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RECENT TRENDS FOR DRY EYE DIAGNOSTIC PROCEDURE – A REVIEW

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Abstract: *It has been hypothesized that the prevalence of eye disorders increases indifferent age groups in a rural population in India. Therefore, middle-income countries should prioritise providing health preventive and rehabilitation programmes. The study aimed to determine the pattern of ocular eye disorder in patients attending the outpatient eye department of a rural eye hospital in Naraingarh, Ambala, India. It is Hospital-based descriptive cross-sectional study. This study incorporated all the patients reported in secondary eye care hospitals and initially written consent forms taken formally the participants, followed by demographic information and detailed case history. A detailed ocular examination was done for all the participants to determine any ocular morbidity. All the data were entered in a Microsoft Excel 2020andanalyzedusing IBM Statistical Package for Social Sciences (SPSS) version 20. Descriptive statistics such as frequency and percentage were calculated. Out of a total of 3321subjects,1562(47.01%) were male, and1759(52.9%) were females. The most common ocular morbidity was cataract (19.59%), followed by Presbyopia (15.32%), Refractive error (13.51%), allergic conjunctivitis (12.13%), and dry eye (5.29%). The percentage of low-vision patients was 8.98%. Refractive error was the most common ocular morbidity in the 4-17 age group, followed by allergic conjunctivitis and dry eye. Prevention and treatment of ocular disease can be made easy by regular screening of the eye, simple, safe, easy, and cost-effective tools of few surgical procedures. Education about health should be imparted to the community regarding healthy eye care practices.*

Introduction

Dry eye which is also known as 'keratoconjuntivitis sicca'. It is an increasing public health burden and the most common cause for seeking optometrist and ophthalmologist interventions. "Dry eye is 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." (Craig et al., 2017). Prevalence rate of symptoms with or without a sign has been estimated to be somewhere between 5% and 50% (Stapleton et al., 2017) Despite its high prevalence, it is frequently overlooked. It is a negative impact of the vision dysfunction and the person quality of life.

Diagnosticsassessment

Findings of ocular surface diseases is based on medical history and the ocular symptoms included with questions about general, systemic, and topical medication. To find the most suitable diagnosis and their treatment the currently available tests and diagnostics tool are play a bigger role. Symptoms based questionnaire are allowed to collect the efficient information about the ocular surface disorder. Several questionnaires are available for ocular surface disorder according to their symptoms. There's no universally recognized questionnaire worldwide for the dry eye disease (DED) but most frequently used are OSDI and DEQ5. The recommended chronological sequence of dry e diagnostic methods is history, examination,

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followed by a questionnaire associated with symptoms, (TBUT) tear film break-up time, and staining on ocular surface (e.g., fluorescein), Schirmer test, meibomian morphology and expression, meibomian expressibility and morphology, lid and meibomian morphology (Stapleton et al., 2017). A standard diagnostic should be non-invasive, objective, specific, and cost- and time-reproducible (Lin & Yiu, 2014). Most of the non-invasive tests require blinking and strong illumination, the order in which they are completed can have an impact on the results. The tests should be conducted in order of least to most intrusive.

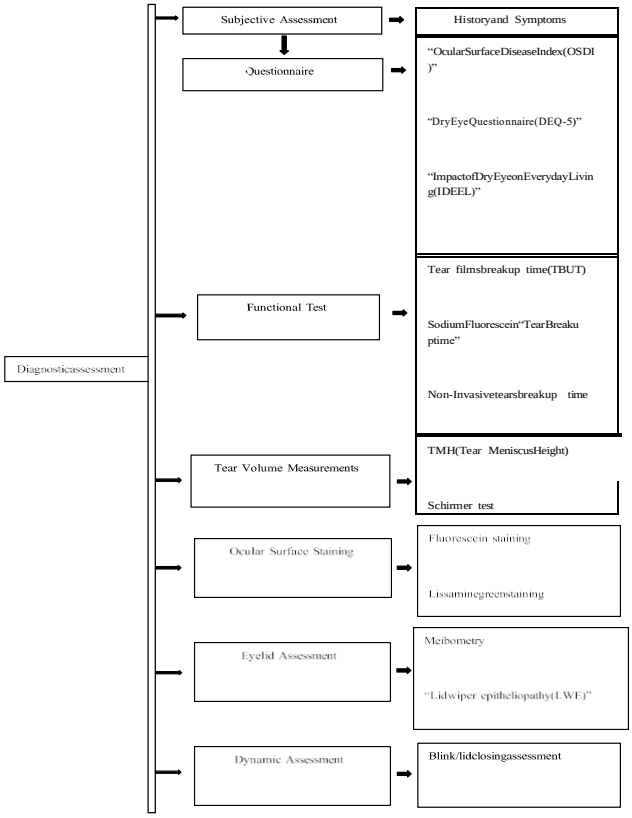

Figure1:AmodularDEDdiagnosticflowchart (Original)

