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DRY EYE DISEASE IN PATIENTS WITH DEPRESSIVE DISORDERS

Ophthalmology

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ABSTRACT

Introduction: Dry eye disease (DED) is a multifactorial disease of the tear film and ocular surface that results in symptoms of discomfort such as pain, heaviness, grittiness, burning, dryness, itchiness, foreign body sensation, visual disturbances, and tear film instability. DED is a common ophthalmological disease with reported prevalence rates as high as 54%. **Aim and Objective:** To investigate dry eye disease (DED) and risk factors in patients with depressive disorders. **Material and Methods:** The Cross-sectional study was performed at the department of ophthalmology, SMS Hospital and attached group of Hospitals, Jaipur, Rajasthan, India. Subjects ($16 years) who had depressive disorders were evaluated with history, questionnaires (Self-rating Anxiety Scale, Self-rating Depression Scale, and Ocular Surface Disease Index), and eye examination. **Result:** The study included Sample size of 944 Patients. DED was present in 566 patients (60%). Compared with patients who did not have DED, patients with DED were significantly older, had longer duration of psychiatric disease and use of antidepressant medication, and more frequently were using a selective serotonin reuptake inhibitor (SSRI). Logistic regression analysis showed that older age, duration of psychiatric disorder, and use of an SSRI were significant independent predictors of the presence of DED. Older age, Self-rating Anxiety Scale >52, and use of tricyclic antidepressants were significant independent predictors of worse vision-targeted health-related quality of life (higher Ocular Surface Disease Index). **Conclusion:** Attention should be paid to DED patients, particularly to those with inconsistent dry eye symptoms and signs and poor response to conventional treatment, for associated psychiatric or neurological disorders, and an integrated treatment approach could be helpful for the patients. Further research is necessary for the elucidation of the mechanisms underlying the association of DED with psychiatric or neurological disorders and the development of treatment methods for DED associated with these conditions.

KEYWORDS

Ophthalmology, psychiatry, depression, quality of life.

INTRODUCTION

Dry eye disease (DED) is a multifactorial disease of the tear film and ocular surface that results in symptoms of discomfort such as pain, heaviness, grittiness, burning, dryness, itchiness, foreign body sensation, visual disturbances, and tear film instability.[1] It is associated with comorbidities such as hypothyroidism, systemic lupus erythematosus, myasthenia gravis, liver diseases, depression, and psychoses to state a few. DED is a common ophthalmological disease with reported prevalence rates as high as 54%. and patients with DED have been found to be more anxious and depressed than those without DED. The discomfort and disturbances in DED decreases vision-related quality of life (VRQL) as well as having an adverse effect on daily tasks, It is also important to note that DED not only affects VRQL but also affects overall quality of life (QOL).[2]

In a study by Wen et al., DED was more prevalent among older patients with a longer history of psychiatric disease and was associated with antidepressant usage especially selective serotonin reuptake inhibitors. Antidepressants increase the risk of DED which is believed to be caused by anticholinergic mechanisms: 'if a systemic medication causes dry mouth it may also cause dry eye'. Serotonin has also been found in human tears and serotonin receptors have been demonstrated in conjunctival tissue contributing to the theory that depression causes DED. DED represents a heterogeneous collection of clinical disorders caused by various pathophysiological etiologies. Disparity between common dry eye symptoms and signs has been reported, which makes the diagnosis and treatment of DED difficult.[3] A number of epidemiological studies have investigated the association of DED with depression and anxiety. These studies have postulated potential explanations for their association, by looking into the prevalence of mental disorders in DED patients or vice versa. However, the prevalence of DED varies with disease definition, sex, age, lifestyle, and geography.[4]

The purpose of this cross-sectional, interdisciplinary, clinical study was to assess the prevalence of DED and self-reported vision-related dysfunction in patients with depressive disorders. We hypothesized that DED is common in patients with depressive disorders.

MATERIALS AND METHODS

The study was performed at the department of ophthalmology, SMS Hospital and attached group of Hospitals, Jaipur, Rajasthan, India. All consecutive patients with depressive disorders (age, $16 years) were treated in the study. All enrolled patients had been diagnosed by professional psychiatrists using criteria for depressive disorders listed in the Diagnostic and Statistical Manual of Mental Disorders (Third Edition). Psychiatric exclusion criteria for participation in the study included a history of seizure disorder, serious or unstable medical illness, substance abuse disorder (active within the past year), serious suicidal risk, schizophrenia, or major antisocial personality disorder. Other medical exclusion criteria included current pregnancy or lactation. Ophthalmic exclusion criteria included ocular topical treatment within the past 6 months, previous ocular laser or surgical treatment, history of ocular trauma, use of contact lenses within the past 12 months, active ocular infection, or other common ocular diseases, including pterygium, glaucoma, or retinal detachment.

RESULT

There were 944 psychiatric patients included in the study . There were 82 other patients who were excluded because of the use of contact lenses within the past 12 months (28 patients), previous cataract surgery (16 patients), previous laser-assisted in situ keratomileusis surgery for correction of refractive error (12 patients), history of glaucoma medication or surgery (10 patients), unstable psychiatric illness (8 patients), and history of ocular injury (4 patients) and serious suicidal risk (4 patients).

