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RESEARCH ARTICLE

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Dry Eyes Illness in Psychiatric Patients Placed on Antipsychotic Medications

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ABSTRACT

Introduction: Psychosis is used to describe conditions that affect the mind where there has been loss of contact with reality. Most psychotic disorders are treated with a combination of medications and psychotherapy. A significant ocular side effect of anti-psychotic drugs is dry eyes which often do not get adequate attention thus leading to great discomfort to the patient.

Methodology: The study was a hospital-based, case-control prospective study where patients diagnosed with a psychotic disorders within the age groups of 18 to 70 years and who have been on anti-psychotic treatment for at least one year were examined by a consultant ophthalmologist. Healthy adults were enrolled from the Ophthalmology outpatient clinic as the control for the study.

Result: The case group comprised 53(44.9%) males and 65(55.1%) females. The age group with the highest representation amongst the cases- 29.7% was the 29-38-year-olds. On the medication history, 65(55.1%) started taking antipsychotic drugs within 1-5 years. 65.3% of the respondents were on antipsychotic monotherapy-commonly Olanzapine tablets.

Schirmer's test was normal in most of the participants in both cases 50.8% and control 53.4% but those that have been on medication for 5 years or less demonstrated the highest occurrence of severe dry eyes with a prevalence rate of 23.1% while those on medication for over 10 years showed a higher prevalence of mild dry eyes accounting for 20.8% of the cases.

Tear film Break-up Time (TBUT) showed Dry eyes in 50.8% of cases. A significant proportion (56.9%) of those who had been on medication for 1-5 years were found to be exhibiting dry eyes.

Conclusion: An association was observed between Dry eye disease and antipsychotic medication as early as within 1-5 years of using the medication. Ophthalmic assessment should be incorporated early in the course of treatment.

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Introduction

Psychiatric disorders are behavioural, emotional, or cognitive dysfunctions that are not readily controlled by the individual and are related to clinically significant distress or impairment in one or more areas including social, occupational, and interpersonal functioning [1]. Psychotic disorder is said to affect more than 23 million people worldwide [2]. In a study done in Nigeria, a lifetime prevalence of 2.1% was found with more males affected than females [3]. Psychotic disorders pose a burden to the patient, caregiver, and the nation at large as they are not able to undertake their usual responsibilities relating to family, work, school, or social activities and in some cases may face stigmatization or discrimination.

Most psychotic disorders are treated with a combination of medications and psychotherapy. The medications are first-generation antipsychotic drugs that work by inhibiting dopaminergic neurotransmission, they also have noradrenergic, cholinergic, and histaminergic blocking actions. The second-generation antipsychotics work by blocking D2 dopamine receptors as well as serotonin receptor antagonist action [4]. Some of the antipsychotics are glutamate receptor antagonists and some improve with nicotina alpha 7 cholinergic receptor

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(CHNAR 7) agonist [5]. The adverse side effects of these drugs include sedation, hypotension, weight gain, constipation, dry mouth, and blurred vision [6].

A significant ocular side effect of anti-psychotic drugs is dry eyes which often do not get adequate attention thus leading to great discomfort to the patient. The possible mechanism is due to the anti-cholinergic action of these drugs as they block the muscarinic receptors over the lacrimal gland leading to decreased tear secretion and unstable tear aqueous layer [7]. Schizophrenic patients on neuroleptics showed a decreased blink rate which may be another cause of dry eyes in these patients [8].

Dry eye is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles [9]. The disease is a common ocular condition that significantly reduces quality of life and it affects 6-34% of the global adult population [10]. Dry eyes are caused by a variety of causes that disrupt the healthy tear film either as a result of inadequate production of tears or due to excessive evaporation of tears.

The parasympathetic branch of the autonomic nervous system controls the lacrimal gland through the neurotransmitter acetylcholine through both the nicotinic and muscarinic receptors [11]. The mechanism by which antipsychotic medications cause dry eye is by blocking the muscarinic and nicotinic receptors and the muscarinic-3 receptor in the conjunctiva and lacrimal gland leading to decreased mucous and aqueous secretion [7]. Though the dry eyes is rarely clinically significant [12], but can have adverse effects on already burdened individuals as it may cause psychological stress, symptoms of depression, and reduced quality of life as seen in a study done on Korean women [13].

