Original research article

Analysis of tear film in patients on long-term antipsychotic treatment

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Abstract

Introduction: Dry eye syndrome is very common these days. Tear film properties are altered by systemic variables such as medicines and the environment, tear film is vital to maintaining a healthy ocular surface. In a psychiatric setting, anti-psychotic medications are routinely prescribed and often taken for the rest of a patient's life. Consequences are therefore frequently experienced.

Materials and methods: This study was conducted at the Department of Ophthalmology, Narayana Medical College and Hospital, Nellore, Andhra Pradesh, India between August 2021 to January 2023. A cross-sectional observational study was conducted on 300 eyes of 150 chronic anti-psychotic patients. 90 men and 60 women comprised 150 patients. Schizophrenia was treated in 92 patients, delusional disorder in 30, psychoses in 15 and other diseases in 13.

Results: Our research showed that 48 of 150 patients using these medications were affected by dry eye illness. It was found that patients who had been receiving treatment for longer than 8 years were more likely to develop dry eye disease. Patients on many medications, especially Chlorpromazine, then haloperidol, then risperidone, were found to be at a higher risk of developing dry eye.

Conclusion: As a result, our research suggests that patients receiving long-term treatment with antipsychotics should have routine ocular follow-up visits for early diagnosis and treatment of dry eye. **Keywords:** Tear film analysis, antipsychotic, chlorpromazine, haloperidol

Introduction

The prevalance of dry eye disease has been increasing in recent years, leaving many people with varied degrees of ocular discomfort. Due to the lack of consensus on how to define dry eye illness and the absence of a reliable diagnostic test or battery of tests, little is known about this disorder ^[1-3]. Due to this, emphasis is being placed on symptom-based examination in clinical diagnosis than traditional medical tests. The prevalence of dry eye reported in the literature varies widely, from 7.8% in one research conducted in the Western Hemisphere to 93.2% in another conducted in Asia. This is likely due to the lack of standardization in the chosen demographic, dry eye questionnaires, objective tests, and dry eye diagnostic criteria, as well as the location of the study population ^[4-6]. Research in Northern and Eastern India has indicated that the prevalence of dry eye was 54% higher at high altitude. Some people who suffer from dry eye syndrome end up going blind as it is a chronic condition. Tear film properties are altered by systemic variables such as medicines and the environment, all of which are vital to maintaining a healthy ocular surface. Medical professionals might help the patients see clearly and feel comfortable for the rest of their lives even though they would always be dealing with an incurable illness, if they had greater knowledge about this condition and how to manage it ^[7-10].

When treating patients with psychoses or delusional condition, anti-psychotic drugs are frequently employed. Due to the long course of treatment, adverse effects are frequently observed. Anti-psychotic drugs typically cause damage to the liver and, secondarily, the eyes. Causes of impaired vision in the eye include corneal deposition of medications, dry eye, stellate capsular deposits, oculogyric crises, and others ^[11]. Dry eye illness is one of several ocular side effects that doesn't get enough attention and causes sufferers a lot of discomfort. Dry mouth, blurred vision, and urine hesitancy are all indications of antipsychotics' strong dose-related anticholinergic adverse effect. Possible mechanism of dry eye is: The anti-cholinergic activity of these medications blocks the muscarinic receptors found over the lacrimal gland ^[12]. The result is decrease in the production of tears, which might cause the tear film to become unstable. One possible explanation of dry eye in people with schizophrenia who take neuroleptics is that they blink less frequently, as found in a research by Mcintosh *et al.* Our research tries to address this

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issue with antipsychotic medication.

Materials and Methods

This study was conducted at the Department of Ophthalmology, Narayana Medical College and Hospital, Nellore, Andhra Pradesh, India between August 2021 to January 2023. A cross-sectional observational study was conducted on 300 eyes of 150 chronic anti-psychotic patients. 90 men and 60 women comprised 150 patients. Schizophrenia was treated in 92 patients, delusional disorder in 30, psychoses in 15 and other diseases in 13.

