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Review Article

Dry eye disease - are we underselling it? An epidemic in the offing and future management trends

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Abstract
Dry eye definition and management has seen a complete overhaul over the past two decades. With increasing life style changes the incidence of DED has exponentially increased and it's not relevant only to the developed world anymore. The earlier thought demography of patients susceptible for dry eye has also changed considerably. In India the prevalence of dry eye ranges from 18.4% to 40.8%. This increasing incidence of DED has provided a sling shot for many pharmaceutical industry leaders to come up with novel innovative treatment methodologies for holistic management of dry eye disease. In our brief communication we look at the history of dry eye diagnosis and management and future treatment options available for treating clinicians to tackle the epidemic of DED.

Keywords: DED, Epidemic, DEWS, Dry eye

1. Introduction
We have progressed a long way from a 5th century BC belief that tears came via the brain, to the present advances in defining and management of dry eye. It was only around the 17th century Steno was able to demonstrate that tears coursed via the lacrimal gland, along the tear ducts. By the 1900's sympathetic and parasympathetic control of basal and reflexive secretions respectively was proved. Further tests and advancements followed in the 20th century, which led to the development of various testing protocols and dyes like fluorescein to study the ocular surface [1, 2].
Similar to the diagnostic revolution of dry eye which took place with time, path breaking discoveries were constantly occurring at pace in the management of dry eye. As early as 5th century oat herbs were used and till around 11th century hearsay treatments like grapewine, vinegar and honey was used to treat dry eye. Around 1900's the majority belief was that lacrimal gland dysfunction should be held at knife point, while many others believed in other archaic forms of treatment like rubbing the eyes with honey and antimony could cure dry eye [2]. 20th century heralded the shot in the arm for dry eye diagnosis and management methodologies. Many innovations like tear substitutes, hormones like estrogen and androgens were tested [4].

2. Incidence & prevalence: So where are we today?
The prevalence of DED is increasing globally, accounts for about 25-30 million patients diagnosed with DED. In India the prevalence of DED, has experienced a dramatic rise in the preceeding 20 years, ranging from 18.4% to 40.8% [5].

3. Etiopathogenesis
As the diagnostic and management strategies have evolved, so has the epidemiology of dry eye. Dry eye disease (DED) patients till recently mostly were post-menopausal woman, computer programmers, and patients with autoimmune diseases but the recent trend of DED suggests patients of all age groups can be affected. Risk factors leading to DED can vary according to the age, geography, environment, co morbidities, life style and any other auto immune pathologies [6].
In children the main risk factors include undiagnosed blepharokeratoconjunctivitis, antihistaminics, allergies, increased screen time and PEM, whereas in adolescent and in early adulthood mostly its due to increased screen time, lack of sleep, excess caffeine, alcohol, life style, lack of contact lens hygiene, abuse of vasoconstrictors, allergies and antihistaminics.

Patients in the age group of 30 to 50 risk factors for DED are hormonal changes, women approaching menopause, increased screen time, reduced blink rate, lack of sleep, excessive caffeine, drugs and medications, poor nutrition, autoimmune or other systemic diseases causing dry eye. Patients above 50years, along with the above mentioned risk factors, drugs (diuretics, anti-glaucoma medications, pantoprazole, anticholinergics, tricyclic antidepressants and antipsychotics, antihistamines, antispasmodics and antiparkinson medications) diabetes, rheumatoid arthritis, lupus, vitamin A deficiency, thyroid disorders, radiation therapy, Sjögren's syndrome menopause and meibomian gland dysfunction can worsen DED [6, 7].

DEWS in 2007 defined DED as "A multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles". DED was further classified as aqueous deficiency and evaporative dry eye. In the aqueous deficient variant – Sjogrens (Primary & Secondary) and Non Sjogrens (lacrimal system abnormality). In the evaporative variant- intrinsic (meibomian gland dysfuction and structural lid anamolies) extrinsic (nutritional Vit A deficiency, contact lens, allergies) [8].

Tear deficient dry eyes: Sjögren's syndrome
Non-Sjögren's syndrome
Evaporative dry eye: Reduced blinking, Vit A deficiency, allergies
Environmental factors, contact lens
Blepharitis/meibomian gland dysfunction
Eyelid problems

4. Diagnostic approaches

Diagnostic developments for dry eye have come a long way in helping the prognosticating and management of DED. Various testing modalities have evolved over the years like schirmer test, epithelial staining, tear function index, impression cytology, fluorophotometry, tear fluid protein immunoassays, tear ferning test, meibometry, meibography and many more. According to the DEWS 2007 diagnostic algorithm, a diagnosis of dry eye disease includes a multitude of testing protocols starting from Questionnaire's, risk factor analysis, symptomatology, non-invasive testing procedures like TBUT, tear fluid osmolarity and ocular surface staining. Based on these testing parameters, criteria for diagnosis of DED was developed: Positive symptomatology (Dry Eye Questionnaire-5 >5 or OSDI >13), plus noninvasive BUT <10 seconds, or Osmolarity >308 mOsm/L or interocular difference >8 mOsm/L, or Ocular surface staining (>5 corneal spots, >9 conjunctival spots, or lid margin) [7, 8].

