Dealing with dry eye disease in general practice

Smit DP, MBChB, Dip Ophth(SA), FC Ophth(SA), MMed(Ophth)(Stell)
Department of Ophthalmology Faculty of Health Sciences, Stellenbosch University, Tygerberg Hospital
Correspondence to: Derrick Smit, dpsmit@sun.ac.za
Keywords: dry eye disease, DED, keratoconjunctivitis

Abstract

Dry eye disease (DED) is a very common condition with significant morbitity. It is under-diagnosed by healthcare practitioners, since the presenting symptoms are often non-specific or misleading, and clinical signs may be subtle, or absent. To help overcome this problem, validated symptom questionnaires have been developed to aid the diagnosis, and grading of severity, of DED. Recent advances in the understanding of the multifactorial aetiology of this condition have also permitted the development of modalities aimed at treating specific underlying causes, rather than merely alleviating symptoms. An awareness of the causes and risk factors involved in this disease will assist the family practitioner in recommending lifestyle and dietary changes that, on their own, may provide sufferers with considerable symptomatic relief. A better understanding of the pathophysiology will, in turn, allow the family practitioner to make informed choices when prescribing initial treatment, and also guide the practitioner to know when to refer a patient for specialist management.

Ⓟ **Peer reviewed. (Submitted: 2011-10-23. Accepted: 2011-11-14.)** **S Afr Fam Pract 2012;54(1):14-18**

Introduction

Dry eye disease (DED), also known as keratoconjunctivitis sicca (KCS), is a very common condition that often prompts patients to seek help from eye-care professionals. In the past decade, understanding of the multifactorial aetiology of this disease has improved considerably, permitting the development of specific therapeutic options to treat the condition more effectively.

The purpose of this review is to provide the family practitioner with an updated insight into the pathophysiology, clinical picture, and treatment options of DED to facilitate confident assessment and management of this often under-diagnosed condition.

Definition

For many years, DED was considered to be the result of a simple imbalance between tear production and tear evaporation. However, understanding of the disease has improved significantly, and now permits the formulation of a far more accurate definition.

In 2007, the International Dry Eye Workshop (DEWS) compiled the following definition:

"Dry eye is a multifactorial disease of the tears and ocular surface, which 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."[1]

It is clear from this definition that dryness of the ocular surface is only one component of the disease. The term "dysfunctional tear syndrome" (DTS) provides a more accurate description of the condition, but has not, as yet, superseded the use of the term "DED".[2]

Demographics

DED most commonly occurs in postmenopausal women and in the elderly, with the reported prevalence varying from 7.4-33.7% in different studies.[3-6] Patients with autoimmune disease have a higher prevalence of DED than the general population.[7] Other factors, such as cigarette smoking and pterygium, are also associated with an increased prevalence.[8]

Pathophysiology

It is traditionally taught that the precorneal tear film consists of three distinct sandwiched layers. The outer lipid layer is secreted by the meibomian glands in the eyelids, the middle aqueous layer is secreted mainly by the lacrimal glands, and the inner mucin layer originates from the conjunctival goblet cells.[9] Recent reports suggest a more complex model, where the tear film forms a dynamic mucinous

gel, although the role played by each component remains largely unchanged.[10]

The outer lipid layer stabilises the tear film and prevents evaporation. Therefore, a deficient lipid layer may cause evaporative dry eye (EDE). The middle aqueous layer supplies dissolved atmospheric oxygen to the corneal epithelium. It washes any unwanted substances from the ocular surface, and also contains antimicrobial proteins, such as lysozyme, lactoferrin and immunoglobulin A. Decreased production of the aqueous layer causes aqueous deficiency dry eye (ADDE). The inner mucin layer enables the aqueous layer to attach itself to the corneal epithelium by converting the hydrophobic epithelial surface to one that is hydrophilic. Deficiency of the mucin layer occurs when conjunctival goblet cells are damaged.

