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ROSACEA AND DRY EYE DISEASE: A CLINICAL STUDY

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Abstract

Background: To evaluate the results of various tear functions in rosacea. **Material and Methods:** This prospective study includes 118 eyes of 59 rosacea patients and 118 eyes ofeyes of 59patients as control group without any signs or symptoms of rosacea. Tear functions of all were evaluated with ocular surface disease index (OSDI) questionnaire, and measurements of by Schirmer I test(ST)without anaesthesia, Tear film break-up time (TF-BUT) and rose Bengal score (RBS). **Results:** The mean Schirmer test result was 16.44 ± 4.49in study group and 18.10 ± 3.75mm/5 min in control group (t-value= -3.06, p-value=<0.05). The mean TBUT in study group was 7.38 ± 0.53and in control group was 12.84 ± 1.93 (t-value= -19.18p-value=<0.05).. Mean OSDI score in study group was 27.01 ± 63and was 11.72± 7.57 in control group (t-value=11.18 , p-value=<0.05). **Conclusion:** Our study demonstrated lower tear function tests in patients of ocular rosacea, TBUT more affected than Schirmer test leading to unstable tear film and evaporative dry eye. Ocular rosacea is a common disease that frequently remains undiagnosed and more recent authors have echoed this impression. When we talk about dry eye and its symptoms the rosacea cannot be overlooked. Early diagnosis and treatment with lubricants is must to save eyes.

INTRODUCTION

Rosacea is a syndrome of unknown etiology involving the skin and eye. Rosacea is a relatively common disorder of the 'blush area' of the skin of face, which has been known for centuries. Reviews by Holloway(1910),Doggart (1931) and Wise (1943) on Rosacea were earliest of the 20th century.[1] Ocular findings in rosacea are grouped as either minor or major, non-sight to sight threatening. Minor complications are much more common. Prevalence of ocular involvement in patients with Rosacea has been reported as low as 3 %1 to as high as 58 %.[2] Symptoms frequently go undiagnosed because they are too nonspecific. Ocular signs and symptoms may occur before cutaneous manifestations in up to 20%of patients with ocular rosacea. Meibomian gland dysfunction presenting as Chalazion 0r chronic staphylococcal infection as manifested by hordeolum (stye) are common signs of rosacea- related ocular disease.[3]

Patients with ocular rosacea experience many of the same symptoms of ocular irritation as those with aqueous tear deficiency, although aqueous tear production is normal, as measured by the Schirmer-I test, often is normal. Thepossible cause of ocular irritation in patients with rosacea include an unstable tear film and elevated tear film osmolarity associated with increased tear evaporation secondary to deficiency in the lipid component of the tear film.[4]

The present study was designed keeping the same objective in consideration and every attempt was made that every patient with complaint of itchy, soaring, burning and gritty sensations had to be examined by dermatologist for skin involvement and by an ophthalmologist for ocularrosacea and detailed evaluation of dry eye is required in rosacea cases.

Aims and Objectives

To evaluate the results of varioustear functions in rosacea andto assess an association of dry eye with rosacea.

MATERIALS AND METHODS

The present study was a clinicalcase control study, which was conducted in a period of one year. All consecutive patients of rosaceapresenting in the Department of Dermatology and Department of

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Ophthalmology, during this time,who were interested,were included in this study and were examined byboth the departments Informed consent was taken from all the patients.On screening out of total 114 patients of rosacea,59 had ocular involvement. Equal number of age and sex matched patients without any features of rosacea were taken as controls.

Inclusion Criteria

All patients having ocular manifestations with or without cutaneous were subjected to ocular examination and were included in study. Inclusion criteria for patients having only ocular involvement, without cutaneous involvement, were the classical symptoms and signs of ocular rosacea.

