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Safety of Psychiatric Medications in Glaucoma. A Review of Current Medical Knowledge

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Abstract

Glaucoma is a leading cause of irreversible blindness, and psychiatric patients are at increased risk of ocular adverse effects from pharmacotherapy; this review summarizes the safety of psychiatric medications with respect to glaucoma type, including open-angle and angle-closure forms. A search of PubMed, Scopus, and Web of Science covering studies from 2020 to 2026, including observational studies, meta-analyses, and systematic reviews, assessed associations between psychiatric drugs, glaucoma risk, and intraocular pressure. Selective serotonin reuptake inhibitors demonstrate a favorable profile in open-angle glaucoma, with modest intraocular pressure reduction and decreased risk, whereas benzodiazepines are associated with increased glaucoma risk, particularly in angle-closure glaucoma. Topiramate shows a strong association with acute angle-closure glaucoma, while tricyclic antidepressants, despite anticholinergic effects, do not consistently increase glaucoma risk. Antipsychotics, especially olanzapine, may precipitate acute angle closure, whereas lithium appears neutral or potentially protective. Overall, psychiatric medications exhibit heterogeneous ophthalmic safety, and particular caution is warranted with topiramate and benzodiazepines in patients with narrow angles or angle-closure glaucoma, alongside regular ophthalmologic monitoring.

Keywords: glaucoma; psychiatric medications; intraocular pressure; angle-closure glaucoma; antidepressants; benzodiazepines

1. Introduction

Glaucoma is a heterogeneous group of optic nerve disorders characterized by progressive neuropathy and irreversible visual field loss, constituting a leading cause of permanent blindness worldwide. It is estimated that by 2040 the number of people living with glaucoma worldwide will exceed 111.8 million. Glaucoma is essentially divided into two main types:

open-angle glaucoma (OAG), which is by far the more common form (approximately 90% of all cases), and angle-closure glaucoma (ACG), which predominates in Asian patients. In OAG, patency of the iridocorneal angle is preserved, but outflow of aqueous humor through the trabecular meshwork is impaired, whereas in ACG there is mechanical blockage of the anterior chamber angle, preventing the outflow of aqueous humor. [1][2][3]

Patients diagnosed with a mental disorder are characterized by significantly greater overall morbidity and are more commonly exposed to ocularly toxic effects of pharmacotherapy. According to epidemiological data, patients with glaucoma show significantly higher rates of depression (RR = 5.92; 95% CI: 3.29–10.66) and anxiety (RR = 2.99; 95% CI: 1.93–4.64) compared with the general population. Data from a large cross-sectional study showed that among 1,492 patients with glaucoma, 13.2% had diagnosed anxiety disorders and 12.2% had a major depressive episode. In a screening study using standardized psychometric tools (PHQ-9 and GAD-7), conducted in 249 patients with glaucoma, 34.9% met criteria for depression and as many as 42.2% for anxiety disorders, whereas formal diagnoses of these disorders had been made in only 11.2% and 1.2% of them, respectively. These data indicate a common and thus far underestimated coexistence of mental disorders and glaucoma, generating a need for frequent use of psychiatric medications in patients at risk of or already affected by this ophthalmic condition.[4][5][6]

Psychotropic drugs may influence the risk of glaucoma through several mechanisms: (1) pupillary dilation induced by an anticholinergic or sympathomimetic effect, leading to angle closure in eyes with anatomical predisposition; (2) ciliary body effusion resulting in displacement of the lens–iris diaphragm; (3) modulation of aqueous humor secretion and dynamics through serotonergic receptors. Knowledge of the risk profiles of individual psychiatric drugs therefore has direct clinical implications for both psychiatrists and ophthalmologists. [2][7]

The aim of the present study is to systematize current knowledge—based on literature from 2020–2026—regarding the safety of the use of particular groups of psychiatric medications in patients with glaucoma or with risk factors for its development. The findings are discussed separately for open-angle and angle-closure glaucoma, and the conclusions were formulated with reference to specific active substances.

