Management of Dry Eye

Essay submitted in partial fulfillment

Of the master degree of ophthalmology

By

Saleh Kamel Saleh Darwish

M.B.B.ch

Under Supervision of

Prof.Dr.Abdallah Hussein Hamed

Professor of ophthalmology

Alazhar University

Prof. Dr.Mohamed Zakaria Eid

Professor of ophthalmology

Alazhar University

Faculty of Medicine

Alazhar University

Cairo-Egypt

2013


وقل رب زدنی علما

Acknowledgement

First of all, thanks to ***Allah*** *the most merciful for giving me the strength to complete this work.*

I wish to express my deepest thanks and respect for ***Prof. Dr. Abdallah Hussein Hamed,*** *Professor of Ophthalmology, Faculty of Medicine, Alazhar University, for his valuable supervision, guidance and kind advice throughout this work.*

Also, I wish to express my deep gratitude to ***Dr. Mohamed Zakaria Eid,*** *assistant Professor of Ophthalmology, Faculty of Medicine, Alazhar University, for his good support, continuous supervision and unlimited help during this work.*

I would like also to thank my family for their kindness, support and much needed encouragement.

Dedication

To the soul of my father,

To my family,

And To the greatest revolution in the history the 25th of January Egyptian revolution.

Contents

List of Abbreviations

AAO	American academy of ophthalmology
BAC	Benzalkonium chloride
BUA	Break-up area
BUT	Break-up time
CGVHD	Chronic graft-versus-host disease
CLs	Contact lenses
CMC	Carboxymethylcellulose
CsA	Cyclosporin A
DCR	Dacryocystorhinostomy
DED	Dry eye disease
DES	Dry eye syndrom
DHA	Docosahexaenoic acid
DMEM	Dulbecco's minimum essential medium
DTS	Dysfunctional tear syndrome
EFAs	Essential fatty acids
EGF	Epidermal growth factor
ELISA	Enzyme-linked immunosorbent assay
EPA	Eicosapentaenoic acid
FDA	Food and Drug Administration
FK	Filamentary keratitis
GLA	Gamma-linolenic acid
GVHD	Graft-Versus-Host Disease
HIV	Human immunodeficiency virus
HP	Hydroxypropyl
HPMC	Hydroxypropyl Methylellulose
HRT	Hormone replacement therapy
IgG4	Immunoglubulin G4

IL-1a	Interleukin-1 a
IL-1b	Interleukin-1b
KCS	keratoconjunctivitis sicca
LASIK	Laser in situ keratomileusis
LFU	Lacrimal functional unit
LMN	Lower motor neurone
LR-CLAL	Living-related conjunctival limbal allografting
LSCD	Limbal stem cell deficiency
LTB5	Leukotriene B5
MGD	Meibomian gland dysfunction
NK	Natural killer
NSAIDs	Non-steroidal anti inflammatory drugs
OTC	Over-the-counter
PGE3	Prostaglandin E3
Rpm	Revolution per minute
PRK	Photorefractive keratectomy
PVA	Polyvinyl Alcohol
S.C.T	Stem cell transplantation
SLE	Slit lamp examination
S.L.K	*Superior limbic kerato-conjunctivitis*
S.L.S	Sjögren-like syndrome
SS	Sjogren syndrome
TCR	Tear clearance rate
TFBU	Tear film break-up time
TFI	Tear Function Index
TGF-B	Transforming growth factor B
TMS	Topographic modeling system
TNF-α	Tumor necrosis factor alpha
WHS	Women’s Health Study

List of Tables

List of Figures

Introduction

Dry eye is the most frequent disorder in ophthalmology (Boyd,2001).

Although chronic dry eye occurs in both men and women, it affects women tow-to-three times more often and most common in post-menopausal women because of the hormonal changes associated with aging (Schumberg et al.,2003).

In Japan, 33 percent in a trial comprising 2500 participants responded to having dry eye syndrome (Schimmura et al.,1999). In Canada, the prevalence of patients reporting any level of symptoms of dry eye was approximately 1 in 5 (Doughty et al.,1997).

