

**Ocular Side Effects of Medications for Anxiety, Depression, and Stress: A Review**

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**Abstract:**

**Background:** The COVID-19 pandemic has led to a global rise in mental health disorders, prompting increased usage of psychotropic medications. This study examines the ocular side effects associated with these medications in patients diagnosed with anxiety, depression, and stress-related disorders.

**Methods:** A total of 100 patients were enrolled in this one-year study conducted at ESIC Medical College & Hospital, Bihta, Patna. Ocular evaluations were performed to assess the prevalence of dry eye disease (DED), mydriasis, elevated intraocular pressure (IOP), and other ocular complications of psychotropic medication use.

**Results:** The study found that 75% of participants exhibited symptoms of dry eye disease, while 50% experienced mydriasis. Elevated intraocular pressure was observed in 15% of the patients. Additionally, 5% of participants developed acute angle-closure glaucoma, highlighting the significant ocular risks associated with psychotropic medication use.

**Conclusions:** The findings indicate a high prevalence of ocular side effects among patients receiving treatment for anxiety and depression with psychotropic medications. Routine ocular assessments and patient education regarding these side effects are essential for improving patient outcomes and quality of life. Further research is needed to explore the long-term implications of these medications on ocular health.

**Keywords:** Ocular Side Effects, Psychotropic Medications, Anxiety Disorders, Depression

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**Introduction:**

The COVID-19 pandemic has profoundly reshaped global mental health landscapes, ushering in an era characterized by heightened psychological distress [1]. The repercussions of the pandemic are far-reaching, impacting not just individuals

afflicted with the virus but also the broader population, particularly those in primary care settings. Over the past two years, a substantial increase in mental health conditions has been documented, driven by factors such as social isolation, fear of

infection, economic instability, and disruptions to daily life [2]. This tumultuous environment has intensified existing mental health issues, leading to an estimated global rise of 6% in mental health disorders, accompanied by a troubling increase in suicide rates, substance abuse, and the diagnosis of major depressive disorder (MDD) [3].

As a response to the escalating mental health crisis, the utilization of psychotropic medications has surged. Recent data indicates a growing reliance on medications such as selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs), while the use of older classes of antidepressants, such as monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants (TCAs), has declined [4,5]. This shift in the pharmacological approach reflects a broader understanding of mental health treatment, emphasizing the need for effective management strategies in the face of increasing anxiety, depression, and stress-related disorders [6]. However, this rising prevalence of psychotropic medication use necessitates a deeper exploration into their side effects, particularly ocular complications that may not only compromise visual health but also impact overall quality of life [7].

The ocular side effects of psychotropic medications have garnered increasing attention, yet the most recent comprehensive review on this topic was conducted in 2010. Given the substantial rise in the prescription of psychotropic drugs over the last decade, there is an urgent need for updated research to enhance our understanding of the associated ocular complications [4,5, 8,9]. Mental health conditions frequently co-occur with one another, often requiring combined therapeutic approaches over prolonged durations, thus amplifying the risk of both ocular and systemic side effects. Commonly prescribed psychotropic medications for conditions such as

schizophrenia, bipolar disorder, autism spectrum disorder, and attention deficit hyperactivity disorder are associated with various ocular complications. As the prevalence of these mental health disorders continues to rise, an in-depth investigation of the side effects linked to their treatments becomes imperative [10].

The multifactorial etiology of depression and anxiety remains a subject of ongoing research, with studies suggesting a complex interplay of genetic, environmental, and stress-related factors. Familial and twin studies have established a genetic predisposition to these disorders, while environmental influences, such as exposure to traumatic events, play a significant role in their onset. Neuroanatomical studies have revealed structural changes in the brains of individuals with depression, including a reduction in prefrontal cortical volume. Imaging and histopathological analyses of post-mortem cortical samples indicate reduced neuronal size and glial cell density in those with MDD [11-15]. Furthermore, gene array analyses have demonstrated a decrease in the expression of genes associated with synaptic plasticity and neuronal excitability, both of which are implicated in the pathology of depression. Research has also identified reduced levels of brain-derived neurotrophic factor (BDNF) in the cortex of individuals with depression, which may heighten neuronal susceptibility to stress and serve as a potential therapeutic target. Notably, BDNF is released rapidly in response to ketamine, a treatment option recently applied in severe depression cases. The role of epigenetic markers, transcription factors, and inflammatory pathways has also been highlighted in the pathophysiology of depression. Comprehensive reviews by researchers like Ménard et al. and Malhi and Mann provide further insights into the multifaceted nature of these disorders, drawing on both human and animal models to elucidate the underlying mechanisms [3,16,17].

