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Association Of Depression With Diagnosed Cases Of Dry Eye Disease: A Prospective Observational Analytical Study

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Abstract

Introduction: Dry eye is a disorder of the ocular surface due to insufficient secretion of aqueous tears and/or excessive tear evaporation characterized by instability and hyperosmolarity of tear film causing inflammation of the ocular surface. Many psychological problems, particularly depression, are associated with ocular surface diseases which deserve more attention.

Aim: To evaluate the association of depression in cases diagnosed with dry eye after ruling out diagnosed cases of depression/already on anti-depressants.

Material And Methods: 100 patients under treatment attending Out Patient Department of Department of Ophthalmology, Government Medical College, Patiala were selected. Institutional ethical clearance was obtained and we adhered to the tenants of declaration of Helsinki. Patients underwent the OSDI questionnaire and 3 tests- Schirmer test, Tear Film Break up time and Rose Bengal staining. Diagnosis of dry eye was established when the OSDI score was more than 12 with minimum one test positive. Positive cases were subjected to Cohen's Perceived Stress Scale and the Hamilton Depression Rating Scale.

Results: Incidence of depression in dry eye cases was 21.0%. The association of depression with OSDI, Pain/Soreness, Blurring, Difficulty in Reading, difficulty in Watching TV, grittiness, poor vision, vision in dry areas and areas with AC and schirmer test was found to be statistically significant.

Conclusion: There was a significant increase in incidence of depression in dry eye patients. Diagnosis of depression had highest association with OSDI questionnaire followed by Schirmer test, Rose Bengal test and TBUT. Age and female sex also had a positive correlation with depression

Keywords: Dry eyes, Dry eye diseases, Depression

Introduction

Dry eye disease is a chronic debilitating condition that affects physical, mental and social wellbeing of a patient. Dry eye is a disorder of the ocular surface due to insufficient secretion of aqueous tears and/or excessive tear evaporation and is characterized by instability and hyperosmolarity of tear film leading to inflammation of the ocular surface. It is a multifactorial disease of the ocular surface that results in symptoms of discomfort, visual disturbance and tear film instability with potential damage to the ocular surface. It remains largely a symptomatic diagnosis, without a single defining diagnostic test.[1]

Dry eye is a highly prevalent disorder affecting 14% to 33% of the adult population worldwide. It does not have an effective therapy and causes a significant loss of productivity at work. It incurs a socioeconomic burden on many societies and is more common in Asia.[2]

It has been recognized that the lacrimal glands, ocular surface (cornea, conjunctiva and meibomian glands), lids, and the sensory and motor nerves that connect them – act as an integrated functional unit (Lacrimal functional unit or LFU) to maintain the tear production and to clear used tears.[3] Disease or any dysfunction of this unit results in an unstable and poorly maintained tear film that causes ocular irritation and epithelial disease called keratoconjunctivitis sicca (KCS).[4]

Decreased tear secretion and clearance initiates an inflammatory response on the ocular surface that involves both soluble and cellular pro-inflammatory mediators (cytokines). Clinical and basic research suggests that this inflammation plays a role in the pathogenesis of KCS mediated by T-cell lymphocytes.[5.6]

On the basis of the underlying pathological processes, dry eye disease can be classified as tear deficiency or hyposecretive dry eye and evaporative or hyperevaporative dry eye.[7]

The term 'tear-deficient dry eye' implies that this condition is caused by lacrimal acinar destruction or dysfunction with reduced lacrimal tear secretion and volume.[7]

Evaporative dry eye may be intrinsic due to meibomian lipid deficiency, poor lid congruity and lid dynamics, low blink rate and the effects of drug use. Extrinsic evaporative dry eye embraces those etiologies that increase evaporation including vitamin A deficiency, the action of toxic topical agents such as preservatives (benzalkonium chloride) and topical anaesthesia. Patients wearing contact lenses are more prone to have dry eye symptoms. Disease of the exposed ocular surface including allergic eye disease may also lead to destabilization of the tear film.[7]

Many studies have paid attention to psychological problems and suggest that mood disorders, particularly depression, are associated with eye diseases.[8,9,10] The chronic ocular discomfort induced by dry eye disease (DED)(11) or inflammatory disorders may be related to the deteriorating mood status as well. Timely and effective detection of the psychological changes will contribute to management of ocular symptoms, improvement of life quality, and also, maintaining peaceful communication between physicians and patients.[8]