2. Methodology

2.1. Review design and search strategy

This study is a narrative literature review. The PubMed/MEDLINE, Scopus, and Web of Science databases were searched. The following search terms were used: *glaucoma*, *intraocular pressure*, *psychotropic drugs*, *antidepressants*, *antipsychotics*, *benzodiazepines*, *mood stabilizers*, *topiramate*, *selective serotonin reuptake inhibitors (SSRI)*, *tricyclic antidepressants*, *angle-closure glaucoma*, *open-angle glaucoma*, and combinations of the above terms using the Boolean operators AND/OR. The search was aimed at identifying publications from January 1, 2020 to May 13, 2026, with particular emphasis on studies published in 2020–2025.

2.2. Inclusion and exclusion criteria

The review included: (1) observational studies (cohort, case-control, case-crossover) and randomized clinical trials assessing the relationship between psychiatric medications and glaucoma or IOP; (2) systematic reviews and meta-analyses addressing this issue; (3) articles published after January 1, 2020; (4) publications in English. Animal or in vitro studies, purely narrative works without quantitative data, and conference abstracts lacking full peer-reviewed versions were excluded. Exceptionally, key earlier studies were cited as methodological background for studies from 2020–2026. [1][3]

2.3. Data extraction and quality of evidence

For each included study, the following data were extracted: authors, year of publication, country, study design, number of participants, investigated medication, type of glaucoma as the endpoint (OAG, ACG, or glaucoma overall), effect measure (OR, RR, HR, or Hedges' g) with 95% confidence interval. The quality of evidence was assessed using the ROBINS-I tool for non-interventional studies. Due to the high heterogeneity of the available data, emphasis was placed on the results of meta-analyses and systematic reviews as evidence with the highest level of credibility. [3]

3. Results

3.1. Characteristics of included studies

A total of 22 primary observational studies concerning the risk of glaucoma and/or changes in IOP during the use of psychotropic medications were identified, including more than 293,228 users of these medications altogether. The studies originated mainly from the USA and Canada (7 studies), South Korea (5 studies), Taiwan (6 studies), and Turkey (3 studies); a geographical disproportionality with predominance of Asian populations is evident. One systematic review with Bayesian meta-analysis (Jannini et al., 2025) included a total of 293,228 patients using psychotropic medications and constitutes the strongest available quantitative evidence. Additional data come from a cohort study based on the FAERS (FDA Adverse Event Reporting System) database concerning atypical antipsychotics (2025), a Danish population-based study concerning lithium (n = 7,683,398), and a large meta-analysis of the European E3 consortium (n = 143,240). [1][3][8][9][10]

3.2. Selective serotonin reuptake inhibitors (SSRIs)

Data on SSRIs in glaucoma are complex and depend on the analyzed subtype of the disorder. With regard to open-angle glaucoma (OAG), the Bayesian meta-analysis by Jannini et al. (2025), including 22 studies and 293,228 patients, demonstrated a significantly lower risk of OAG in patients using SSRIs compared with unexposed individuals (OR = 0.832; 95% CrI: 0.753–0.921). These results are consistent with the observations of Khawaji et al., cited by the E3 consortium, indicating a 30% reduction in POAG risk associated with SSRI use. The protective mechanism is attributed primarily to stimulation of 5-HT1A receptors in the ciliary body, which decreases aqueous humor production and lowers IOP; at the same time, 5-HT7 receptors present in the ciliary body–iris complex may induce mydriasis through relaxation of the pupillary sphincter. This meta-analysis further demonstrated a small but consistent reduction in IOP by SSRIs (Hedges' g = −0.332; 95% CrI: −0.487 to −0.179), with low heterogeneity of results (I^2 = 31.3%). [1][2][3]

