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REVIEW

Smoking and alcoholism: Risk factors for papillitis?

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Introduction: Papillitis is the inflammation of the optic nerve at the level of the optic papilla or optic disc. We did not find enough published studies that corroborate smoking and alcoholism as absolute risk factors for papillitis; however, it has been raised, so we were motivated to conduct this research, with the aim of identifying a statistically significant causal association between these factors and papillitis in our hospital.
Methodology: An analytical study of cases and controls was carried out in patients with papillitis treated at the Ophthalmology Centre of Santiago de Cuba (2017–2019). Group 1 (cases): 42 patients; group 2 (controls): 84 patients' companions who attended in the same period and did not present ophthalmological entities.
Results: In the association of smoking with papillitis, we obtained an odds ratio (OR) = 1.60, with confidence interval (CI): [0.74; 3.48], but $p > 0.05$. Alcoholism with papillitis resulted in an association with OR = 1.19, with CI: [0.53; 2.68] and $p > 0.05$.
Conclusion: In this study, smoking and alcoholism had no statistically significant causal association with papillitis.

Keywords: alcoholism, smoking, papillitis, optic nerve, optic neuropathy

1. Introduction

Optic is the most common cause of optic nerve injury in young adults (1). It can be anterior (also called papillitis) or posterior (retrobulbar). The American Academy of Ophthalmology (AAO) defines papillitis as inflammation of the optic nerve at the level of the papilla or optic disc (2). In this research, we will focus our attention on this ophthalmological entity, as it is a frequent reason for consultation in neuro-ophthalmology, and its sequelae can significantly affect the vision. Many studies have been carried out over the past decade with the aim of clarifying its main causes (3–5).

Papillitis is caused by different aetiologies, from common causes such as infections to less reported ones such as lightning strikes (6). Other associations include papillitis with intraocular disease; in the course of systemic, connective tissue or autoimmune diseases; (7) secondary to insect bites or stings; (8) among others. The risk factors for papillitis are closely related to its aetiology, with some studies (7, 9) mentioning infections, autoimmune diseases, alcohol consumption and smoking as risk factors.

We will focus our attention on the latter two. Tobacco use is well established as one of the leading causes of death in the world, accounting for around 5–6 million deaths per year globally. Under current patterns of consumption, during the 21st century, some 1 billion deaths may occur from smoking, in contrast to only 100 million deaths in the 20th century from the same cause (10).

In the United States, in 2017, 34.3 million adults aged 18 years and older (14% of US adults) were estimated to be smokers, and smoking prevalence is higher among men than women (15.8% vs. 12.2%) (11). In the same year, 7.4 million adults (15.1% of adults) in the United Kingdom were estimated to be smokers (17% of men and 13.3% of women) (12). In Russia, the prevalence of smoking is considered by WHO to be one of the highest in the world and has been estimated at 60% (13). In Cuba, smoking prevalence is estimated to be one of the highest in the world.

In Cuba, smoking prevalence has been considered high for as long as information has been available. The first data on national smoking prevalence in Cuba dates back to 1978, from a survey conducted by the Ministry of Internal Trade, in which 68.9% of the population aged 17 years and older smoked (14, 15). Among 78 WHO member countries, Cuba ranks 28th in smoking prevalence, which is currently 38.2% (15).

Tobacco smoke contains up to 4,000 active compounds, the majority of which are toxic in acute or long-term exposure (16). Smoking has been linked to systemic diseases such as lung cancer, cerebrovascular and cardiovascular diseases, and gastrointestinal disorders, (10) as well as to different ocular diseases; among them, age-related macular degeneration (AMD) is the most common in people aged over 50 years in industrialized countries. It is caused by smoking in the United Kingdom, Canada, the United States of America, and Australia (17). Both the development of cataracts and AMD are directly accelerated by smoking (18).

There are other diseases where well-documented studies have demonstrated the influence of smoking, including polypoidal choroidal vasculopathy, (19) diabetic retinopathy, (20) ocular inflammations (uveitis, scleritis and episcleritis), (21) dysthyroid orbitopathy, (22) as well as toxic-nutritional optic neuropathy, formerly called tobacco-alcoholic amblyopia, (20) and Cuban epidemic optic neuropathy. Fuentes Pelier D. Epidemiological and clinical evolution of patients with Cuban epidemic optic neuropathy in Santiago de Cuba. Doctoral thesis (23).

As for alcohol, it is important to bear in mind that it is a psychoactive substance with dependence-causing properties, which has been widely used in many cultures for several centuries (24). According to the WHO, (25) 3 million deaths occur each year worldwide due to the harmful use of alcohol, representing 5.3% of all deaths; it is a causal factor in more than 200 diseases, and 5.1% of the global burden of disease and injury are attributable to alcohol consumption.

In the United States of America, with 300 million inhabitants, there are currently 20 million alcoholics, and the expectation that those born today may have alcoholism is 13.7%. The comparative situation in Latin America, whose population is twice that of North America, is also at risk, with the current existence of some 40 million alcoholics (26).

In Cuba, it is considered that 45.2% of the population over 15 years of age consumes alcoholic beverages, mainly in the 15–44 age range, and the majority of alcohol-dependents are between 25 and 42 years of age. In the last 15 years, there has been an increasing trend in consumption on a societal scale (24).

Alcohol use causes death and disability at a relatively young age. It is associated with the risk of developing health problems such as mental disorders, major non-communicable diseases such as cirrhosis of the liver, some types of cancer and cardiovascular diseases, as well as injuries resulting from violence and road traffic accidents (25).

