Dry Eye Syndrome and Two Commonly Overlooked Causes of Dry Eyes

Dry eye syndrome is currently a very prominent topic in optometry. Increased awareness has caused a surge in articles written on the topic and research performed in the field. However, there are still patients slipping through the cracks that are even more at risk for dry eye syndrome or dry eye disease (DED) than the general population.

Most optometrists are aware of the most common systemic conditions and other causes of dry eyes including, Sjögren's syndrome, Rheumatoid arthritis, lupus, and thyroid-related conditions.

Diabetes and glaucoma are two conditions that should be at the top of that list and every optometrists' mind considering the increased risk for dry eye syndrome.

Here's a 36 page guide on understanding dry eye and meibomian gland dysfunction. Learn how you can treat MGD using LipiFlow, and how to bring this technology to your practice.

Dry Eye Syndrome and Diabetes

According to the American Diabetic Association, 29.1 million Americans, or 9.3% of the population, had diabetes in the last year reported (2012) and that number is on the rise.[1]

Diabetes is also one of the leading causes of blindness in persons aged 20-74. Cataracts and diabetic retinopathy are the most thought of cause of blindness; however, ocular surface complications such as superficial punctate keratopathy, trophic ulceration, and persistent and recurrent

epithelial erosions need to be realized as a common reason for decreased vision and blindness.[2]

Read more on treatment methods for recurrent corneal erosion.

Secondary complications from diabetes-induced dry eye syndrome include corneal scarring and bacterial infections.

There are **three** proposed mechanisms of DED complications related to systemic diabetes:[3]

1. Neuropathy
2. Metabolic dysfunction
3. Abnormal lacrimal secretions

1) Neuropathy and Dry Eye Syndrome

Decreased corneal sensitivity through neuropathy of the ophthalmic branch of the Trigeminal nerve (CNV) and the long ciliary nerves leads to decrease feedback, decreased healing and basement membrane abnormalities.

This can lead to such things as neurotrophic ulcers, SPK, RCE, and non-healing corneal abrasions. This is of utmost concern for optometrists because a patient may not be complaining of symptoms, but signs of ocular surface disease may be present. It is important for optometrists to astutely assess the corneal structures looking for the aforementioned signs.

2) Metabolic dysfunction

It has been postulated that aldose reductase, which is the first enzyme in the sorbital pathway, may be involved in the process. Decreasing aldose reductase increased healthy tear dynamics in patients.

3) Lacrimal Gland Secretions

Studies using the Schirmer test to measure tear secretion values have shown a reduction in lacrimal secretions in diabetic patients compared to controls, possible due to dysfunction of the autonomic nervous system or due to damage to the microvasculature of the lacrimal glands. Furthermore, there was a decreased TBUT in diabetic patients.[2] It has also been shown that diabetics' tear protein composition differs from that of healthy individuals.[3]

The prevalence of dry eye disease in patients with concomitant diabetes ranges widely from high teens to over 50%. One study examined 199 diabetic patients for signs of dryness using a diagnostic criteria of decreased TBUT less than 15 seconds or Schirmer test value less than 15mm after five minutes.

The examiner also confirmed the diagnosis with ocular surface dye staining with fluorescein. They found the prevalence of dry eye syndrome in diabetic patients to be 54.3%.[2] The study also found a clinically **significant association between duration of diabetes and dry eye disease** ($p = 0.01$).

Dry eye disease was also more frequent in patients with diabetic retinopathy ($p = 0.02$).[2]

Another study used a 308 mOsm/L cutoff to diagnose dry eye disease using an osmolarmeter. They found the prevalence of dry eye disease in diabetic patients to be 27.7% and also confirmed a correlation between dry eye disease and retinopathy ($p = 0.01$).[3] The study also showed a significant odds ratio for dry eye disease with increased HbA1C levels ($p = 0.04$).[3]

Optometrists should be routinely examining for dry eye disease in patients, but should employ more tactics when dealing with an at-risk population.

Including TearLab® Osmolarity testing and a dry eye questionnaire, such as

the OSDI or SPEED, as part of your diabetic examination can not only help your patients but can be a source of new revenue.

Treatment should be initiated based on exam findings with special attention given to those patients with high HbA1C levels, long duration of diabetes, or with diabetic retinopathy, all of whom may need a higher level of dry eye disease treatment.

Dry Eye Disease and Glaucoma

It is estimated that three million Americans have glaucoma, half of which do not know they have it yet.[4] According to WHO, glaucoma is the second leading cause of blindness in the world.[4]

While glaucoma is not as prevalent as diabetes in the United States, optometrists are the sole primary doctors responsible for treating glaucoma and are more likely to use multiple topical medications for treatment versus our ophthalmologist counterparts.

The cause of dry eye disease is most likely multifactorial in nature. Glaucoma is more common in an older population where dry eye disease is also more common. In addition, multiple topical glaucoma medications, especially those containing the **preservative benzalkonium chloride (BAK)** and topical carbonic anhydrase inhibitors **(CAI)**, are toxic to the ocular surface.