With regard to angle-closure glaucoma (ACG), the situation is less clear. Subgroup analysis in the same meta-analysis did not demonstrate a significant increase in ACG risk in SSRI users (OR = 1.529; 95% CrI: 0.590–4.009). Nevertheless, in a large cohort study from a Canadian database—covering a total of 865,546 patients, among whom 589 cases of acute

angle-closure glaucoma (AACG) were recorded—an attempt was made to compare the risk of AACG between individual SSRIs and venlafaxine. The results indicated a trend toward lower AACG risk in users of citalopram (RR = 0.52), escitalopram (RR = 0.94), and venlafaxine (RR = 0.79) compared with sertraline as the reference drug, but none of these differences reached statistical significance. These data suggest that the risk of AACG is not identical for all substances in the SSRI class, yet they remain insufficient to formulate categorical data-based recommendations. [3][11][12]

It is worth noting that case reports in the literature have described AACG in patients using escitalopram, citalopram, paroxetine, fluvoxamine, sertraline, and SNRIs (duloxetine, venlafaxine). This mechanism—associated with a weak anticholinergic effect and serotonin-dependent mydriasis through 5-HT7 receptors—is plausible; however, large-scale epidemiological data do not confirm a clinically relevant population risk. In summary, SSRIs may be considered relatively safe in patients with OAG; in patients with an anatomically narrow iridocorneal angle—particularly before laser iridotomy—caution should be exercised. [2][3]

3.3. Serotonin and norepinephrine reuptake inhibitors (SNRIs)

The safety profile of SNRIs in glaucoma is similar to that of SSRIs, although with emphasis on the noradrenergic effect, which may be more conducive to the development of glaucoma than a purely serotonergic effect. In the Bayesian meta-analysis, the influence of SNRIs on IOP did not reach statistical significance (Hedges' g = −0.143; 95% CrI: −0.600 to 0.329), although the directional trend was consistent with the SSRI effect. In a prospective Turkish study assessing the effect of duloxetine (50 patients with depression, 6-month follow-up), no significant changes in IOP after treatment were demonstrated. Numerous case reports describe AACG following venlafaxine and duloxetine in patients with anatomical predisposition. Cases of choroidal effusion as a mechanism triggering AACG by SNRIs have also been described, analogous to the topiramate mechanism. The E3 meta-analysis, including 143,240 European participants, did not demonstrate a significant association between the use of any antidepressants (combined SSRIs, SNRIs, and TCAs) and glaucoma. In summary, SNRIs are considered medications with an acceptable risk profile in OAG, whereas in patients with a narrow iridocorneal angle they should be used with particular caution because of the possibility of triggering AACG. [2][3][10]

3.4. Tricyclic antidepressants (TCAs)

Tricyclic antidepressants (TCAs)—including amitriptyline, imipramine, clomipramine, nortriptyline, and desipramine—have for decades been regarded as a high-risk group in patients with glaucoma because of their strong anticholinergic effect. The mechanism potentially increasing glaucoma risk consists in anticholinergic blockade of the pupillary sphincter and ciliary body, leading to mydriasis and pupillary block in anatomically predisposed eyes with a narrow angle. Numerous cases of AACG induced by TCAs have been described in the literature, including severe visual field damage after amitriptyline. Standard textbooks as well as Canadian and FDA guidelines recommend avoiding TCAs in patients with a narrow angle or ACG. [2][7][13]

Paradoxically, currently available quantitative data do not unequivocally confirm an increased glaucoma risk at the population level. The Bayesian meta-analysis by Jannini et al. (2025) showed that TCAs were not associated with a statistically significant increase in glaucoma risk (OR = 1.466; 95% CrI: 0.700–3.338), although with very high heterogeneity of results (I^2 = 98.2%). The authors emphasize that the lack of statistical significance is probably due to heterogeneity of the included studies, rather than absence of an effect. Data from a case-control study conducted on a Korean cohort database (Ik Na et al., 2022) demonstrated a significantly increased risk of ACG in the case of amitriptyline use (OR = 3.08; 95% CI: 1.56–6.08) and nortriptyline. The clinical conclusions therefore remain unchanged: TCAs are contraindicated in patients with ACG or a narrow iridocorneal angle, and in patients with OAG they should be used with caution and under ophthalmological supervision. [2][3][7][14]