5. Conventional management trends

Management of dry eye has varied among different clinicians. To enhance uniformity DEWS gave out treatment guidelines in 2007 for DED. In early to moderate severity life style modifications like reduce caffeine, alcohol, quit smoking, good sleep hygiene, contact lens hygiene and lid hygiene. Medications like artificial tears, punctal occlusion, moist chamber glasses, treat underlying lid abnormalities and infections, topical steroids, topical cyclosporine, oral tetra cyclines and macrolides. In moderate to severe cases oral secretagogues, allogenic/ autologous serum eye drops, soft bandage lenses and rigid scleral lenses may help. In very severe cases amniotic membrane grafts and permanent surgical punctual occlusion and salivary gland transplantation may be needed [8].

Even with all of these medications and advancements the problem of DED has seen an upward trend in recent years. The cause maybe inadequate awareness among the general population, life style, increased technological/ screen time since the turn of the century in all age groups and environmental aspects all of which are contributing to this increased prevalence and early incidence of DED. In school going children, the teachers should be made aware of the symptomatology of dry eye and should act as primary screeners of DED. Education about the harms of increased screen time should be conveyed to both teachers and parents so that they can relay the same and take active steps to decrease the screen time in children. One of the most important ways by which we as clinicians can tackle this problem is early awareness and patient education of DED, along with better diagnostic modalities which would help us in early diagnosis and characterizing of the DED. Any case of belpharokerato conjuctivitis should be followed up so as to not miss any secondary dry eye and all cases of MGD should undergo complete course of treatment. All medication history, co morbidities and auto immune diseases should be evaluated and the root cause of DED should be treated rather than just treating the symptomatology of DED. Nutritional supplements like vitamin A, and fish offer resistance to ocular surface disorders and should be part of a balanced diet [9]. Patients who are working on computers should be advised about visual hygiene (Anshel's 20/20/20 rule is: Every 20 minutes, take 20 seconds and look 20 feet away from the screen). Employing all these steps would help us prevent ocular morbidity and improve treatment outcomes [10].

6. Future management ideas: What's ahead in management of DED?

The pharmaceutical market of dry eye has consistently increased over the last 10 to 15 years with expected figures for 2025 of about 7.7billion US dollars. From the early age development of artificial tears to devices for combatting dry eye, the dry eye pharma sector has undergone a considerable change. Recent advances in treatment of DED include, Cyclosporine A (0.05%) which acts against the T lymphocytes, inhibit apoptosis and also increase number of goblet cells. Vitamin A & Omega 3 fatty acids decreases inflammation and alters the composition of meibomian lipids [9]. Lifitegraft 5% (LFA-1 integrin antagonist) is currently in phase 3 of development acts by prevents interaction with ICAM-1, thereby inhibiting cytokine release and migration of inflammatory mediators [11]. Rebapimide, a quinolinone derivative mucin secretogogue increases the number of goblet cells, although initially used for gastritis, now is approved for DED in Japan although it is yet to be approved by USFDA [12]. MIM-D3 nerve growth factor (NGF) peptidomimetic that has completed phase 3 clinical trial for the treatment of dry eye acts as a mucin secretogogue and helps in corneal wound healing [13]. OTX-DP: Sustained release dexamethasone loaded punctal plug 0.4 mg, acts by dispensing a tapered release of dexamethasone onto the ocular surface over 30 days after insertion. OTX-DP has primarily been investigated for treatment of inflammation and pain in the postoperative period. In 2015 was proposed for treatment of DED, is in phase 2 of drug development [14]. Other drug targets like Protein-Based IL-1 Inhibitor EBI 005 for topical ophthalmic use and has completed phase 2 clinical testing [15]. Diquafosol, a agonist of the ocular surface P2Y2 receptor,

acts by stimulating the phospholipase pathway which promotes fluid transfer and mucin secretion, recently concluded phase 3 study in the US [16]. Others along the pipeline are RU-101:Recombinant human serum albumin, and Loteprednol Etabonate mucus-penetrating particle and many more [17].

