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Review Article

Dry eye, Contact lenses and Preservatives in Glaucoma Medication

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Abstract

Current review focus on hidden links between glaucoma, contact lenses and Ocular Surface Disease (OSD). In glaucoma the most important treatment is the control of progression through targeted pharmaceutical protection, keeping low intraocular pressure, by prescribing ophthalmic medications. On the other hand, use of preservatives in glaucoma medications is a common practice in order to maintain their effectiveness for an extended period of time. Anti-glaucoma medications enclose preservatives and the 70% of them contain a very common preserving agent, the Benzalkonium chloride (BAK). In glaucoma medications BAK toxicity includes, loss of tear film stability, direct damages to the cornea and conjunctival epithelium, and possible immune allergic reactions. Other types of preservatives may exhibit less toxicity but are still irritating agents. Of course, concentration and duration of treatment determine the extent of side effects of the preservatives. High content hydrogel contact lenses, absorb BAK molecules and release them slowly onto the corneal epithelium over time. So, patients that use contact lenses may wear them better 15 minutes after the medication. The prolonged exposure to BAK is well known to increase symptoms of ocular inflammation. A diminish of patient's life quality is observed and patient compliance to the specific anti-glaucoma medication, is also undermined. Conversely, there are more causes of dry eye in glaucoma patients, as the majority of the glaucomatous patients are elderly. Such factor is the decrease of tear production with increasing of age and numerous changes in the composition of the tear film. At the same time, elderly often suffer from other pathological diseases that encourage the development of dry eye and eye irritations. Adding the anti-glaucoma eye drops containing preservatives along with the constant use of contact lenses, we are led to a serious multifactorial dry eye condition. The last years several antiglaucoma agents have been marketed such as preservative-free or benzalkonium chloride-free formulations in an attempt to reduce the side effects related to the preservatives.

keywords: Benzalkonium Chloride; Contact Lenses; Dry Eye; Glaucoma Medications; Preservatives ; Preservatives Free; Ocular Surface Disease

Introduction

Glaucoma is the second most common cause of blindness in the world. It is estimated that 4.5 million people around the world are blind due to glaucoma and that number will rise to 11.2 million by 2020. The main treatment of the disease is to control progression through targeted protection of high intraocular pressure, prescribing ophthalmic medication. Medication involves systematic use, occasionally for an extended period, perhaps weeks or months, either for ocular hypertensive or primary open-angle glaucoma patients. The use of preservatives extends the shelf-life of medications by far. Therefore, preservatives continue to be in widespread use in ophthalmic medications due to the convenience they provide, regulatory requirements and the higher cost of alternatives. On the other hand, Benzalkonium chloride (BAK) remains the most commonly used preservative but there is a trend towards the use of Preservative-Free (PF) drops for glaucoma, although at a higher price [1].

Specifically, benzalkonium chloride preservative (BAK) is a common cause, contained in a small concentration (0.004%) or slightly higher dose (0.02%) in 70% of glaucoma medications.

These drops can cause side effects in glaucomatous patients affecting their quality of life and which in turn may reduce the patient's compliance with glaucoma treatment. According a series of laboratory, non-randomised controlled studies BAK have provided some supporting evidence of its toxicity in patients, mainly in those with pre-existing Ocular Surface Disease (OSD) or on multiple medications [2].

Hidden Links Between Glaucoma, Contact Lenses and Ocular Disease (OSD)

Monitoring glaucoma progression can be challenging, but as it turns out, medication is not the only tool in the Ophthalmologist's toolbox. Many factors affect the development of glaucoma in patients, some of which may not be related to the disease itself.

Although inflammation of the ocular surface may sound simple and specific, but it actually encompasses much more than what appears in the eye. The disorder affects the cornea, limbus, conjunctiva and even the eyelids, with dry eye by far the most common diagnosis for patients. In case, the glaucoma patients that receive eye-medications wear contact lenses the situation turns more complicated. It is well known that (hydrogel) soft contact lenses absorb a significant percent of medication that is slowly released in tear layers after major time. Contact lenses, especially high content hydrogel lenses, absorb BAK molecules and release them slowly into the corneal epithelium over time [3].

The benzalkonium chloride molecule, disrupts the corneal epithelium by damaging the DNA of the epithelial cells, disrupting their consecutive chain of growth and increasing inflammation. Such a disorder can be of particular concern when the patient is wearing contact lenses, as prolonged exposure to BAK is known to increase symptoms. It is also, well known that there is a higher prevalence of OSD in patients with glaucoma, which is mainly related to reduced tear production and tear film Breakup time. These symptoms may not be related to glaucoma, but instead are due to medications used by patients to manage glaucoma symptoms. The US Food and Drug Administration (FDA) recommends patients that use anti-glaucoma medications containing preservatives and wear contact lenses, after applying eye-drops to wait at least 15 minutes, before to wear their lenses [4].

Therefore, clinicians should be aware of the hidden links between the symptoms of glaucoma, medication and contact lenses according to the way the disease of the Ocular Surface Disease (OSD) affects the course of glaucomatous patients

Preservatives in Glaucoma Eye Medications

Any multidose format includes preserving agents for maintaining the sterility of the contents throughout its intended length of use. The most commonly used preservative in topical drops of any form is benzalkonium chloride (BAK).