3.5. Other antidepressants: mirtazapine, bupropion, trazodone

With regard to bupropion, data from several studies are available. The Bayesian meta-analysis demonstrated a trend toward reduction in glaucoma risk (OR = 0.757; 95% CrI: 0.506–1.011), which, however, did not reach the threshold of statistical significance. The authors postulate that this effect may result from the inhibitory effect of bupropion on TNF-α, which protects retinal ganglion cells against apoptosis. Earlier case-control studies indicated a possible increase in ACG risk in patients under 50 years of age (OR = 1.98; 95% CI: 1.02–3.84), but these findings were not confirmed in more recent analyses. Data concerning mirtazapine in glaucoma are limited. A single case of AACG after combined use of escitalopram and

mirtazapine has been described, with rapid regression after discontinuation of the medication. Taking into account the mechanism of action of mirtazapine (blockade of alpha-2 adrenergic receptors and antagonism of H1, 5-HT2A, 5-HT3), a potential risk of mydriasis exists, but it is not well documented epidemiologically. Regarding other antidepressants, including trazodone, vortioxetine, and vilazodone, there are insufficient data to formulate unequivocal evidence-based recommendations. [3][14][15][16]

3.6. MAO inhibitors (MAOIs)

Data concerning monoamine oxidase inhibitors (MAOIs) in the context of glaucoma are extremely limited. Mechanistically, due to their sympathomimetic properties—resulting from catecholamine accumulation—MAOIs may theoretically lead to pupillary dilation and increased ACG risk. A disproportionality analysis from the FAERS database (Cambridge, 2024) demonstrated significant safety signals for many antidepressant classes, including MAOIs (ROR: 1.034–21.17); however, these data should be interpreted with caution due to the nature of a spontaneous reporting database. MAOIs are currently used rarely in clinical practice, mainly in cases of treatment-resistant depression. [14][15][17]

3.7. Antipsychotics

The safety profile of antipsychotics in the context of glaucoma is complex and ambiguous, which made it impossible to conduct a quantitative meta-analysis in the study by Jannini et al. (2025). Data from the FAERS database analyzed by Li et al. (2025) demonstrated a significant disproportional signal for olanzapine and ACG, with all four applied statistical measures exceeding the established thresholds (ROR = 4.64; 95% CI: 3.07–7.01; PRR = 3.33; 95% CI: 2.53–4.38; IC = 1.70, IC025 = 1.16; EBGM = 3.26, EBGM05 = 2.30). For other atypical antipsychotics—quetiapine and aripiprazole—some measures showed an upward trend, but did not simultaneously meet all signal-threshold criteria. The authors emphasize that the results of disproportionality analysis generate hypotheses rather than prove a causal relationship; therefore, further prospective studies are required. [3][8]

The mechanism of triggering AACG by antipsychotics—particularly atypical ones—includes blockade of muscarinic receptors (anticholinergic effect) leading to pupillary dilation and blockade of serotonergic receptors (5-HT2A) affecting relaxation of the iris sphincter. Olanzapine is characterized by one of the highest anticholinergic affinity indices among atypical neuroleptics, which explains its distinctive risk profile. Case reports of AACG after

olanzapine have been described in the literature—including in a 59-year-old patient diagnosed with schizophrenia, in whom unilateral ocular pain with elevated IOP >40 mmHg was observed, and gonioscopy revealed 360° angle closure in the anterior chamber. Analogous cases have been reported for aripiprazole, ziprasidone, quetiapine, and clozapine. The study by Darwich et al. (2024), based on the large PharMetrics Plus database, further showed that clozapine is associated with increased risk of OAG, whereas haloperidol shows a potentially neuroprotective effect on retinal cells in laboratory data. [2][7][8][14][18][19][20]

Data from the review by Cavaco et al. (2022) indicate that first-generation (typical) antipsychotics may be associated with a lower risk of IOP increase than second-generation (atypical) agents, although evidence on this matter is inconclusive. The study by Behera et al. (2025), conducted in an Indian tertiary-care center, showed that psychiatric medications with anticholinergic/sympathomimetic properties (SSRIs, TCAs, BZDs) caused narrowing of the iridocorneal angle measured by gonioscopy and AS-OCT compared with patients treated with lithium. This constitutes indirect evidence that cholinergic antagonism may exert a chronic effect on the morphology of the iridocorneal angle. [2][14][21]

Taking the above into account, antipsychotics require caution in patients with an anatomically narrow iridocorneal angle or diagnosed ACG, with particular attention to olanzapine and other substances with a high anticholinergic burden. In patients with OAG, the risk is lower, although regular ophthalmological monitoring remains indicated.