Exclusion Criteria

Patients Ocular disease such as injuries, chemical conjunctivitis, viral and bacterial conjunctivitis, immunological diseases that might interfere with evaluation. Contact lens wear, Patients previously diagnosed as cases of keratoconjuctivitis sicca i.e. with arthritis, xerostomia, parotid & lacrimal gland enlargement and abnormal Schirmer Test-I, Exposure resulting from lagophthalmos, neurotropy and neuroparalysis.

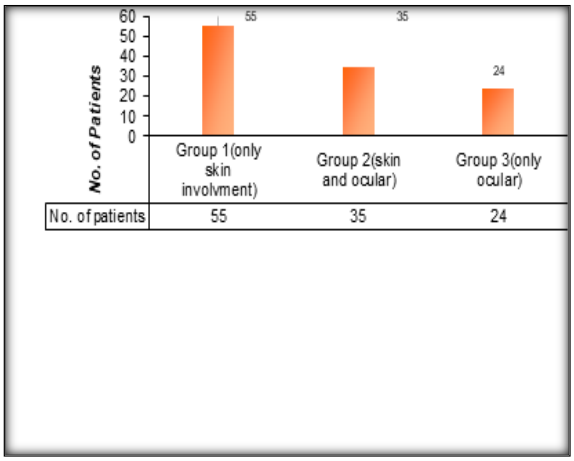

Figure 1: Showing number of patients with various types of presentations

Table 1: Theocular symptoms and signs were taken into consideration.[25]

Sn. No.	Symptom	Sign
1	Dryness	Erythema/ Telangiectasia of lid margin
2	Itching	Meibomian gland dysfunction
3	Blurred Vision	Ciliary base injection
4	Photosensitivity	Bulbar injection/ conj. hyperemia
5	Irritation	Crusts/Sleeves/ Blepharitis
6	Foreign body sensation	Papillary hypertrophy
7	Mattering/Crusting	Vascularization
8	Redness	Tear foaming
9	Tearing/Watering	Trichiasis/Lash loss
10	Stinging	Styes / Chalazion
11	Styes	Infiltrates/Keratitis
12	Eye lid bumps	Tear volume/Keratoconjuctivitis sicca
13	Swelling	Scarring
14	Scaling	Iritis
15	Any other symptom	Any other sign

Ocular symptomsand signswere analyzedandgraded asmild as2 or fewer, moderate as 3-6.and severe as 7 or more.

Slit Lamp bi-microscopic examination was done in all cases for both eyes. Status of Meibomian glands and their secretions was assessed. The lid margin was assessed and conjunctiva was seen for telangiectasia and cornea for superficial punctate keratitis and marginal infiltrates, with white light before and after installation of rose Bengal dye and through cobalt blue filter after installation of Fluorescein. In preparation for slit-lamp microscopy of the ocular surface, we instilled 2µL of a preservative-free dye (1 %Rose Bengal and 1 % Fluorescein) into the conjunctival sac or touched saline-moistened Rose Bengal strip and Fluorescein strip into the conjunctival sac. Fluorescein staining was assessed through Cobalt blue filter and was graded from 0 to 3 for each of the upper, middle, and lower thirds of the cornea. Rose Bengal staining of the temporal conjunctiva, cornea, and nasal conjunctiva was also graded from 0 to 3 after examination with ordinary light without any filter. The grading scale was defined according to the staining extent: 0 for negative; 1, scattered minute; 2, moderate spotty; and 3, diffuse blotchy staining.

Tear Film Break Up Time (TF-BUT): A saline-moistened Fluorescein strip was touched to the inferior temporal bulbar conjunctiva, and the patient was asked to blink several times to distribute the dye. The patient was then asked to look straight ahead, without blinking or holding the lids, and observed the tear film with cobalt blue light, x16 and 3mm wide beam, for development of a dry spot on the cornea. The TF-BUT was recorded as the time between the last blink and the appearance of dry spot. The test was repeated 3 times in each eye and average TF-BUT was taken. An attempt was made to maintain constant temperature humidity and airflow. A normal TF-BUT greater than 10 seconds was taken as normal.[5]

