle glaucoma (POAG)**, now recognized as a neuroinflammatory disease with mitochondrial origins.

Conclusion: Primary open-angle glaucoma is a neuroinflammatory disease of the optic nerve and central nervous system that leads to systemic neurodegeneration. To positively influence the progression of glaucoma, the avoidance of iatrogenic risk factors is essential. Smoking has numerous unfavorable influences on the glaucomatous process, which are summ arized in this mini-review. This makes it absolutely necessary to refrain from smoking in the case of glaucoma.

Key words: smoking, glaucoma, mitochondriopathy, neurodegeneration, microcirculation.

Introduction

Smoking is a socially recognized psychotropic substance that is still widely used. From the Bureau of National Statistics Agency for Strategic Planning and Reforms of the Republic of Kazakhstan, an annual survey of the adult population on tobacco consumption was conducted in July 2024 [1]. The results showed that of the total number of household members surveyed, 20.7 percent of the population, or 39.8 percent of men and 7.6 percent of women, currently smoke tobacco.

Smoking is the single most significant health risk in industrialized nations and the leading cause of premature mortality. Diseases that occur more frequently in smokers include cardiovascular, gastrointestinal, respiratory, endocrine, and cancer diseases [2].

Globally in 2019, 1.14 billion individuals were current smokers, who consumed 7–41 trillion cigarette-equivalents of tobacco in 2019. Globally in 2019, smoking tobacco use accounted for 7.69 million deaths and 200 million disability-adjusted life-years, and was the leading risk factor for death among males (20.2% of male deaths). 6.68 million of 7.69 million deaths attributable to smoking tobacco use were among current smokers [3].

Material and methods

This study is an evaluation review. The literature was searched in the databases PubMed, Scopus, Web of Science, and Springer. Duplicate publications have been checked and deleted. The literature search was carried out using the terms “smoking” and “primary open-angle glaucoma” in the period 1990 to 2024. The selection of papers was made in the context of microcirculation and neurodegeneration of glaucoma..

Results and discussion

Burning a cigarette produces about 2 liters of smoke. According to the American Lung Association, cigarettes contain around 600 ingredients. Burning cigarettes produces more than 7,000 chemicals. At least 69 of these chemicals are known carcinogens, and many are toxic (4).

In principle, a distinction is made between mainstream smoke and sidestream smoke. The mainstream smoke is the smoke inhaled by the smoker (25%), while the sidestream smoke is the smoke emitted from the smoldering cigarette tip between puffs (75%). The sidestream smoke together with the exhaled mainstream smoke is considered pas- sive smoking. Passive smoking is often neglected in discussions, although the carcinogenic substances in sidestream smoke are up to 130 times higher than in mainstream smoke due to the combustion process.

Cigarette smoking, smoking with an electronic cigarette and passive smoking all lead to significant mitochondrial dysfunction (5). The consequences are a depolarization of the mitochondria, which leads to accelerated apoptosis. In addition, there is increased intracellular lipid peroxidation and protein oxidation as well as DNA damage. This triggers a far-reach- ing inflammatory reaction that attacks the immune system and can also trigger autoimmune processes (6,7). The toxic effect of smoking on the vascular endothelium leads to endothelial dysfunction and is partly responsible for the development of arterial hypertension (8). Smoking is also neurotoxic. In the cerebrospinal fluid, there is a significant increase in beta-amyloid, a classic marker for Alzheimer's disease, as well as an increase in tumor necrosis factor-alpha (TNF-α), a cytokine that is involved in almost all inflammatory reactions (9). TNF-α is the first cytokine released in the signaling cascade of activated macrophages. Its most important function is the activation of various immune cells. Furthermore, the neuronal growth factor BDNF (brain derived neurotrophic factor) is significantly reduced in the cerebrospinal fluid (9), which plays an important role in the formation of functional synapses in the nervous system and has neuroprotective properties (10). This leads to neuroinflammation in the central nervous system, which favors central neurodegeneration in POAG (9,11). These processes are supported by an unfavorable influence of smoking on the enteric microbiome, the bacterial composition of the intestine, which can lead to a disruption of the gut-brain axis (12).

These findings are of great importance for primary open-angle glaucoma (POAG), as POAG is now regarded as a neuroinflammatory disease that has its origin in a primary mitochondriopathy [13,14]. The resulting mitochondrial dysfunction manifests itself, among other things, in a reduced metabolism of free radicals and thus increased oxidative stress, reduced ATP production, instability of the cellular plasma membrane with uncontrolled influx of messenger substances and calcium into the cell as well as in the induction of metabolic dysfunctions [15]. This results in an excessive cellular immune response and an inflammatory reaction, which leads to an acceleration of cellular ageing and apoptosis. These inflammatory processes have demonstrated for POAG [16], which cause ocular and cerebral neuroinflammation [17] and later lead to generalized neurodegeneration [18]. Not only the visual tract, but the entire brain is involved [19]. In addition to the detection of primary mitochondrial genetic defects, the extent of damage the mitochondria is also modified by concomitant systemic diseases, in which, for example, arterial hypertension, diabetes mellitus and dyslipidemia themselves lead to secondary mitochondriopathy and thus exacerbate the primary mitochondriopathy in POAG [20,21,22]. This is of great importance because in Germany, arterial hypertension occurs in 75.5% of POAG, dyslipidemia in 50% and diabetes mellitus in 30% [23].

Whateffectsdoessmokinghave on POAG?

In a meta-analysis published in 2024, no association between smoking and the occurrence of POAG was found (24). However, smoking does have an influence on glaucoma progression. In optical coherence tomography, a significant loss of the retinal nerve fiber layer (25) could be detected in those affected after more than 8 pack years (1 pack year = smoking 20 cigarettes per day for 1 year), and accelerated visual field progression (26) after 20 pack years in achromatic perimetry. In addition to the direct neuroinflammatory and neurotoxic effects of smoking on the nerve fibers, the impairment of ocular perfusion may also be responsible for the accelerated progression. Laser Doppler flowmetry showed reduced retinal blood flow with increased retinal perfusion pressure (27). A reduced capillary perfusion of the optic nerve (28,29) as well as a reduced reactivity of the retinal and papillary vessels to oxygen (30) could be demonstrated with scanning laser Doppler flowmetry. In a recent study, a progressive thinning of the vessel density at the optic nerve was found in OCT angiography after exceeding 22.2 pack-years (31).

In addition to these local perfusion defects, a prospective longitudinal study showed that smoking in

combination with obesity, lack of exercise and malnutrition causes a 2.6 times higher risk of cardiovascular disease in POAG patients (32).

Conclusion

In summary, smoking is extremely unfavorable for POAG patients. It exacerbates the already existing neuroinflammation and neurodegeneration in POAG and additionally worsens ocular and systemic perfusion. For this reason, it is absolutely essential to advise POAG patients to give up nicotine and to make it clear to them that electronic cigarettes are not an alternative. Since smokers usually do not manage to stop smoking themselves (33), smoking cessation therapy should be strongly recommended.

Only when we as doctors consciously position ourselves against smoking can a convincing impetus to stop smoking be given (34).

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