In one hospital-based cross-section study that was conducted in India, 50 patients diagnosed with schizophrenia and on anti-psychotic medications were examined for dry eyes. About one-third of the 50 patients had dry eye diseases and 50% of those with dry eye disease were on treatment with anti-psychotic agents for more than 10 years [14]. In another hospital-based study, 200 eyes of 100 patients on chronic anti-psychotic therapy attending the psychiatric OPD were examined and 32 of the 100 had dry eye disease. Patients on typical antipsychotics and multidrug regimes showed more prevalence of dry eyes [15]. The study also concluded that the risk of dry eye disease in patients on antipsychotic medications is dose-related if the patient is on monotherapy or polytherapy.

Despite the seriousness of the association of dry eye disease with neuroleptic medications, studies on such topics after electronic and manual searches were found to be scanty in studies in Africa and other developing countries. For this reason, it is, necessary to investigate such associations in the Nigerian context. This study was, therefore, designed to investigate if the antipsychotic medication prescribed at the psychiatric outpatients' clinic of the Lagos State University Teaching Hospital, Ikeja, Lagos, caused dry eyes and if found to be significantly high and also to recommend routine eye checks in patients on antipsychotic medications. The other objectives of the study were to find out significant associations between antipsychotics and dry eyes, and whether dry eyes were caused by mono-pharmacy or poly-pharmacy.

Methodology

The study was a hospital-based, case-control prospective study conducted at the Lagos State University Teaching Hospital (LASUTH) in the Department of Behavioural Medicine Outpatients' Clinic and Ophthalmology Clinic between January 2022 and June 2023. All patients diagnosed with a psychotic disorder within the age groups of 18 to 70 years and who have been on anti-psychotic treatment for at least one year were examined by a consultant ophthalmologist. Healthy adults were enrolled from the Ophthalmology outpatient clinic as the control for the study. All the recruited patients had ophthalmic examination of both anterior and posterior segments including a visual acuity check with the Snellen's chart. Schirmer's test 1(without anaesthesia) was done to measure both basic and reflex tears and Tear Break-up time (TBUT) was done and the average time taken [16]. Central Corneal Thickness (CCT) was measured using the ultrasound pachymeter.

Ethical approval to conduct the study was obtained from the Health Research Ethics Committee (HREC) of Lagos State University Teaching Hospital (LASUTH). Permission was also taken from all the participants willing to participate in the study.

Data Collection and Analysis

Demographic data was derived from the questionnaire. Statistical analysis was done using Statistical Package for Scientific Solutions (SPSS Software 25). Quantitative data analyses with students' T-test, and Chi-square test for comparison of the group parameters, and correlation analysis was done. The influence of duration on anti-psychotic medications, mono-therapy, or multi-therapy on Schirmer's test, and TBUT was investigated by multivariate regression. The determined results were expressed as means ± Standard deviation (SD) and percentages with a 95% confidence interval; P-value <0.05.

Results

The study included 236 participants evenly divided into 2 study groups of 118 each: the case and control groups. The case group comprised patients on antipsychotic medications for at least 1 year. The case group comprised of 53(44.9%) males and 65(55.1%) females with an M:F ratio of 1:1.2. similarly, the control group had a higher proportion of females 79 (66.8%) Figure 1.

The participants were categorized into different age groups. The age group with the highest representation amongst the cases- 29.7% was the 29-38-year-olds and in the control was 22.0% in the 56-68-year-olds Figure 2.

