TREATMENT OF DRY EYE SYNDROME

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Abstract: *Dry eye syndrome is a chronic, progressive disorder. Depending on its cause and severity, it may not be completely curable. In most cases, dry eyes can be treated successfully, usually resulting in visible eye comfort, fewer dry eye symptoms and clearer vision. Because dry eye syndrome may have many causes, there are a variety of treatment approaches.*

Treatments for tear insufficiency

1. Eye lubricants replacement approaches

The products called "artificial tears" try to replace and/or supplement the natural tear film. These products are not focusing on the basic pathophysiology of the dry eye.

Regarding the mild cases of dry eye syndrome due to long term computer use, reading, school, the best treatment can be the use of artificial tears or other lubricating drops. On the market, there are available a wide variety of ingredients and viscosity. High viscosity tears are only recommended for use during sleep. Ingredients from artificial tears may be more effective for dry eyes with water deficiency or for dry eyes by evaporation.(1)

Biological tear replacements

Autologous serum. Serum is the fluid component of the blood that remains after clotting. The autologous serum contains some specific epitheliotrophic factors, such as epithelial growth factor (EGF), nerve fibers murine growth factor (NGF), high protein levels such as albumin and fibronectin. Autologous serum supports the proliferation and migration of epithelial cells directly and, indirectly it enhances epithelial viability by binding and neutralizing the inflammatory cytokines.(2)

2. Tearing conservation approaches

2.1. Occlusion point. The concept of temporary or permanent occlusion of one or both of the lacrimal points is to retain tears on the ocular surface by blocking drainage.

Indications and contraindications: Sjogren's syndrome, autoimmune diseases, dry eyes associated with a short tear break-up time (BUT), systemic drugs leading to film production reduction, upper limb keratoconjunctivitis, any corneal irregularities or scarring affecting lacrimal stability, toxic epitheliopathy.(4)

2.2. Moisture glasses. There are specially designed glasses to slow tear evaporation by providing a damp environment and minimizing airflow.

3. Lacrimal stimulation approach. On certain markets, there are commercially available topical pharmacological technologies that stimulate aqueous, mucin and/or lipid secretion.

Different methods of lacrimal stimulation.

A variety of other new methods have been reported to stimulate lacrimal production. Here, we can mention abdominal breathing for 3 minutes, which has accentuated the increase in the volume of the lacrimal meniscus in healthy women. The stimulation of corneal thermoreceptors could increase the production of tears. Finally, caffeine, probably the most consumed psychoactive substance, seems to stimulate the secretion of tears in healthy subjects. Immunomodulatory drugs are sold only by prescription and are recommended to change the local immune system around the tear glands. They act to increase the production of tears.(5)

Damaged eyelids treatment

- Anterior blepharitis
- Hygiene of the eyelids can reduce lipid production. The crusts in the anterior blepharitis will be removed using foams, solutions and wipes.
- Reduction of bacterial colonization

Topical antibiotics. Hygiene to reduce bacterial load on the eyelid edge is usually performed in dry eye management associated with blepharitis. A short dose of local antibiotic has been recommended. Anofloxacin ointment was recommended for the treatment of patients with obstructive meibomial gland dysfunction (MGD). Topical azithromycin (a macrolide antibiotic) has been used in the treatment of dry eye, but has anti-inflammatory action rather than simply reducing bacterial eyelid flora.(5)

- Dysfunction of the Meibomius gland. Obstruction from the terminal channel and the ductal system of the meibomian glands. There has been recognized the significant role of conventional treatments in managing MGD, including eye lubricants, hygiene and warm compresses.
- Eye Lubricants. The following are also used: liposomal spray; eyelid cleansing massage, hypoallergenic soap, Blephaclean napkins, Blephagel cleansing solution, neutral eyelid shampoo, TheraTearsSteriLid eyelid cream, and TheraTears Nutrition supplements with omega-3 oral.
- Hot compresses. Their results have shown that eyelid warming with a non-wet device improves lacrimal function in healthy individuals and may have good results both on the lacrimal film and regarding the function of the meibomian gland in patients with MGD. Non-wet devices

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use for 2 or 4 weeks has made a stable improvement in normal patients and in MGD patients. An eye study recommended that hot compresses, heated to 45°C, should be applied for at least 5 minutes. Optimal contact between the compresses and the eyelid should be made and the compress must be replaced every 2 minutes to ensure temperature is maintained. It should be avoided that the skin of the eyelids warm up to more than 45°C to avoid thermal damage. To educate the patient on how to perform the procedure optimally, it was considered necessary to know the risks of increased corneal temperature. In addition to home compresses, a wide variety of devices are now commercially available for raising eye temperature for a long period of time: Blephasteam (Thea Pharmaceuticals, Newcastleunder Lyme, UK) resembles to swimming glasses and is connected in an electrical outlet to provide latent, non-pressurized heat to the MGD eye. Rx EyeBag® is used twice a day for two weeks. The benefits lasted up to 6 months with repeated sessions that led to increased comfort. The EyeGiene® Mask (Eyedetec Medical, Danville, CA, USA) employs pressurized heating units. The infrared heater can also be used.(5)

