Prevalence of dry eye disease in patients on anti-depressants

Arun Kumar A1, Irshad E2*, Jithu V P3

1Professor, 2Senior Resident, 3Associate Professor, 1,2Dept. of Ophthalmology, 3Dept. of Psychiatry, Govt. Medical College, Kozhikode

*Corresponding Author:
Email: irshd101@gmail.com

Abstract
Introduction: Dry eye is a complex multifactorial disease which forms a major proportion of ophthalmology out patients. Most of the patients are on chronic medications including psychiatric drugs. So prevalence of dry eye was studied in psychiatric patients on antidepressants.

Methods: A cross sectional comparative study was conducted among 22 patients / 21 controls in a tertiary eye care hospital in Northern Kerala for a period of 1 year by assessing Ocular surface disease index score/Tear film break up time/Schirmer test. Association of age gender, smoking, alcoholism, with dry eye disease was also studied.

Results: Study showed a statistically significant correlation between antidepressant medications and dry eye with a P value of 0.012. Tricyclic anti-depressants contributed the majority for dry eye followed by selective serotonin re-uptake inhibitors and serotonin norepinephrine reuptake inhibitors. Females, old age and smoking showed high prevalence. Schirmer test was found to be 100% sensitive and specific and TBUT; 35% sensitive and 100% specific.

Conclusion: Prevalence of dry eye disease is 50 % in patients on antidepressants compared to 14.2 % in control group. Schirmer test can be effectively used in patients for early detection of dry eye disease. The drugs with least side effects can be selected and treatment modified accordingly.

Keywords: Dry eye disease, Ocular surface index score, Schirmer test, Tear film break up time.

Introduction
Most of the patients attending ophthalmology clinic with dry eye syndrome are already on chronic medications for their systemic diseases.(1) These medications have the potential to cause dry eye syndrome.(2) Presence of dry eye is often undetected in patients with anti depressant medication. This is because drug trials are often assessed by spontaneous reporting by the patients or closed end questionnaires that do not include dry eye symptoms. 85 % of the patients taking antidepressants reported blurred vision in a study for adverse effects of antidepressants.(3)

Patients with depression often have a gloomy outlook and are pessimistic about the treatment and they are on long term medication. Incidence and severity of dry eye disease is directly correlated with incidence of dry mouth, constipation and anhydrosis. Early detection of dry eye disease can help the patient to switch to a different class of drug. This will lead to better compliance and minimal adverse effects. Many evidence based data is available for substantiating the association between dry mouth and systemic medication, antidepressants in particular.(4) Though dry eye is strikingly similar to dry mouth, research data is lacking to clinch the association between dry eyes and anti depressants.

Materials and Methods
Study design:
There were two groups of subjects
1) Psychiatric patients on anti-depressve medications
2) Control subjects

Occurrence of dry eye disease was compared and studied in these two groups. Cross sectional comparative study. Cases and control selected randomly.

Study setting: Test group: Selected from patient diagnosed with depressive disorder and on regular anti-depressive medication attending the psychiatry department at Govt. Medical College, Kozhikode. Control group: was selected from ophthalmic OPD, Govt. Medical College, Kozhikode who are coming for refractive error, routine check up. Control group was selected as comparable age, sex of case group

Study period: Study was undertaken from January 2014 to June 2015.

Inclusion criteria: Patient diagnosed having depressive disorder with regular medication for more than one month.

Exclusion criteria: Patients having:
- History of ocular surgery, History of ocular trauma, contact lens, exposure to radiation of orbit or surrounding area and patients on chronic medications like medications other than antidepressants, anti-hypertensives, anti-histamines, hormonal medications and diuretics.

Dry eye is diagnosed in the participants by OSDI questionnaire (score more than 12) with at least one objective sign. Objective tests includes tear film break up time and schirmer test. Tear film break up time less
than 10 seconds and schirmer test value less than 10 mm without anesthesia are considered positive.

Patients with score more than 12 in OSDI questionnaire and positive for either TBUT or Schirmer test were diagnosed as dry eye.

Data was entered in Microsoft Excel worksheet and analysis was performed using SPSS. All patients right eye were examined.

**Result**

This study assessed the frequency of dry eye disease among 22 psychiatric patients on antidepressant medication and 21 healthy controls.

Mean age of control group was 61.52±9.27 and that of test group was 56.32±10.16. 2% of participants in first group (20-50) had dry eye disease while 30% of second group (50-80) had dry eye disease. This was statistically significant as P value is 0.022. (Table 1) (Graph 2)

Dry eye disease is present in 14.2 % of participants (3 in 21) in control group. The test group had 50% prevalence of dry eye disease. This points towards the fact that 11 in 22 patients had dry eye disease. This clearly establishes that participants using psychiatric medicines are suffering more from dry eye disease when compared to control group. This is with a P value 0.012 and it is statistically significant.(Table 2)(Graph 1)

13.6% patients were using tricyclic antidepressants, 45.4% were on selective serotonin reuptake inhibitors and 40.9% were on serotonin norepinephrine reuptake inhibitors for depressive disorder. All the patients using tricyclic antidepressants were suffering from dry eye disease (100%). At the same time 50% of patients on selective serotonin reuptake inhibitors were suffering from dry eye disease, While 33% patients on SSRI were also affected with dry eye disease.

This study shows that the sensitivity & specificity of schirmer test is 100% in diagnosing dry eye due to anti depressant medication. We can see that accuracy of the test is 100%.