A systematic review and meta-analysis performed to estimate the prevalence of depression among different eye disease patients reported that amongst different eye disease subgroups, the highest depression prevalence was revealed for DED patients 29%, followed by glaucoma, AMD and cataract patients. It indicated that the prevalence of depression and depressive symptoms in DED patients was higher than that of other eye disease patients and ranged from 5.4%(12) to 57.0%.[13,14]

This result may also be caused by social factors, multiple doctor visits and medical expenses. The depressive symptoms of eye disease patients deserve more attention.[15]

Several mechanisms play role in association between DED and depression. Female sex, menopause and an increased ratio of omega-6 and omega-3 are the common risk factors, seen in both the diseases, thus suggesting an overlapping pathogenesis. Dry eye symptoms due to production of pro-inflammatory cytokines are worsened by chronic depression. It also lowers the threshold for pain perception or discomfort caused by DED by affecting cognitive modulation of attention. Somatization, which is frequently seen in depression, may predispose to more of dry eye symptoms.[11,16]

The present study was conducted to determine the incidence of depression in patients diagnosed with dry eye.

Material And Methods

This prospective observational analytical study was carried out in Department of Ophthalmology, Government Medical College, Rajindra Hospital, Patiala. A total of 100 patients fulfilling the inclusion criteria and after verifying the exclusion criteria were enrolled in the study. Inclusion Criteria included, diagnosed cases of dry eye of any gender, above 18 years of age and willing to participate in the study. Exclusion Criteria included patients already on anti-depressants, history of previous corneal surgery or trauma in concerned eye or having corneal opacity and keratitis. Patients with known hypersensitivity to any component of procedural medication such as stain or anaesthetic agents or those who refused to participate in the study were also excluded from the study. A written informed consent was taken from the patients. The procedures followed were in accordance

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with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975 that was revised in 2013.

History regarding Symptoms, Presenting complaints (Irritation, tearing, burning, stinging, dry or foreign body sensation, mild itching, photophobia, blurry vision, contact lens intolerance, redness, mucous discharge, increased frequency of blinking, diurnal fluctuation, and symptoms that worsen later in the day), Duration of symptoms and Exacerbating conditions (e.g. wind, air travel, decreased humidity, prolonged visual efforts associated with decreased blink rate such as reading or watching TV.) was taken.

Ocular history details about any topical medications used, their frequency, and their effect on symptoms, contact lens wear, any chronic allergic eye disease, ocular surgical history, ocular surface disease, punctal occlusion, eyelid surgery, Bell's palsy were recorded.

Medical history details eg. Menopause, Systemic inflammatory diseases, Atopy (e.g. dermatitis, rhinitis, bronchial asthma), Systemic medications (e.g., antihistamines, diuretics, hormones and hormonal antagonists, antidepressants, cardiac antiarrhythmic drugs, isotretinoin, diphenoxylate/atropine, beta-adrenergic antagonists, chemotherapy agents, any other drug with anticholinergic effects), Chemical injury (e.g. lime burn or any other), Neurological conditions (e.g., Parkinson disease, Bell's palsy, trigeminal neuralgia), Smoking or exposure to passive smoking were recorded.

Ocular examination included Visual acuity with correction (Best Corrected Visual Acuity), eyelids, adnexa and detailed anterior segment examination under slit lamp biomicroscope.

Tear film break up time (TBUT) was measured after instilling fluorescein dye. The interval between the last blink and the appearance of first dry spot around the central cornea is the TBUT. A TBUT of less than 10 seconds was considered as abnormal.

Ocular surface dye staining was performed using one drop of 1 percent of Rose Bengal stain without prior instillation of topical anaesthetic. Level of staining was determined 2 minutes after instilling the Rose Bengal stain. Grading of staining was done at the slit lamp biomicroscope for each of temporal and nasal conjunctiva as well as the cornea to make a maximum of 9 scores. A cumulative score of 3 or more was regarded as positive while a total score of less than 3 was regarded as negative.

Schirmer test done using 5 mm x 35 mm Whatman filter paper no. 41 with no prior instillation of topical anaesthetic drops. A reading of less than 10 mm was considered as indicative of dry eye and that of less than 5 mm as severe dry eye.