- LipiFlow. LipiFlow® TearScience, Morrisville, NC, USA. The LipiFlow thermal pulse system is an automatic dry eye treatment that combines the best features of hot compressing therapy and the expression of the meibomian glands. The unique 12-minute procedure of the LipiFlow® system has been proven to be safe and effective for the treatment of MGD and the effect is sustained. The patented device designed and manufactured by TearScience uses a precisely controlled combination of heat and pressure to open the blocked meibomian glands. This is called thermal pulse. LipiFlow is designed to treat the main cause of the dry eye, MGD.(6)
- Intense pulse light (IPL). For more than 10 years, the FDA has approved the use of intense pulsed light (IPL) to treat skin redness. Often, it may be accompanied by rosacea on skin and eyelids as well. In IPL treatment, a portable device sends a strong light onto the skin. Light is filtered to allow only wavelengths that can be absorbed by the dilated blood vessels. This treatment can lead to the resolution of dilated vessels and associated inflammation. Patients typically require four to six intense pulsed light treatments, with one month break between each treatment.
- Soft therapeutic contact lenses (bandage lenses). The availability of soft, hydrogel-like materials with oxygen rapid transmission has encouraged the use of these devices in the therapeutic management of ocular surface disorders (OSD), including recurrent corneal erosion, corneal abrasion, bullous keratopathy and corneal surgery. The therapeutic lenses can help managing corneal pain by isolating the corneal nerves sensitized by the stimulation of the environment. A protective effect may occur to prevent the ocular surface from drying or cooling or to protect the nociceptors from the ocular surface.(6)
- Gas permeable scleral lenses. There is a growing appreciation that the daily use of the gas-permeable rigid scleral lens plays an important role in dry eye management, maybe as a result of the fact that they can provide a reposition of tears between the lens and the eye surface.

Antinflammatory therapy

- Topical Ciclosporins A 0.05% (RESTASIS®, IKERVIS) were approved by the FDA as a dry eye treatment associated with an inflammatory process. Modulation of the inflammatory process of the ocular surface may increase the neural reaction, improving lacrimal secretion. Topical cyclosporins are used early in the development of this disease; a small number of patients may experience a long-term improvement after completion of the initial treatment with cyclosporins. Approximately 70% of patients with moderate to severe dry eyes appear to benefit from topical cyclosporine treatment, with minimal side effects.(7)

Cyclosporin is an immunomodulatory drug with anti-inflammatory properties, as well as other actions relevant to the treatment of dry eyes. Cyclosporin inhibits IL-2 activation of lymphocytes. Life quality studies have concluded that local cyclosporin is more effective for the treatment of dry eye compared to the use of eye lubricants. One study also reported the added value of local cyclosporin therapy in patients with punctal plugs. Tacrolimus 0.03% may be a good alternative for the patients with intolerance to topical cyclosporin or in patients in whom the response to topical cyclosporin is low.(7)

The efficacy of lifitegrast has been demonstrated for long. The FDA approved Xiidra™ (Lifitegrast 5% ophthalmic solution Shire, Lexington, MA, USA) in a single dose format for the treatment of the signs and symptoms of the dry eyes.

Xiidra aims at reducing inflammation associated with the signs and symptoms of dry eyes syndrome. After 12 weeks of Xiidra use, there has been observed a significant reduction in dry eye symptoms. The most common side effects of Xiidra which were reported in studies were: altered taste and reduced visual acuity, eye irritation, which occurred in 5 to 25% of patients.(7)

Surgical approaches

1. Tarsorrhaphy;
2. Surgical treatment for conjunctival candidiasis;
3. Essential treatment for blepharospasm with botulinum neurotoxin;
4. Eyelid correction;
5. Conjunctival surgery and amniotic membrane grafts. Individuals with conjunctival conditions such as pterigion, pinguecula, Stevens-Johnson syndrome often develop dry eye syndrome. Conjunctival autograft reduces pterygium recurrence. Amniotic membranes may be taken into consideration in cases of persistent epithelial defects, ocular cicatricial pemphigoid, Stevens-Johnson syndrome and other severe ocular surface disorders. These membranes contain a wide variety of neuropeptides and neurotransmitters, including acetylcholine and catecholamine
6. Transplantation of salivary glands (7)

Dietary changes

There is increasing evidence that nutritional supplementation and individuals' diet play a role in dry eye syndrome. The general contributions to hydration and other interventions, such as lactoferrin and antioxidant supplements, are also worth mentioning.