It has been shown that tear cytokines are elevated in patients on topical medications and can cause complications post-trabeculectomy.[5] Bleb dysesthesia can also disrupt normal tear surface properties exacerbating dry eye disease.

A study of 124 glaucoma patients, 23 of which were control patients, examined dry eye disease using the high validity Ocular Surface Disease Index (OSDI) twelve item questionnaire.

Those with an OSDI score greater than or equal to 12 were diagnosed as having dry eye disease.

The study showed that the "OSDI score increased significantly with increasing glaucoma severity".[5] Using univariate analysis, albeit not as strong as a multivariate model, daily dose of BAK greater than four drops and more than two topical glaucoma medications were strong predictors of OSDI score. The opposite of that was true for those taking no glaucoma treatments where the OSDI score was low.

On multivariate analysis, a daily dose of BAK greater than four drops was an independent risk factor for higher OSDI scores.[5] The duration of glaucoma diagnosis also affected the OSDI score in a significant and predictable way. Those with a glaucoma diagnosis of less than six years had a mean OSDI score of 18 indicating mild DED and those with a diagnosis of greater or equal to six years had a mean OSDI score of 23 indicating moderate DED. The scores were statistically significant between the two groups ($p = 0.03$).[6] The difference between OSDI scores with each addition of a topical glaucoma medication was clinically relevant; however, not statistically significant.[6]

Other studies have shown statistically conclusive evidence that there is a correlation between the number of topical medications administered and the severity and presence of dry eye disease.

The same study evaluated the quality of life of the patients diagnosed with glaucoma using the glaucoma quality of life questionnaire (GQL-15). The GQL is a 15-item patient questionnaire aimed at evaluating subjective ability to perform visually demanding tasks in normal daily living.

There are four main categories assessed: reading and recognizing faces (central/near vision), peripheral vision, darkness/glare, and navigating outside and walking along side roads.

Patients are asked to rate their experience with each question on a scale from zero to five (do not perform for non-visual reasons to severe). *The higher the score, the worse the quality of life for the patient. The test has been validated and has shown high reproducibility and consistency.*

It is well known that peripheral vision loss decreases quality of life (increasing the raw score of the GQL); however, Skalicky et. al. showed that patients with DED had higher GQL-15 raw scores than those without DED. 5. GQL-15 summary scores were found to be the strongest independent predictor of OSDI score. It must be noted however that a patient's subjective response to a questionnaire may be influenced by psychosocial factors and that there may be overlap between conditions causing worsening of quality of life. However, Skalicky et. al. go on to say "the correlation between the two scores [GQL-15 and OSDI] indicates a significant additive impact of both factors with an increased burden from each condition [Glaucoma and DED]."[5]

Due to the effects of glaucoma on dry eye disease, I recommend having all glaucoma patients fill out a qualified DED questionnaire and have their tears tested with an osmolarmeter. This can identify patients at risk for a decreased quality of life and improve ocular health. It should also be noted that topical glaucoma medications are created and tested on eyes with a normal tear osmolarity and having a high tear osmolarity may have detrimental effects on the effectiveness of topical medications.

BAK is the most widely used preservative in ophthalmic topical medications.[6] Unfortunately, it has also been proven to have toxic effects on the cornea and other ocular tissues.

These known toxic effects have pushed pharmaceutical companies to produce preservative-free glaucoma medications as well as alternative preservatives.

Prostaglandins are considered a first-line therapy for glaucoma

management in most patients. For those with BAK sensitivities or DED symptoms, **Zioptan (tafluprost) is the only preservative-free option** in the prostaglandin drug class. It should be noted that bottles of Zioptan not in current use should be stored in a refrigerator. The only other preservative free IOP lowering medications available for our patients are Timoptic (timolol maleate) in Ocudose™ and the combination drug Cosopt PF (dorzolamide/timolol).

There are a few other glaucoma medications that offer an alternative to BAK preservatives. The "P" in Allergan's Alphagan-P alpha-agonist glaucoma medication stands for Purite®. Purite® is a preservative that breaks down when exposed to air. It works by oxidizing microbial cells, but has no significant effect on corneal epithelial cells. SofZia® is found in Travatan-Z and is effective at killing bacteria, which lack specific enzymes, by oxidative destruction. Human cells have the necessary enzymes to protect against the harmful actions of SofZia®.[7]

Glaucoma can easily be treated with non-preservative topical medications for patients with BAK sensitivities or concomitant DED. Prostaglandins and beta-blockers tend to be the most commonly prescribed initial medications for glaucoma, both of which have preservative-free treatment options. If the target IOP is not reached with a combination of these two drops, Timoptic can be replaced with Cosopt PF.

As optometrists, we must consider the cost to the patient and weigh it against the possible benefits. Preservative free topical IOP-lowering drugs can cause a budget burden on our patients. For example, according to goodrx.com, 30 days worth of Zioptan costs about $175 versus $100 for Lumigan and only $15 for generic latanoprost.

We must talk with each patient to understand their concerns and issues and consider their OSDI score, osmolarity score, and quality of life when prescribing topical glaucoma medications.

Sources

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