Dry Eye Syndrome in the Elderly: Challenges and Treatment Options

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9.1 Introduction

The term dry eye was initially introduced by Roetth in 1953, who described dry eye as low flow of tears measured with the Schirmer test (de Roetth 1953). Now in the twenty-first century, our understanding of the underlying mechanisms and multiple possible etiologies underlying this form of ocular surface disease is more complex and nuanced, but the term "dry eye" is still prevalently used worldwide (Morube 2004).

Dry eye disease (DED) has received different denominations in attempt to better define this condition: keratoconjunctivitis sicca, dry eye syndrome, and dysfunctional tear syndrome (DTS) (Lemp 2008a).

Most recent attempts to define this entity vary from Roetth in that they do not require a reduced flow of tears and are not linked to any particular diagnostic test (such as the Schirmer test). The National Eye Institute, in 1995, defined DED as "disorder of the tear film due to tear deficiency or excessive tear evaporation which causes damage to the interpalpebral ocular surface and is associated with symptoms of ocular discomfort" (Lemp 1995).

In a 2007 report of the International Dry Eye Workshop (DEWS), dry eye was defined as a "multi factorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface" (Lemp et al. 2007).

9.2 Epidemiology

According with World Health Organization (WHO), 650 million people aged 60 years and over are alive today. In 2050 the elderly population is expected to reach two billion, reflecting improvements in nutrition and healthcare in modern societies (WHO 2011). This aging of the world's population portends a dramatically increasing burden of ocular surface disease from dry eye.

Dry eye is a public health problem with major quality of life impact (QOL), frequently associated with social, physical, and psychological disturbance. In addition, it is a chronic disease and usually requires long-term clinical follow up (Friedman 2010).

Many diagnostic tests are currently available in the clinic and used variably in attempts to define DED; however, there is no consensus of which diagnostic test must be employed. Because it is a symptomatic condition, symptoms questionnaires are usually applied as auxiliary instrument to help establish the diagnosis (Smith et al. 2007). These questionnaires can provide significant

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information, however, may not truly represent the reality of an epidemiologic study because of its subjective aspect (Uchino et al. 2011).

The prevalence of dry eye in the USA among adults aged 50 years and older has been estimated about 3.23 million of women (approximately 7 %) and 1.68 million of men (about 4 %). DED is considered a common condition among women 50 years old and over in USA (Schaumberg et al. 2003, 2009).

According with Koumi study, the high prevalence of DED among Japanese might be related with ethnicity (Uchino et al. 2011), and some studies from Asia suggested higher prevalence among this population. Lin has demonstrated that Taiwanese women are at high risk to develop dry eyes symptoms and positive dry eye tests (Lin et al. 2003).

9.3 Risk Factors

Aging is considered the most important risk factor for DED. There are others ophthalmologic comorbidities aging related as cataract, glaucoma, aging macular disease, and diabetic retinopathy (Tsubota et al. 2010).

Consistent factors for dry eye include older age, female sex, and use of hormone replacement therapy, particularly estrogen (Schaumberg et al. 2001), decrease of androgen levels, vitamin A deficiency, malabsorption, and eating disorders are also included as factor risks for DED (Jaworowski et al. 2002; Sullivan et al. 2000).

Some medical conditions and systemic medications have been recognized as risk factor for development of DED. Galor et al. have shown that patients who present with psychiatric illness, autoimmune disease, benign prostatic hyperplasia (BPH), sleep apnea, rosacea, and human immunodeficiency virus are roughly two times more likely to also present with DED (Galor et al. 2011).

Patients taking antihistamines, antianxiety agents, antidepressant, and agents used to manage BPH were also almost two times more expected to develop DED (Galor et al. 2011). Manaviat et al. showed higher prevalence of DED among type 2 diabetic patients with diabetic retinopathy (Manaviat et al. 2008).

The Beaver Dam Eye Study showed that current and past smoking, multivitamin use, and history of heavy alcohol consumption in the past were related with increased risk for DED whereas caffeine consumption was associated with decreased risk (Moss et al. 2000).

9.3.1 Patient History

Patient history has a relevant role to establish the diagnosis and appropriate therapy, to identify causes of DED, and to principally relieve patient discomfort and prevent related complications.