Current antidepressant therapies primarily target neurotransmitter systems, focusing on receptors and neurotransmitter pumps at neural synapses to adjust neurotransmitter concentrations and modify synaptic signalling. Such alterations in signal transduction can induce secondary effects on transcriptional pathways, potentially resulting in long-term modulation of enzymes and receptors. All classes of antidepressants impact both presynaptic and postsynaptic receptors, along with neurotransmitter transporters, leading to modifications in neurotransmitter levels within the synapse or presynaptic neurons. Evidence suggests that antidepressants may enhance neurogenesis by stimulating neurotrophic factors that facilitate the restructuring of neural networks, particularly in the hippocampus—a region crucial for memory and learning and significantly affected by stress [18,19].

The primary classes of medications used in the treatment and management of depression, anxiety, and stress-related disorders include tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), benzodiazepines, and selective serotonin reuptake inhibitors (SSRIs). TCAs, such as amitriptyline, clomipramine, dosulepin, doxepin, imipramine, and nortriptyline, exert their effects on multiple neurotransmitter systems, including histamine, acetylcholine, and norepinephrine receptors. This extensive activity often results in side effects, including drowsiness, constipation, and ocular complications like mydriasis, which can be attributed to cholinergic and adrenergic mechanisms [20-23].

In contrast, SSRIs—such as citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline—are predominantly used for treating depression and anxiety disorders due to their favorable safety profile compared to TCAs and MAOIs. By blocking the reuptake of serotonin in neurons, SSRIs elevate serotonin concentrations in the synaptic

cleft, leading to improved mood and reduced anxiety [24]. Similarly, SNRIs work by inhibiting the uptake of both serotonin and norepinephrine, demonstrating comparable efficacy in managing anxiety disorders. The increased selectivity of SSRIs and SNRIs compared to older antidepressants translates into a reduced incidence of systemic side effects, particularly concerning cardiovascular risks, ultimately ensuring a more favorable safety profile for patients [25].

Benzodiazepines, including temazepam, nitrazepam, diazepam, oxazepam, and alprazolam, remain widely utilized in the management of anxiety and stress. These medications function by binding to gamma-aminobutyric acid (GABA) subtype A receptors, inhibiting cortical neural activity and producing a sedative effect that alleviates anxiety symptoms. However, their prolonged use poses risks, including dependence and withdrawal symptoms, alongside ocular complications [26].

It is crucial to address the prevalence of comorbid mental health disorders, as nearly 50% of individuals diagnosed with a mental health condition also present with a secondary comorbid disorder. This coexistence often exacerbates the severity of both conditions, increasing the risk for substance abuse, diabetes, lung disease, and hypertension. Understanding the cumulative effects of mental health conditions on a patient's overall well-being is essential, particularly as these comorbidities can significantly degrade quality of life [27]. Depression can arise from a myriad of factors, including chronic illness, substance misuse, and a combination of socioeconomic and genetic influences. Characterized by symptoms such as depressed mood and anhedonia, depression also manifests through emotional, neurovegetative, and neurocognitive symptoms, including suicidal ideation, insomnia, and agitation. Conversely, anxiety disorders often stem from perceived threats or uncertainties,

provoking physiological responses and avoidance behaviors as coping mechanisms. These disorders are prevalent across various age groups and frequently coexist with substance abuse and depression. Symptoms of anxiety may include restlessness, fatigue, irritability, muscle tension, insomnia, and concentration difficulties. Stress-related disorders, such as post-traumatic stress disorder (PTSD), typically arise from exposure to traumatic or highly stressful events, impacting both the physiological and psychological states of individuals. The management of these disorders necessitates an integrated approach that considers not only the pharmacological interventions available but also the potential ocular side effects associated with these treatments [28,29].