Ocular Surface Disease Index (OSDI): Standardised 12 questions were asked from the patients, and the number in the box that best represents each answer was circled. The OSDI is assessed on a scale of 0 to 100, with normal eye having 0-12, Mild dry eye 13-22, Moderate dry eye 23-32 and severe dry eye having 33-100 score (table 1). OSDI score was calculated by the below given formula

$$\text{OSDI score} = \frac{(\text{Sum of all answered questions}) \times 25}{\text{Total number of answered questions}}$$

Cohen perceived stress scale (PSS) was used for measuring the perception of stress by asking questions to the subject about his feelings and thoughts during the previous month. In each case, the subject was asked to indicate by circling how often did he feel or think a certain way. PSS scores were obtained by reversing the responses (e.g., 0 = 4, 1 = 3, 2 = 2, 3 = 1 & 4 = 0) to the four positively stated items (items 4, 5, 7, & 8) and then summing across all the scale items.

The Hamilton Depression Rating Scale (HAM-D) is a useful proven way to determine level of a patient's depression before, during, and after treatment was used. The HAM-D form lists 21 items in total, but the scoring is based on the first 17 items. Eight items are scored 0,1,2,3 or 4, where 0 = not present and 4 = severe. Nine are scored from 0-2. Add the scores from the first 17 items. Result : 0-7 = Normal, 8-16 = Mild Depression, 17-24 = Moderate Depression, >24 = Severe Depression.

Stastical Analysis

SPSS version 20.0 software was used to analyze the descriptive statistics, where continuous variables were expressed as mean ± SD and categorical

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variables as frequencies (no. of patients) and percentages. Chi-square test was used to compare the nominal categorical data between the groups and P value <0.05 was considered statistically significant.

Results

A total of 100 patients were enrolled in the study, 42 were males and 58 females. Distribution of patients according to age was 26.0% of total 100 patients in 41-50 years age group, 36.0% patients in 51-60 years age group, 30.0% patients in 61-70 years age group, 8.0% patients in >71 years age group. Mean age ±SD was 57.98±10.01 years with a range of 42-85 years.

17 out of 100 patients in our study had mild depression and 4 had moderate depression. Thus the incidence of depression in dry eye cases in our prospective study came out to be 21.0% (Table2).

The association of depression with OSDI was calculated and was found to be statistically significant (p-value 0.001) and chi square value of 93.97. The association of depression with Pain/Soreness, Blurring, Difficulty in Reading and difficulty in Watching TV was also found to be statistically significant (p-value 0.001). The association of depression with grottiness, poor vision, vision in dry areas and areas with AC also found to be statistically significant (p-value <0.05) (Table 3).

The association of depression with age and sex was calculated and was found to be statistically significant (p-value< 0.05) (table 4).

The association of depression with Schirmer test was found to be statistically significant (p-value< 0.05) (Table 5).

Discussion

Dry Eye can be highly detrimental to the quality of life as well as the mental state of the patient. It is, therefore, very important to assess ant treat the psychological and mental aspect of the disease such as depression and anxiety. Dry eye is a highly prevalent disorder affecting 14% to 33% of the adult population worldwide, without an effective therapy and causes a significant loss of productivity at work. It incurs a socioeconomic burden in many societies and is more common in Asia.[2] Also the prevalence of depression occupies the fourth leading contributor to the global disease burden.[17] The present study was done considering the increasing incidence of depression and the perspective of growing importance of its implications in ocular surface diseases.

The incidence of depression in dry eye cases enrolled in our study was 21%. Kim et al [11] in an elderly Korean population aged ≥ 65 years, found the prevalence rate of depression in dry eye to be 33% while Labbe et al [18] examined a random sample of 1957 subjects from the Beijing Eye Study for dry eye disease (DED) and found out that 14% of the subjects suffered from depression. Our study was in conformity with most of the above studies. Stepwise regression analysis of the data revealed that there was significant correlation of the PSQI and HADS scores with both age (P<0.05) and the presence of dry eye (P<0.05).

The association of depression with advancing age was statistically significant (p-value=0.045) in our study. Van Der Vaart et al[19] found that the age group of >65 years had maximum patients with incidence of depression in dry eye and age group of 18-35 years had minimum patients with incidence of depression in dry eye (p-value 0.004) whereas Labbe et al[18] found that the age group of 65-85 years had maximum patients with incidence of depression in dry eye and age group of 41-50 years had minimum patients with incidence of depression in dry eye (p-value 0.9).