A factor which may precipitate and/or exacerbates the symptoms of DED is long-term contact lens wear. Guillon and Maissa showed that tear film evaporation at normal humidity when a patient is wearing contact lenses is similar to evaporation at low humidity in eyes without contact lenses (Guillon and Maissa 2008).

Detailed history of ocular surgeries must be investigated because most surgical procedures which cause cornea denervation may exacerbate preexisting dry eye symptoms, including cataract (Cho and Kim 2009) and refractive surgery, presumably due to damage of corneal nerves during the corneal incision (Albietz et al. 2004). The chronic use of eyedrops containing preservatives can lead to ocular surface damage, as the consequence of allergic reaction and reactions, and direct epithelial damage (Mantelli et al. 2011).

Modern living, including work in indoor air-conditioned environments, computer use, prolonged reading, watching television, and driving appear to negatively impact on DES; hence, it is often helpful to investigate the patient's everyday activities with the goal of possibly alternating environmental stresses (Miljanovic et al. 2007).

9.3.2 Secondary Mechanical Conditions

Elderly populations are more susceptible to conditions that can lead to eyelid malpositions or

dysfunction and consequently DED symptoms. Examples of these conditions include involutional entropion and ectropion, loss of inferior eyelid tonicity, nocturnal lagophthalmos, and neurological conditions as Parkinsonism with reduced blink rate and paralysis of cranial nerve VII (Bashour and Harvey 2000). Damasceno et al. showed that entropion is more often associated with DED symptoms and also is more prevalent among women (Damasceno et al. 2011).

Conjunctivochalasis is also a condition increasingly prevalent with age and may result in DED symptoms by aggravating a preexisting DED condition, caused basically by aqueous tear deficiency (Yokoi, et al. 2005).

The recognition of these mechanical conditions is crucial for an effective treatment (Di Pascuale et al. 2004), because once detected and treated, the DED symptoms tend to recover (Henstrom et al. 2011).

9.4 Symptoms

Dry eye is considered the most typical cause of chronic eye irritation in patients 50 years and older. The most frequent symptom related is sandy-gritty sensation or burning, which gets worse with the course of the day (Gilbard 2009).

Others symptoms, also frequent, include tearing, blurring vision, and sometimes, redness, mainly when associate with blepharitis. The patient with DED usually refers symptoms intensification after exposition to air-conditioning, wind, prolonged staring, or any situation that causes diminishing of blink rate. Reflex tearing, a paradox symptom, may occur even before establishment of irritated and uncomfortable eyes (Terry 2001).

DED affect directly the QOL and has considerable impact on daily activities and psychological, physical, and social life, especially if the symptoms of dry eye are persistent. However, QOL is an effective tool to evaluate whether the therapy applied was sufficient to improve the symptoms (Friedman 2010).

9.5 Etiopathogenesis

One classification scheme divides DED in two major categories: *aqueous tear-deficient dry eye* and *evaporative dry eye*. Mathers and Lane verified a reduction in tear film function with aging; there is a decrease of tear flow and volume and an increase of tear film evaporation and osmolarity (Mathers and Lane 1998).

9.5.1 Aqueous Tear-Deficient Dry Eye (ADDE)

ADDE is considered to represent an inefficient lacrimal secretion due dysfunction or destruction of lacrimal gland tissue, reducing tear production and secretion. Consequently to this process, a modification of increased tear osmolarity is believed to occur, and this hyperosmolarity is thought to be responsible for the inflammatory response and subsequent damage to the ocular surface. Furthermore, ADDE also have two subclasses: Sjögren syndrome dry eye and non-Sjögren syndrome dry eye (Lemp et al. 2007).

9.5.1.1 Sjögren Syndrome Dry Eye (SSDE)

Sjögren syndrome is an autoimmune endocrinopathy in which the main targets are lacrimal and salivary glands. There are two ways SSDE becomes manifest: primary (PSS) or secondary (SSS). PSS correspond clinically aqueous-deficient dry eye, associated with reduction of salivary secretion (Zoukhri 2006). Two age peaks are found on PSS, the first, around 20–30 years old and the second, in the mid-50s (Fox 2005). SSS represents the same characteristic of PSS associated with other autoimmune disorders including rheumatoid arthritis and systemic lupus erythematosus (Zoukhri 2006).

