Glaucoma has been described as a “sick eye in a sick body,” and there has been much research on systemic diseases that may cause or correlate with the development of glaucoma.

Likewise, the medical treatments often prescribed for glaucoma can affect a patient’s systemic health and underlying medical comorbidities. This article concentrates on the relationship of primary open-angle glaucoma with systemic illnesses.

WHICH SYSTEMIC DISEASES CORRELATE WITH GLAUCOMA’S DEVELOPMENT?

Systemic Hypotension

There is reasonable evidence to support the concept that systemic hypotension, whether caused primarily or by the overtreatment of systemic hypertension, can cause glaucoma to develop and worsen its progression.\(^3\) This is particularly true for normal-tension glaucoma (NTG), and the effects of hypotension seem to be even worse if the patient’s blood pressure dips too low nocturnally.\(^3\)

Systemic Hypertension

Although there seems to be a relationship between systemic blood pressure, as it relates to ocular perfusion pressure, and glaucoma, the evidence is contradictory about systemic hypertension and glaucoma.\(^3\) It has been suggested that the extremes of blood pressure, both too low and too high, may be deleterious for glaucoma.\(^5\) Blood pressure measurements, however, do not correlate well with IOP measurements. Many large-scale studies have addressed the hypertension question, but the results are not conclusive. More research is needed to obtain better answers.

Migraine and Vasospasm

Migraine and vasospasm appear to be related to the development of NTG in particular.\(^3\) At this point, however, there is no good evidence to show that treating migraine or vasospasm offers benefits in terms of glaucoma (Figure 1).
THE RELATIONSHIP BETWEEN SJÖGREN AND DRY EYE

By Paul Singh, MD

For many patients, dry eye disease (DED) is a persistent problem that leads to a level of discomfort highly detrimental to their quality of life. During counseling, these patients often tell me that they have visited three or four doctors in an attempt to get relief from the burning, itching, fluctuating vision, and redness. Although we eye care professionals aggressively treat conditions such as uveitis and corneal abrasion, we often have a more relaxed approach to treating DED. Not only should we be more diligent in relieving the uncomfortable—even painful—symptoms of this syndrome, we should also consider every manifestation of DED as a hallmark of a potential systemic disease. Diagnosing Sjögren syndrome in patients with DED, for example, can help provide a clearer, targeted treatment path.

DIAGNOSIS

As many as 4 million people in the United States suffer from Sjögren syndrome, but only 1 million have been diagnosed.1-3 This discrepancy is largely due to the fact that biomarkers associated with traditional Sjögren syndrome testing—Sjögren-specific antibody A, Sjögren-specific antibody B, rheumatoid factor, and antinuclear antibody—are not specific or sensitive enough to accurately identify the disease at an early stage. A new serology test for Sjögren syndrome (Sjo; Nicox) includes the identification of three novel biomarkers—salivary gland protein-1, carbonic anhydrase-6, and parotid secretory protein—in addition to the aforementioned traditional biomarkers. This comprehensive diagnostic panel helps to detect Sjögren syndrome earlier and with a high specificity and sensitivity.4 The test also displays markers indicative of other autoimmune diseases such as rheumatoid arthritis.

THE TEST IN PRACTICE

I use Sjö in my practice to identify a potential systemic etiology in DED patients whom I suspect of having deeper problems. I have found that close to 40% of my DED patients also experience dry mouth and dry skin, yet some do not notice those symptoms until I question them. This is valuable information, as it relates to the possibility of systemic disease, particularly Sjögren, which attacks the lacrimal and salivary glands and, if left untreated and unmonitored, increases patients’ risk of developing lymphoma.5 Knowing if an autoimmune cause underlies a patient’s DED enables me to tailor my treatment plan accordingly and ultimately improve his or her outcomes.

Once my colleagues and I decided to start screening for Sjögren syndrome in our practice, we leveraged our established relationships with rheumatologists, who are able to manage affected patients from a systemic standpoint. When an autoimmune disease has been diagnosed, many promising medications can be prescribed, including hydroxychloroquine and other immunosuppressors. Just as with numerous other diseases, beginning treatment early in the disease state increases the chances of controlling symptoms and progression.