Despite this prevalence, dry eye is worledwide underdiagnosed problem. It is estimated that 89percent of Americans and Canadians have not heard of it.Most people assume that gritty, red, watery eyes are just part of their life. Accordingly, one out of five may be suffering from dry eye syndrome and is unaware of it (Kaercher, 2001).

The management of dry eye syndrome requires ophthalmologists first to identify the underlying cause(s) of patients' symptoms. It is important to take a careful medical history and search for potential etiologies. They can include radiation therapy and status post refractive surgery (LASIK, astigmatic keratotomy, and cataract surgery) as well as systemic diseases such as rheumatoid arthritis, diabetes, lupus, scleroderma, Sjögren’s syndrome, vitamin A deficiency, chronic recurrent herpetic keratitis, and Bell’s palsy. Other potential instigators are medications, including antihistamines, decongestants, birth control pills, diuretics, angiotensin-converting enzyme inhibitors, narcotic analgesics, antidepressants, and acne medications. Finally, several environmental factors can cause dry eye. Common triggers include computer usage, reading, prolonged driving, wind, heat exposure, altitude, low humidity, smoke, and contact lens usage(Noble et al., 2004).

In order to assess the degree of concordance between common dry eye diagnostic tests, researchers evaluated the tear film and ocular surface by meibomian gland pathology, ocular surface grading, conjunctival epithelial and goblet cells, phenol red thread test, and fluorescein tear breakup time (TBUT). Statistical correlations among all tests were evaluated using a McNemar’s test to compare results. Dry eye symptoms were assessed using McMonnie’s dry eye

questionnaire. A statistically significant difference was reported between phenol red thread results and those of all other tests. The MGD pathology, McMonnie's dry eye questionnaire, and TBUT results correlated with McNemar's test results. A lack of concordance was found among all other tests (Moore et al., 2009).

Over the past two years, several international groups have met to discuss consensus within the field of dry eye in an effort to improve patient care and collectively move the field forward. They proposed a new term for dry eye disease: dysfunctional tear syndrome (DTS), which, they say, would accurately reflect patient symptoms and take into account lid margin disease and\or tear composition abnormalities (Behrens et al.,2006).

It has been confirmed that dry eye is related to the inflammation of ocular surface which is based on immune response and induced by many cytokines (Nagelhout et al.,2005).

In recent studies, topical corticosteroids have shown promising results for treating dry eye. Steroids may help increase goblet cell density and reduce the accumulation of inflammatory cells within ocular surface tissues (Avunduk et al.,2003).

Various treatment modalities are being tried. Conventionally, therapy of dry eye follows a staged concept including topical normal saline (NS) or normal saline with high molecular weight polymers, tear replacement in the form of cellulose esters (methyl cellulose hydroxypropyl) or polyvinylalcohol & saline artificial tears, serum eye drops, punctum plugs, novel anti-inflammatorydrugs (cyclosporin A), and surgical procedures. Interdisciplinary care, especially of patients with autoimmune disease, is recommended and is best provided in a specializes dry eye outpatient clinic (Cursiefen et al., 2006).

Surgical treatment of dry eye has many advantages including punctual patch technique (Boyd,2001), amniotic membrane transplantation (Azuaro-Blanco et al.,1999), stem cell transplantation (Lubniewski and nelson,1990) and submandibular gland transfer (Seig et al.,2000)

As the aetiology and pathogenesis of dry eye is increasingly understood, management of dry eye expects promising days (Boyd,2001).

Aim of the work

The aim of this study is to review the literature as regard the current diagnostic and therapeutic means in addition to the latest progress and achievement in the field of management of dry eye.

A- Anatomy of The Lacrimal Secretory System

The main lacrimal glands produce about 95% of the aqueous component of tears and the accessory lacrimal Glands of Krause and Wolfring produce the remainder (Kanski., 2003).

1- Anatomy of The main Lacrimal Gland

The Lacrimal gland lies above and anterolateral to the eye ball.It appears in all vertebrates except fish.
It is formed of tow parts:
A large orbital (Superior) part and a small palpepral (inferior) part. The tow parts continue with each other (Snell and Lemp,1998).

The orbital (superior) part:

It alies in a fossa in the anterolateral part of the orbital roof.It is almond-shaped displaying superior and inferior surfaces,anterior and posterior borders as well as medial and lateral extremities. The superior surface is convex and lies in the fossa and connected to it by weak trbeculae. The inferior surface is slightly concave and lies successively on the levator muscle, its lateral extension and The lateral rectus.