9.5.1.2 Non-Sjögren Syndrome Dry Eye (NSSDE)

Non-Sjögren syndrome dry eye is a subdivision of ADDE when systemic autoimmune etiology was discharged. For many years, this entity was considered synonymous with keratoconjunctivitis sicca (KCS). There are different forms of NSSDE,

and they are classified as: primary and secondary lacrimal gland deficiencies, obstruction of the lacrimal gland ducts, and reflex hyposecretion. Age-related dry eye is included in the first classification of primary lacrimal gland deficiencies (Lemp et al. 2007).

9.5.2 Evaporative Dry Eye (EDE)

Evaporative dry eye form is characterized by excessive tear evaporation from the ocular surface; however, the lacrimal secretory function is considered normal. There are two different types described: intrinsic and extrinsic. The intrinsic type, as the name suggests, occurs due to an intrinsic dysfunction of the palpebral structures or functions, for example, meibomian gland dysfunction (MGD), low blink rate, and Parkinson disease (Lemp et al. 2007). In MGD an abnormal lipid excretion results in increased tear evaporation rate and consequently evaporative DED. The major prevalence of MGD is age related, mainly thought to relate to decreased androgen levels (Bron and Tiffany 2004). The extrinsic type includes ocular surface disorders (vitamin A deficiency, topical drugs, and preservatives), contact lens wear, and allergic conjunctivitis (Lemp et al. 2007).

9.6 Mechanisms of Dry Eye

Two mechanisms are listed as a potential trigger for inducing DED, *hyperosmolarity* and *tear film instability*, and both may have a concomitant contribution to dry eye symptoms.

9.6.1 Hyperosmolarity

The main mechanisms of hyperosmolarity are considered to be the reduced aqueous tear flow and/or elevated evaporation rate of tear film. Hyperosmolarity stimulates the inflammatory cascade by increasing expression and production of proinflammatory cytokines and chemokines. After establishment of DED, inflammation becomes cause and consequence of cell damage (Baudouin 2001). Inflammatory cytokines are up-regulated in the dry eye condition, including interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and MMP-9 (Yoon et al. 2007).

9.6.2 Tear Film Instability

A normal superficial lipid layer is thought to stabilize the tear film due to controlling the physiologic evaporation rate. Once both aqueous and mucin layers become thinner, a focal tear breakup can happen because of tear fluid surface tension (Tsubota 1998). During tear film instability, a temporary increase of tear film hyperosmolarity has been noted. Liu et al. demonstrated that corneal nerves can detect changes in osmolarity, and corneal sensory neurons react by increasing tear film osmolarity, causing ocular discomfort (Liu et al. 2009); subsequently the epithelial cells respond with inflammation and apoptosis (Luo et al. 2007).

9.7 Diagnosis

A considerable challenge with the diagnosis, severity-grading, and monitoring response to treatment of DED is the absence of a gold standard test for diagnosis (Schein et al. 1997). In addition, patient symptoms are not often in accordance with the clinical signs; some patients may be extremely symptomatic despite modest visible slit lamp findings, while other patients with beginning epithelial breakdown and other worrisome clinical features will describe minimal subjective complains (Nichols et al. 2004).

An appropriate identification of precipitating factors and quantification of disease severity is necessary for an adequate approach to management.

9.8 Classification

One report describes four severity levels for DED, without lid margin disease, based on symptoms and signs. Discomfort, severity, and visual disturbance are included in symptoms

and can vary from none or episodic, mild to severe, and constant. The signs include conjunctival injection and staining and corneal staining and can also vary from none/mild to severe (Behrens et al. 2006).

9.9 Treatment

Based on patient signs and symptoms, four severity levels are considered to indicate the treatment, and therapeutic options are recommended according with the severity (Pflugfelder et al. 2007). An appropriate range of therapeutic options should be followed in attempt to avoid treatment of patient level one applying therapeutics approaches for level four (Wilson and Stulting 2007).

The treatment of DED may involve four different options: *tear supplementation*, *tear stimulants, tear retention,* and *antiinflammatory therapy*. Avoiding exacerbating factors, dietary modifications, and eyelid hygiene are examples of nonpharmacologic approaches that also must be considered (Lemp 2008b).

For patients with anterior eyelid margin disease, eyelid hygiene and topical antibiotic are indicated. Posterior eyelid margin disease requires warm massage, oral tetracyclines, and topical steroids if necessary (Behrens et al. 2006).