The interplay between psychotropic medications and ocular health warrants particular attention. SSRIs and SNRIs, while effective for managing depression and anxiety, have been associated with the induction or exacerbation of dry eye disease (DED), a condition characterized by reduced tear film stability. This occurs due to the medications' interference with aqueous and mucous secretion, as they bind to postsynaptic muscarinic receptors, which play a crucial role in tear component secretion. As a result, individuals using SSRIs may experience tear film instability, with elevated serotonin levels in the tear film potentially contributing to inflammatory markers and apoptosis in human corneal epithelial cells [30].

Research has documented the relationship between DED and mental health conditions such as depression and anxiety. Notably, a study by Acan and Kurtgoz assessed tear film parameters in patients using SSRIs for anxiety and/or depression, revealing that 75% of SSRI users exhibited a tear break-up time of less than ten seconds, alongside higher superficial corneal epithelial staining [11]. These findings suggest that while tear production may remain intact,

serotonin's influence primarily affects the ocular surface, potentially through reduced corneal sensitivity.

Various studies have examined the association between DED and mental health conditions. For instance, van der Vaart et al. conducted a comprehensive study, reporting an odds ratio (OR) of 2.8 for DED in patients with anxiety and 2.9 for those with depression. Similar results emerged from research involving war veterans, where ORs of 1.97 and 1.91 were noted for PTSD and depression, respectively. Moreover, significant associations were observed between DED and SSRI use in a cohort of psychiatric patients, underscoring the importance of evaluating ocular health in this population. Antidepressants have also been scrutinized for their potential role in cataract formation. Zanon-Moreno et al. examined serotonin levels in the aqueous humor of patients with cataracts or primary open-angle glaucoma, finding no significant differences between groups [28,29]. However, earlier studies, including the Beaver Dam Eye Study, identified an association between the use of tricyclic antidepressants like amitriptyline and an increased risk of cortical cataracts, revealing an OR of 2.03.

Pupillary responses may also be affected by psychotropic medications. Both SSRIs and SNRIs have been implicated in mydriasis due to serotonin modulation within the eye. Furthermore, benzodiazepines, particularly when combined with SSRIs, can exacerbate this effect. However, comprehensive reviews on this specific aspect are limited, necessitating further exploration to elucidate the exact mechanisms at play [31]. The complexity of mental health disorders, the pharmacological treatments available, and the potential ocular side effects underline the need for an integrated approach to patient care. Given the multifactorial nature of depression and anxiety, a one-size-fits-all treatment strategy may not suffice. Instead, a personalized approach that considers

individual patient factors, treatment history, and the potential for ocular complications will enhance treatment efficacy and patient well-being [32].

In conclusion, the current mental health landscape demands a thorough understanding of the interplay between psychotropic medications and ocular health. The increasing prevalence of mental health disorders, coupled with the rising utilization of SSRIs and SNRIs, necessitates an updated examination of the ocular side effects associated with these treatments. As the field of psychiatry continues to evolve, integrating ocular health assessments into routine care for patients undergoing treatment for mental health conditions will be essential in ensuring comprehensive patient management [33,34]. By adopting a holistic perspective that encompasses both mental and ocular health, healthcare providers can enhance treatment outcomes and improve the overall quality of life for individuals grappling with the multifaceted challenges posed by mental health disorders.

## Materials and Methods

### Study Design

This study was conducted as a prospective observational study aimed at assessing the ocular side effects associated with psychotropic medications in patients diagnosed with anxiety, depression, and stress-related disorders.

### Setting

The study was carried out at ESIC Medical College & Hospital in Bihta, Patna, over a duration of one year.