Inclusion criteria

Patients on Anti-psychotic medications for more than 2 years.

Exclusion criteria

- People who have used antipsychotic drugs for less than two years.
- Patients who experienced a severe case of the illness.
- Patients taking antipsychotics combined with other drugs.
- Patients who have additional ocular conditions that may impair tear film.
- Additional systemic illnesses.

Results

Dry eye illness was present in 48 of the 150 patients who were receiving prolonged anti-psychotic treatment. 15 of these 48 patients displayed symptoms that were consistent with having dry eye illness.

Age Distribution

Table 1: Age distribution of patients with dry eye disease

Age groups	Number of patients with dry eye disease	Number of eyes without dry eye disease
< 18	6	28
20-40	16	34
41-60	26	40
Total	48	102

The majority of individuals suffering from dry eye disease fell into the age bracket of 41-60 years old, making up 54.1% of the total number of eyes affected by the condition.

Grading of dry eye disease

Dry eye illness was seen in 90 of the 300 eyes examined.

Table 2:	Grading	of dry	eye	disease
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Dews severity grading	Number of eyes
2	4
3	36
4	32
9	18
Total	90

Dry eye disease was detected in a total of 90 eyes, and Grade 4 dry eye disease was present in 32 of those eyes.

Table 3: Symptoms of patients

Symptoms	Number of patients with dry eye
Irritation/ Foreign Body Sensation	16
Burning Sensation	4
Discomfort To Bright Light/ Wind	10
No Symptoms	18
Total	48

Taking this into consideration, we ought to accord significance to their symptoms and conduct additional, objective evaluations of them. 18 out of the 48 customers had no complaints whatsoever. Due to the fact that the majority of patients fell into the Grade 4 dry eye illness group, it is imperative that we evaluate these individuals, even if they are exhibiting no symptoms.

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Tear Film Meniscus Height

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Tear film meniscus height	Number of eyes with dry eye
Abnormal	75
Normal	15
Total	90

 Table 4: Tear film meniscus height

Aberrant tear film height was found in 75 of those eyes.

 Table 5: Number of eyes with conjunctival injection

Conjunctival injection	Number of eyes with dry eye
Absent	75
Present	15
Total	90

In 75 out of 90 eyes, which is equivalent to approximately 83.33% of positive instances, there was no evidence of conjunctival injection.

Conjunctive staining	Number of eyes with Dry eye
Absent	15
Mild	45
Moderate	20
Severe	10
Total	90

Table 6: Number of eyes with conjunctival staining

The use of fluorescein to stain the conjunctiva revealed a positive result in 75 of the 90 eyes that were diagnosed with dry eye illness.

Corneal staining	Number of eyes with dry eye
Absent	20
Mild Staining	45
Marked Central Staining	15
Diffuse Punctate Staining	10
Total	90

Table 7: Number of eyes with conjunctival staining

The corneas of the majority of the patients exhibited just slight discoloration.

Lable 0. I can min break up time

TBUT	Number of eyes with dry Eye
Abnormal	75
Normal	15

Aberrant tear film break up time was found in 75 of those eyes.

Table 9: Number of eyes with dry eye schirmer's test

Schirmer's Test 1 (in mm)	Grade of dry eye disease	Number of eyes with dry eye
6-10	Mild	45
3-5	Moderate	35
0-2	Severe	10
Tot	al	90

The majority of the patients, 45 out of 90 eyes, had a mild form of dry eye disease.

Discussion

We find that Chlorpromazine, Haloperidol, and Risperidone are the most useful anti-psychotic medications. Risperidone is part of a newer class of antipsychotic medications called Atypical Antipsychotics.

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Derection	Dry eye	Tatal	
Duration	Present	Absent	Totai
<5 Years	4	22	26
5-8 Years	8	50	58
>8 Years	36	30	66
Total	48	102	150

Table 10: Duration of drug therapy

Almost eight years of anti-psychotic medication use was associated with dry eye condition in nearly 75 percent of patients. Since the P value is less than 0.01, it is clear that there is a highly significant connection between treatment duration and the prevalence of dry eye illness.

