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THE ROLE OF MEIBOGRAPHY IN THE EVALUATION OF DRY EYE DISEASE IN A SOUTH INDIAN COHORT

Opthalmology

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ABSTRACT

Purpose: To evaluate the role of meibography in the detection of dry eye disease in a South Indian cohort. **Study Design:** Cross sectional observational study. **Primary Outcome Measure:** Non-contact infrared meibography to evaluate dry eye. **Methods** The Ocular Surface Disease Index (OSDI) questionnaire was used to diagnose dry eye disease. All participants underwent a detailed anterior segment slitlamp biomicroscopic evaluation including Tearfilm Break Up Time (TBUT). The Schirmer's test (ST) and noncontact infrared meibography, using a non-mydriatic fundus camera were then performed. The results of meibography, TBUT and ST were compared between different OSDI groups. The Chi-square test and Kendall's tau-b test were used to evaluate the presence and strength of any association between the three diagnostic modalities. **Results** A total of 170 participants were included. On the basis of OSDI responses, 101 participants had mild dry eye or less, and 69 had moderate dry eye or worse. There was a statistically significant association of increased severity of dry eye with higher meiboscores on meibography, ($p<0.05$). The strength of association of meibography was greater between TBUT (τ: 0.507, $p<0.05$), than ST(τ: 0.254, $p<0.05$). Nearly 49% of the participants with mild OSDI showed moderate or more advanced changes on meibography. **Conclusion** Non-contact infrared meibography is a useful technique in detecting dry eye disease. It is a simple test, which is as effective as conventional dry eye detection tests. It may also have a role in early detection of severe dry eye disease, and as a screening tool in places like India, where dry eye disease is estimated to reach epidemic proportions.

KEYWORDS

Dry Eye, Meibography, Meibomian Gland Dysfunction

INTRODUCTION

Dry eye disease (DED) is an abnormality of the tear film with the resultant sequelae of visual disturbance, and ocular discomfort. It may be associated with inflammation of the ocular surface.[1] Various tests have been developed over time to diagnose dry eye. These include tests for tear production including Schirmer's test (ST), tests for ocular surface abnormalities including Rose Bengal Staining, and tests for evaluation of the tear film distribution including Tear film Breakup Time (TBUT). Tests for inflammatory mediators in tears include the lysozyme assay. The quality of life due to dry eye has also been assessed by various questionnaires.[2] A single definitive test for dry eye is lacking, and often, treatment is initiated based on the symptoms of the patient.[1]

Meibomian gland health is crucial in the maintenance of a stable tear film.[3] Meibography is a specialized imaging modality that helps to directly visualize the meibomian glands in vivo. [4] Contact meibography was introduced in the 1970's. [5] Non-contact meibography is the novel method which is quicker, more patient friendly and simpler to use.[6]

With the projection of this condition reaching epidemic proportions,[7] an ideal screening test which is simple, efficient and cost-effective, in identifying dry eye patients, is needed. The nonmydriatic portable fundus camera used in community diabetic retinopathy screening has an infrared camera feature, and can be used for noncontact meibography.

MATERIALS AND METHODS

A cross sectional, observational study was conducted at the Ophthalmology department of a tertiary care University teaching hospital in south India between October 2015 and June 2017. Institutional Ethics Committee approval was obtained (IEC: 450/2015) and the study was carried out as per the regulations of Declaration of Helsinki.

The patients visiting the department who were willing to participate were consecutively enrolled. The patients having any active ocular infection, history of using topical ocular medications, and those who had undergone any ocular surgery one month prior to the study, were excluded.

The basic demographic profile of the participants was noted. Their response to the structured Ocular Surface Disease Index (OSDI) questionnaire was recorded. A clinical ocular evaluation was performed including slit lamp biomicroscopic evaluation of the anterior segment and the TBUT. The ST was subsequently performed after an interval of 20 minutes, followed by meibography. The objective tests were performed in the right or eye with worse symptoms.

The OSDI score was calculated as follows:[8]

- OSDI = (Sum of scores for all the questions asked) x100 / (Total number of questions answered) x 4
- A score of less than 12 was normal, between 13 and 22 mild, between 23 to 32 moderate and between 33 to 100 was considered severely symptomatic. [9]

The stability of the tear film was assessed by the TBUT. This was performed by staining the inferior bulbar conjunctiva with 2% fluorescein dye. The participant then underwent slitlamp evaluation with cobalt blue filter, after blinking so as to evenly distribute the fluorescein over the cornea. The time taken for the first dry spot, after a blink was noted.[10] It was considered normal $\geq$ 10 seconds and severe if less than 5 seconds.[11]

The tear production was assessed by the ST without anesthesia. [12] Whatman No 1 Schirmer's strips were inserted over the lower eyelid margin at one third the margin length, medial to lateral canthus. The length of the Schirmer's strip that had been wet was read at the end of 5 minutes. It was considered to be normal if > 10 mm, mild to moderate if 6 to 10 mm and severe tear film deficiency if lesser than 5 mm.