Schirmer Test-1,without topical anesthesia, was done to assess tear volume in each eye at each visit. No. 41 Whatman filter paper strip (5 x 35 mm), designed for same, was inserted between the lower lid margin and bulbar conjunctiva, at junction of

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lateral 1/3rd and medial 2/3rd of eye lid, eyes were kept open with spontaneous blinking allowed. Wetting of tear strip after 5 minutes was measured. A value above 15.0 mm was considered normal.[6]

Rose Bengal staining with 1% impregnated strip of the temporal conjunctiva, cornea, and nasal conjunctiva was graded from 0 to 3 after examination with ordinary light without any filter. The grading scale was defined according to the staining extent: 0 for negative; 1, scattered minute; 2, moderate spotty; and 3, diffuse blotchy staining. Van Bijsterverd grading scale was used which evaluates the intensity of staining based on a scale of 0-3 in three areas: nasal conjunctiva, temporal conjunctiva and cornea. Score 0-3 for each zone. 1+ = few separated spots, 2 + = many separated spots, 3 + : confluent spots and Maximum possible score is 9.Rose Bengal staining score of more than 3 was considered abnormal.[7]

The pH of tears was assessed with strip in case and control group.

On basis of symptoms, the severity of dry eye assessed in form of ocular surface disease index (OSDI) calculated in both groups. This 12-item questionnaire assessed the dry eye symptoms and the effects it has on vision-related function in the past week of the patient's life. The questionnaire has 3 subscales: ocular symptoms, vision-related function, and environmental triggers. Patients rate their responses on a 0 to 4 scale with 0 corresponding to "none of the time" and 4 corresponding to "all of the time." A final score is calculated which ranges from 0 to 100 with scores 0 to 12 representing normal, 13 to 22 representing mild dry eye disease, 23 to 32 representing moderate dry eye disease, and greater than 33 representing severe dry eye disease.[8,9,28]

Statistical Analysis

Was done using paired t-test. All the data was analyzed using student's 't' test.'p' value was calculated at 5 % level. 'p' value less than 0.05 implied that the data was statistically significant at 5 % level (95 % confidence limits) and a value of more than 0. 05 was taken as statistically insignificant.

RESULTS

Among diagnosed rosacea patients 59 had ocular manifestations. Thesepatients were divided into two groups on the basis of type of manifestation of rosacea at the time of presentation, Group-1Patients with Both Skin andOcular manifestations with 35 (59.32%) patients and Group-2 Patients with Ocular manifestations only with had 24 (40.67%) patients. In Group 1 (Patients with both Skin and Ocular manifestations only) of 35 patients, 15 (42.85%) were male patients and 20 (57.15%) were female patients. In Group 2 (Patients with Ocular manifestations only) of 24 patients, 11 (45.84%) were male patients and 13 (54.16%) were female patients. [Table 2]

59 patients, with ocular involvement 'reported experiencing one or more symptoms, in 118 eyes, occasionally, frequently or as a constant feature in their eyes. Among the symptoms analyzed burning sensations in 76 eyes (64.40%), itching in 62eyes (52.54%), redness in 56 eyes (47.45%) , foreign body sensations in 42 eyes (35.59%), watering in 32 eyes (27.11%), stinging sensations in 26 eyes (22.03%), Eye lid bumps in 19 eyes (16.10%) Dryness in 18 eyes (15.25%) Foaming in 16 eyes (13.55%) Styes in 14 eyes (11.86%) Mattering/Crusting in 12 eyes (10.16%) Scaling in 12 eyes (10.16%) Swelling in & around eyes in 8 eyes (6.77%) Photosensitivity in 7 eyes (5.93%) Blurred vision in 7 eyes (5.93%) and Pain in eyes in 4 eyes (3.38%) were found.

For ocular symptoms, patients reported them experiencingone or more symptom occasionally, frequently or as a constant feature in their eyes. For them burning sensations, itching, redness, foreign body sensations, watering, stinging sensations and dryness were frequent or constant symptom(Table-2). Their were74.3% eyes to be reported of occurrence of at least 1 symptom frequently. 42.6% eyes had occurrence of 2 symptoms frequently and there were 3 symptoms occurring frequently in 35.7%of eyes as reported by patients.