General hydration condition. The process of body hydration has been suggested to have a potential in dry eye syndrome control. Observational data suggests that the body's hydration status can influence the clinical expression of dry eye syndrome directly.

Essential fatty acids are called "essential" because they are necessary for the healthy metabolic processes. Two essential fatty acids are omega-3 fatty acids and omega-6 fatty acids with 18 carbon atoms. There are both short subtypes and long chain subtypes. Both subtypes can be obtained from food. Common omega-3 foods include flaxseeds, walnuts and soybean oil, oily fish (such as tuna, salmon, trout, sardines and mackerels) and to a lesser extent crustaceans (such as shrimps, oysters and mussels). Omega-6 is usually obtained from

vegetable oils such as corn oil.(8)

Omega-3 base studies are recognized as having a wide range of systemic anti-inflammatory effects and preventing the proliferation of T lymphocytes, processes that have been involved in the pathogenesis of dry eye syndrome.

Human observation data. The study on women's health described an association between low dietary intake of omega-3 and dry eye syndrome in women. This study reported a 30% reduction in the risk of dry eye syndrome with each additional gram of omega-3 consumed per day. A higher ratio of u-6: u-3s was also correlated with an increased risk of dry eye syndrome. Furthermore, it has recently been shown that the ratio of u-6 u-3 lacrimal lipids is increased in people with dry eye syndrome and that this is proportional to the degree of dysfunction of the tear film and corneal dye.

Lactoferrin is a multifunctional lacrimal glycoprotein with antibacterial, anti-inflammatory and anti-angiogenic properties. Lacrimal lactoferrin levels are seen as an indicator of the function of the lacrimal secretion. Low levels of lacrimal lactoferrin have been reported in many people with dry eye syndrome.(8)

Other dietetic considerations. Oxidative stress generates damaging reactivity to the cell. Daily supplementation with oral antioxidants resulted in relative improvement in dry eye symptoms and Schirmer scores compared to baselines, over months. The alpha-lipoic acid, a natural disulfide compound, also has an antioxidant capacity.

Local environment considerations

Several environmental factors have been involved in the dry eye syndrome, including systemic and topical medications, dehydration conditions, the use of digital devices and contact lenses wearing. Taking these risk factors into account is important because they can provide additional information regarding the patient's individual response to prescribed therapy. Any initial change in the eye surface culminating with the dry eye syndrome can be prevented by eliminating environmental risk factors.

Chronic topical drugs. Preservatives may be associated with allergic, toxic or inflammatory reactions, particularly in patients who use long-term topical drugs.

Preservatives such as BAK irritate the eye surface and both symptoms (such as burning, dryness and foreign body sensation) and signs are significantly more common in patients using glaucoma-preserved medicines.(9)

Systemic medications. Many drugs used to treat chronic diseases can contribute to dry eye syndrome.

A higher incidence of dry eye has been reported in people using antihistamines, beta-blockers, antidepressants, diuretics, anxiolytics, antipsychotics, antiparkinsonian drugs, estrogen therapy and systemic chemotherapy.

Symptoms of dry eyes may be increased as a result of topical glaucoma medication. The chronic use of both topical betablockers and miotic agents may decrease the density of mucus-secreting conjunctival cells. Topical betablockers have been associated with an increased incidence of dry eye cases, possibly due to reduced corneal sensitivity.

Oral administration of drugs, such as carbonic anhydrase inhibitors (e.g. acetazolamide and metazolamide) may reduce the production of tears.

Along with aging, the frequency of glaucoma is increased, and dry eye syndrome is more common. These pathologies often influence each other.

Many treatments for dry eye increase the risk of aggravation or the appearance of glaucoma and have an impact on surgery, and the use of antiglaucoma topical agents may cause dry eye occurrence or exacerbation

There is evidence of correlation of benzalkonium chloride with corneal, conjunctival, trabecular, crystalline, macular and retinal integrity. The increased toxicity of topical treatments may also decrease tolerability and compliance with treatment with decreased therapeutic success. Thus, the treatment of these two pathologies must be considered together.

Decrease in blinking rate

Blinking is essential to keep the tear film homeostasis on the eye surface.

Decreasing the blink rate affects the rupture dynamics, prolonging the period when the ocular surface is exposed to water loss before the next blink, thus contributing to the development of the dry eye syndrome.

Dehydration conditions and environmental pollutants.

The eye surface is most exposed to light, low relative humidity, extreme temperatures, UV radiation, irritants, pollutants and tobacco smoke. Exposure to adverse conditions leads to increased instability and evaporation.

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