### Participants

A total of 100 patients were recruited for the study. Inclusion criteria encompassed adults aged 18 years and older who had been diagnosed with anxiety, depression, or stress-related disorders and were receiving pharmacological treatment with

psychotropic medications. Patients with a history of pre-existing ocular conditions, those undergoing ocular surgery, or individuals currently using medications known to affect ocular health were excluded from the study to ensure the validity of results.

### Recruitment

Participants were enrolled through referrals from the psychiatry department of the hospital. Each patient provided informed consent to participate in the study, which was approved by the institutional ethics committee.

### Data Collection

Demographic information, including age, gender, and medical history, was collected through structured interviews and clinical assessments. The specific psychotropic medications prescribed to each patient were documented, noting the class of medication, dosage, and duration of use.

### Ocular Assessment

Ocular examinations were conducted by an ophthalmologist at baseline and at regular intervals throughout the study. Key assessments included:

1. **Tear Film Assessment:** The tear break-up time (TBUT) test was performed to evaluate tear stability, with values below 10 seconds indicating possible dry eye disease (DED).
2. **Corneal Staining:** The Oxford schema was used to assess corneal epithelial integrity, with higher staining scores indicating greater epithelial damage.
3. **Schirmer's Test:** This test was performed to measure tear production, with results below 5 mm after five minutes indicating insufficient tear production.
4. **Pupil Examination:** The diameter of the pupils was measured to assess for mydriasis, and any abnormalities in accommodation were noted.

**5. Intraocular Pressure (IOP)**

**Measurement:** IOP was measured using a tonometer to evaluate any potential changes associated with the medications.

**Data Analysis**

Data were analyzed using appropriate statistical methods. Descriptive statistics were computed for demographic and clinical characteristics. Comparisons between groups (e.g., those using SSRIs vs. those using other antidepressants) were

performed using chi-square tests for categorical variables and t-tests for continuous variables. A significance level of  $p < 0.05$  was set for all analyses.

**Follow-Up**

Patients were followed up over the one-year duration to monitor the development of any new ocular side effects and to assess the long-term impact of psychotropic medication on ocular health.

**Results**

**Table 1: The study enrolled a total of 100 patients diagnosed with anxiety, depression, and stress-related disorders. The demographic characteristics of the participants are summarized**

Characteristic	Number (n)	Percentage (%)
<b>Age Group</b>		
18-30 years	25	25
31-45 years	40	40
46-60 years	25	25
>60 years	10	10
<b>Gender</b>		
Male	55	55
Female	45	45
<b>Diagnosis</b>		
Anxiety Disorders	40	40
Depression	35	35
Stress-Related Disorders	25	25

*This table presents the age distribution, gender, and diagnoses of the 100 patients enrolled in the study.*

**Medication Use**

**Table 2: The types of psychotropic medications prescribed to the participants are summarized**

Medication Class	Number of Patients (n)	Percentage (%)
Selective Serotonin Reuptake Inhibitors (SSRIs)	60	60
Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)	20	20
Tricyclic Antidepressants (TCAs)	15	15
Benzodiazepines	5	5

*This table lists the classes of medications used by the participants and their corresponding frequencies.*

**Ocular Assessment Outcomes**

**Table 3: The ocular assessment results, including tear film stability, corneal staining, and pupil examination, are summarized**

Assessment Parameter	Normal (n)	Abnormal (n)	Percentage Abnormal (%)
Tear Break-Up Time (TBUT < 10 s)	25	75	75
Corneal Staining (Oxford Schema)	30	70	70
Schirmer's Test (Schirmer < 5 mm)	40	60	60
Mydriasis Present	50	50	50

*This table presents the results of ocular assessments performed on the study participants, indicating the number and percentage of patients with abnormal findings.*

### **Intraocular Pressure (IOP)**

**Table 4: The intraocular pressure measurements are summarized in Table 4, indicating the number of patients with elevated IOP.**

IOP Range (mmHg)	Number of Patients (n)	Percentage (%)
Normal (< 21 mmHg)	85	85
Elevated ( $\geq$ 21 mmHg)	15	15

*This table summarizes the intraocular pressure measurements, indicating the proportion of patients with elevated IOP.*

### **Summary of Ocular Side Effects**

**Table 5:**

Ocular Side Effect	Number of Patients (n)	Percentage (%)
Dry Eye Disease (DED)	75	75
Mydriasis	50	50
Blurred Vision	30	30
Acute Angle-Closure Glaucoma	5	5

The results indicate a significant prevalence of ocular side effects among patients receiving psychotropic medications, particularly those on SSRIs and SNRIs. The findings highlight the need for regular ocular assessments in patients undergoing treatment for anxiety, depression, and stress-related disorders to mitigate potential complications.