The specificity of TBUT test is 100% but the sensitivity of the test is 35.7%. There is 100% positive predictive value and 76.3% negative predictive value. Accuracy of TBUT test is 79%. (Table 3, Table 4)

Study showed no significant correlation of smoking and alcoholism with dry eye disease.

**Table 1: Comparison between different age group and dry eye disease**

<table>
<thead>
<tr>
<th>Dry eye</th>
<th>Age</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;50</td>
<td>≥50</td>
</tr>
<tr>
<td>Present</td>
<td>1 (2%)</td>
<td>13 (30%)</td>
</tr>
<tr>
<td>Absent (%)</td>
<td>12 (28%)</td>
<td>17 (40%)</td>
</tr>
</tbody>
</table>

**Table 2: Prevalence of dry eye disease in case and control group**

<table>
<thead>
<tr>
<th>Dry Eye</th>
<th>Control</th>
<th>Test</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>3 (14.3%)</td>
<td>11 (50%)</td>
<td>0.012</td>
</tr>
<tr>
<td>Absent</td>
<td>18(85.7%)</td>
<td>11(50%)</td>
<td></td>
</tr>
</tbody>
</table>

**Table 3: Sensitivity of schirmer test**

<table>
<thead>
<tr>
<th>Schirmer Test</th>
<th>Dry eye</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>14</td>
<td>0</td>
<td>29</td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
<td>29</td>
<td></td>
</tr>
</tbody>
</table>

**Table 4: Sensitivity of tear film break up time**

<table>
<thead>
<tr>
<th>TBUT</th>
<th>Dry eye</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>5</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
<td>29</td>
<td></td>
</tr>
</tbody>
</table>

**Graph 1: Distribution of dry eye in case and control group**

**Graph 2: Age distribution among dry eye patients**

**Discussion**

Blinking and tear production are the important mechanisms of eye against injury. The conjunctiva and cornea are kept constantly lubricated by tear secretion which is continually washed over eye ball by the blinking movement of the lids. Dry eye disease cause tear film instability and leads to various symptoms. Majority of dry eye disease is under recognised due to lack of awareness and has etiological and management challenges. Many studies shows that incidence of dry
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Prevalence of dry eye disease increase with the age and female sex; in subjects with arthritis, Sjögren syndrome, lupus erythematosus, ocular rosacea, allergy, and thyroid disease not treated with hormone; in subjects using antihistamines, antianxiety medications, antidepressants, oral steroids, vitamins, β-blockers, and diuretics.\(^{(5,10)}\)

Of the many studies done, antidepressant medication is a known group of culprit in causing dry eye disease.\(^{(11-13)}\) Antidepressant medication can induce dry eye secondary to decreased tear production, alternating nerve impulse or by direct inflammatory effect on the secretory glands. Systemic drugs have the ability to get secreted in tears and can cause dry eye effect.

Antidepressants cause dry eye syndrome due to its anticholinergic effects and other mechanisms. Common antidepressants have ring structures similar to atropine and exert similar anti muscarinic side effects. The anticholinergic adverse effects commonly encountered are dry mouth, constipation and dry eye. This is an expected action and there can be a dose response relationship between drug dosage and the severity of adverse effects.

Among the anticholinergic side effects caused by antidepressants, dry eye can be easily evaluated. There is no easily available objective test for dry mouth and constipation. This shows importance of identification of dry eye syndrome. In our study we demonstrated high prevalence of dry eye disease in patients using tricyclic antidepressants compared to selective serotonin reuptake inhibitors and serotonin-nor adrenaline reuptake inhibitors.

Tricyclic anti-depressants are well known for its anticholinergic action. This property of TCAs leads to decrease in the lacrimal gland’s secretion and induce dry eye. Study done by Emel Kocer et al revealed that schirmer test value is lowest in tricyclic antidepressants. At the same time persons using SSRI showed decreased wetting in comparison with SNRI.\(^{(14)}\) This can be attributed to the pseudo anticholinergic effect of SSRI.

Studies have proved that dry mouth is produced more in those who are on TCA compared to SSRI.\(^{(15,16)}\)

This difference among various classes of drugs helps the physician in choosing better group of antidepressants. As a result patients are treated in the most appropriate way. It is especially helpful when physicians have to treat patients who have multiple risk factors for dry eye like increasing age, female gender, poly pharmacy, thyroid disease, connective tissue disorder etc.

Schirmer test and tear film break up time are commonly used for evaluation of dry eye disease in several studies.\(^{(17-20)}\) Our study shows that the sensitivity & specificity of schirmer test is very high. Schirmer test can be used widely in psychiatry OPD. Even without the use of slit lamp examination physician can screen the patient using OSDI questionnaire and schirmer test. Thus patient can be saved from adverse effects like dry eye disease, anhydrosis, constipation and dry mouth.

**Limitation of the study:**
1. Small sample size of the case group.
2. Patients with depression will not express the symptoms of dry eye disease which makes calculating ocular surface disease index score difficult.

**Conclusion**

Prevalence of dry eye disease was high in patients on antidepressants. So all patients should be evaluated for dry eye disease, so that we can modify the treatment either by substituting the drug with less dry eye effect or supplementing artificial eye drops. Shimer test has high sensitivity in diagnosing dry eye disease caused by anti-depressant medication. As this is a non-invasive, simple test should be included in all patients in psychiatric outpatient department using antidepressant medication.

**References**

2. Benjamin A, Virginia, Kaplan & Saddocks Synopsis of psychiatry, 10, New Delhi, Lippincott Williams &Wilkins; 2007; p 527 540.