The symptoms were graded into Grade-1 (Mild) <3 symptoms, Grade-I2 (Moderate) 3-6 symptoms and Grade-III (Severe) >6 symptoms as per no. of symptoms patient had: 48 eyes (40.67%) had Grade-I ,60 eyes (50.86%) had Grade-II and 10 eyes (8.47%) had Grade-III (Severe) symptoms. [Table 3]

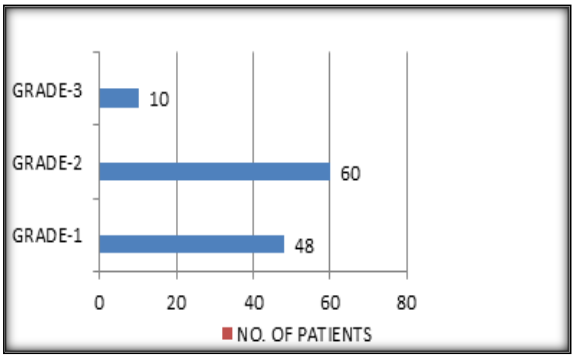

Figure 2: Grades of symptoms among patients with ocular involvement (n = 118)

Dry eye manifesting as dry, lusterless conjunctiva, tear lake deficiency, mucus debris and filaments were observed in 32 (35.59%) eyes. Schirmer's score were lower and rose bengal scores were mainly high in these eyes. Of the118 eyes examinedof 59 patients, in various groups, when analyzed had Grade-I signs in 5 eyes (Rt.eye-1, Lt. Eye-4),Grade-II signs in 87 eyes (Rt.eye-45, Lt. Eye-42) and Grade-II signs in 26 eyes (Rt.eye-13, Lt. Eye-13)

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On data analysis of Schirmer's test (ST-1) we found that the out of 118 eyes with ocular manifestations of rosacea, 79 eyes were categorized in grade-0 i.e. >15 mm in 5 minutes,25 eyes were categorized in grade-I i.e. 11-15 mm in 5 minutes,14 eyes were categorized in grade-II i.e. 0-10 mm in 5 minutes.

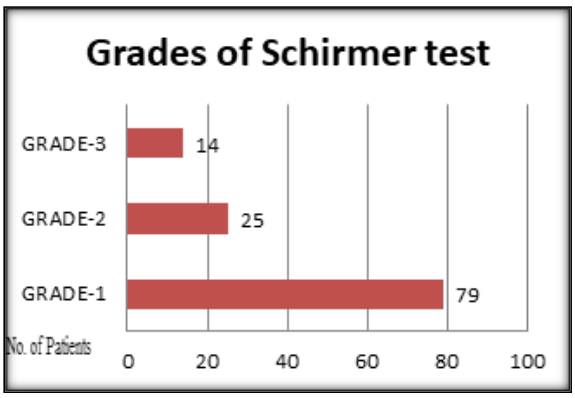

Figure 3:Grades of Schirmer tests among patients with ocular involvement (n =118)

Tear break up timeTF-BUT was assessed in both eyes of all patients and average of three readings in each eye was recorded. We observed that in the values of TF-BUT were normal (i.e.>10 seconds) in 13 patients and were categorized as Grade-0, whereas in patients having ocular manifestations (n=118 eyes), 71 eyes were found to be in Grade-I (i.e.6-10 seconds) and 34 eyes were in Grade-II(i.e. 0-5 seconds).