Another novel method is the neurostimulation of lacrimal functional unit (LFU) - Oculeve Neurostimulator Device: Intranasal lacrimal stimulator for dry eye, is inserted into the mucous membrane of the nasal cavity. Tear production stimulation is then modulated by a wireless controller [17]. Better drug delivery devices like Ocular Iontophoresis with EG-437 (40 mg/ ml Dexamethasone Phosphate Solution) is an ocular iontophoriesis system designed to deliver drugs to the conjunctiva and sclera. In ocular iontophoresis, a small current is applied to the ocular surface creating an electrical field, which enhances the mobility of charged particles across the anterior and posterior segments. A drug delivered by ocular iontophoresis may achieve higher concentrations than it would via topical drop form [8].

7. Conclusion

In reality we are at crossroads with regards to treatment of DED. The pharmaceutical market for treating DED is growing and more options are available for the treating clinician. Although various long term safety studies are yet to be done, the results are encouraging. With availability of newer treatment options perhaps DED treatment should be approached in a more holistic manner than the ones till recently, when only symptomatology was treated. With advent of newer advancements in treatment of DED perhaps newer treatment protocols has become a more pressing necessity in the current scenario.

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No conflict of interests

8. References

1. Kraus A. Assyro-Babylonian Ophthalmology. Annals of Medical History 1934;6:42-55.
2. Andersen SR. The eye and its diseases in Ancient Egypt. Acta Ophthalmol Scand 1997;75:338.
3. Hirschberg J. The History of Ophthalmology, Antiquity. Translated by FC Blodi. Bonn, West Germany: Verlag JP Wayenborgh, 1982, 1.
4. Moshirfar M, Pierson K, Hanamaikai K, Santiago-Caban L, Muthappan V, Passi SF. Artificial tears potpourri: a literature review. Clinical ophthalmology (Auckland, NZ) 2014;8:1419.
5. Prevalence of Dry Eye in Patients Presenting With Symptoms Suggestive of Dry Eye. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) 2018;17(3):7-12.
6. Phadatare SP, Momin M, Nighojkar P, Askarkar S, Singh KK. A comprehensive review on dry eye disease: diagnosis, medical management, recent developments, and future challenges. Advances in Pharmaceutics 2015.
7. Messmer EM. The pathophysiology, diagnosis, and treatment of dry eye disease. Deutsches Ärzteblatt International 2015;112(5):71.
8. Craig JP, Nichols KK, Akpek EK, Caffery B, Dua HS, Joo CK *et al*. TFOS DEWS II definition and classification report. The ocular surface 2017;15(3):276-83.
9. Rand AL, Asbell PA. Current opinion in ophthalmology nutritional supplements for dry eye syndrome. Current opinion in ophthalmology 2011;22(4):279.
10. Anshel JR. Visual ergonomics in the workplace. AAOHN J 2007;55(10):414-20.
11. Sheppard JD, Torkildsen GL, Lonsdale JD *et al*. Lifitegrast ophthalmic solution 5.0% for treatment of dry eye disease: results of the OPUS-1 phase 3 study. Ophthalmology 2014;121(2):475-83.
12. Kashima T, Itakura H, Akiyama H, Kishi S. Rebamipide ophthalmic suspension for the treatment of dry eye syndrome: A critical appraisal. Clin Ophthalmol 2014;8:1003-10.
13. Meerovitch K, Torkildsen G, Lonsdale J *et al*. Safety and efficacy of MIM-D3 ophthalmic solutions in a randomized, placebo-controlled Phase 2 clinical trial in patients with dry eye. Clin Ophthalmol 2013;7:1275-85.
14. Borgia M, Chaouk H, Cui H, Laredo W, Li Z, Nathan A, Trezza M, inventors; Johnson, Johnson Vision Care Inc, assignee. Punctal plugs for the delivery of active agents. United States patent application US 11/759,281. 2008.
15. Goldstein MH, Tubridy KL, Agahigian J *et al*. A phase 2 exploratory study of a novel interleukin-1 receptor inhibitor (EBI-005) in the treatment of moderate-to-severe allergic conjunctivitis. Eye Contact Lens 2015;41(3):145-55.
16. Keating GM. Diquafosol ophthalmic solution 3%: a review of its use in dry eye. Drugs 2015;75(8):911-22.
17. Vickers LA, Gupta PK. The future of dry eye treatment: a glance into the therapeutic pipeline. Ophthalmology and therapy 2015;4(2):69-78.
18. Gungor S, Delgado-Charro MB, Ruiz-Perez B *et al*. Trans-scleral iontophoretic delivery of low molecular weight therapeutics. J Control Release 2010;147(2):225-31.