The images of the meibomian glands were captured using a portable non mydriatic camera [3 nethra, Forus Health Pvt Ltd, Bengaluru, India] with a 40 degrees' field of view and optical resolution of 10 microns. The everted upper and lower eyelids were imaged for every patient. The image was then graded on the basis of the area of meibomian gland area loss. Grade 0 implied no loss, Grade 1 and 2 represented a loss of lesser and greater than one-third the area respectively. A loss of more than two-thirds of the area of meibomian glands, was classified as Grade 3. [13] A total of the grades of both lids were taken to determine the meiboscore.

On the basis of the OSDI scores, the participants were divided into two major groups - one with normal to mild symptoms and the other having

moderate to severe dry eye symptoms. The TBUT, ST and meibography results were compared between these two groups. For the ease of calculation, the TBUT and ST were divided into two groups, i.e. those with severe dry eye and those without. The meibography results were also divided into two groups, with those having a meiboscore of greater than 4, being severe meibomian gland loss.

Anticipating 85% proportion of correct detection of dry eye, with 0.085 relative precision at 95% confidence level, a minimum of 68 participants were required to be screened.

Statistical analysis was done by the Chi square test and a $p<0.05$ was considered statistically significant. Kendall's Tau-b test was performed to study the strength of association between meibography and the TBUT and Schirmers' tests.

RESULTS

A total of 170 participants were included in the study. On the basis of the OSDI score, 101 participants were classified into the normal to mild dry eye group, and 69 participants in the severe dry eye group. The demographics of the patients in these groups are shown:

Table 1 : Age and gender distribution on the basis of Ocular Surface Disease Index(OSDI) score

	Normal to Mild Dry eye	Severe Dry eye
Median Age (years)	43 (19-75)	56 (19-75)
Gender N(%)		
Male	46 (45.5)	29 (42)
Female	55 (54.5)	40 (58)
Total	101(100)	69 (100)

There was a significant association noted with the increased severity of the symptoms as noted by the OSDI and the severe grades of dry eye as detected by TBUT, Meibography and the ST.

Nearly 79% of the participants with severe symptoms on the OSDI had severe dry eye as per TBUT and meibography values. Similarly, 84 % of the participants with severe symptoms on the OSDI, had moderate to severe decrease in tear production as per ST. A detailed distribution is depicted :

Table 2: The classification of participants on the basis of their OSDI and comparison with TBUT, Meibography and Schirmers test values.

OSDI (Total)	TBUT		Meibography		Schirmer's Test	
	Mild	Severe	Mild	Severe	Mild	Severe
Mild (N=101)	74	27	52	49	79	22
Severe (N=69)	15	54	15	54	11	58
Total	89	81	67	103	90	80
P-value	<0.05		<0.05		<0.05	

It was noted that nearly 49% of patients with mild dry eye on the basis of OSDI, had a meiboscore suggestive of severe meibomian gland loss. Meibography had a stronger association with TBUT compared to ST, although both were statistically significant with $p<0.05$.

Table 3: The strength of association of meibography with TBUT and Schirmer's test.

Meibography (Total)	TBUT		Schirmer's Test	
	Mild	Severe	Mild	Severe
Mild (N=67)	56	11	46	21
Severe (N=103)	33	70	44	59
Total	89	81	90	80
T	0.504		0.254	
P-value	<0.05		<0.05	

Meibomian gland drop-out was noted to be more in the age group above 50 years. However, it had no significant association with gender.

Table 4: Age and Gender distribution in Meibography results

Meibography			
	Mild	Severe	
Gender			Total
Females	38	57	95
Males	29	46	75
Total	67	103	170
P value	0.859		
Age			
<50 years	51	39	90
>50 years	16	64	80
Total	67	103	170
P value	<0 .05		

DISCUSSION

In our hospital based single center study from coastal south India, on the basis of the OSDI questionnaire, around 40% were noted to have moderate to severe dry eye. This necessitates the need for an efficient but simple non-invasive objective screening test for dry eye disease.

Meibography is a novel technique used to directly image the meibomian glands and assess meibomian gland drop out. Although earlier devices involved the use of a transilluminating probe which had to be applied to the eyelid, [14] newer devices are based on infrared video camera based image acquisition. This has an advantage of being non-contact and thus, patient friendly. Meibography is still not being routinely practiced in many clinics, probably because of the need for operator expertise and the finances involved. However, with the newer non-contact meibography devices being incorporated into topography devices, autorefractometers, and fundus cameras, its utility may be increased. Moreover, with the advent of mobile meibography systems, community screening and therapy is likely to increase.[15]

Gupta et al. found a strong correlation between the OSDI and ST in a North Indian population.[16]] In our study too, a significant association was noted between the severity of dry eye as per the OSDI questionnaire and the TBUT and ST, with objective tests corroborating in nearly 80% of the severe dry eye cases. These conventional dry eye tests have several limitations. The ST has a high tendency for false negatives if not carried out correctly. The illumination, humidity, air velocity and correct placement of Schirmer's strips have a bearing on the test results. [17] The causes of variability in TBUT include poor stain of tearfilm, concentration of the stain used, and delayed recognition of the dry spot by the observer.[18]

Meibography being a more objective test, can to a certain extent overcome these limitations. In our study, OSDI scores showed a significant association with the severity of Meibomian gland loss detected by meibography. But an interesting observation was the occurrence of severe meibomian gland loss noted in nearly 49% of participants having normal to mild OSDI scores. This may point towards its ability to detect dry eye disease prior to the onset of clinically evident symptoms.