3.8. Benzodiazepines and Z-drugs

Benzodiazepines (BZDs) constitute one of the better documented classes of psychiatric medications with an increased glaucomatogenic risk. The Bayesian meta-analysis by Jannini et al. (2025) demonstrated OR = 1.550 (95% CrI: 1.436–1.674) for the association between BZDs and glaucoma, with low heterogeneity of results (I^2 = 20.8%). This effect was observed for both short-acting (OR = 1.647) and long-acting BZDs (OR = 1.538). Case-control studies from Korean population databases confirm these data: Kim et al. (2020) demonstrated increased AACG risk with BZD use (aOR = 1.40; 95% CI: 1.27–1.54), with similar risk for short- and long-acting agents. Park et al. (2019) demonstrated that new BZD use in older adults was associated with AACG risk (aOR = 1.62; 95% CI: 1.09–2.37), and within the first 7 days of exposure the risk was threefold higher (aOR = 3.09; 95% CI: 1.58–5.88). [1][2][3]

The primary mechanism responsible for ACG risk is allosteric modulation of GABA-A receptors by benzodiazepines, leading to pupillary dilation through an effect on the pupillary sphincter muscle. Paradoxically, the results of the review by Cavaco et al. (2022) suggest that in clinical practice BZDs less often trigger clinically overt angle closure than epidemiological data would suggest, and older reports questioned the actual causal relationship. Nevertheless, in light of the most recent Bayesian meta-analysis from 2025 demonstrating a consistent and significant class effect, benzodiazepines should be regarded as medications with increased glaucomatous risk in patients with an anatomically narrow iridocorneal angle. [1][3][14][22]

Data regarding Z-drugs (zolpidem, zaleplon, eszopiclone, zopiclone) are more limited. The cohort study by Ho et al. (Taiwan, included in the Jannini meta-analysis) demonstrated an association between zolpidem and glaucoma overall, but no subgroup analysis by subtype was conducted. Bearing in mind the similar mechanism of action of zolpidem and BZDs (GABA-A modulation) and the possibility of a similar effect on angle morphology, Z-drugs should be used with analogous caution. [3]

3.9. Topiramate

Topiramate occupies a special place in the literature concerning iatrogenic glaucoma, as a substance with the most unequivocally documented association with acute angle-closure glaucoma. This drug is used in psychiatry as an adjuvant in mood disorders, in addiction treatment (alcohol, nicotine), and in body weight reduction. In the meta-analysis by Jannini (2025), OR = 3.930 (95% CrI: 1.784–11.465) was reported for the risk of ACG with topiramate use. Current data from the Epilepsia population study (2026), conducted on the IQVIA electronic database in the United Kingdom, showed that topiramate is associated with higher glaucoma risk than valproate (aHR = 2.66; 95% CI: 1.12–6.32) and lamotrigine (aHR = 3.57; 95% CI: 1.76–7.26); in women, the risk relative to valproate was more than fivefold higher (aHR = 5.31; 95% CI: 1.48–19.08). A significant increase in risk was observed only in the subgroup of patients with epilepsy, whereas no significant association was demonstrated in patients treated for migraine prophylaxis. [1][3][23][24]

The mechanism of triggering AACG by topiramate is unique and different from most other drugs: the medication causes suprachoroidal effusion with ciliary body edema, which leads to relaxation of the zonular fibers, lens swelling, forward displacement of the lens–iris diaphragm, and mechanical angle closure without pupillary block. The clinical picture includes bilateral angle closure, acute myopia, and high IOP, usually developing within the

first 2 weeks after treatment initiation. Treatment consists of immediate discontinuation of topiramate and administration of cycloplegic (not miotic) agents—the use of miotic drugs (pilocarpine) may paradoxically worsen the patient's condition. Laser peripheral iridotomy (LPI), effective in idiopathic angle closure with pupillary block, is not the first-line treatment in topiramate-induced AACG. [23][25][26]