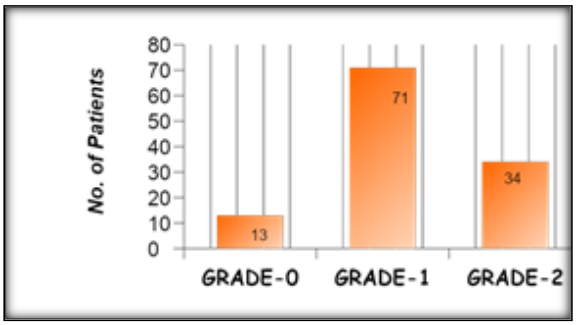

Figure 4: Tear Film break up time among patients with ocular involvement (n=118)

35 of 59 patients (59.32%) with ocular rosacea had cutaneous findings. 11 (31.42%) of these 35 patients had isolated erythema and telangiectasia (stage-I). In 9 of these patients lid margin telangiectasia was prominent, tear break up time (TF-BUT) was affected in 8 patients, and conjunctival hyperemia was observed in 14 eyes of 7 patients of varying degrees. No abnormality in Schirmer's testing was noticed in these patients. 16 of 35 patients (45.71%) exhibited overlap of first and second stage of rosacea, erythema and telangiectasia associated with papulopustular lesions. In 11 patients, conjunctival hyperemia and in 1 patient conjunctival granuloma was noticed, in 10 patients, meibomian gland dysfunction in form of meibomitis and in 6 patients blepharitis was observed. 8 patients had superficial punctate keratitis with positive Fluorescein staining. Conjunctivitis or keratoconjunctivitis was seen in 5 patients. Most of ocular signs were present in these patients including severe fall in TF-BUT, low values of Schirmer's testing, dry eyes and meibomian gland dysfunction in form of meibomitis or in form of chalazia and styes existed. Only in one patient with rhinophyma (stage-III), no specific ocular signs were observed although ocular symptoms such as burning sensations abd irritation and foreign body sensations were present in both eyes. Schirmer's test was lower and rose bengal staining was mildly positive.

The means of all test values (pH, ST-1, TF-TBUT and RBS were significantly lower in study group.It was significantly higher in OSDI study group.Group-1 and Group-2 are significantlydifferent at p <0.05 indicating lower tear function tests in Group-1 (cases). Data revealed that maximum effect was observed on TF-BUT where t stat measure is almost 10 times its critical value as compared to t value of other tests like pH, ST-1and RBS Therefore it has maximum effect on TF-BUT

Theabove table clearly signifies that TF-BUT being more effective than ST-I indicating that deficiencyof tear film in rosacea is due to unstabletear film which leads to development ofevaporative dry eye.

Table 2: Age and Gender distribution of Patients showing number and percentage of male and female patients in various age groups (Decade wise) inGroup-1 and Group-2

Age in yrs.	Group-1 (Patients with skin and ocular manifestations)		Group-2 (Patients with ocular manifestations only)	
	No. & % males	No. & % females	No. & % males	No. & % females
20-29	0 (0%)	0 (0%)	0 (0%)	2 (8.33%)
30-39	1 (2.85%)	6 (17.11%)	3 (8.33%)	2 (8.33%)
40-49	4 (5.71%)	10 (14.28%)	2 (12.55%)	4 (16.66%)
50-59	5 (8.57%)	4 (14.28%)	2 (8.33%)	4(12.55%)
60-69	4 (22.85%)	0 (8.57%)	4 (16.66%)	1(8.33%)
70-79	1 (2.85%)	0(2.85%)	0 (0%)	0 (0%)
Total	15 (42.86%)	20 (57.14%)	11(45.83%)	13 (54.17%)

Table 3: Symptoms reported among Patients (n =118 eyes of 59 patients)

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Symptom	Occasional	Frequent	Constant
Burning sensation	14.8%	69.9%	15.3%
Itching	27.5%	43.6%	29.9%
Redness	19.4%	56.8 %	23.8%
Irritation, F.B. sensation	25.1%	52.2%	22.7%
Watering/ Tearing	16.4%	61.8%	21.8%
Stinging	34.7%	53.8 %	11.5%
Dryness	33.4%	39.8%	26.8%

Table 4: Test values in study group Vs Control Group showing various statistical outcomes oftear tests