The preserving agent benzalkonium chloride is a quaternary ammonium compound that acts as an antimicrobial agent, against a wide variety of common pathogens by denaturing proteins and disrupting cytoplasmic membranes.

Many scientists oppose the use of benzalkonium chloride preservative, significant results concluded from its use in glaucoma medications detailing the side effects it has on the ocular surface when used for an extended period of time. Preservative-free (Pf) glaucoma medications use can reduce the adverse effects related to preservatives [5,6].

Clinical signs associated with the use of BAK-preserved drops include superficial punctate keratitis, conjunctival hyperemia, staining and follicles, blepharitis, increased osmolarity, reduced tear production and reduced tear film break up time. The changes to tear film stability associated with BAK have not only been documented in glaucomatous patients but in healthy subjects too. At a cellular level, histopathological techniques reveal an increase in inflammatory cells in the conjunctival epithelium along with a significant decrease in the number of goblet cells. [5,6,7,8].

Several researches have found that it took 8-12 weeks to see a measurable change in tear film breakup time and staining of the corneal epithelium. It's also possible that after the exposure to a preservative like BAK the damage might become irreversible. Commonly, in glaucomatous patients, such toxicity has implications not only for tolerability, but also for adherence and persistence with therapy that is known to be poor in glaucoma [9].

Alongside with benzalkonium chloride, there are other preservative agents such as etrimide, Polyhexanide, Chlorhexidine gluconate, Polidronium chloride and Chlorobutanol. These include, for example, Polyquad®, PURITE® or the oxychloro complex. These agents are slightly more tolerable than benzalkonium chloride, but they could also irritate the eyes and cause allergies.

Many frequently used medications, such as Xalatan and Travatan (prostaglandin analogues), Timolol and Betagan (Beta-blockers) or even Alphagan (Alpha-blockers) must be used suspiciously by patients wearing contact lenses or to ask medical advice before the use in case of Ocular Surface Disease (OSD) experience Fortunately, vision scientists can mitigate these corneal/drug interactions through patient education [10]. Clinicians must share this information with their patients to ensure that patients understand the potential interaction between contact lenses and medication [2].

Additionally, Optometrists applying contact lenses to patients with glaucoma can use this knowledge when selecting contact lens type. A soft hydrogel lens with a low water content may be preferred if the patient is aware that he will abuse his drops while wearing contact lenses.

Age and Dry Eye

It should also be considered that, the majority of glaucomatous patients are elderly. In aging, both main causes of dry eye usually appear together: (a) the tear product decreases with increasing age and (b) the composition of the tear film changes.

The degree of severity of ocular surface disease increases with age. This is partly due to the fact that the elderly often suffer from other diseases that encourage the development of dry eye and other eye irritations. These include diabetes mellitus or rheumatism. While it's also important to keep in mind, that women

in menopause suffer more from dry eye due to hormonal changes.

Regular intake of certain medicines that worsen dry eye can also be added to the problems of aging. Beta blockers for high blood pressure or antihistamines for allergies are two examples of such drugs.

Adding to all this and the deterioration of the anti-glaucoma eye drops along with the constant use of contact lenses, we are led to a serious multifactorial dry eye, which has to treat each factor separately, eliminating its involvement in the appearance of dry eye.

Promising Treatment of Glaucoma with Drug Release Contact Lenses

Contrary the risk, researchers promise contact lenses equipped with a polymeric drug membrane along the edge of the lens that releases latanoprost slowly - a drug commonly prescribed for glaucoma patients - on the eye surface [11].

Because the drug membrane is on the edge, the center of the lens is clear, allowing everything you would expect from a good contact lens and eliminating much of the hassle associated with the use of eye medications [12].

At the Caunas Lithuanian Institute of Technology, experimented with "Dissolving Contact Lenses" (DCLs) that may absorb medications that would be released as the lens dissolves and at Columbia Univ., USA apply to glaucoma patients a contact lens with an electronic sensor (SMART Contact Lens) which is sending wi-fi signals to a recording device nearby, every change happened in corneal curvature, in this manner controlling Intraocular Pressure (IOP) changes and thus they can alter or continue a successive anti-glaucoma treatment [13].

Conclusions

Selecting medical treatment for glaucoma it is important to understand the primary aim of the therapy but also contraindications and side effects of medication for each patient. Besides efficacy, the choice of therapy must take into account tolerability, related quality of life and adherence to treatment [14]. Preservatives contained within topical eye drop preparations may cause inflammatory conjunctival side effects and toxicity of the ocular surface [5,8]. Factors such as exposure time to treatment, preserving agent concentration, gender, age and general medical status of the glaucomatous patient can determine the severity of the ocular surface damage and likely recovery time. As a general rule, preservative-free eye drops could be likely beneficial to patients with the following characteristics. Pre-existing or concomitant dry eye/ocular surface disease, those receiving a multidrug topical treatment, those whose treatments are expected to last over several years/decades those who are about to undergo glaucoma surgery (trabeculectomy) [6,8,15]. Patients that use contact lenses are more vulnerable to the side effects of BAK and other less toxic preservatives and the risk to loss the compliance to the antiglaucoma medication is very high. FDA advice these patients in case they use contact lenses to wear them at least 15 minutes after the medication was applied [16].

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