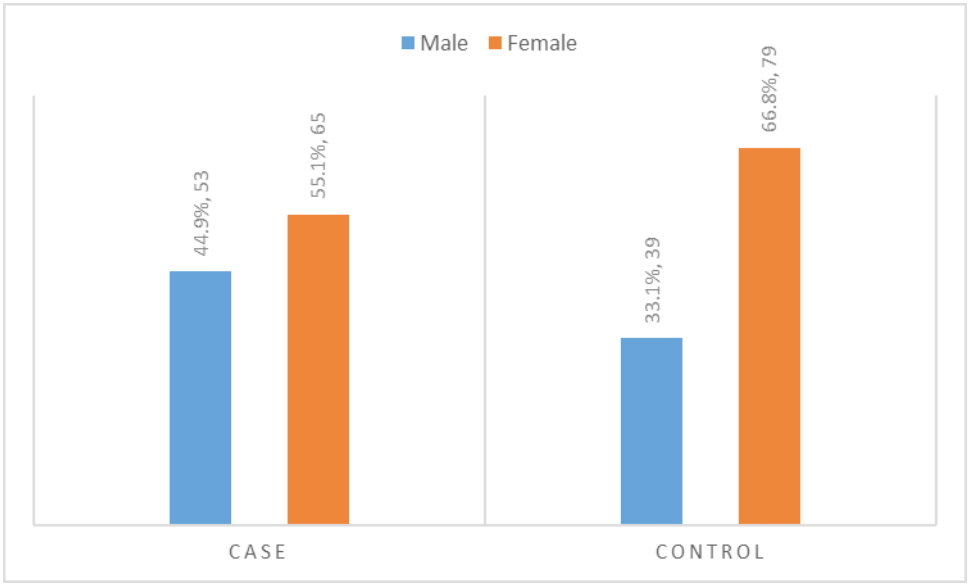

Figure 1: Gender distribution.

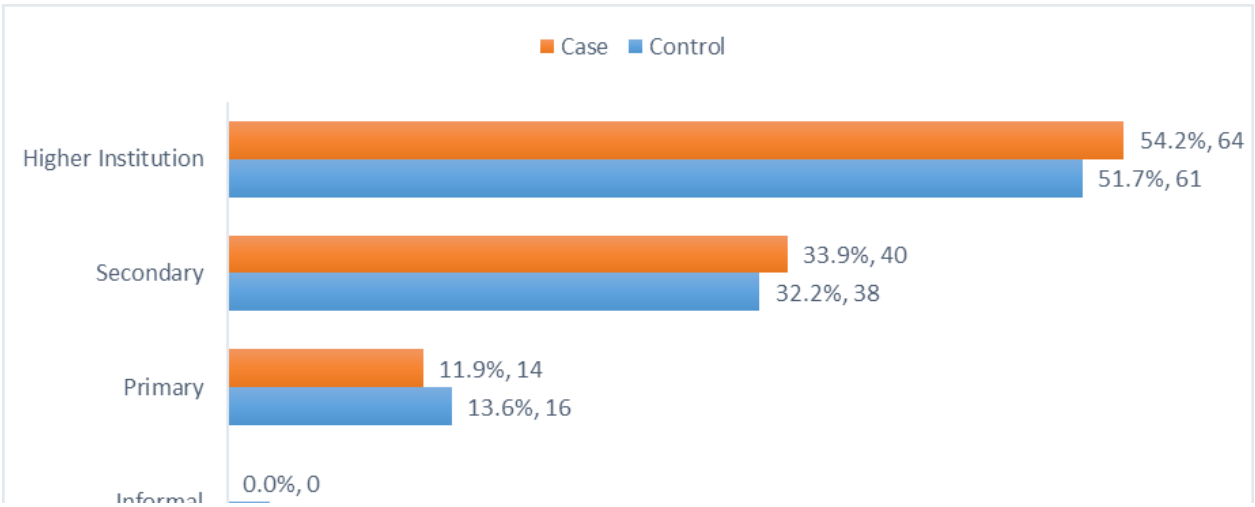

Figure 2: Age distribution.