Test	Group	n	Mean ± SD	t- value	df	P-value
pH	Group-1	118	7.39 ± 0.53	8.01	234	< 0.05
	Group-2	118	6.90 ±0.39			
ST-1	Group-1	118	16.44 ± 4.49	-3.06	234	< 0.05
	Group-2	118	18.10 ± 3.75			
TF-BUT	Group-1	118	7.38 ± 0.53	-19.18	234	< 0.05
	Group-2	118	12.84 ± 1.93			
RBS	Group-1	118	1.38 ± 1.74	4.73	234	< 0.05
	Group-2	118	0.50 ± 1.01			
OSDI	Group-1	59	27.01 ± 63	11.18	113	< 0.05
	Group-2	59	11.72± 7.57			

DISCUSSION

The incidence of dry eye in rosacea is higher than the normal population (39–62% versus 15–34%). Most of the ocular symptoms and signs in rosacea are related to dry eye which is closely associated with inflammation and dysfunction of the meibomian glands. The dysfunction could be secondary to increased production of free fatty acids due to bacterial lipases or facial and angular venous dilation. These changes cause abnormal lipid composition of the tear film leading to shorter TF-BUT and dry eye.[10]

Ornek N et al,[10] after their study conveyed that although considered as a skin disease, rosacea may affect eye in up to 58–72% of the patients. Superficial punctate keratitis, peripheral neovascularization associated with subepithelial marginal infiltrates, stromal ulceration, corneal perforation, recurrent corneal epithelial erosions, pseudodendritic ulcer, pseudokeratoconus, and infectious keratitis have been previously reported. Conjunctival manifestations are chronic conjunctivitis, chronic papillary reaction, cicatricial conjunctivitis, pinguecula, conjunctival fibrosis and symblepharon. Blepharitis and meibomian gland dysfunction are also common findings. Dry eye with abnormal Schirmer's I test (ST) and shorter tear breakup time (tBUT) has also been reported in a majority of patients with ocular rosacea.[11,12,13,14,15,16]

N Zengin et al. in their study foundof 43 consecutive patients that Schirmer test, tear film break-up time, and meibomian gland function values in patients with ocular rosacea (n = 28) were found to be significantly decreased as compared with those of the patients with only cutaneous involvement and control patients ($p > 0.05$). Decreased tear secretion in patients with ocular rosacea would seem to be a result of structural changes secondary to meibomian gland dysfunction, and short break-up time might be due to an abnormal meibum composition.[16] Our findings showed a positive relationship between tear film abnormalities and meibomian gland dysfunction in patients with rosacea.

Abelson and associates compared the tear pH values of 44 normal, 20 patients of ocular disorders other than rosacea, 7 patients with untreated, active ocular rosacea and 5 patients with tetracycline treated, active ocular rosacea, using pH paper and pH electrode in some cases, and concluded that group with untreated, active ocular rosacea had significantly more alkaline pH values than the other groups tested. In patients with tetracycline- treated rosacea, tear pH values were not significantly different from those of normal subjects.[17]

In contrary to above study, Jaros and coles reported that in active ocular rosacea tears are acidic as compared to normal subjects,[18]Coles and Jaros in another study found tear pH to be more alkaline in older females, suggesting that a decreased rate of tear secretion may be contributing,[19] whereas David J Browning in his study using pH meter and a combination of pH sensitive-reference microelectrodes to measure tear pH concluded that tear pH is not characteristic of patients with active ocular rosacea and does not change after course of tetracycline therapy20 In our study we found that in rosacea cases (Mean=7.39 ± 0.53) the pH was towards alkaline side as compared to controls(Mean=6.90 ±0.39) (t-value8.01 , p value<0.05)

Afonso A A et al. intheir study observedthat as compared with normal control subjects, patients with ocular rosacea had a greater delay of tear fluorescein clearence ($p<0.001$), a higher tear IL-1□ concentration ($p<0.001$) and a greater pro-gelatinase B activity ($p<0.001$) in their tear fluid. Elevated gelatinase B activity in ocular rosacea may be involved in the pathogenesis of the irritation symptoms, recurrent epithelial erosions, vascularization and epithelial basement membrane dystrophy that develops in corneas of these patients.[21]