From a safety perspective, topiramate should be regarded as contraindicated in patients with diagnosed angle-closure glaucoma and as requiring particular caution and ophthalmological monitoring in patients with an anatomically narrow iridocorneal angle. Every patient starting topiramate treatment should be informed about the symptoms of AACG requiring immediate ophthalmological assistance. [24]

3.10. Other mood stabilizers: lithium, valproate, lamotrigine, carbamazepine

Lithium (lithium carbonate) is a first-line medication in bipolar disorder. Mechanistically, lithium may influence glaucoma through several pathways: (1) inhibition of GSK-3β kinase with a neuroprotective effect on retinal ganglion cells; (2) potential antioxidant effect; (3) the WNT/β-catenin signaling pathway modulating neuronal survival. A Danish population study (2025) from a registry covering 7,683,398 individuals showed that overall exposure to lithium was associated with a significantly greater risk of glaucoma (HR = 1.10; 95% CI: 1.02–1.19; p = 0.01), but this relationship was not statistically significant in the subgroup of patients with bipolar disorder (HR = 1.07; 95% CI: 0.93–1.22; p = 0.34). The authors conclude that the observed higher incidence of glaucoma in patients exposed to lithium probably results from the general somatic comorbidity of patients with bipolar disorder, rather than from a specific glaucomatogenic effect of lithium. The results of the study by Behera et al. (2025) are consistent with this interpretation: patients treated with lithium showed more widely open iridocorneal angles compared with the group using SSRIs/TCAs/BZDs. [9][27][28][29]

For valproate and lamotrigine, there are no dedicated high-quality epidemiological studies concerning glaucoma risk. The IQVIA database study (2026) used valproate and lamotrigine as active comparators for topiramate, demonstrating clearly lower glaucoma risk in both groups. These data allow indirect inference of the relative safety of valproate and lamotrigine in this context, although they require confirmation in studies in which these agents are the primary interventions. Carbamazepine was not the subject of separate ophthalmic studies after 2020; its weak anticholinergic properties theoretically create minimal risk of pupillary dilation. [24]

3.11. Medications used in ADHD: methylphenidate, amphetamines, atomoxetine

Methylphenidate and amphetamines are sympathomimetics—as such, they are formally listed in FDA labels as contraindicated in patients with angle-closure glaucoma due to the risk of adrenergic mydriasis and increased IOP. The retrospective cohort study by Darwich et al. (2024), including 240,257 new users of ADHD medications in the PharMetrics Plus database, showed that amphetamines and atomoxetine were associated with increased ACG risk (aIRR respectively: 2.27; 95% CI: 1.42–3.63 and 2.55; 95% CI: 1.20–5.43), whereas methylphenidate was associated with increased OAG risk (aIRR = 1.23; 95% CI: 1.05–1.59). These findings have important public health implications due to the widespread use of these medications. [30][31]

Paradoxically, prospective studies in children (Guvenmez et al., 2020, n = 78; 6-month follow-up) did not demonstrate statistically significant changes in IOP after the use of methylphenidate or atomoxetine in the age group of 8–12 years. The Bayesian meta-analysis confirmed no significant effect of methylphenidate on IOP in children (Hedges' g = −0.162; 95% CrI: −0.407 to 0.084). The discrepancy between the results of adult and pediatric studies may result from differences in ocular anatomy, prescribed doses, and follow-up duration. Clinically, in patients with OAG methylphenidate may be used with caution, whereas in patients with ACG or a narrow iridocorneal angle all stimulants should be avoided. [3][30]