In our study, out of 42 males, 6 males (14.29%) had depression. Similarly 15 (25.86%) out of 58 females were diagnosed with depression. The association was found to be statistically significant (p value=0.005). Kim et al[11] concluded that in the binary logistic regression model, female sex (P = 0.014) and depression (P < 0.001) were associated with the risk of DED. Similarly, Ahn et al[20] found that the association between dry eye disease in females and depression was statistically significant (p-value 0.013).

Hallak et al[21] found a linear association between OSDI and depression scale, which was more apparent among DED cases (p-value <0.001). Szakáts et al[22] concluded that the scores of the psychological questionnaires demonstrated significant positive correlations with the OSDI scores (p-value < 0.01). In the present study, in accordance with the above studies the results of the OSDI questionnaire had higher scores in the patients with depression (42.62 ±

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2.50) than in the patients without depression (30.26 ± 2.60) and were statistically significant (p-value 0.001).

In the present study, the comparison of depression and control groups revealed significantly lower Schirmer (5.47 ±1.27 vs. 8.4 ± 3.74 mm) and TBUT (8.36 ± 3.36 vs. 10.61 ± 4.53 sec) scores with a consistently higher HAM-D score (15.62 ± 2.91 vs. 5.61 ±1.09) in the depressive group. Tiskaoglu et al[23] made a comparison of depressive and control groups which revealed significantly lower Schirmer (20.3 ± 9.9 vs. 25.7 ± 9.3 mm) and TBUT (7.8 ± 5.7 vs. 12.5 ± 7.8 s) scores with a consistently higher Oxford depression score (1.8 ± 3.2 vs. 0.2 ± 0.4) in the depressive group. Thus our prospective study was in accordance with the above study.

Association between osdi questionnaire and depression scale was statistically highly significant. (p-value 0.001). Association between schirmer test and depression scale was found to be statistically significant (p-value 0.019 & 0.006 of right & left eye respectively). Association between tear film break up time and depression scale was found to be statistically significant (p-value 0.017).18 of the 21 patients with depression had a Tear Film Break up time < 10 seconds (positive) while 3 of the 21 depression patients had Tear Film Break up time ≥ 10 seconds (negative).

Limitation(S)

The study subjects were selected on the basis of reliability of Visual acuity with correction, Tear film break up time (TBUT) , Ocular surface dye staining, Schirmer test and other criteria, which meant that a larger study group and longer duration of study would have yielded better results. So the demographic characteristics could not be generalised to normal population. A bias may be created by difference in the number of subjects in Dry eye and normal eye group.

Conclusion

In this study, we have tried to determine the association between depression and Ocular surface disease. We found that OSDI questionnaire, Schirmer test, TBUT and Rose Bengal staining all have positive correlation with diagnosis of depression with highest association being of OSDI questionnaire followed by Schirmer test, Rose Bengal test and TBUT respectively. Our study shows that there is a significant increase in incidence of depression in patients suffering from dry eye and further more age and female sex also has a positive correlation with the incidence of depression. There is a desperate need to have a standardized diagnostic criterion to diagnose depression in early stages so as to provide timely treatment and prevent any further debilitation caused by it. Ophthalmology and Psychiatry departments must join hands to provide a better multi-disciplinary treatment which will give better outcomes.

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Tables

Table 1 : Ocular Surface Disease Index (OSDI) questionaire and scoring used in the study

Have you experienced any of the following during the last week?	All of the time	Most of the time	Half of the time	Some of the time	None of the time
1. Eyes that are sensitive to light?	4	3	2	1	0
2. Eyes that feel gritty?	4	3	2	1	0

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3. Painful or sore eyes?	4	3	2	1	0
4. Blurred vision?	4	3	2	1	0
5. Poor vision?	4	3	2	1	0

Have problems with your eyes limited you in performing any of the following during the last week?	**All of the time**	**Most of the time**	**Half of the time**	**Some of the time**	**None of the time**
1. Reading?	4	3	2	1	0
2. Driving at night?	4	3	2	1	0
3. Working with a computer or bank machine (ATM) ?	4	3	2	1	0
4. Watching TV?	4	3	2	1	0

Have your eyes felt uncomfortable in any of the following situations during the last week?	**All of the time**	**Most of the time**	**Half of the time**	**Some of the time**	**None of the time**
1. Windy conditions?	4	3	2	1	0
2. Places or areas with low humidity (very dry)?	4	3	2	1	0
3. Areas that are air conditioned?	4	3	2	1	0

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Table 2 : Assessment of stress and depression in subjects on Cohen's perceived stress scale and Hamilton stress sale