Table 1. Characteristics of 944 Patients with Depressive Disorders Who Were Evaluated for DED

Variable		Mean ± Sd/No. of patients and percentage
Age	41± 15	
Sex	Female	572(61%)
	Male	372(39%)
Education	Illiterate or graduate from primary school	32(3%)
	Graduate from junior high school	220(23%)
	Graduate from senior high school	284(30%)
	Undergraduate	338(36%)
	Graduate or higher	68(7%)
Menopause (if women)		206(36%)
Current smoker		114(12%)
Systemic diseases	Hypertension	94(10%)
	Cardiac diseases	52(6%)
	Gastrointestinal disorders	20(20%)

	Diabetes	18(2%)
	Thyroid diseases	14(2%)
	Rheumatic diseases	12(1%)
Other systemic medications	Antihypertensive drug	28(3%)
	Glucocorticoid or NSAID‡	16(2%)
	Antihistamine drug	4(0.4%)
Use of visual terminals (television, computer)	Scarcely (never use)	234(25%)
	Sometimes (≤1 h/d)	212(23%)
	Often (>1 and ≤5 h/d)	468(50%)
	Always (>5 h/d	30(3%)

Most of the patients were middle-aged women who had depression and most patients used 1 antidepressant medication, primarily a selective serotonin reuptake inhibitor (SSRI) (Table 1). Most patients did not have systemic diseases and did not use systemic medication (Table 1). Half of the patients often used visual terminals (Table 1).

Table 2. Ophthalmic Findings in 944 Patients With Depressive Disorders

Ophthalmic Findings	No. Patients (%)	
Dry eye symptoms	All patients who had $1 symptom	760(81%)
	Dryness	460(49%)
	Blurring	444(47%)
	Itching	304(32%)
	Foreign body sensation	220(23%)
	Photophobia	142(15%)
	Red eye	82(8%)
	Burning	58(6%)
	Pain	58(6%)
Schirmer test	Abnormal (1+)	218(23%)
	Strongly abnormal (2+)	396(42%)
Tear breakup time test	Abnormal (1+)	220(23%)
	Strongly abnormal (2+)	500(53%)
Corneal fluorescence staining test	Abnormal	252(27%)

Most patients had $1 dry eye symptom, primarily dryness, blurring, itching, or foreign body sensation (Table 2). Burning was more frequently observed in patients who had generalized anxiety disorder than other psychiatric disorders (P< 0.03); the patients who had other psychiatric disorders had similar frequency of the presence or absence of dry eye symptoms. Most patients had an abnormal or strongly abnormal Schirmer test and tear breakup time test (Table 2). The frequency of patients who had abnormalities in the objective tests was similar for patients with different psychiatric conditions. Based on the findings of dry eye symptoms and objective studies, most psychiatric patients were diagnosed with DED (Table 2).

Table 3. Comparison of Patients With or Without DED

Variable	With DED	Without DED	P-value
Age (mean± SD), yr	43 ± 14	37 ±14	0
SAS (mean± SD)	47 ± 11	46 ± 11	0
SDS (mean± SD)	40 ± 10	41± 10	0
Duration of psychiatric disease (mean± SD)	54 ± 59	39± 39	0
Duration of antianxiety or antidepressant medication use (mean± SD)	17 ± 25	10 ±18	0
Sex (male/female)	208/358	164/214	0
Education (0/1/2/3/4)	20/130/168/202/44	12/90/116/136/24	0
Type of psychiatric disease (0/1/2/3/4)	200/58/7/218/78	140/52/8/134/42	0
Antidepressant medication (0/1/2/3/4/5)	94/10/354/54/14/40	102/4/204/22/6/40	0
Menopause (if women), n (%)	138(39%)	68(32%)	0
Current smoker, n (%)	66(12%)	48(13%)	0
Systemic disease (0/1/2/3/4/5)	64/10/38/10/12/10	30/8/14/4/8/1	0
Other systemic medication (0/1/2)	4/20/2012	0/8/6	0
Use of visual terminals (television, computer) (0/1/2/3)	124/130/294/18	110/82/174/12	0

Compared with patients who did not have DED, patients with DED were significantly older, had longer duration of psychiatric disease and use of antianxiety or antidepressant medication, and more frequently were using an SSRI (Table 3). After adjustment for age, sex, menopause (if women), current smoking, systemic diseases, systemic medication, and use of visual terminals (television or computer), DED was significantly associated with longer duration of psychiatric disease (P , 0.02), longer duration of antianxiety or antidepressant medication (P <0.02), and use of an SSRI (P <0.007).