Subjective Assessment

History and symptoms–

Dry eye symptoms must be noticed to be extremely severe, even with relatively moderate or mild changes in the surface, yet absurdly once the severity of the dry eye's reaches a definite or certain point, it's time to seek out for medical help, symptoms decrease because of corneal sensitivity loss (McGinnigle et al., 2012).Dry eye assessment invariably begins with symptoms and history; there are often relationship lacking between the sign of the dry eye and severity of the indications (Begley et al., 2003).

Questionnaire–

For Dry Eye Diagnosis the OSDI is the widely use questionnaire. The OSDI assesses the occurrence of symptoms, the causes in the environment, and the quality of life associated with vision problems. Many other questionnaires also developed, and they are validated as OSDI in recent publications.

"Ocular Surface Disease Index (OSDI)"

The outcomes "Research Group (Allergan Inc., Irvine, CA)" developed the tool in 1997, which contains of twelve items that functional constraints, assess symptoms, and environmental factors associated to dry eye. It is made up of a twelve-item questionnaire that allows for a quick evaluation of ocular irritation with symptoms and Dry Eye Disease association with it and depends on their vision-related effect and functions. The questionnaire's12itemsareratedasof0to4scale,"4indicating all the time, 3 indicating most of the time, 2 indicating half of the time 1 indicating some time with 0 indicating no time", and. The total score in OSDI form was then analysed from the following formula "OSDI=[(all questions answered(sum of the scores) × 100 / total number of questions answer × 4". Hence, OSDI score on the level of 0 to 100, highest score represents more disability (Schiffman et al., 2000). There was a comparison of 71 patients without DED, and 87 patients with the DED group had lower OSDI complex and subscale ratings for vision-related function (Li et al., 2012a).

"Dry Eye Questionnaire (DEQ-5)"

Total five questions are found in DEQ-5 which consist of that, discomfort, and dryness (on a range of 0–4), rate the frequency of watery eyes as well as the level of late-day dryness and discomfort (on a scale of 0–5). It can distinguish between patients suffers from "Sjogren's syndrome and non-Sjogren's dry eye, non - dry eye, and dry eye patients, dry eye with Sjogren's syndrome, and dry eye severity", then by adding the specific questions scores and calculated that for the result. The questionnaire has a maximum score of 22(Chalmers et al.,2010).

"Impact of Dry Eye on Everyday Living (IDEEL)"

It was created in 2003 and consists of 57 items (L. Abetz et al., 2003). The IDEEL has exceptional feature that is its measures the aspects (mainly top three) of treatments for dry eye: symptoms bother, quality of life, fulfilment of the treatment, and. Except for yes/no questions, all other questions are responded on a 4- or 5-point Likert scale, and with a range of 0 to 100 points score for each module (Okumura et al., 2020). Statistically significant changes in IDEEL questionnaire responses have been reported across various levels of DED severity (Rajagopalan et al., 1098).

"National Eye Institute's Visual Function Questionnaire (NEI VFQ-25)"

NEI-VFQ, having 25-item form evaluating the impact of ocular conditions on visual acuity-related quality of Life. It scores in DED patients are lower on the scales of vision, general health, ocular pain, visual acuity-related social purpose, need, mental health condition, distance vision activities, intermediate vision activities, and driving (Li et al., 2012b).

"Computer vision symptom scale (CVSS17)"

The CVSS17 was created to give a patient-reported measure of computer-related ocular and visual symptoms among video display terminal workers. It was established, justified, and scored using Rasch analysis. The17-itemscalehasascorerange

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of 17 - 53, with higher score reflecting a symptom with greater intensity (González-Pérez et al., 2018).

