Lacrimal Drainage Obstruction Associated with Topical and Systemic Medications

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A wide array of pathogenic factors has been associated with lacrimal drainage system obstruction including inflammatory conditions originating from the eye, conjunctiva, lacrimal mucosa, nose and paranasal sinuses; trauma; congenital abnormalities; radiotherapy and neoplasms.

Inflammatory conditions initially cause lacrimal mucosal swelling but may lead to fibrotic narrowing or obstruction of the nasolacrimal drainage conduit. Descending inflammation from the eye or ascending inflammation from the nasal cavity may cause swelling of the mucous membranes of the nasolacrimal duct, remodeling of the helical arrangement of connective tissue fibers, or malfunction in the subepithelial cavernous body causing reactive hyperemia and temporary occlusion of the nasolacrimal duct system. The submucosa of the nasolacrimal duct contains arterioles with sphincters and cavernous vessel complexes; these can cause swelling and approximation of the lumen depending on the amount of blood flow. Due to constriction of tissue within a bony canal, any swelling inevitably leads to blockage. Structural epithelial and subepithelial changes may lead to fibrous closure of the lumen or to a nonfunctional segment causing chronic epiphora and discharge, however the system may seem patent to irrigation.

There are reports on induced inflammatory and fibrotic changes in the conjunctival surface in association with medications especially topical anti-glaucoma and systemic anti-neoplastic agents. Such changes may be related to the medications themselves, the preservatives in the commercial preparations, or the duration of treatment. It seems likely that similar changes may occur in the epithelium and subepithelial tissues of the lacrimal drainage system, resulting in stenosis and occlusion. The upper lacrimal system is close to the conjunctiva and fornix and is expected to be more affected by topical medications than the lower lacrimal system; this is now accepted as a fact in the literature. Topical agents including antiglaucoma medications such as timolol, pilocarpine and dorzolamide; antiviral drops such as idoxuridine and trifluridine; and systemic medications such as fluorouracil and docetaxel are now considered as risk factors for upper lacrimal system obstruction.

A more recent question is whether such medications may have a similar effect on the lower lacrimal system, i.e. the nasolacrimal duct. Kashkouli et al conducted a prospective case series in which diagnostic probing of the canaliculi and irrigation of the nasolacrimal duct was performed in 98 glaucoma patients (130 eyes) taking topical antiglaucoma drops and 178 non-ocular patients (280 eyes) who were taking no topical medications. The two groups were matched for age, sex and associated systemic disorders. The authors found significantly more cases of lacrimal drainage system obstruction in the glaucoma group (20% vs 8.57%) and also more instances of upper lacrimal drainage system obstruction (76.9% vs 37.5%). The nasolacrimal duct was the only site of obstruction in 19.2% (5/26) and was associated with other sites in 3.8% (1/26) of subjects in the case group. They concluded that although the puncti and canaliculi are the main anatomical sites of lacrimal drainage system obstruction associated with topical anti-glaucoma medications, the common canaliculus and nasolacrimal duct may also be involved separately or in conjunction with the upper lacrimal

drainage system.

Seider and colleagues compared a group of patients with primary acquired nasolacrimal duct obstruction (209 eyes of 178 patients) with a control group of patients who underwent cataract surgery (183 eyes of 183 patients). They found that the prevalence of primary open angle glaucoma in patients with primary acquired nasolacrimal duct obstruction (23%) was significantly higher than that of controls (6%). The average number of topical glaucoma drugs per glaucomatous eye in patients with primary acquired nasolacrimal duct obstruction (1.58±0.92) was significantly higher than that of the control group (0.73±0.90). Bilateral nasolacrimal duct obstruction was more common among glaucoma patients with primary acquired nasolacrimal duct obstruction (38.2%) as compared to nonglaucomatous patients in the same group (11.8%).

To determine the role of sympathetic and parasympathetic antagonists on the luminal diameter of the lacrimal drainage system, Narioka and associates conducted a comparative case series. They compared the luminal width of the nasolacrimal duct, measured by dacryocystography, in two groups of patients with unilateral nasolacrimal duct obstruction on the unaffected side before and after receiving 100 μl topical bunazosin hydrochloride 0.01% (a potent selective α-1 adrenergic antagonist) in 19 subjects and 100 μl of 0.4% tropicamide (a muscarinic cholinergic antagonist) in another 19 subjects. Bunazosin was found to reduce the luminal diameter significantly; changes were more marked in the nasolacrimal duct, especially in the middle and the lower regions. In contrast tropicamide caused no significant change in the nasolacrimal drainage system. These results may point to the effect of topical sympatholytic medications on the lacrimal drainage system, especially the lower part.

Esmaeli and associates reported 3 patients with gastrointestinal carcinoma who developed upper and lower lacrimal drainage system obstruction following oral S-1 treatment. S-1 is an oral fluoropyrimidine-based antineoplastic agent consisting of the fluorouracil (5-FU) prodrug tegafur, combined with 2 modulators, 5-chloro-2,4-dihydroxypyridine, and potassium oxonate. S-1 is more active and less toxic than intravenous 5-FU and entails fewer gastrointestinal side effects. It has been reported that intravenous treatment with 5-FU may be associated with punctal and canalicular obstructtions. Although these recent studies support the association between topical/systemic medications and lower lacrimal drainage system obstruction, a true causal association needs to be ascertained by large-scale prospective clinical trials.

Suggested Readings

1. Kashkouli MB, Rezaee R, Nilforoushan N, Salimi S, Foroutan A, Naseripour M. Topical antiglaucoma medications and lacrimal drainage system obstruction. *Ophthalm Plast Reconstr Surg* 2008;24:172-175.
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