Mono-pharmacy vs poly-pharmacy

Sixty people out of the 150 were only receiving one medication. 90 of them were receiving treatment with multiple medications. Eight patients in the Multi-drug group were taking Haloperidol in addition to Chlorpromazine and Risperidone, whereas 52 were taking Haloperidol and Chlorpromazine, and 30 were taking Risperidone in addition to Chlorpromazine.

Treatment modality	Dry eye disease		Total	Percentage of dye eye present among each
	Present	Absent	Total	treatment modality
Mono drug therapy	20	40	60	33.3%
Dual drug therapy	35	47	82	42.6%
Multi drug therapy	5	3	8	62.5%
Total	48	102	150	32%

Table 11: Mono-pharmacy VS Poly-pharmacy

Drug combination and dry eye disease

Dry eye illness was present in 48 of 150 patients who had been on anti-psychotics for more than 2 years. Ninety eyes out of 300 tested had dry eye syndrome. Treatment-seeking patients aged 41-60 made up 54.1% of all eyes with dry eye disease ^[13, 14]. According to the Dry Eye Illness Staging System (DEWS), 40% of patients were diagnosed with Grade 3 disease. Almost half of individuals with dry eye illness reported experiencing symptoms. About 33 percent of people report feeling that something is stuck in their body. In 83.3% of cases, the height of the tear film meniscus was decreased ^[15, 16]. It was found that Schirmer's test 1, fluorescein staining, and tear film break up time were excellent predictors of dry eye disease. In addition, no patients experienced any adverse effects from dry eye. Our research showed that dry eye condition was more prevalent with chlorpromazine than haloperidol or risperidone, three of the anti-psychotic drugs tested. With typical antipsychotics, dry eye disease was more common than with atypical antipsychotics. Nearly 62.5% of patients on a multidrug regimen experienced dry eye, which is significantly higher than the prevalence seen in patients on a dual or single medication regimen. More patients on the Haloperidol + Chlorpromazine + Risperidone combination experienced dry eye, followed by those on the Haloperidol + Chlorpromazine combination, and finally by those on the Risperidone + Chlorpromazine combination. People who had been taking anti-psychotics for more than 8 years were more likely to develop dry eye. It was shown that around 32% of patients were suffering from dry eye illness [17-19].

Conclusion

Forty-eight individuals out of a total of 150 on anti-psychotics for more than 2 years had symptoms of dry eye. Ninety eyes out of 300 tested had dry eye syndrome. People between the ages of 41 and 60 had the highest prevalence. Grade 3 dry eye illness was present in nearly 40% of patients, and if left untreated, can worsen. It was found that individuals who had been on anti-psychotics for more than 8 years, and notably those who were on a multi-drug regimen, were significantly more likely to develop dry eye disease. Given the patient's mental state, it's hard to put much stock in their claims of ocular discomfort. On the other hand, our research highlights the significance of paying attention to patient symptoms in order to catch the disease in its earliest stages.

Funding source

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Conflict of interest None

References

1. Dean CE, Thuras PD. Mortality and tardive dyskinesia: long-term study using the US National

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Death Index. The British Journal of Psychiatry. 2009 Apr;194(4):360-4.