Functional tests

For near and distance visual acuity assessment, follow the Modified ETDRS protocol for distance visual acuity recorded at 2 meter and the line documented where all the letters and for near Light House near visual acuity letter card at 16 inches. Both the visual acuity taken before and after installation of the one drop of CMC drop. It has been seen that both symptomatic and asymptomatic patient has temporarily improvement ofvisual acuity with these charts (Nilforoushan et al., 2005).

Recommendation Dry eye diagnostics

Vision disturbances are presently assessed by different ocular symptoms related and quality of life related questionnaire. By the report of TFOS DEWS II report there are no specific recommendation for vision test in Dry Eye Disease (DED) (Wolffsohn et al., 2017).

Assessment of tear film

For the assessment of tear film stability and abnormality various evaluating tools are used for the fundamental diagnostics criteria.

Tear films breakuptime (TBUT)

It's the amount of time which passes between a full or complete blink and the first blink appearing. For non-invasive tear film stability assessed by the Placido disc video keratography. The TBUT was assessed using an E300 corneal topographer, which was based on the high-speed Placido disc video keratography principle, and the dynamic area was evaluated. A video of the reflected mires of Placido disc was obtained for upto after blink 23 seconds utilizing with frame speed or rate of 4 photokeratoscopic images/second (4 Hz). Three-time measurement taken on each eye. It has been seen that the Automated TBUT was less variability than the CNI – TBUT (clinician value who are assessing TBUT manually) (Downie, 2015).

Sodium Fluorescein "Tear Breakup time"

Fluorescein Tear Break up time is widely and generally used in place of any non-invasive measurement for stability of tear film because is low costly as evidenced by several survey of ophthalmologist and optometrist. It's also suggested through "American Academy of Ophthalmology" as a dry eye diagnosis, and it's broadly applied by "Sjogren's International Collaborative Clinical Alliance researchers" (Akpek et al.,2019). Fluorescein can be injected into a micropipette with variable volumes and concentrations, or it can be impregnated onto strips (Golebiowskietal.,2017). The strips were moistened and placed to the superior bulbar conjunctiva with non- preserved saline. An identical method is also necessary, and general instructions given to patient that naturally blink 3 times and later to stop blinking until instructed (Golebiowski et al., 2017). Ask to blink gently twice and then keep the eyes open as much as possible at the end of the second blink, Once the first tear break-up was noticed, a stopwatch was ready for recording the time. The reference for the Na Fl BUT parameters are less than 5 seconds and less than 10 seconds when more controlled volume of fluoresce in are used (M.B.Abelsonetal.,2002;R. Abelson et al., 2012). This technique is dependent onpractitioner to practitioners and having some drawback, but it is the most used diagnostics tools used in DED practice.

Non-Invasive tears breakup time

As we early discussed the E300 corneal topographer use fornon-invasive methods in tear film stability measurement. An inferrometry are also used for the non-invasive technique with tear film stability. More recently, a device which is used to define the lipid layer thickness by using inferrometry. It is for clinical usage. (Tear Science® Lip iView®, Tear Science, Morrisville, NC) (Blackie et al., 2009). The standard rates for tear breakup time described as to be greater non-invasive methods, "mean difference of 3.7 s" being stated. However, the differences between the two strategies are said to be minor. While breakup times are shorter (Finis et al., 2013a).

Thermography

A newly use analytical device that have non-invasive technique with infrared thermography. It measures the temperature of ocular surface mainly relation with to tear film. The research suggests that in people with DED, the ocular surface cools faster than in healthy eyes, which is believed to be because of a faster percentage of the tear film evaporation (Acharyaetal.,2015). In advanced thermography its measures with more accuracy with high resolution and differentiate the etiological factors. "With the greatest cooling and temperatures with lowest rates being reported for assumed ADDE, and lower rates in dry eyes of presumed evaporative aetiology" (Abreau et al., 2016). Furthermore, it has been shown that in patients with DED, the subjective experience of discomfort occurs earlier in the inter blink phase than in uses and symptoms are linked to lower temperatures of corneal and increased tear evaporation (Versura et al., 2015). There have been reports of sensitivity and specificity levels of about 80%. (Su et al., 2011).

Tear evaporation rate

To keep the tear evaporation rate low, the lipid layer must stay intact. Around 10% of the overall tear volume evaporates, whereas 90% drains through the lacrimal punctum, according to research (Tsubota, 1998).Tear evaporation rates are being measures by different advance and newly method and technique such as vapour pressure gradient, rate of relative humidity increase with google cup placed over the eye (Wolffsohn et al., 2017). Also, by using the infrared thermography camera we can also measures the evaporation rate with the exclusion of surrounding skin and sealed chamber. "According to Jen-Hong Tan and E. Y. K. NgA et al. research, the corneal rate of evaporation in older people is higher than in younger people" (Tan et al., 2010).