Table 4. Results of Evaluation of Vision-Targeted Health-Related Quality of Life as Assessed With the OSDI

Variable	Normal	Mild to Moderate	Severe	P-value
OSDI	0–15	15.1-30	>30	0
No. patients (%)	376(40%)	386(41%)	182(19%)	0
Age (mean ±SD), yr	39± 14	41±15	45±14	0
SAS (mean ± SD)	46±11	45±10	51±11	0
SDS (mean ± SD)	40± 10	40±9	42±10	0
Duration of psychiatric disease (mean ± SD), mo	46± 52	49±52	52±53	0
Sex (male/female)	164/212	148/238	60/122	0
Education (0/1/2/3/4)	14/88/102/138/2	8/94/118/142/24	10/38/64/58/10	0
Type of psychiatric disease (0/1/2/3/4)	126/62/14/134/40	144/42/4/152/44	70/6/4/66/36	0
Menopause (if women), n (%)	60(27.9%)	68(30%)	56(45%)	0
Current smoker	48	46	20	0
Systemic disease (0/1/2/3/4/5)	82/10/14/8/10/4	40/4/22/0/4/4	30/4/16/6/6/4	0
Other systemic medication (0/1/2)	2/12/8	2/12/4	2/4/6	0
Use of visual terminals (television, computer) (0/1/2/3)	82/96/184/14	110/76/184/16	42/40/100/0	0

Assessment of vision-targeted health-related quality of life, quantified with the OSDI, showed significantly better quality of life in patients who were younger, had shorter duration of psychiatric disease, and did not use antidepressant medication (Table 4). After adjustment for age, sex, menopause (if women), current smoking, systemic diseases, systemic medication, and use of visual terminals (television or computer), there was a significant association between greater OSDI (worse vision-targeted health-related quality of life) and greater frequency of obsessive–compulsive disorder (P<0.05) and use of tricyclic antidepressants (P <0.0008).

DISCUSSION

The present results confirmed the hypothesis that DED frequently occurs in patients who have depression and/or anxiety disorders (Table 2). There was a greater prevalence of DED (60%) and dry eye symptoms (81%) in the present study of patients with depression and/or anxiety disorders (Table 2) than that previously reported in several studies of Asian populations.[5]

A strength of the present study was the use of objective ophthalmic tests, instead of symptoms alone, to evaluate the prevalence of DED in a psychiatric population. Furthermore, the study showed that specific antidepressants or antianxiety medication may influence DED and vision-targeted health related quality of life (Table 6).

Age was an important risk factor for DED in the present study (Tables 3, 6). Other studies of varied racial groups also have reported a greater prevalence of DED with increased age,but some studies have shown no dependence on age.[6] The greater prevalence of DED in older people may be attributed to several factors, including a decline of tear function and tear flow in older people20; decreased lacrimal gland function, decreased tear secretion, and instability of the tear film associated with changes in the lipid layer; and age related changes of the meibomian glands, demonstrated by infrared meibography.[7]

Population-based studies have shown the association of DED with depression, anxiety and stress. In a study on elderly Koreans of age 65 years or older, Kim et al[8] revealed that depression was related to dry

eye symptoms in patients with normal or mildly reduced tear production. In a large population-based study including 6,655 women of $19 years of age, Na et al[9] revealed that subjects with DED showed increased risk of experiencing severe psychological stress, anxiety and depression. Yilmaz et al[10] also reported that subjects with depression, stress and anxiety are more prone to DED.

Several previous studies have shown sex to be a risk factor for DED.[5,6] However, sex was not a risk factor for DED in the present study of patients with depression and/or anxiety disorders (Table 3). The greater prevalence of DED in patients with psychiatric disorders may have been caused by psychiatric-related factors, such as the duration of psychiatric disease and use of SSRIs (Table 6), and these factors may have been stronger in these patients than the sex-related factors observed in previous studies in general populations.

Several studies had demonstrated a greater prevalence of DED in people with medical comorbidities, including hypertension,[11] diabetes,[12] cardiac disease,[13] thyroid disease,[13] gastrointestinal disorders,[13] rheumatic diseases,[6] and systemic medication (antihistamine drugs,[14] antihypertensive drugs, glucocorticoids, nonsteroidal antiinflammatory drugs,[14] and hormone replacement therapy[6]). Other studies suggested that visual terminals may have adverse effects on the ocular surface.[15] Although these factors were evaluated in the present study, none were associated with DED in patients with depression and/or anxiety disorders (Tables 3, 6). This disparity may be explained by the low frequency of medical comorbidities in the present population (Table 1) and the greater importance of age and psychiatric factors on DED than medical comorbidities in these patients (Tables 3, 6).

Anxiety disorders and depression are among the most common psychological disorders. A previous epidemiologic study showed that patients with DED were more likely to have depression (odds ratio, 2.11) and psychosis (odds ratio, 1.87),[16] but anxiety was not identified as a risk factor.[16] In the present study, the type of psychiatric disease was not associated with DED (Tables 3, 6), but this study was limited to patients with depression and anxiety disorders.

CONCLUSION

The study concluded that attention should be paid to DED patients, particularly to those with inconsistent dry eye symptoms and signs and poor response to conventional treatment, for associated psychiatric or neurological disorders, and an integrated treatment approach could be helpful for the patients. Further research is necessary for the elucidation of the mechanisms underlying the association of DED with psychiatric or neurological disorders and the development of treatment methods for DED associated with these conditions.

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