4. Discussion

4.1. Iatrogenic mechanisms and glaucoma type

The present review confirms that iatrogenic mechanisms differ between OAG and ACG and have distinct clinical implications. Medications with anticholinergic or sympathomimetic activity (TCAs, BZDs, atypical antipsychotics, stimulants) threaten primarily patients with a narrow iridocorneal angle and predisposition to ACG, through pharmacologically induced pupillary dilation and pupillary block. Topiramate constitutes an exception—its mechanism is independent of angle width and consists in ciliary body effusion, which makes topiramate-induced AACG a unique and unpredictable complication even in patients without an anatomically narrow angle. The influence on OAG is more subtle: SSRIs, through modulation of serotonergic receptors in the ciliary body, may reduce aqueous humor

production and lower IOP, showing potentially neuroprotective action on retinal ganglion cells. [1][2][3][7][23][25]

4.2. Data heterogeneity and methodological limitations

The high heterogeneity of the available data constitutes the main limitation for interpretation. In the Bayesian meta-analysis, I^2 values for TCAs were 98.2%, and for SSRIs in ACG—94.9%, indicating enormous discrepancies between studies. These result from differences in: (1) studied populations (particularly overrepresentation of Asian populations with naturally higher prevalence of ACG); (2) definitions of glaucoma as the endpoint; (3) medication exposure (dose, duration, indication); (4) methods of controlling confounders (age, sex, family history, ocular morphology). The current lack of randomized clinical trials concerning the iatrogenesis of glaucoma by psychiatric medications prevents causal inference and limits the strength of recommendations to the level of observational studies. [3][10]

4.3. Implications for differentiation of clinical safety

These data have significant implications for clinical practice. In patients with OAG, the only absolute contraindication is topiramate; TCAs should be used with caution, with preference for alternative medications; BZDs and some atypical antipsychotics require regular ophthalmological monitoring. SSRIs—in light of current data—may be the medications of choice in patients with OAG, both because of psychiatric indications and a potentially beneficial ophthalmic effect. In patients with ACG or a narrow iridocorneal angle (especially before treatment with laser iridotomy), particular caution should be exercised when using TCAs, BZDs, topiramate, atypical neuroleptics with a high anticholinergic burden (particularly olanzapine), and all stimulants. [1][2][3][7][8][21]

The study by Behera et al. (2025) indicates that long-term exposure to psychiatric medications with an anticholinergic effect may lead to chronic narrowing of the iridocorneal angle through a mydriatic mechanism, which provides an additional argument for implementing ophthalmological screening examinations before and during long-term psychiatric pharmacotherapy. This study demonstrated that patients taking SSRIs, TCAs, and BZDs had significantly narrower iridocorneal angles on gonioscopy (8/50 patients with a Shaffer grade 2 angle), whereas in the lithium group no patient demonstrated a narrow angle (0/22). [2]

4.4. Relationship between mental illness and glaucoma

An important clinical context is the bidirectional relationship between glaucoma and mental disorders. Glaucoma, as a chronic disease leading to visual deterioration, is a strong predictor of depression and anxiety disorders. It has been demonstrated that anxiety correlates with 40% poorer adherence to ophthalmic treatment, accelerated progression of visual field damage (−1.5 dB/year), and a 30% higher risk of postoperative complications. Conversely, glaucoma by its very nature requires the use of IOP-lowering medications, the interaction of which with psychiatric medications is insufficiently studied. Data from a large cross-sectional study showed that glaucoma is associated with a significantly higher number of diagnoses of anxiety (OR = 1.36; 95% CI: 1.17–1.58), MDD (OR = 1.4; 95% CI: 1.20–1.64), and schizophrenia after adjustment for confounding factors. [4][6][32]

5. Conclusions

The present literature review allows the following clinical conclusions to be formulated regarding the safety of psychiatric medications in patients with glaucoma:

5.1 Medications safe or beneficial in glaucoma:

- **SSRIs** (fluoxetine, sertraline, escitalopram, citalopram, paroxetine) — moderately reduce the risk of OAG (OR = 0.832) and show a small but consistent hypotensive effect on IOP; they may be the medications of choice in patients with OAG; in patients with a narrow angle, caution is required before iridotomy treatment. [1][3]