For severity level one (mild disease), counseling and patient education, environmental changes, and artificial tear substitutes are suggested. If level one measures fail to satisfactorily improve the patient, level two therapies are added: antiinflammatory drugs as topical cyclosporine and corticosteroids, nutritional supplements, and secretagogues, and non-pharmacological approach including punctual plugs and moist chamber. Treatment for level three (severe disease) includes tetracyclines, autologous serum, and punctal plugs. Finally, with severity level four "end stage," systemic immunosuppressive and surgical alternatives may be necessary (Wilson and Stulting 2007).

9.9.1 Tear Supplementation

Tear substitutes are hypotonic or isotonic buffered solutions with electrolytes, surfactants, and different levels of viscosity; they can provide additional humidity to the ocular surface, improving the lubrication. There are many ocular lubricants available in the USA; they vary in concentration of electrolytes, osmolarity, viscosity, and presence or absence of preservative. The principal advantage of nonpreserved eyedrops is the possibility of frequent administration without toxic effects, found in preservatives preparations (Pflugfelder et al. 2007).

Sodium hyaluronate is a glycosaminoglycan, and that is able to hold large amounts of water and consequently lubricate adjacent structures. Its relatively high viscosity can stabilize the precorneal tear film and maximizes the residence time on eye surface (Snibson et al. 1990; Shimmura et al. 1995). Hyaluronate has viscoelastic properties, humidifies the ocular surface, and has beneficial effect on the cornea and conjunctival epithelium (Aragona et al. 2002).

Tears supplements used outside the USA often contain hyaluronate, but this molecule has not been approved by US Food and Drug Administration (FDA) (Pflugfelder et al. 2007).

Topical lubricants may help improving symptoms and signs; however, there is no evidence that they can improve the underlying pathology and inflammation found in DED (Pflugfelder et al. 2007).

9.9.1.1 Biological Tear Substitutes

Tear factors are known to be indispensable for the maintenance of normal cornea and conjunctival epithelium. Some of them, including epidermal growth factor, vitamin A, transforming growth factor β (TGF-β), cytokines, and fibronectin, can be found in serum. Tsubota et al. evidenced that autologous serum applied as a tear substitute can improve signs and symptoms of DED (Tsubota et al. 1999).

9.9.2 Tear Retention

9.9.2.1 Punctal Occlusion

Punctal plugs are commonly employed to slow tear drainage and can improve DED symptoms and signs. Plugs can be placed into upper, lower, or both puncta. Absorbable punctal plugs type

may be made of collagen or a labile polymer and may last for a few days to about 2 weeks, while nonabsorbable plugs made of silicone or hydrophilic acrylic may remain in place unless spontaneously dislocated or removed by a physician. The most common side effect of occlusion is epiphora (Lemp 1994).

Intracanalicular SmartPlug™ (Medennium, Irvine, CA) is a thermosensitive hydrophobic acrylic polymer, solid at room temperature and soft gel at 37 °C, accommodating into canalicular space (Chen and Lee 2007). Kojima et al. evaluated the SmartPlug™ in patients who had previously been treated with conventional plugs, and they showed clinical and symptoms improvement (Kojima et al. 2006). If plugs become located within the canalicular system, they may be difficult to retrieve and may serve as a nidus for inflammation of infection.

Punctal occlusion may promote immediate tear conservation but may also aggravate the ocular surface irritation because the changes in lacrimal tears composition may be toxic to the cornea and conjunctival epithelium. In addition, the concomitant use of preserved artificial tears in patients with punctal occlusion may raise the eye surface inflammation (Roberts et al. 2007).

9.9.2.2 Moisture Chamber Spectacles

With the objective of increase humidity around the eye, small moist sponges may be attached to the side panels of the patients' eyeglasses or swimming goggles can be used. These devices are able to maintain a humidity rate; however, patient adherence may be poor due cosmetic reasons (Tsubota et al. 1994).

9.9.2.3 Contact Lenses

Boston sclera lens is a rigid gas-permeable lens that vaults over the cornea and rests on the sclera. Tear film is retained between lens and eye surface, and it may be useful to promote healing of persistent epithelial defect refractory to other treatments. Advantages of wearing this lens include decrease of ocular pain and photophobia, besides the improvement of vision acuity (Rosenthal and Corteau 2005).

9.9.3 Tear Stimulants

Pilocarpine and cevimeline, cholinergic parasympathomimetic agonists' agents, are FDA approved for dry mouth associated with Sjögren syndrome, but not for DED treatment (Lemp 2008a).