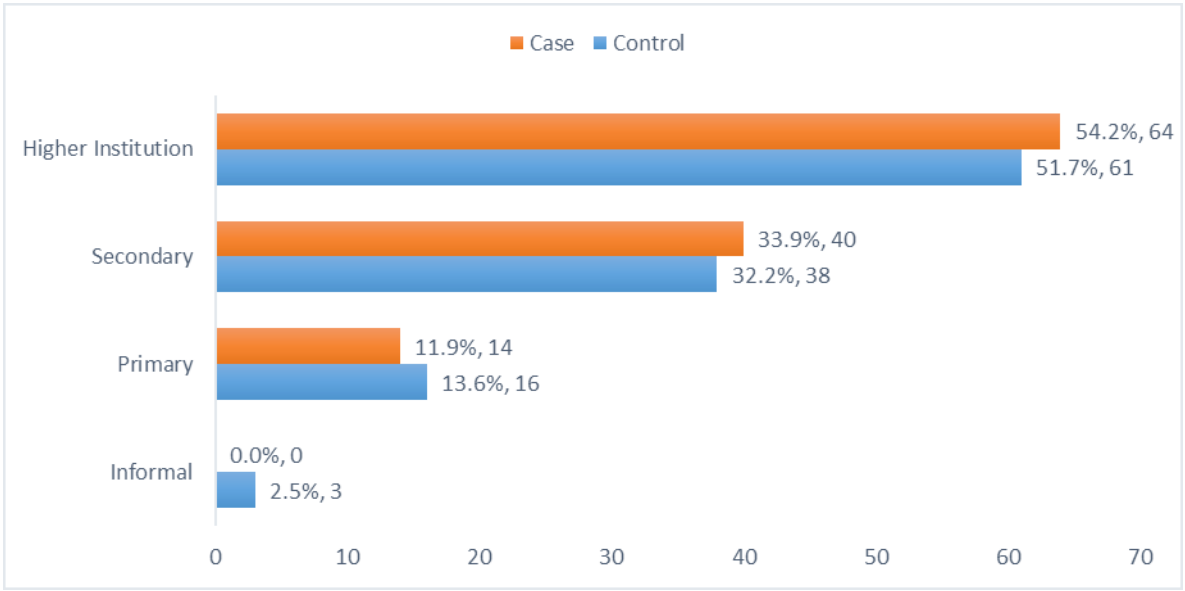

Figure 3: Educational level.

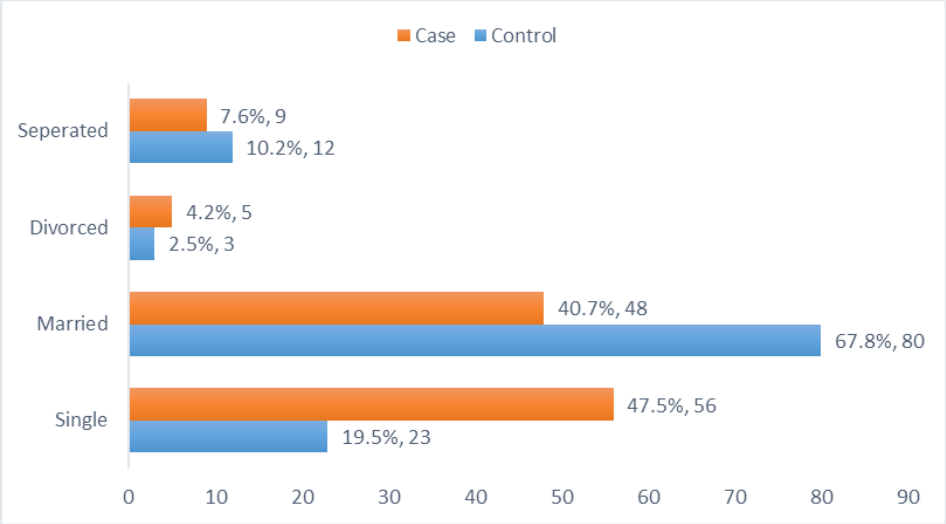

Figure 4: Marital status.

The educational status of the respondents showed a significant proportion of the case group 64(54.2%) and the control group 61(51.7%) have obtained higher institution education figure 3.

Most of the respondents that are cases were within the singlehood category 47.5% while significant number of the control cases were married 67.8% Figure 4.

The medication history of the case group comprised of individuals using various antipsychotic medications. A higher percentage of respondents. 65(55.1%) started taking antipsychotic drugs within 1-5 years Table 1. The respondents were also evaluated based on the number of medications used, categorized as monotherapy, two-drug combination, and multi-drug combination. The result indicated that 65.3% of the respondents were on antipsychotic monotherapy-commonly Olanzapine tablets (41.5%) Table 1.

Table 1: History and Medication Details of the Case Group Using Various Antipsychotic Medications.

Variable	Frequency (n=118)	Percentage (%)
Years of Medication		
1 - 5	65	55.1
5 - 10	29	24.6
> 10	24	20.3
Mono drugs	**77**	**65.3**
Olanzepine tab	49	41.5
Clozapine tab	2	1.7
Chloropromazine tab	7	5.9
Risperidone tab	11	9.5
Aripriprazole tab	3	2.5
Haloperidol tab	2	1.7
IM Fluephenazinedecanoate	3	2.5
Two drug Combination	**35**	**29.7**
IM fluphenazine &Olazepine	15	12.7
IM fluphanazine & Carbamazepine	6	5.1
Olanzepine & Soduimvalporoate	2	1.7
IM fluenphenazine & Risperidore	12	10.2
Multi drug combination	**6**	**5.0**
Olanzipine tab, Amitryptyline tab and IM fluphenazine	5	4.2
IM fluphenazine, olazopineand cholorpromazine	1	0.8

A high proportion of the control 73(61.9%) had normal visual acuity within 6/4-6/9. Cases that had been on medication within 1-5 years 46(70.8%) had visual acuity within the same range Table 2.