Tear film instability may result from any alteration in its normal composition. A change in either the quality, or quantity, of any important tear film constituent, will destabilise the tear film, and lead to symptoms of DED. These changes are often caused by an inflammatory process affecting the meibomian glands, the conjunctival goblet cells, the lacrimal glands, or any combination of these structures. This underlying inflammation is usually mediated by T lymphocytes, and may occur in patients both with, and without, a systemic inflammatory disease.[11,12]

It is important to note that tear film instability allows the precorneal tear film to break up sooner than it normally would. This leads to the formation of transient, microscopic dry areas on the corneal surface, which causes the eye to feel dry or gritty. However, these dry areas may also stimulate the reflex secretion of aqueous tears by the lacrimal glands in an effort to decrease the perceived dryness, and thereby cause the paradoxical tearing that patients with DED often complain about. This illustrates why DTS is a better term than DED, since the problem is caused by tear film dysfunction, rather than by a mere lack of tears.

Classification, causes and risk factors

As indicated above, DED is often divided into two main classes, namely EDE and ADDE, although many patients experience a combination of the two. Table I provides more detail regarding specific conditions that predominantly cause either EDE or ADDE.[9]

Several other factors have also been identified that have a significant effect on dry eye symptoms. Many of these factors exacerbate the symptoms, while some tend to alleviate them.

Table II provides a summary of these factors.[7,12]

Table I: Classification and causes of dry eyes

Classification	Causes
Aqueous deficiency dry eye	
Sjögren syndrome	
Other causes	
Neurological	Decreased sensation (contact lens wear, refractive surgery)
	Parkinson's Disease
Decreased lacrimal tissue function	Surgical removal
	Tumour
	Inflammation
	Congenital absence (rare)
Obstructed lacrimal ductules	Chemical burns
	Stevens-Johnson syndrome
	Ocular cicatricial pemphigoid
Age-related hyposecretion	
Vitamin A deficiency	
Evaporative dry eye	
Meibomian gland disease	Blepharitis
	Rosacea
	Atopic keratoconjunctivitis
Prolonged exposure	Severe proptosis
	Facial nerve palsy
	Eyelid scarring
Environmental factors	Air conditioning
	Dry, windy conditions
Contact lens wear	

Adapted from reference 9

Table II: External factors that increase, or relieve, dry eye symptoms

Increase symptoms	Relieve symptoms
Increasing age	Increased intake of omega-3 fatty acids
Female sex	High ambient relative humidity
Hormone replacement therapy (oestrogen alone)	
Long-term contact lens wear	
Systemic medications	
Refractive surgery (LASIK,[a] PRK[b])	
Smoking and alcohol use	
Extended visual tasks (reading, computer work)	

a = laser-assisted in-situ keratomileusis, b = photo refractive keratectomy
Adapted from references 7 and 12

It is especially important for family practitioners to be aware of the multitude of systemic medications that may cause, or worsen, the symptoms of DED. Table III highlights a number of drugs associated with dry eye symptoms.[10]

Table III: Systemic drugs associated with dry eye symptoms

Drug class	Examples
Antiarrhythmia	Amiodarone
Antihistamine	Diphenhydramine, hydroxyzine
Anti-Parkinson	Benztropine, trihexyphenidyl
Antipsychotics	Chlorpromazine, haloperidol
Antispasmodics	Hyoscine butylbromide, oxybutinin
Tricyclic antidepressants	Amitriptyline, nortriptyline
Diuretics	Hydrochlorothiazide
Beta blockers	Atenolol
Retinoids	Isotretinoin
Sex hormones	Estrogen supplements
Selective serotonin-reuptake inhibitors	Fluoxetine, paroxetine, sertraline
Chemotherapy	Cyclophosphamide, 5-fluorouracil

Adapted from reference 10

Clinical features

Patients often complain about a feeling of dryness, grittiness, or burning, that tends to get worse during the day. They may also report transient blurring of vision, or increased tearing.

The signs are often very subtle, and may not match the severity of the presenting complaints. Findings may vary from a completely normal-looking eye, to one with variable crusting or foaming on the eyelid margins, mild conjunctival redness, or punctate staining of the cornea when viewed under cobalt blue light, after the installation of fluorescein dye (Figure 1). Corneal epithelial defects, and even corneal perforation, may occur in severe cases.

