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Ocular lubricants (Introduction)

What is the Technology

Ocular lubricants (encompassing artificial tears and non-medicated eye ointments) are used widely for dry eye syndrome. Some are classified as medicinal products with Summary of Product Characteristics (SPCs) but increasingly the products available are classified as medical devices. These do not have SPCs and only require safety data to gain the CE mark.

There is a wide range of products available for dry eyes, including hypromellose, polyvinyl alcohol, carbomers and sodium hyaluronate. Presentations include multi-dose preserved eye drops, multi-dose preservative-free eye drops, preservative-free single dose units and eye ointments.

This document presents an overview of the use of ocular lubricants. Subsequent documents will look at each product and its various presentations.

What is the evidence for effectiveness of the device?

Dry eye syndrome occurs when there is a problem with the tear film that normally keeps the eye moist and lubricated[2].

Tears are a complex mixture of water, salts, lipids, proteins, and mucins. The tear film is comprised of three layers; aqueous, lipid and mucin[1-3]. The mucin layer is closest to the eye and acts as a foundation for the other tear layers. It is produced by the conjunctival goblet cells. The aqueous layer, produced by the lacrimal glands, provides moisture to the eye and oxygen, electrolytes, antibacterial lysozyme and proteins to the cornea. These tears also help wash away any foreign bodies in the eye. The lipid layer, produced by the meibomian glands, is furthest from the eye and forms a seal over the aqueous layer to retain moisture, prevent evaporation and ensures the tear film is evenly spread over the eye.

The term ‘artificial tears’ is somewhat of a misnomer because most products do not mimic the composition of human tears. The mode of action of ocular lubricants is poorly understood but plausible mechanisms include a lubricating action, replacement of certain missing tear constituents, reduction of tear film osmolarity, dilution of inflammatory substances, or a combination of these[2]. There is a lack of placebo-controlled trials assessing ocular lubricants, thus it is not clear which of the 'active' components is effective, or whether there is a more general lubricating effect of the overall product.

Preparations and formulations

Preparations[2]

Hypromellose is the most commonly used product but requires frequent administration.

Products containing carbomers, polyvinyl alcohol, hydroxypropyl guar, soybean oil or sodium hyaluronate are longer acting.

Sodium chloride is short acting and suitable as 'comfort drops' or for use with contact lenses.

Eye ointments containing paraffin can be used but may be uncomfortable and blur vision. They should only be used at night, and never with contact lenses.

There is limited trial-based evidence showing that any particular product is superior to any other. However, their effect is sufficiently rapid and dramatic for the individual to know if they are helping or not[3]. As the majority of newer ocular lubricants are registered as medical devices, there is no requirement for clinical trials to be performed. It may be necessary for a patient to try several different preparations to find one which is most effective in relieving symptoms.

Preservatives and excipients

Many multi-dose eye drops contain preservatives to reduce bacterial contamination during use.

The most commonly used preservative in eye-drops is benzalkonium chloride. Benzalkonium chloride can damage the corneal and conjunctival epithelium[1,4]. Its toxicity is related to its concentration, the frequency of dosing, the level or amount of tear secretion, and the severity of disease. In the patient with mild dry eye, benzalkonium chloride-preserved drops are usually well tolerated when used 4-6 times a day or less. In patients with moderate-to-severe disease, the potential for benzalkonium chloride toxicity is higher, due to decreased tear secretion and

decreased turnover and potentially more frequent use of drops. Patients may also be using other ocular preparations (eg, glaucoma medications) that contain benzalkonium chloride, increasing their overall exposure to the agent.

Cetrimide or polyquaternium-1 (Polyquad®) are also used as preservatives, although less frequently than benzalkonium chloride. Cases of hypersensitivity have been reported following repeated application of products containing these preservatives[5,6].

Another additive used in ophthalmic products is disodium edetate (EDTA). This, in itself is not a sufficiently effective preservative but can be used to augment the efficacy of other preservatives[1,4]. A lower concentration of the preservative may therefore be possible. However EDTA itself may cause irritation to the ocular surface.

Ocular lubricant preparations, including preservative-free formulations, often contain excipients or buffers to control pH or osmolarity. Some excipients have also been reported, rarely, to cause allergy or contact sensitivity[4].

Preservative-free drops

Preservative free products have an increasing role in the management of patients with severe dry eye and those using concurrent topical therapy for other eye conditions. If a patient is receiving more than 4-6 drops per day in total from all ocular medication, preservative-free drops could be considered[2]. Preservative-free formulations are also indicated for those with a known history of allergy to preservatives, those with pre-existing corneal disease and those who wear contact lenses. Preservatives and other excipients accumulate on the surface of contact lens and may cause irritation and possible damage to the surface of the eye.

It should be noted that irritation can still occur with preservative-free drops due to other excipients (for example buffers or electrolytes) in the preparation[4].

Preservative-free formulations are available in a variety of delivery systems. Many are supplied as single-dose units. These are often small tubes or plastic ampoules designed to administer one drop and to be discarded. These can usually be used to administer a drop into both eyes before discarding, although some medical devices can be used for up to 12 hours after opening.

Some preservative-free formulations are available in 10ml bottles. These are usually patented designs containing either a filter or valve to prevent the entry of micro-organisms. As these preparations are registered as medical devices, they are not subject to medicinal product licensing requirements. Thus the requirement for eye drops to have a 4 week shelf-life after opening does not apply and these multi-dose products can be used for 2-6 months after opening.

Other formulations contain what have been described as 'vanishing' preservatives, for example sodium chlorite or sodium perborate[1]. Sodium chlorite degrades to sodium and chloride free radicals and water upon exposure to UV light after instillation[1,6]. Sodium perborate is converted to sodium borate, hydrogen peroxide, water and oxygen on contact with the tear film. In higher concentrations, sodium perborate has been reported to be an eye irritant[7]. For patients with severe dry eye, even vanishing preservatives may not totally degrade, due to a decrease in tear volume, and may be irritating[1].

Presentations

Multi-dose bottle preparations of ocular lubricants are convenient to store and transport. Those licensed as medicinal products must have a 28 day expiry after opening but many ocular lubricants registered as medical devices have extended shelf lives of up to six months after first opening.

Single dose units are bulky to store, particularly if several different eye drops are used. They are less convenient for the patient to carry, especially if they are being used many times a day. They have a greater unopened shelf-life than multidose vials but generate more waste.

Eye ointments may be uncomfortable and blur vision. They should only be used at night, and never with contact lenses.

References

1. Anon 2007 Report of the International Dry Eye WorkShop (DEWS) The Ocular Surface 2007: 5(2)
2. NICE Clinical Knowledge Services Dry eye syndrome Last revised in September 2012 Available at www.cks.nice.org.uk, [Accessed 8th August 2013]
3. RNIB and Royal College of Ophthalmology. Understanding Dry Eye March 2013 (http://www.rcophth.ac.uk/page.asp?section=365&sectionTitle=Information+Booklets)
4. Moorfields Eye Hospital NHS Foundation Trust Pharmacists Handbook 2006 Moorfields Pharmaceuticals
5. Sweetman SC (ed), Martindale: The Complete Drug Reference, 2010. London: Pharmaceutical Press. Available from www.medicinescomplete.com [accessed on-line 6/9/13]
6. Freeman PD, Kahook MY Preservatives in Topical Ophthalmic Medications: Historical and Clinical Perspectives Expert Rev Ophthalmol. 2009;4(1):59-64
7. Scientific Committee on Consumer Safety (SCCS) Opinion on sodium perborate and perboric acid (2010) SCCS/1345/10 (Available from http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_031.pdf, Accessed 19/9/13)