Schirmer's test which denotes the quantity of tears was normal in most of the participants in both cases 50.8% and control 53.4% but those that have been on medication for 5 years or less demonstrated the highest occurrence of severe dry eyes with a prevalence rate of 23.1% while those on medication for over 10 years showed a higher prevalence of mild dry eyes accounting for 20.8% of the cases. Tear film Break-up Time (TBUT) that indicates the stability of tears showed Dry eyes in 50.8% of cases and 47.5% of the control. A significant proportion (56.9%) of those who had been on medication for 1-5 years were found to be exhibiting dry eyes Table 2.

Table 2: Association of Medication Duration with Dry Eye Characteristics.

Variable	Duration of Medication (yrs)				X^2 (P-value)
	No Medication (%)	1 – 5 (%)	5 – 10 (%)	> 10 (%)	
Schirmer test (mm)					
Severe dry eyes (0 – 5)	29 (24.6)	15 (23.1)	5 (17.2)	4 (16.7)	9.034 (0.434)
Moderate dry eyes (5 – 10)	11 (9.3)	10 (15.4)	6 (20.7)	5 (20.8)	
Mild dry eyes (10 – 15)	15 (12.7)	4 (6.2)	4 (13.8)	5 (20.8)	
Normal tear function (> 15)	63 (53.4)	36 (55.4)	14 (48.3)	10 (41.7)	
TBUT test (S)					
Dry eyes (< 10)	56 (47.5)	37 (56.9)	12 (41.4)	11 (45.8)	2.513 (0.473)
Normal eyes (>10)	62 (52.5)	28 (43.1)	17 (58.6)	13 (54.2)	
Visual Acuity					
Normal (6/4 – 6/9)	73 (61.9)	46 (70.8)	18 (62.1)	13 (54.2)	13.09 (0.158)
Mild (6/12 – 6/18)	30 (25.4)	6 (9.2)	7 (24.1)	4 (16.7)	
Moderate (6/18 – 6/60)	13 (11.0)	11 (16.9)	4 (13.8)	5 (20.8)	
Severe (6/60 – 3/60)	2 (1.7)	2 (3.1)	0 (0.0)	2 (8.3)	

Table 3: Association of Medication Combination with dry eyes characteristics.

Variable	Type of Medication				X^2 (P-value)
	No Medication (%)	Mono drug (%)	Two drug Combination (%)	Multi-drug combination (%)	
Schirmer test					
Severe dry eyes	29 (24.6%)	15 (19.5%)	7 (20.0%)	2 (33.3%)	
Moderate dry eyes	11 (9.3%)	14 (18.2%)	6 (17.1%)	1 (16.7%)	5.824
Mild dry eyes	15 (12.7%)	9 (11.7%)	3 (8.6%)	1 (16.7%)	(0.824)
Normal tear function	63 (53.4%)	39 (50.6%)	19 (54.3%)	2 (33.3%)	
TBUT test					
Dry eyes	56 (47.5%)	39 (50.6%)	20 (57.1%)	1 (16.7%)	3.632
Normal eyes	62 (52.5%)	38 (49.4%)	15 (42.9%)	5 (83.3%)	(0.304)
Visual Acuity					
Normal	73 (61.9%)	50 (64.9%)	26 (74.3%)	1 (16.7%)	
Mild	30 (25.4%)	13 (16.9%)	1 (2.9%)	3 (50.0%)	21.16
Moderate	13 (11.0%)	13 (16.9%)	6 (17.1%)	1 (16.7%)	(0.012)*
Severe	2 (1.7%)	1 (1.3%)	2 (5.7%)	1 (16.7%)	

The association between the various eye tests and different therapeutic groups, i.e., mono-drug, two-drug combination, and multi-drug combination showed 50.0% of those on multi-drug combination experienced mild visual impairment. 18.2% of those on monotherapy have moderate dry eyes while 33.3% of participants on multi-drug therapy were diagnosed with severe dry eyes Table 3.