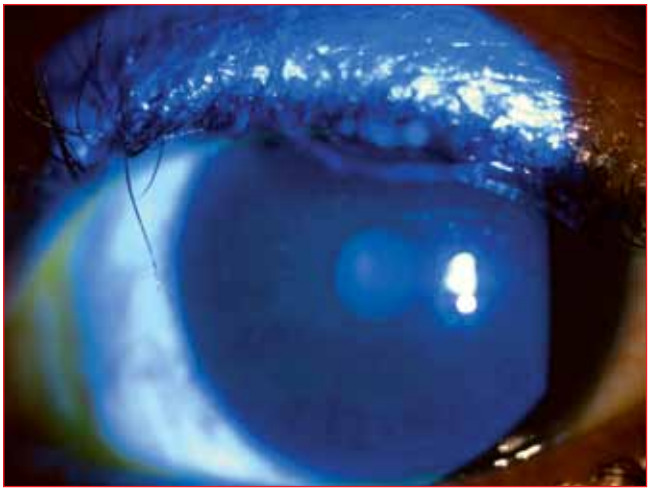

Figure 1: Punctate staining of the cornea when viewed under cobalt blue light, after the installation of fluorescein dye

Several different symptom questionnaires have been designed to aid busy practitioners in the diagnosis of DED, and these may be extremely useful when a diagnosis of DED is suspected, but little evidence is found on clinical examination. The Ocular Surface Disease Index© (OSDI), for example, asks a patient 12 simple questions, and then allows the practitioner to decide whether or not DED is present, and if so, to grade the severity thereof. It has been shown to discriminate effectively between normal eyes, eyes with mild-to-moderate DED, and eyes with severe DED. It may also be used to monitor the response to any treatment that the patient receives.[13] An example of the OSDI is available at www.dryeyezone.com/documents/osdi.pdf

Treatment options

DED treatment aims to improve quality of life by relieving the symptoms, and enhancing visual acuity. It also aims to restore the normal homeostasis of the ocular surface and tear film, and to address any underlying disease processes.[1] Several treatment options are available, and the appropriate choice is based on the severity of the patient's symptoms, as elicited from the taking of a clinical history, or completion of a symptom questionnaire, or both.

Mild cases

These cases are ideally suited to management by a family practitioner, since the necessary interventions include lifestyle changes, dietary measures, a review of systemic medications, and the initiation of topical lubricants. The recommended lifestyle and dietary adjustments are summarised in Table IV.

Table IV: Recommended lifestyle and dietary changes for patients with dry eye disease

Avoid allergens and control allergies	
Humidify the home and work environment	Beware of heaters, air-conditioners
Avoid rubbing the eyes	
Stop smoking	Reduce exposure to environmental smoke
Limit periods of television watching, reading	Encourage frequent breaks
	Use artificial tears during the activity
Ensure correct use of contact lenses	
Encourage a diet rich in omega-3 fatty acids	Eat fish (salmon, mackerel, sardines, tuna)
	Plant oils (canola oil, flax seed oil)
	Reduce alcohol consumption

Adapted from reference 10

Systemic drugs implicated in causing or exacerbating dry eye symptoms should, if possible, be replaced with more suitable alternatives, and the patient should be given artificial tear drops to supplement their precorneal tear film. These

preparations usually contain hypromellose, carmellose, polyvinyl alcohol or polyacrylic acid. It should be noted that a preservative such as benzalkonium chloride, which is found in many ophthalmic drops, may also contribute to dry eye symptoms if used more than four times a day. Therefore, patients should change to preservative-free preparations if they require more frequent application to control their symptoms.

Moderate cases

Patients with moderate symptoms of DED require the same initial management as those with mild disease. However, they are likely to require more frequent application of topical lubricants, and should be given preservative-free drops from the outset. Oral omega-3 fatty acid supplements may also be prescribed if dietary intake is not sufficient. If symptoms persist despite all the treatment modalities already employed, referral should be considered for slit lamp examination, and other special investigations. This will allow more specific and individualised management of the underlying problem.