COHEN'S PERCEIVED STRESS SCALE			
Cohen's Perceived Stress Scale	Range/Score	Frequency	Percentage
Mild	1-12	17	17%
Moderate	13-24	68	68%
Severe	25-40	15	15%
Total		100	100%
HAMILTON SCALE			
Hamilton Scale	Range/Score	Frequency	Percentage
No Depression	0-7	79	79%
Mild Depression	8-16	17	17%
Moderate	17-24	4	4%
Severe	>24	0	0%
Total		100	100%

Table 3 : Association of depression with OSDI questionnaire.χ2=chi square value

Symptoms	Depression	Response to OSDI Questionnaire						χ^2	p-value
		4	3	2	1	0	NA		
Sensitivity to Light	Yes	0 (0%)	12 (100%)	8 (36.36%)	1 (1.52%)	0 (0%)	0 (0%)	0.65	0.421
Grittiness	Yes	0 (0%)	4 (50%)	14 (66.67%)	3 (4.35%)	0 (0%)	0 (0%)	3.94	0.047
Pain/Soreness	Yes	0 (0%)	2 (100%)	8 (88.89%)	11 (12.50%)	0 (0%)	0 (0%)	11.03	0.001
Blurring	Yes	0 (0%)	0 (0%)	7 (53.85%)	12 (22.64%)	2 (5.88%)	0 (0%)	10.72	0.001
Poor Vision	Yes	0 (0%)	0 (0%)	6 (85.71%)	12 (32.43%)	6 (10.71%)	0 (0%)	5.56	0.018
Difficulty in Reading	Yes	0 (0%)	1 (100%)	9 (37.50%	11 (14.67%	0 (0%)	0 (0%)	13.84	0.001

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				)	)				
Night Driving	Yes	0 (0%)	3 (100%)	7 (58.33%)	3 (5%)	0 (0%)	8 (32%)	2.17	0.141
Working with Computer	Yes	0 (0%)	0 (0%)	0 (0%)	18 (18.56%)	0 (0%)	0 (0%)	0.00	1.000
Watching TV	Yes	0 (0%)	13 (26.53%)	4 (7.84%)	0 (0%)	0 (0%)	0 (0%)	11.90	0.001
Windy Conditions	Yes	0 (0%)	0 (0%)	5 (10%)	0 (0%)	0 (0%)	0 (0%)	0.00	1.000
Dry Areas	Yes	0 (0%)	0 (0%)	20 (26.32%)	1 (4.17%)	0 (0%)	0 (0%)	4.74	0.029
Areas with AC	Yes	0 (0%)	0 (0%)	20 (25.97%)	1 (4.35%)	0 (0%)	0 (0%)	4.74	0.029

Table 4 : Association of depression in dry eye with age and sex. χ2=chi square value

Age	**Patients**	**Depression**		χ^2	**p-value**
	Frequency (%age)	**Yes (%age)**	**No (%age)**		
41-50	26 (26%)	2 (7.69%)	24 (92.31%)	38.78	0.045
51-60	36 (36%)	5 (13.89%)	31 (86.11%)		
61-70	30 (30%)	10 (33.33%)	20 (66.67%)		
≥71	8 (8%)	4 (50%)	4 (50%)		
Total	100 (100%)	21 (21%)	79 (79%)		
Sex	**Patients**	**Depression**		χ^2	**p-value**
	Frequency (%age)	**Yes (%age)**	**No (%age)**		

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Female	58 (58%)	15 (25.86%)	43 (74.14%)	26.45	0.005
Male	42 (42%)	6 (14.29%)	36 (85.71%)		
Total	100 (100%)	21 (21%)	79 (79%)		

Table 5 : Association of depression with Schirmer test. χ2=chi square value

Eye	Schirmer Test	Score (in mm)	Patients	Depression		X^2	p value
			Frequency (%age)	Yes (%age)	No (%age)		
Right Eye	Positive	<10	78 (78.0%)	17 (21.79%)	61 (78.21%)	21.92	0.019
	Severe	<5	11 (11.0%)	4 (36.36%)	7 (63.64%)		
	Negative	>10	11 (11.0%)	0 (0%)	11 (100%)		
Left Eye	Positive	<10	81 (81.0%)	15 (18.52%)	66 (81.48%)	22.75	0.006
	Severe	<5	8 (8.0%)	6 (75.0%)	2 (25.0%)		
	Negative	>10	11 (11.0%)	0 (0%)	11 (100%)		

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