Tear Volume Measurements

As per TFOS DEWS II definition of Dry Eye Disease, it's very important to assess the tear film volume which will plays thekey mechanism in Dry Eye Diagnostic.

TMH (Tear Meniscus Height)

Tear meniscus is an element of precorneal tear film which is made by the tear reservoir. The tear meniscus height (TMH), a hypersensitive indication of tear film volume, is used to diagnose aqueous-deficient dry eye (Kawaietal.,2007). The

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TMH has been determined by the slit lamp biomicroscope graticule in 0.05 mm unit. Advance technology like e Keratography 5M (based on Placido disc video keratography) and "Fourier Domain Optical Coherence Tomography are useful for accurate measurement of tear meniscus height". The menisci are containing tear fluid by, produced by tears staying at the intersections of the bulbar conjunctiva and margins of both the lower and upper eyelids (Wolffsohn et al., 2017). Blink after some time, measuring lid margin along locus, the humidity, air speed, illumination, time of day, temperature and canal have an impact on Meniscometry (Wolffsohn et al., 2017). OCT Meniscometry advantages are non-invasive, and that picture acquisition will be quick and easy; though, image processing can be complicated, time-consuming, and depends upon the operator.

Schirmer test

These has been made by utilizing autoclaved, "35-mm-long, and 5-mm-wide Schirmer strip". One millimetre of rounded end of strip was folded and inserted temporal one third lower lid margin and the patient was asked not to close the eyes, and blink normally. The strip was removed after 5 minutes, and the score is the measured length of the wetting from the notch (Vashisht& Singh, 2011; Wolffsohn et al., 2017). Interpretation of results are as follows :>10 mm means normal tear production, ≤10 mm means borderline dry eye, ≤5 mm means severe dry eye (Vashisht & Singh, 2011). Without anaesthesia that means Schirmer test II is the standardized measurement methods for the reflex tear flow. In Dry Eye Disease diagnosis, the Schirmer test II might be more objective and reliable.

"PRT (Phenol Red Thread Test)"

For the PRT test,a"75-mm-longphenol-redimpregnated thread with a3-mmcurved"endwas autoclavedandputfor15seconds in the lower fornix. When alkaline tears meet phenol red, the colour changes from "white to yellow-orange, yellow, and finally red". After 15 seconds, thread was taken off, and the red section was calculated from the very tip, regardless of fold. The following is how the findings were interpreted: Severe dry eye is well-defined when the wet length is of less than 10 mm, borderline dry eye is described as a wet length of less than 19 mm, and normal tear production is defined as a wet length of more than 20 mm (Vashisht & Singh, 2011). These factors recommend that PRT test gives a realistic and indirect measurement of existing tear volume(Wolffsohnetal.,2017).A study found a Kappa value of 0.96 between PRT and Schirmer, indicating high agreement between the two. As a result, PRT can be used to identify dry eye just as well (Vashisht & Singh, 2011).

Tear Film Osmolarity

One of the mostly use objective assessment is the Osmolarity of tearfilm,asshowningtheDEWSreport(Wolffsohnetal.,2017).
Mostlythediagnostictest that apply forthetearfilmOsmolarity is "TearLab Osmolarity System", the system is non-invasive, very friendly and gives the result in just one minute. TearLab isahand-heldgadgetthat collectstearswithoutbeing invasiveand takes less than one second to sample. The assessment or testcard is utilised as tear collection device also it is a measurement system. After collecting the sample, the pen begins measuring and docked into the "Tear Lab Reader", it shows a quantitative value (Benelli et al., 2010). Osmolarity rises with severity ofthe disease,withnormallimit,mild-to-moderate,severebeingthe most common (Bron et al., 2015a). Tear film osmolarity is decease by any artificial tear drop installation.

Ocular Surface Staining

These dyes are mostly used Lissamine green, rose Bengal, and sodium fluorescein for the ocular surface staining.