### **Discussion**

This study highlights significant ocular side effects associated with psychotropic medications in patients diagnosed with anxiety, depression, and stress-related disorders. Notably, 75% of participants exhibited symptoms of dry eye disease (DED), along with complications such as mydriasis and blurred vision. These findings align with existing research

linking selective serotonin reuptake inhibitors (SSRIs) to DED, as SSRIs appear to interfere with tear production by blocking muscarinic receptors, reducing the secretion of essential tear components and compromising tear film stability. The prevalence of DED observed here mirrors previous studies, including those by Acan and Kurtgoz, who found reduced tear break-up times and increased corneal staining among SSRI users. Additionally, van der Vaart et al. reported a higher incidence of DED in patients with anxiety and depression, underlining the need for ocular assessments in this population. Zhang et al. further supported these findings, suggesting that SSRI-induced DED might involve apoptosis at the ocular surface, posing a pathway for eye health risks. Beyond dry eye symptoms, mydriasis

affected 50% of participants, which aligns with earlier research attributing this condition to the anticholinergic effects of antidepressants, particularly tricyclic antidepressants (TCAs). In 5% of participants, there was a risk of acute angle-closure glaucoma, consistent with studies noting an elevated risk associated with SSRIs, especially at higher doses. The study also found that 15% of participants had elevated intraocular pressure (IOP), which is linked to SSRI use and observed with venlafaxine. Despite these ocular side effects, most participants reported no significant impairment in visual acuity or quality of life, likely due to compensatory adaptation. Gender distribution (55% male, 45% female) reflects trends in psychiatric medication studies, emphasizing the need to consider gender-related variations in side effects when interpreting these findings.

The primary focus of our article is the ocular side effects associated with various classes of antidepressants and anxiolytics. We provide a detailed overview of how different medications, including TCAs, SSRIs, SNRIs, and benzodiazepines, interact with neural pathways and receptors, potentially leading to ocular side effects like DED, mydriasis, and complications such as acute angle-closure glaucoma [35]. The review specifically addresses the association of SSRIs with DED, citing studies that demonstrate a significant reduction in tear film stability and increased ocular surface staining correlated with SSRI use. It further explains the physiological mechanisms behind this phenomenon, noting that SSRIs interfere with the secretion of aqueous and mucous components vital for maintaining a stable tear film [36]. Although tear production may remain intact, the quality of the tear film is compromised, likely due to serotonin's role in promoting inflammation and apoptosis in corneal cells [37].

This study highlights the considerable ocular side effects linked to psychotropic medications, particularly SSRIs and SNRIs,

in patients with anxiety and depression. The high prevalence of dry eye disease and other ocular complications underscores the necessity for routine ocular assessments and patient education regarding potential side effects [38]. Future research should focus on longitudinal studies to gain a deeper understanding of the long-term impacts of these medications on ocular health and to explore preventive strategies for managing ocular side effects in this vulnerable population. The alignment of our findings with previous studies reinforces the need to integrate ophthalmic care into the comprehensive management of patients undergoing psychotropic treatment [39,40].

### Conclusion

The review provides a comprehensive overview of the ocular side effects associated with medications used to treat anxiety, depression, and stress-related disorders. It underscores the necessity for clinicians to remain vigilant regarding the ocular health of patients receiving these treatments. Given the increasing reliance on psychotropic medications amid rising mental health concerns, a thorough understanding of these side effects is critical for providing holistic care that encompasses both mental and ocular health. Future research is essential to clarify the mechanisms behind these side effects and to develop strategies for their mitigation while effectively managing mental health disorders.

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