CONCLUSION

As eye care practitioners, it is important for us to take advantage of improvements in the diagnosis and treatment of diseases such as Sjögren syndrome that were previously misunderstood and underdiagnosed. By taking this front-line approach, we gain relevance and, more importantly, become better physicians.

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Hyperthyroidism

Graves disease is associated with glaucoma, most likely due to the orbital congestion that can raise IOP (Figure 2). No clear relationship between hypothyroidism and glaucoma, however, has been established in the literature.2,3

Diabetes Mellitus

Some large studies have implicated diabetes mellitus as a risk factor for glaucoma, but other studies have not found such an association.3 At this point, there is no net conclusive evidence supporting the relationship between the two diseases, so screening glaucoma patients for diabetes is not recommended.2

Sleep Apnea

Although recent studies have suggested a relationship between sleep apnea and glaucoma, the evidence is conflicting overall. IOP has been shown to rise during
continuous positive airway pressure treatment of obstructive sleep apnea. More research is needed to determine if a link between these diseases truly exists.

Miscellaneous
Several small studies have implicated increased blood viscosity, particularly dysregulated platelet aggregation, as a risk factor for glaucoma. Other studies suggest a relationship between autonomic nervous system dysfunction and glaucoma, particularly in the case of NTG. There is also weak evidence supporting autoimmune diseases as contributing to glaucoma’s development. Although a possible link between the pathophysiology of Alzheimer dementia and glaucoma is tantalizing, evidence does not yet exist to support this correlation. Further work must be done to clarify these relationships.

WHICH GLAUCOMA TREATMENTS CAN AFFECT SYSTEMIC DISEASES?

ß-blockers
ß-blocker eye drops such as timolol act upon ß-1 and ß-2 receptors. The ß-1 blockade can decrease cardiac contractility and heart rate, lower systemic blood pressure, and cause an irregular pulse. The ß-2 blockade can increase bronchospasm in patients with underlying asthma or chronic obstructive pulmonary disease. For these reasons, ß-blocker eye drops are generally contraindicated in patients with asthma, bronchospasm, chronic obstructive pulmonary disease, heart failure, sinus bradycardia, atrioventricular block, and cardiogenic shock. Betaxolol, a selective ß-1 blocker, may not have the bronchospastic effects of nonselective ß-blockers.

ß-blockers can also affect the central nervous system, leading to headaches, depression, anxiety, confusion, dysarthria, hallucinations, a tendency to somnolence, and lethargy.

α-2 Blockers
This category of eye drops includes brimonidine and apraclonidine. These agents can cause decreases in blood pressure and pulse, drowsiness, dizziness, and dry mouth.

Carbonic Anhydrase Inhibitors
Particularly when taken orally as acetazolamide or methazolamide, carbonic anhydrase inhibitors (CAIs) can cause dysesthesia of the fingers and around the lips, frequent urination, a lack of energy, anorexia, weight reduction, urolithiasis (kidney stones), metabolic acidosis, and hematopoietic cell restraint anemia. CAIs can potentiate the metabolic effects of other diuretics when taken concurrently, necessitating the monitoring of patients for hypokalemia and hyperuricemia. These systemic side effects, while theoretically possible, do not generally occur when the eye drop forms of CAIs (ie, dorzolamide and brinzolamide) are used.

Parasympathomimetic Drugs
This category of eye drops, including pilocarpine, can activate secretory glands and smooth muscles. Systemic side effects can therefore include drooling, sweating, diarrhea, nausea/vomiting, stomach ache, asthma, bradycardia, hallucinations, and depression.

CONCLUSION
Research has clarified some of the complex relationships between glaucoma and systemic diseases, but others remain unclear and deserve further investigation. In general, patients can reduce the systemic side effects of eye drops by closing their eyes or performing 5 minutes of punctal occlusion immediately after instillation. If the eye provider is not certain whether or not a glaucoma treatment may negatively affect a patient’s systemic issues, his or her primary care provider should be consulted.

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