A multicenter, double-blind, placebo-controlled trial evaluates the efficacy of pilocarpine tables for Sjögren syndrome patients with dry eye symptoms. Patients who were treated with 5 mg tablets 4 times per day had a significant change comparing with the placebo group. The most frequent adverse reactions were sweating, followed by urinary frequency, flushing, and increased salivation (Vivino et al. 1999).

Ono et al. evaluated the efficacy of cevimeline in patients with Sjögren syndrome and concluded that 20 mg 3 times daily can effectively improve the symptoms related to dryness compared to placebo (Ono et al. 2004).

9.9.4 Antiinflammatory

9.9.4.1 Corticosteroids

Corticosteroids (CEs) have been worldwide used to treat a diversity of eye surface inflammation, because of their cytokines inhibition capacity. De paiva et al. showed that 1 % methylprednisolone, a very potent CE, can preserve apical corneal barrier function and can promote a great clinical improvement (de Paiva et al. 2006; Pflugfelder et al. 2007). Nonpreserved 1 % methylprednisolone solution had a remarkable improvement in ocular irritation symptoms. Marsh and Pflugfelder evaluated the efficacy and side effects of topical methylprednisolone and found that this CE is an effective treatment option for patients with severe DED secondary to Sjögren syndrome (Marsh and Pflugfelder 1999).

Due the reduced intraocular effect and/or penetration of "soft steroids" such as fluorometholone and loteprednol etabonate, they might be unlikely to modify the intraocular pressure IOP (de Paiva and Pflugfelder 2008). Pflugfelder et al. performed a study evaluating loteprednol etabonate ophthalmic 0.5 % suspension for treatment of DED in

patients with moderate inflammatory component; after 4 weeks of treatment no elevation of IOP was observed (Pflugfelder et al. 2007).

Although topical CEs for DED have been shown to be of benefit, their long-term use may stimulate cataract formation, glaucoma, and ocular infection. For this reason, CE should be used for short-term periods, during disease exacerbations (Pflugfelder et al. 2007).

9.9.4.2 Topical Cyclosporine

Cyclosporine, an immunomodulatory drug, is considered the second most common drug, followed by CEs, used in treatment of immune-mediated ocular surface illness. Currently, it is the only pharmacologic treatment FDA approved particularly for DED that aims to normalize tear composition and production (Lemp 2008a).

The efficacy, safety, and patient tolerability of this drug have been demonstrated for assorted eye surface disorders (Utine et al. 2010; Foulks 2006). Yüksel evaluated the efficacy of topical cyclosporine by clinical and cytologic methods in patients with DED and demonstrated that after 6 month of therapy, severe dry eye patients had no satisfactory response as mild to moderate severity patients had (Yüksel et al. 2010).

9.9.4.3 Tetracyclines

Tetracyclines and derivatives have both antiinflammatory and antibacterial properties. Oral tetracyclines have been used off-label to DED treatment (Lemp 2008a).

Doxycycline is a therapeutic agent FDA approved for inflammatory skin lesions of rosacea, however, not for ocular rosacea (Lemp 2008a). The main action of doxycycline in patients with rosacea may be the capacity that this drug has to inhibit angiogenesis (de Paiva and Pflugfelder 2008).

Clinical reports propose that doxycycline has a successful effect in the treatment of inflammatory ocular diseases due its capacity of decrease collagenase, phospholipase A2 activity, and inhibition of proinflammatory cytokines (Smith and Cook 2004; de Paiva and Pflugfelder 2008).

Shine et al. suggested that minocycline may reduce inflammation reaction by decreasing meibomian gland lipid degradation products and consequently decrease neutrophil recruitment (Shine et al. 2003).

Yoo et al. verified improvements in dry eye symptoms after ingestion of doxycycline in patients with chronic meibomian dysfunction, who had performed the conventional therapy including warm eyelid massage and topical antibiotic therapy, with no success (Yoo et al. 2005).

9.9.4.4 Essencial Fatty Acids

Essential fatty acids are considered potential modulator of inflammatory activity and must be taken from food. Miljanovic et al. demonstrated a reduction of prevalence of DED among women with a higher consumption of n-3 fatty acids than those with lowest intake (Miljanovic et al. 2005).