As for ophthalmological conditions, the most recognized is toxic-nutritional optic neuropathy of multifactorial aetiology (27). It is the most frequent cause of bilateral optic neuropathy, especially in adults (28). Toxic optic neuropathy has also been described in cases of ingestion of 600–700 ml of methanol (29). The clinical picture is characterized by acute central visual loss. The patient usually inadvertently ingests the toxin, which is often present in alcoholic beverages distilled at home. Other sources of methanol poisoning include ingestion of paint solvents, gasoline additives, antifreeze and windshield fluid (30).

Regarding the latter two, we did not find enough published studies to corroborate them as absolute risk factors for papillitis, so we were motivated to conduct this research with the aim of identifying statistically significant causal associations between smoking and alcoholism with the development of papillitis.

2. Materials and methods

This is an analytical, case-control study of patients with papillitis seen at the Ophthalmology Centre of Santiago de Cuba (2017–2019). Group 1 (cases): 42 patients; and group 2 (controls): 84 patients' companions, who attended in the same period and did not present ophthalmological entities. Due to the number of cases, it was decided to select two controls for each case. To calculate the sample size, we used an expected proportion of 45% of exposed cases and 20% of unexposed cases, an expected odds ratio (OR) of 2, two controls for each case and a confidence interval (CI) of 95%. The Declaration of Helsinki was taken into account during the research, as well as the ethical principles and regulations established by the Ethics Committee of our institution.

A literature search was conducted in the PubMed, ClinicalKey, ClinicalTrials.gov, Lilacs, EBSCO, Hinari and SciELO; Index Medicus and Cuban Medical Journals. To identify possible associations between variables, contingency tables were designed, whose analysis made it possible to estimate the OR, its CI, as well as the level of statistical significance of the difference between the groups.

3. Results and discussion

In this study, regarding the causal association of smoking with papillitis, we obtained an OR = 1.60, but its CI: [0.74; 3.48] and $p > 0.05$ reflect that it is not a direct risk factor for developing the disease, as shown in **Table 1**. Similar results were found by Ciesielski et al. (31) who analyzed the immediate effect of smoking on the optic nerve and macular perfusion measured in healthy regular smokers. Their results have shown a lack of immediate effects of cigarette smoking on the vascular density of the central retina and optic disc region in healthy regular smokers. This is in agreement with

TABLE 1 | Cases and controls according to smoking status.

Smoking	Cases		Controls		Total	
	n	%	n	%	N	%
Exposed	13	31.0	23	27.4	36	28.6
Unexposed	29	69.0	61	72.6	90	71.4
Total	**42**	**100.0**	**84**	**100.0**	**126**	**100.0**

OR = 1.60, CI: [0.74; 3.48], $p > 0.05$.

TABLE 2 | Cases and controls according to alcoholism.

Alcoholism	Cases		Controls		Total	
	n	%	n	%	N	%
Exposed	13	31.0	23	27.4	36	28.6
Unexposed	29	69.0	61	72.6	90	71.4
Total	**42**	**100.0**	**84**	**100.0**	**126**	**100.0**

OR = 1.19, CI: [0.53; 2.68], $p > 0.05$.

Holló (32) who suggested that both macular and peripapillary vessel density values in healthy middle-aged smokers were not influenced by acute cigarette smoking.

Nevertheless, it is important to consider smoking in the toxic history and habits when evaluating patients with papillitis, as these aforementioned researchers did not evaluate the long-term effect of smoking. Furthermore, in our study, there was a higher frequency of smoking (40.5%) in the case group than in the control group (29.8%), although it was not statistically proven to be a risk factor.

In this NOInA case report, as we have mentioned, no causal association of smoking with the disease was observed, since smoking is not frequently described in studies on papillitis as it generates another specific type of neuropathy, the toxic-nutritional one. This clinical entity often presents with a gradual, symmetrical and bilateral decrease in visual acuity, scotomas and pallor of the optic disc (33).

As for the pathological mechanism, it is presumed that free radicals in tobacco impair the mitochondrial DNA respiratory chain, resulting in changes in mitochondrial morphology leading to demyelination (34). Toxic optic neuropathy attributed to smoking (especially cigar or pipe smoking) is a diagnosis of exclusion, and other aetiologies should be explored, including mitochondrial optic neuropathies, for example, Leber hereditary optic neuropathy (30).

As an interesting fact, we found that the use of electronic cigarettes in several developed countries is applied as a smoking cessation mechanism (35). However, it is controversial, as some studies have reported that their use has become very common among young people and has induced them to start smoking real cigarettes (36). This is to draw attention to disease prevention; not starting or stopping smoking are the best ways to prevent and avoid the development of smoking-related neuropathies.

As for alcoholism and papillitis, as can be seen in **Table 2**, there was no causal association, as we obtained OR = 1.19, with CI: [0.53; 2.68] and $p > 0.05$. This means that it does not constitute a direct risk factor for suffering from the disease; similar to what occurs with smoking, as both toxic habits generate a specific type of neuropathy, which is not the previous inflammatory type, as we have explained.

Some authors (30) even argued that alcohol is no longer considered a direct cause of toxic optic neuropathy, but it is associated with a higher incidence of nutritional deficiencies, some of which may cause optic neuropathy. In the cases group, those exposed were 31.0%, which is higher than the controls group, where those exposed represented 27.4%, so this issue remains controversial, and it is important to evaluate this history carefully in each patient.

4. Conclusion

In this study, smoking and alcoholism were not statistically significant risk factors for papillitis.

Author contributions

DH-F, MV-M, and DF-P: information research, data collection, proofreading, and editing. DH-F and EZ-Á: statistical analysis. DH-F, MV-M, DF-P, and EZ-Á: manuscript writing. All authors contributed to the article and approved the submitted version.

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