EYE-HEALTH CAN START ON THE LIPS

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ABSTRACT:

Primary open-angle glaucoma (POAG) is a progressive optic nerve disease characterized by neurodegeneration of retinal ganglionic cells and their axons. Local inflammatory responses are implicated in the pathology of glaucoma. Despite the large number of studies conducted to identify non-genetic risk factors, only race, age, intraocular pressure, and corneal thickness were consistently identified. Of these, only intraocular pressure is a modifiable factor and also the only means we have at our fingertips to influence the development of glaucomatous disease. Tooth loss or periodontal disease is associated with systemic endothelial dysfunction, which has been implicated in primary open-angle glaucoma. The main hypothesis behind this correlation is that infectious and inflammatory processes located in the teeth can produce factors that will be released into systemic blood circulation. At the eye level, these factors are responsible for triggering the inflammatory response, neurodegeneration and, in some cases, open-angle glaucoma. Mounting evidence suggests that neuroinflammation is a key process in glaucoma, while the precise roles are yet to be discovered. In this article we reviewed the literature on neuroinflammation in glaucoma triggered by oral cavity microbiota and infiltration of peripheral immune cells. In conclusion, if an association between dental health, the oral microbiome and POAG were established, this would have potentially significant implications for the understanding and management of glaucoma and possibly other neurodegenerative diseases and we will be able to work together in order to prevent both glaucoma and dental diseases.

Key words: glaucoma, neuroinflammation, oral microbiota, periodontal disease.

INTRODUCTION

The oral cavity will always be an individual business card. Each element, starting with the smell, quantity and composition of saliva, gum health, and aspect of the teeth can provide information on the body of the person concerned.

Oral infections which could lead to loss of teeth or periodontal disease, have been correlated with a series of systemic conditions such as diabetes, cardio-vascular diseases, rheumatoid arthritis, certain types of cancer and neurodegenerative diseases (1-6).

Periodontitis is a bacteria-induced oral inflammatory condition, which can trigger endothelial dysfunctions and a chronic inflammatory response to other extraoral tissues (7-9).

Moreover, the inflammatory markers generated by the inflamed periodontal tissue, can reach other organs through the blood flow. For example, in neurodegenerative diseases such as Alzheimer's or Parkinson's, there are more and more evidence that the peripheral inflammation exacerbates the loss of neuronal cells (3,4). A third mechanism is the immune response triggered in the presence of bacteria, involving antibodies generation for the bacteria and toxins released by them, which may have off-target effects in extraoral tissues (10).

Open-angle glaucoma (OAG), one of the most common causes of blindness on a global level, is a chronic condition characterized by neurodegeneration of retinal ganglionic cells and their axons. Considering the increased prevalence of this pathology and the extremely delicate clinical aspects and public health aspects, we have very few accurate data concerning the risk factors that trigger the neurodegeneration process.

The risk of OAG development in first-degree relatives is 7-10 times higher than in the general population (11) and there is a high consistency with monozygotic twins (12). There are researches that associate OAG with 15 different genomic regions (OMIM GLC1A-GLC1P), further emphasizing the polygenic nature of this pathological condition. In addition, there are specific genes such as myocilin and optineurin, which however, have been identified in too few cases of glaucoma. Despite the large number of studies conducted to identify non-genetic risk factors, only race, age, intraocular pressure, and corneal thickness were consistently identified (13-17). Of these, only intraocular

pressure is a modifiable factor and also the only means we have at our fingertips to influence the development of glaucomatous disease.

In recent years, more and more studies have confirmed that gum inflammation can be a risk factor for the development of OAG. The main hypothesis behind this correlation is that infectious and inflammatory processes located in the teeth can produce factors that will be released into systemic blood circulation. At the eye level, these factors are responsible for triggering the inflammatory response, neurodegeneration and, in some cases, OAG (18,19).

Dr. Louis Pasquale and his team investigated approximately 40.000 men for the Health Professionals Follow-up Study between 1986 and 2012 (20). The men chosen for the study were under the observation of an ophthalmologist and did not suffer from OAG. Every two years, the participants reviewed the number of teeth they had, the number of teeth lost and other signs of periodontal inflammation and bone loss. During the study, there were 483 cases of confirmed OAG that were classified as having paracentral visual field loss or only peripheral visual field loss. The risk of developing OAG was 43% higher in patients who reported loss of one or more teeth compared to those who managed to keep their dentures integral. The risk of OAG was even 86% higher in patients who reported tooth loss associated with periodontal disease (21).

The research team assumed that the vascular bed at the base of the tooth may the overflow pipeline of cytokines and microbes into the systemic circulation, leading to dysfunction of endothelial cells that finally compromise retinal nerve cell axons. Periodontal disease is associated with a vasodilatation mediated by blood flow, and treatment of periodontal inflammation has led to decreased vasodilation. It is important to underline that OAG has also been correlated with vasodilatation associated with deranged blood flow, and some studies on genetic and environmental aspects have reported altered endothelial cell function as the basis of the paracentral scotoma in OAG (21).

Although the association may be random and not in a cause-effect relationship, the results may influence the anamnesis, screening methods for glaucoma, and may be even revealing about disease pathogenesis and treatment.

In support of these statements, there is a study (19) conducted at the SUNY

Downstate Ophthalmology clinic, where the researchers wanted to observe whether the reason for the exacerbation of present neurodegeneration is supported by chronic subclinical inflammatory processes. For this purpose, they collected the oral bacterial load from patients diagnosed with OAG. Moreover, they administered bacterial components (lipopolysaccharide – LPS) to groups of laboratory mice. As for the mice, they were divided into two groups: a model with spontaneous glaucoma and one with induced glaucoma. During the experiments, it was observed that the subcutaneously administered LPS treatment induced an increase in components of the immune system (TLR4 and complement) and an acceleration of the optic and retinal nerve damage in both groups of mice. Toll-like receptors (TLR) immunological components are known to be involved in neurodegenerative diseases, including in glaucoma (18). In terms of the amount of bacterial species found in oral microbiota of patients, these were much more prevalent in patients with OAG, both gram positive and gram negative ones.

Another case-control study, performed on a group of 119 adults with OAG and 78 healthy controls, revealed a higher number of Streptococcus bacteria in patients with OAG. The findings are similar to those of the previous studies, namely that bacteria play the role of catalyst in triggering inflammatory reactions that cause oxidative stress in the neuronal cell and including death. It is intriguing that contrary to expectations, patients with milder POAG had slightly (but statistically) increased signs of periodontal disease compared to those with more severe disease. This would suggest that at the moment, periodontal infections precede the development of severe glaucomatous damage and may thus contribute to ongoing glaucomatous neurodegeneration. If so, improved dental care may become relevant even to patients with established glaucoma (22).

The questions that arise from these researches generate new study subjects regarding the way in which severe periodontitis influences the progression of glaucoma and whether or not prompt treatment of oral pathologies can inhibit the development of glaucoma.

In conclusion, if other studies will prove the causality between oral hygiene and glaucoma, then we will identify a new weapon in the fight against vision loss, and we will be able to work together to prevent both glaucoma and dental diseases.

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