Barabino et al. verified that systemic linoleic and gamma-linolenic acid administered twice a day has an antiinflammatory activity in patients with DED, with improvement of ocular irritation (Barabino et al. 2003). A study performed by Aragona et al. showed increase of prostaglandin (PGE1), which has antiinflammatory properties, and improvement of symptoms of ocular discomfort and signs of corneal epithelial defects (Aragona et al. 2005).

9.9.5 Potential Dry Eye Treatment

There are some potential options for DED treatment that are in various stages of phase II and III clinical trials. Promising results have been shown, and new treatment alternatives may help alleviate DED symptom.

9.9.5.1 SAR 1118

The SAR 1118 ophthalmic solution (SAR-code Bioscience, Brisbane, Calif) has the property of inhibiting T-cell-mediated inflammation acting on cellular surface proteins. The phase II trial was a randomized, placebo-controlled, multicenter study. SAR 1118 was reported to be well tolerated, with improvement in corneal staining and significant increase in tear production (Semba et al. 2012). Currently, SAR 1118 is in phase III trials.

9.9.5.2 CF101

CF101 is an adenosine receptor agonist, shown in preclinical and clinical studies to have antiinflammatory effect. In at phase II study, CF101 was administrated orally, as monotherapy for 12 weeks, by patients with moderate to severe dry eye. The drug was reportedly well tolerated and safe, without serious adverse events (Avni et al. 2010). Currently, the drug is in phase III clinical trial.

9.9.5.3 Dexamethasone Phosphate (EGP-437)

A single center, double-masked, randomized, placebo phase II trial evaluated ocular iontophoresis of EGP-437 (40 mg/mL) in patients with moderate to severe DED. Iontophoresis is a drug delivery technique which applies electrical field at ocular surface with the purpose of propelling charged drug, increasing ocular drug concentration. The results showed improvement of symptoms of dryness over 3-week study period relative to placebo (Patane et al. 2011).

9.9.5.4 Bromfenac

Bromfenac is a nonsteroidal antiinflammatory drug being evaluated as a potential therapy for DED.

9.9.5.5 Acupuncture

The Korea Institute of Oriental Medicine has completed a phase III trial. The purpose of this study was to verify if acupuncture is more effective than artificial tears for treatment of DED. In one group, seventeen acupuncture points were selected and acupuncture needles were placed on these points. The other group received preservative-free lubricant once a day for 4 weeks. Results have not yet been published.

9.10 Management Challenges

Aging populations are more susceptible to manifest visual impairment. Both DED and glaucoma are chronic conditions that require long-term care compliance with topical drop administration. Prolonged use of eyedrops containing preservatives can increase tear evaporation with subsequent discomfort (Rossi et al. 2009).

According with Department of Health and Human Services, in 2008, 68 % of the adult incident cases of diabetes were diagnosed between 40 and 64 years old and 17 % at age 65 or older (Department of Health and Human Services 2010).

Diabetes itself may decrease corneal sensation due peripheral neuropathy and also reduced tear secretion. Dogru et al. showed considerable changes in tear function and impression cytologic parameters in diabetic patients. Furthermore, fluctuations in glycemic levels may change the lacrimal gland function (Dogru et al. 2001).

Niti et al. demonstrate depression in 13.3 % of population aged 55 and older. There is a connection between depression and chronic diseases, principally if the chronic illness can cause any functional incapacitation (Niti et al. 2007).

Managing patients with dry eye associated with depression might be harder to quantify because these group may overestimate their symptoms and not believe that treatment will improve the symptoms, leading to noncompliance. Studies have shown depressive symptoms among older populations principally caused by physical disorder and functional disability (Lépine and Bouchez 1998). The psychological disturbance may be caused because of eye discomfort, disappointment with treatment results, and diminished QOL (Li et al. 2011).

Burns and Mulley demonstrated that practical issues were frequent among elderly patients, and they presented difficulties in self-application medication. The main difficulty seems to be the capability of the patient to precisely place the medication on the eye (Burns and Mulley 1992). Winfield et al. evaluated patient problems during self-medication with eyedrops, and they verified that 14 % had difficulties with reading labels and identifying bottle, 13 % poor visibility of tip of dropper, and 8 % with shaky hands (Winfield et al. 1990).

Some others age-related factors have a relevant influence in noncompliance to medication as decrease quality of vision, hearing, and memory; reduced cognitive and physical functions; and limited social and financial funds (Murray et al. 2004).

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