- **Lithium** — no direct anticholinergic effects; neutral or potentially beneficial ophthalmic profile; patients with bipolar disorder have a generally higher risk of glaucoma because of comorbidity, not because of lithium action. [9][29]

- **Lamotrigine and valproate** — lower glaucoma risk than topiramate; no specific glaucomatogenic mechanism has been demonstrated. [24]

- **Haloperidol (first generation)** — according to available data, it shows a potentially beneficial effect; lower affinity for muscarinic receptors than second-generation drugs. [14][21]

5.2 Medications requiring caution or monitoring:

- **SNRIs** — acceptable profile in OAG; caution in patients with a narrow angle because of the potential to trigger AACG. [2][3]
- **Mirtazapine, bupropion, trazodone** — equivocal or insufficient data; if use is necessary, ophthalmological monitoring. [3][14]
- **Atypical antipsychotics** (quetiapine, aripiprazole, risperidone) other than olanzapine — isolated cases of AACG; caution in patients with a narrow angle; insufficient population data. [8][19][33]
- **Methylphenidate** — possible increased risk of OAG in adults; no significant effect on IOP in children; do not use in patients with ACG. [31]

5.3 Medications contraindicated or requiring avoidance in patients with ACG or a narrow iridocorneal angle:

- **Topiramate** — strong association with AACG (OR = 3.930); unique mechanism (ciliary body effusion); absolutely avoid in patients with ACG or a narrow angle; every patient should be monitored ophthalmologically during the first 2 weeks of treatment. [1][3][24]
- **TCAs** (amitriptyline, imipramine, clomipramine, nortriptyline) — contraindicated in ACG because of their strong anticholinergic effect and the risk of AACG; use with caution in OAG. [2][7][14]
- **Benzodiazepines** — significantly increased risk of ACG (OR = 1.550); avoid in patients with a narrow iridocorneal angle; if necessary—minimize duration of use and provide ophthalmological monitoring. [1][3]
- **Olanzapine** — the strongest safety signal among atypical antipsychotics for ACG (ROR = 4.64); avoid in patients with ACG or a narrow angle; consider alternative medications. [8]
- **Amphetamines and atomoxetine** — increased risk of ACG (aIRR = 2.27–2.55); contraindicated in patients with ACG or a narrow iridocorneal angle. [31]

5.4 Medications with insufficient data:

- Clozapine, amisulpride, paliperidone, lurasidone, brexpiprazole, cariprazine — insufficient epidemiological studies concerning glaucoma risk; further observation and spontaneous reports are required.
- MAOIs — theoretical risk of mydriasis; no population data.
- Z-drugs (zolpidem, zaleplon, eszopiclone) — mechanism similar to BZDs; no dedicated studies. [3]

5.5 Recommendations for clinical management:

Patients diagnosed with glaucoma or risk factors for its development (narrow iridocorneal angles, Asian race, hyperopia, advanced age, family history) should undergo ophthalmological evaluation including IOP measurement, gonioscopy, and optic disc assessment before initiation of psychiatric pharmacotherapy. During long-term therapy with medications carrying potential ophthalmic risk, regular ophthalmological follow-up is indicated, and patients should be informed about the symptoms of acute angle closure (sudden eye pain, redness, blurred vision, halos, nausea/vomiting) requiring immediate ophthalmological intervention. Cooperation between the psychiatrist and the ophthalmologist is a key element of safe care for this group of patients. [2][7]

5.6 Directions for future research:

The current state of knowledge is burdened by numerous gaps. There is a lack of prospective randomized studies regarding the risk of iatrogenic glaucoma caused by psychiatric medications, and the available data are based almost exclusively on observational studies. Further studies are necessary to assess: (1) the risk of individual atypical antipsychotics in European cohorts; (2) the effect of long-term exposure to psychiatric medications on iridocorneal angle morphology; (3) the potential neuroprotective effect of SSRIs on retinal ganglion cells in prospective clinical studies; (4) interactions between ophthalmic medications (beta-blockers, prostaglandin analogues) and psychiatric medications. [1][3][24]

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AUTHORS'S CONTRIBUTION

Conceptualization: KI, WP, DG, NN, NR
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