Fluorescein staining

The most valuable and important tool that is use for corneal staining is fluorescein staining, it helps to find different ocular surface diseases including DED. When seen via a cobalt blue exciter filter, fluorescein is usually implanted at a concentrated volume that will colour the tear film a vivid green. In the fluorescein stripes one drop of saline solution was placed and then injected in the eye to do the conjunctival and corneal staining. The colouring was graded on a scale of 0 to 4 (no staining on surface and complete ocular surface stained) (Bronet al., 2015a). When live cells' integrity is compromised, as example by a break in superficial cell tight junctions or a faulty glycocalyx, fluorescein staining appears clinically (Wolffsohnet al., 2017). Fluorescence staining visibility is greatly enhanced using a yellow barrier filter because it absorbs light in the blue spectrum. This is especially useful when seen in the conjunctiva section because, without using a barrier filter, the fluorescenceis masked by the sclera's high scatter of blue light (Whitcher et al., 2010).

Lissaminegreen staining

Lissamine green is an organic sulfonic acid which is different from fluorescein and rose bengal staining. It is easily tolerated after installation and has a lower inherent toxicity than rose bengal. Healthy epitheliumand conjunctival cellsareunaffected by Lissamine green. Strips of Lissamine green placed to the conjunctival sac. Stains are stable and fade in a long time (Whitcher et al., 2010). After the installation wait 1 to 4 min because of the fade out of the stain beyond this period due to certain light exposure. And this is also scaled into 0 to 4. A positive score is > 9 conjunctival spots (Bron et al., 2015b).

Rose Bengal Staining

Rose bengal staining is equivalent to fluorescein staining. The best staining results come from injecting a full drop into the sac oftheconjunctivaandusingtopicalanaesthetictoalleviatepain.
Epithelial cells of ocular surface that are not covered by mucinor glycocalyx, also dead or degraded cells (Whitcher et al., 2010). It is also toxic but more as compared to Lissamine green, so the irritation is more. Because of that it induces reflex tears. The ocular surface staining can be visible in red-free absorption filter or white light, when rose bengal is used clinically at the slit-lamp. When examined under low magnification with white light, staining corneal epithelial cells appear as red dots (Whitcher et al., 2010). Due to high contrast in the sclera and its white background the visibility is clearer in rose bengal staining of conjunctiva.Because of the iris colour the contrastis affected andshowsthecornealstainingsimilarity.Whentheiriscolouris dark brown, contrast is weak, and the lesion is difficult to see; when the blue colour iris, rose bengal staining stands outbrightly compared to the light backdrop (Whitcher et al., 2010; Wolffsohn et al., 2017).

"LidParallel ConjunctivalFolds(LIPCOF)"

The conjunctival folds are folds parallel to the lower lid edge in thelateral,lowerquadrantofthebulbarconjunctiva.LIPCOF

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may reflect the earliest moderate stages of conjunctivochalasis and hence contribute to the aetiology, although clinically, they differslightly(Wolffsohnetal.,2017).Itmayberelatedwiththe tear film viscosity, completeness of blink and speed of blink. During slit lam examination it is very easy to evaluate LIPCOF and grade it. Patient with higher LIPCOF grade is likely to be suffer from DED. Even though Central tear meniscus does not affect by LIPCOF the, which underestimated the central height of the tear meniscus measurement (Pult & Bandlitz, 2018).

Ocular surface sensitivity

Sensitivity of ocular surface measured using "Cochet-Bonnet or non-contact air-jet esthesiometers". Corneal sensation may give rise to epithelial disorders e.g., neurotrophic keratosis (Wolffsohn et al., 2017).

Eyelid Assessment

Anterior

Anteriorlyassesstheanteriorblepharitisandotherdifferential diagenesis associated with DED.

Posterior

Meibometry

Meibography is an established, non-invasive study enabling visualization and meibomian gland documentation. Currentlythe mostly choice is infrared meibography (Lekhanont et al., 2019). It gives the quantitative assessment of the meibomian gland, so it is easy to diagnosis the MGD. For the evaluation of meibography, many different scoring schemes, e.g., the meiboscore, have been used. Recent developments in meibography have been made by the creation of mobile phones, handheld devices, pen-shaped devices, and multiuse systemstake videos and photographs with light emitting diodes and an infrared camera (Arita et al., 2013; Pult & Riede-Pult, 2012).