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Lemp et al using Schirmer-I testing, as a measure of aqueous tears creation, found a significantly greater prevalence of dry eyes in patients of ocular rosacea than normal controls. He also suggested that incidence of rosacea and keratoconjuctivitis sicca is high in general population, particularly from 4th to 6th decade and both conditions may be associated.[22]

Gudmundsen et al concluded that dry eyes frequently occur in Rosacea. In their study of rosacea patients, 56.3% had less than 8 mm of strip wetting compared with 25% of control patients($p<0.02$).Of rosacea patients, 40.6% had less than 5 mm of strip wetting compared with 18.75% of controls ($p<0.10$).[23]

Kocak-Altintas AG, Kocak-Midillioglu et al found that Schirmer tests and tear film break up time (TBUT) were significantly lower in patients with ocular rosacea than in normal controls ($P<0.05$) and concluded that patients with ocular rosacea not only had decreased tear production but also tear lnstability. Ocular surface epithelium had significant degeneration in patients compared with normal controls.[24]

Mark J. Quartermanetal,[25] in their study concluded thatAll patients with cutaneous rosacea had some degree of ocular involvement. Tear break-up time is abnormal in patients with rosacea. Ocular erythema and telangiectasia, meibomian gland dysfunction, and short tear break-up time in patients with cutaneous rosacea are indicators of ocular rosacea. Doxycycline, 100 mg daily, will improve ocular disease and increase the tear break-up time.

Yaylali V and Ozyuart C conducted study on patients proven of ocular rosacea, after histopathological studies and clinical diagnosis of acne rosacea, and suggested that in addition to tear function tests, rose bengal staining and impression cytology can be successfully used in the early diagnosis of dry eye and in monitering medical treatment in ocular rosacea, Meibomian glands play an important role in the pathogenesis of ocular disease.[26]

MelisPalamaretal. in their study compared rosacea cases and control groupin terms of tear film stability and volume, meibomian gland dysfunction, dry eye disease, and ocular surface staining found tear film parameters (tear meniscus height ($p=0.338$), noninvasive tear film rupture time ($p=0.228$), invasive rupture time ($p=0.471$), Schirmer's test scores ($p=0.244$)and concluded that ocular rosacea causes dry eye and significant meibomian gland loss, as well aslipid secretion impairment that can objectively be demonstrated with meibography, leads to evaporative dry eye, ocular surface dysfunction, and inflammation.[27]

Our study is in consistent to previous studies. In our study we found that the means of all test values (pH, Schirmer test, TF-TBUT and RBS were significantly lower in study group where as It was significantly higher in OSDI study group.Group-1 and Group-2 are significantly different at $p < 0.05$ indicating lower tear function tests in Group-1 (cases). We observed that maximum effect was on TF-BUT where t stat measure is almost 10 times its critical value as compared to t value of other tests like pH, ST-1and RBS Therefore it has maximum effect on TF-BUT.TF-BUT being more effective than ST-I indicating that deficiencyof tear film in rosacea is due to unstabletear film which leads to development ofevaporative dry eye.

CONCLUSION

Our study demonstrated lower tear function testsin patients of ocular rosacea, TF-BUT more affected than Schirmer test leading to unstable tear film and evaporative dry eye. Ocular rosacea is a common disease that frequently remains undiagnosed and more recent authors have echoed this impression. As the pathogenesis of disease is unknown and no undisputed histopathological or laboratory hallmarks of the disease exists, the diagnosis rests largely on a constellation of clinical signs. When we think and talkaboutdry eye and its symptoms therosacea cannot be overlooked.Early diagnosis and treatment with lubricants is must to save eyes.

Financial Implications: Nil
Conflict of Interest: Nil.

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