For instance, if significant eyelid inflammation is present, a combination of short-term topical antibiotics and long-term, low-dose oral tetracycline may be indicated. If aqueous deficiency is diagnosed, patients may also require plugging, or cautery of the lacrimal puncta, to decrease tear drainage. Ocular surface inflammation should also be addressed by the initial prescription of low-potency corticosteroids, such as fluorometholone. If effective, the corticosteroids may later be replaced by cyclosporine A, which prevents T-cell activation and has been shown to improve DED both subjectively and objectively.[12] Cyclosporine A is now commonly used by ophthalmologists in a topical preparation, as part of the treatment for moderate and severe DED.

Severe cases

Severe cases require specialist management. In addition to all the treatment modalities discussed so far, several other interventions may be needed. Patients may require moisture-retaining eyewear, or special contact lenses to preserve whatever aqueous tears they are able to produce themselves. They may also require the preparation of eye drops from their own serum, which contains a variety of anti-inflammatory factors. Many studies have shown a beneficial response to 20% autologous serum drops, when used in patients with severe DED.[10] Systemic immunosuppressive therapy should also be considered if the patient has an underlying systemic inflammatory condition. Surgical procedures, such as tarsorrhaphy, or even salivary

gland or duct transplantation, may become necessary in very severe cases.[12]

Conclusion

DED is very common, and poses a significant problem to its sufferers. It is now well established that this disease has a multi-factorial aetiology, and therefore requires several different modalities to treat it effectively.

Symptom questionnaires are able to accurately diagnose and grade the severity of DED, and can assist healthcare practitioners in the management of this condition. Mild disease should preferably be managed by family practitioners, who are in an ideal position to assess and alter environmental, dietary, and iatrogenic factors that cause, or exacerbate, the disease. Moderate-to-severe DED generally requires more specialised intervention, thus the family practitioner should consider referral to an ophthalmologist.

References

1. International Dry Eye Workshop (DEWS). The definition and classification of dry eye disease: report of the definition and classification subcommittee of the International Dry Eye Workshop. Ocul Surface. 2007;5(2):75-92.
2. Behrens A, Doyle JJ, Stern L, et al. Dysfunctional tear syndrome: a Delphi approach to treatment recommendations. Cornea. 2006;25(8):900-907.
3. Schaumberg DA, Sullivan DA, Buring JE, et al. Prevalence of dry eye syndrome among US women. Am J Ophthalmol. 2003;136(2):318-326.
4. Moss SE, Klein R, Klein BE. Prevalence of and risk factors for dry eye syndrome. Arch Ophthalmol. 2000;118(9):1264-1268.
5. Lin PY, Tsai SY, Cheng CY, et al. Prevalence of dry eye among an elderly Chinese population in Taiwan: the Shihpai eye study. Ophthalmology. 2003;110(6):1096-1101.
6. McCarty CA, Bansal AK, Livingston PM, et al. The epidemiology of dry eye in Melbourne, Australia. Ophthalmology. 1998;105(6):1114-1119.
7. Gayton JL. Etiology, prevalence and treatment of dry eye disease. Clin Ophthalmol. 2009;3:405-412.
8. Lee AJ, Lee J, Saw S, et al. Prevalence and risk factors associated with dry eye symptoms: a population based study in Indonesia. Br J Ophthalmol. 2002;86(12):1347-1351.
9. Kanski JJ. Clinical ophthalmology: a systematic approach. 6th ed. Philadelphia: Elsevier, 2007; p. 205-214.
10. Jackson WB. Management of dysfunctional tear syndrome: a Canadian consensus. Can J Ophthalmol. 2009;44(4):385-394.
11. Stern ME, Gao J, Schwalb TA, et al. Conjunctival T-cell subpopulations in Sjögren's and non-Sjögren's patients with dry eye. Invest Ophthalmol Vis Sci. 2002;43(8):2609-2614.
12. Bhavsar AS, Bhavsar SG, Jain SM. A review on recent advances in dry eye: pathogenesis and management. Oman J Ophthalmol. 2011;4(2):50-56.
13. Schiffman RM, Christianson MD, Jacobsen G, et al. Reliability and validity of the ocular surface disease index. Arch Ophthalmol. 2000;118(5):615-621.