Discussion

This study investigated if the antipsychotic medications prescribed for patients experiencing mental disorders with psychotic features caused dry eyes and if found to be significantly high and also to recommend routine eye checks in patients on antipsychotic medications. The study also determined significant associations between antipsychotics and dry eyes, and whether dry eyes were caused by mono-pharmacy or poly-pharmacy. In that light, two hundred and thirty-six (236) participants were studied.

Both case and control groups had a higher proportion of females, 55.1 % and 66.8% respectively. This is comparable to studies done on US adults [17] and on the urban population in Ilam province in Iran [18] where the majority of the participants seen with psychosis were females but contrary to studies done in Nigeria [3] and Ethiopia [19] that showed a higher prevalence of males in their studies. The high prevalence of females in this study could be due to the fact that they are more prone to stress which may be attributed to their biological reactions [18]. The age group with the highest representation amongst the cases was the 29-38-year-olds. This is comparable with other studies but contradictory with others where older age groups were more seen with psychotic illnesses [17,18,20-22].

The educational status of the respondents in both cases (54.2%) and the control group (51.7%) have obtained higher institution education. Similar findings were observed in other studies whereas some other studies showed lower educational status in the respondents [17-19,21]. Though some studies have demonstrated significantly reduced risk with increasing educational attainment [23]. The increase in the respondents with higher educational attainment seen in this study could be a result of increased awareness about mental health and the need to seek medical help instead of attributing the illness to a "spiritual attack".

A significant proportion of participants in the case group (47.5%) were singles. This is similar to a study done in Finland where singlehood was associated with poorer mental well-being but contrary to a study done in Iran that showed prevalence of psychiatric disorders to be higher in widows, married and divorced individuals than in singles [24,25].

A higher percentage of respondents (53.1%) have been on antipsychotic medications within 1-5 years and 65.3% of these were on mono-drug mainly Olanzapine tablets which is a second-generation antipsychotic medication. A study done in France showed majority of the participants were on mono-drugs and atypical antipsychotic was more common [26]. This is contrary to other studies where the majority of the participants were on a combination therapy [20].

Visual acuity was within normal range in 65.3% of participants on antipsychotic medications and those on medications for over 10 years showed a predominant presence of moderate visual impairment-20.8% and severe visual impairment-8.3% suggesting that a longer duration of medication use may be associated with an increased likelihood of visual impairment. This may be as a result of ocular complications such as cataracts which is a common side effect with high doses of typical antipsychotics over a long period or due to optic nerve atrophy secondary to Glaucoma or Corneal endothelial deposits especially in prolonged use of Chlorpromazine [20]. Of the total participants, 49% of those on antipsychotic medications exhibited reduced Schirmer's test with the majority on medication within 5 years or less and on mono-drug therapy. Among the cases, severe dry eye was noticed in 20.3%, moderate in 17.8%, and mild in 11%. This is contrary to a study in India that showed a high prevalence of cases with mild dry eyes and severe dry eyes 16.94% [15].

Tear-film Break-up time (TBUT) showed more than half of the cases –(50.8%) exhibiting dry eye conditions with higher prevalence in those using drugs within 1-5 years and on mono drug therapy. This is similar to the studies done in India where TBUT was found to be abnormal in the cases seen [14,15].

Amongst the side effects of antipsychotic medications are anticholinergic effects that cause constipation, dry mouth, blurred vision, and dry eyes [6]. Through the anticholinergic action,there is blockage of the muscarinic, nicotinic, and muscarine-3 receptors on the conjunctiva and lacrimal gland leading to decreased mucous and aqueous secreation and this can affect tear stability which may consequently affect the ocular surface and vision [27]. Decrease blink rate noticed in a study[8] may be another cause of Dry eyes.

Conclusion

An association was observed between Dry eye disease and antipsychotic medication. Dry eye disease was observed as early as within 1-5 years of using the medications and also in those on mono-drug therapy as well as polytherapy. We hereby suggest that psychiatrists must be aware of this potential medication-induced side effect and incorporate ophthalmic assessment early in the course of treatment in the form of a pretreatment ocular assessment and annual ocular examination for early detection of any drug-related abnormalities.

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