The anterior border is well-defined and in contact with the orbital septum. Hence, skin, orbicularis and orbital septum must be divided to reach the gland.
The posterior border is rounded and lies in contact with the orbital fat in a level with the posterior pole. The medial extremity rests on the levator while the lateral extremity on the lateral rectus(Bron et al.,1997).

The palpebral (inferior)part:

It is flattened horizontally and one-third the size of the orbital part. The palpebral part is separated from the orbital part by the lateral expansion of the levator except behind where they continue with each other. The

palpebral portion lies mainly on the fornix palpebral conjunctiva and the levator palpebrae superiosis.
The anterior end of the palpebral part lies just above the lateral border of the superior conjunctival fornix. Thus, it is visible through the conjunctiva when the upper lid is everted and up to 12 ductular openings may be seen with biomicroscopy(Snell and Lemb,1998).

Ducts of the lacrimal gland:

Approximately 11 ducts pass from the orbital lobe through the palpebral lobe of the lacrimal gland and most enter the conjunctiva above the lateral canthus in the superolateral fornix(Sanderson et al.,1995). Additional ductules arise directly from the palpebral lobe and empty into the superolateral fornix. Inadvertent resection of the palpebral lobe or superolateral conjunctival fornix may result in loss of tear secretion and dry eye symptoms (Shovlin et al., 1994).

Structure of the lacrimal gland:

The lacrimal gland is serominous tubulo-acinar with short branched tubules resembling the parotid gland in structure. The smallest intra-lobular ducts are lined with a layer of low columner or cuboidal cells and have myo-epithelial cells at the periphery. The larger inter-lobular ducts have a tow-layered epithelial lining (Bron et al., 1997).

Blood supply of the lacrimal gland:

- Arterial supply : The lacrimal artery is the main arterial supply of the gland, which is a large branch that arises from the ophthalmic artery close to its emergence from the optic canal(Snell and Lemb, 1998).
- Venous drainage : The lacrimal vein has the same course of the artery and ends in the superior ophthalmic vein. The latter passes through the superior orbital fissure to end in the cavernous sinus (Snell and Lemb,1998).
- Lymphatic drainage of the lacrimal gland: Lymphatics pass from the gland to the conjunctival channels and then to pre-auricular lymph nodes.

Nerves of the lacrimal gland:

The lacrimal gland receives both autonomic and sensory nerve fibres.

The parasympathetic secretomotor nerve supply is derived from the superior salivatory nucleus of the facial nerve.The preganglionic fibres reach the pterigopalatine ganglion throw the nervus intermedius and its great Petrosal nerve and through the nerve of the pterygoid canal.Post-ganglionic fibres leave the ganglion and join the maxillary nerve. They then pass into the zygomatic branch and the zygomatico-temporal nerve. They reach the lacrimal gland within the lacrimal nerve.

The sympathetic postganglionic fibres arise from superior cervical sympathetic ganglion and travel in the plexus of nerves around the internal carotid artery. They join the deep petrosal nerve,the nerve of the pterygoid canal, the maxillary nerve,the zygomatic nerve, the vidan nerve, the zygomaticotemporal nerve and finally the lacrimal nerve.

The sensory fibres reach the lacrimal gland in the lacrimal nerve, a branch of the ophthalmic division of the trigeminal nerve(Hurwitz,1996).

2- Anatomy of Accessory Lacrimal Glands

The gland of Krause:

They are resembling in structure the main lacrimal gland They are present deeply in the subconjunctival Connective tissue mainly in the upper fornix. Their number is about 42 in the superior fornix and 6-8 in the lower fornix. Their ducts have been united into another long ducts which open into the fornix (Snell and Lemb,1998).

The glands of Wolffring:

They are larger than glands of Krause. They are 2-5 glands in the upper lid situated in the upper border of the tarsus and tow in the lower edge of the lower tarsus. Their ducts are short,wined and lined by epithelium made of two layers deep cubical and superficial cylindrical cells(Snell and Lemp,1998).

Henel's glands and Glands of Manz:

They are present in some animals.