Studies comparing meibography for meibomian gland loss with TBUT have shown an inverse correlation. [19,20] In our study too, a significant association was established between meibography and TBUT. The strength of association with meibography was greater for TBUT than ST.

Den et al concluded that the meibomian gland dropout was more evident in men as compared to women, above 40 years, and was more severe with increasing age. [21] Our study also showed that meibomian gland drop out increases with age. However, it did not show any gender predilection.

The major limitation of the study was its hospital based recruitment of participants. This may not be truly representative of a south Indian population. Moreover, the utility of the device in diagnosing DED in a community set up is not evaluated.

To conclude, noncontact meibography is a simple, non-invasive technique to assess meibomian gland structure. Although it is unable to determine effects of the altered meibum quality on DED, meibomian gland dropout is detected. It may also help in identifying cases of dry eye missed by the conventional dry eye tests. There is limited data on the role of meibography in dry eye disease in the Indian population. The role of meibography in community screening and management of the evolving epidemic of dry eye disease needs to be studied further.

REFERENCES

1. The epidemiology of dry eye disease: report of the Epidemiology Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf. 2007;5(2):93–107.
2. Tiffany JM. Tears in health and disease. *Eye (Lond)*. 2003;17(8):923–926.
3. Lemp MA, Crews LA, Bron AJ, Foulks GN, Sullivan BD. Distribution of aqueous-deficient and evaporative dry eye in a clinic-based patient cohort: a retrospective study. *Cornea*. 2012;31(5):472–478.
4. Schaumberg DA, Sullivan DA, Dana MR. Epidemiology of dry eye syndrome. *Adv Exp*

Med Biol. 2002;506(Pt B):989–998.
5. Wise RJ, Sobel RK, Allen RC. Meibography: A review of techniques and technologies. Saudi J Ophthalmol. 2012;26(4):349–356.
6. Robin JB, Jester JV, Nobe J, Nicolaides N, Smith RE. In vivo transillumination biomicroscopy and photography of meibomian gland dysfunction. A clinical study. Ophthalmology. 1985;92(10):1423–1426.
7. Donthineni PR, Kammari P, Shanbhag SS, Singh V, Das AV, Basu S. Incidence, demographics, types and risk factors of dry eye disease in India: Electronic medical records driven big data analytics report I. Ocul Surf. 2019;17(2):250–256.
8. Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. Arch Ophthalmol. 2000;118(5):615–621.
9. Yu X, Guo H, Liu X, Wang G, Min Y, Chen SS et al. Dry eye and sleep quality: a large community-based study in Hangzhou. Sleep. 2019;42(11):zsz160.
10. Lee JH, Kee CW. The significance of tear film break-up time in the diagnosis of dry eye syndrome. *Korean J Ophthalmol*. 1988;2(2):69–71.
11. Lin H, Yiu SC. Dry eye disease: A review of diagnostic approaches and treatments. Saudi J Ophthalmol. 2014;28(3):173–181.
12. Phadatare SP, Momin M, Nighojkar P. A Comprehensive Review on Dry Eye Disease: Diagnosis, Medical Management, Recent Developments, and Future Challenges. Advances in Pharmaceutics. 2015; Hindawi Publishing Corporation; Article ID 704946.
13. Nichols JJ, Berntsen DA, Mitchell GL, Nichols KK. An assessment of grading scales for meibography images. *Cornea*. 2005;24(4):382–388.
14. Mathers WD, Daley T, Verdick R. Video imaging of the meibomian gland. Arch Ophthalmol. 1994;112(4):448–449.
15. Arita R. Meibography: A Japanese Perspective. Invest Ophthalmol Vis Sci. 2018;59(14):
16. Gupta N, Prasad I, Jain R, D'Souza P. Estimating the prevalence of dry eye among Indian patients attending a tertiary ophthalmology clinic. Ann Trop Med Parasitol. 2010;104(3):247–255.
17. Nichols KK, Mitchell GL, Zadnik K. The repeatability of clinical measurements of dry eye. Cornea. 2004;23(3):272–285.
18. McCulley JP, Shine WE. The lipid layer of tears: dependent on meibomian gland function. Exp Eye Res. 2004;78(3):361–365.
19. Feng Y, Gao Z, Feng K, Qu H, Hong J. Meibomian gland dropout in patients with dry eye disease in China. Curr Eye Res. 2014;39(10):965–972.
20. Finis D, Ackermann P, Pischel N, König C, Hayajneh J, Borrelli M .et al. Evaluation of Meibomian Gland Dysfunction and Local Distribution of Meibomian Gland Atrophy by Non-contact Infrared Meibography. Curr Eye Res. 2015;40(10):982–989.
21. Den S, Shimizu K, Ikeda T, Tsubota K, Shimmura S, Shimazaki J. Association between meibomian gland changes and aging, sex, or tear function. *Cornea*. 2006;25 (6):651–655.