"Lidwiperepitheliopathy (LWE)"

Lid wiper epitheliopathy (LWE) is the staining with lid wiper done with dyes such as Lissamine and fluorescein green, which is most common in Dry eye disease patients (Wolffsohn et al., 2017). The lid wiper is thought to be the region of the upper eyelid's marginal conjunctiva that serves as a wiper to disseminate the tear film across ocular surface (Efron et al., 2016). "LWE appears on both upper and lower lids, but most of survey shows only upper LWE"(Wolffsohn et al., 2017) . In severalresearch,"theysuggestedstainingLWEwithfluorescein and Lissamine green in combination, with Lissamine green instillation repeated before the examination of LWE" (Korb et al., 2010). There are also some new methods for assessing the LWEsuchasconfocalmicroscopywheretheminutesdetailsare observed with hyper reflexive dots. After staining immediately evert the lid and check length with mm scale and width of lid margin. There are also some grading scales which are used for the documentation of the LWE (Korb et al., 2005, 2010).

Interferometry

Lipid layer thickness of tear film can be measured using interferometry (Wolffsohn et al., 2017). The LipiView II interferometer is the first clinically accessible tool that analyses the tear film's interferometric pattern to allocate automated determination of LLT with nanoscale accuracy(Finis et al., 2013b).Inshort,theinvestigationofthepatientwithaspeciality camerawhichrecordsavideoof20-secondininterference pattern form of tear film (Finis et al., 2013b). It is resulted in interferometric colour unit for each eye separately recorded. "Guillon et al. constructed a clinical interferometer that uses broadband illumination to visualise the dynamics of the lipid layer of the tear film, demonstrating that distinct patterns of interferometric fringe are generated depending on the thickness of the lipid layer" (Guillon et al., 1997).

Expressibility of Meibomian gland

Glands of meibomian produce meibum, which includes components of the tear film lipid layer. The expressibility quantity and quality of meibum are assumed to represent the function of the glands. The expressibility of meibum, as an indicator of meibum secretion, is commonly established using digital compression to glands, eyelid length, through the eyelid skin surface (Mathers et al., 1991; Pult & Riede-Pult, 2012; Wolffsohn et al., 2017). The ranging of meibomian gland expressibility having different grading scale. "Meibomian gland expressibility: central 8 glands of UL or LL 0: all gland expressible; 1: 3-4 gland expressible; 2:1-2 gland expressible;3: No gland expressible Meibum quality: - 0: Clear fluid; 1:Cloudy fluid; 2: Cloudy particulate fluid; 3: Dry, toothpaste like".

Dynamic Assessment Blink/

lidclosingassessment

Lid closure and blinking plays a bigger role in ocular surface healthandopticalperformanceoftheeye.Theactionblinkingis washes out debris, gives mechanical protections and modifications of tear film (Wolffsohn et al., 2017). The usual rate of spontaneous blinking is said to be between 10 and 15 blinks per minute(Pult et al., 2013). As a result, it's critical to check the blink rate, as insufficient blinking might lead to DED and exposure keratopathy(Pult et al., 2013). Some studies also found some systemic disease because of incomplete blink such as Parkinson disease(Pult et al., 2013).

Sensitivity of the Lids

The main role of lid sensitivity is to maintain the ocular surface and its homeostasis(Wolffsohn et al., 2017).In healthy people, lid sensitivity was shown to be halfway between sensitivity of cornea and sensitivity of conjunctiva in many studies. Some studies found that upper eyelid is less sensitive than the lower eyelid(NORN, 1973). In DED, Lid sensitivity found to benormal (NORN, 1975).

Conclusion

Dry eye is a multifactorial disorder of tear film with manyocular symptoms that don't always match diagnostic testing. It may be overlooked by the professional because it is not causing ocular morbidity. Many times, DED is missed due to unawareness of right diagnostics techniques which should be utilize at those times. There are also some newer studies that indicate DED has a more effect of visual function disfunction and everyday quality of life (Kaštelan et al., 2013). As digital screen uses has increased due to covid pandemic, so most of the population have started symptoms of dry eye, but proper diagnostictoolsareneeded forconfirmationofseverity ofDED. So that DED can be managed in better way and patients can be benefitted. For screening purpose online questionnaires can be utilized and for confirmation in clinical set up NIBUT or TBUT canalsobeutilizedforfastassessment.Forquantitativeanalysis

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oftearfilmTearLabandMeibometry givesbetterunderstanding of the tear quality, which is very essential for ocular health and contact lens use.

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