- 2. Schmidl D, Schmetterer L, Witkowska KJ, Unterhuber A, dos Santos VA, Kaya S, Nepp J, Baar C, Rosner P, Werkmeister RM, Garhofer G. Tear film thickness after treatment with artificial tears in patients with moderate dry eye disease. Cornea. 2015 Apr 1;34(4):421-6.
- 3. Arai H, Nakamura Y, Taguchi M, Kobayashi H, Yamauchi K, Schneider LS, J-CATIA Study Group. Mortality risk in current and new antipsychotic Alzheimer's disease users: large scale Japanese study. Alzheimer's & Dementia. 2016 Jul, 1;12(7):823-30.
- 4. Kanahara N, Yamanaka H, Shiko Y, Kawasaki Y, Iyo M. The effects of cumulative antipsychotic dose on brain structures in patients with schizophrenia: Observational study of multiple CT scans over a long-term clinical course. Psychiatry Research: Neuroimaging. 2022 Jan 1;319:111422.
- 5. Messmer EM. The pathophysiology, diagnosis, and treatment of dry eye disease. Deutsches Ärzteblatt International. 2015 Jan;112(5):71.
- Keikhayfarzaneh MM, Aghazade-Amiri M, Akhgary M, Dibajnia P. Tear film break-up time: comparison between patients using psychiatric drugs and healthy individuals. Zahedan Journal of Research in Medical Sciences. 2014 Sep 30;16(9).
- 7. Lang DJ, Kopala LC, Vandorpe RA, Rui Q, Smith GN, Goghari VM, Honer WG. An MRI study of basal ganglia volumes in first-episode schizophrenia patients treated with risperidone. American Journal of Psychiatry. 2001 Apr 1;158(4):625-31.
- 8. Gilmer TP, Dolder CR, Lacro JP, Folsom DP, Lindamer L, Garcia P, Jeste DV. Adherence to treatment with antipsychotic medication and health care costs among Medicaid beneficiaries with schizophrenia. American Journal of Psychiatry. 2004 Apr 1;161(4):692-9.
- 9. Siegel SJ, Winey KI, Gur RE, Lenox RH, Bilker WB, Ikeda D, Gandhi N, Zhang WX. Surgically implantable long-term antipsychotic delivery systems for the treatment of schizophrenia. Neuropsychopharmacology. 2002 Jun;26(6):817-23.
- 10. Lidow MS, Song ZM, Castner SA, Allen PB, Greengard P, Goldman-Rakic PS. Antipsychotic treatment induces alterations in dendrite-and spine-associated proteins in dopamine-rich areas of the primate cerebral cortex. Biological psychiatry. 2001 Jan 1;49(1):1-2.
- 11. Bickmore TW, Puskar K, Schlenk EA, Pfeifer LM, Sereika SM. Maintaining reality: Relational agents for antipsychotic medication adherence. Interacting with Computers. 2010 Jul;22(4):276-88.
- 12. Allen CG, Sugarman MA, Wennerstrom A. Community health workers: A resource to support antipsychotic medication adherence. The Journal of Behavioral Health Services & Research. 2017 Apr;44:341-6.
- 13. Ballard C, Hanney ML. Long-Term Antipsychotics Increase Mortality Risk in AD Patients.
- Ruiz MJ, Puente BF, Olivares OP, Revuelta MG, Rodríguez RL, Blanco LS, de Santayana Jenaro GP, Herrera MP, Van Son JM. Effect in antipsychotic-induced hyperprolactinemia after switching to long-acting injectable aripiprazole: A 1-year study. European Psychiatry. 2017 Apr;41(S1):s815-6.
- 15. Watson-Wolfe K, Galik E, Klinedinst J, Brandt N. Application of the antipsychotic use in dementia assessment audit tool to facilitate appropriate antipsychotic use in long term care residents with dementia. Geriatric Nursing. 2014 Jan 1;35(1):71-6.
- 16. Wong J, Lan W, Ong LM, Tong L. Non-hormonal systemic medications and dry eye. The ocular surface. 2011 Oct 1;9(4):212-26.
- 17. Haley J. The effect of long- term outcome studies on the therapy of schizophrenia. Journal of Marital and Family Therapy. 1989 Apr;15(2):127-32.
- 18. von Maffei C, Görges F, Kissling W, Schreiber W, Rummel-Kluge C. Using films as a psychoeducation tool for patients with schizophrenia: a pilot study using a quasi-experimental prepost design. BMC psychiatry. 2015 Dec;15:1-7.
- 19. Taylor GM, Taylor AE, Thomas KH, Jones T, Martin RM, Munafo MR, Windmeijer F, Davies NM. The effectiveness of varenicline versus nicotine replacement therapy on long-term smoking cessation in primary care: a prospective cohort study of electronic medical records. International journal of epidemiology. 2017 Dec 1;46(6):1948-57.