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# Angle closure glaucoma secondary to psychotropic medications

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## CASE STUDY

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## ABSTRACT

**Background**
Psychotropic medications are commonly associated anticholinergic side-effects. In susceptible patients, this can result in angle closure induced permanent loss of vision

**Aims**
To review the mechanism of angle closure and which psychotropics are most likely to precipitate this complication.

**Methods**
Literature review surrounding the mechanism of angle closure and pharmacology of various psychotropics

**Results**
Mydriasis, forward-displacement of the lens-iris diaphragm and ciliary body swelling are the mechanisms by which angle closure occurs. Anticholinergic side effects of psychotropic medications are most implicated in causing this.

**Conclusion**
Screening patients for risk factors of angle closure and either having them formally assessed or choosing psychotropics with minimal anticholinergic effects may avoid inducing angle closure.

**Key Words**
Psychotropics, angle closure, vision loss, glaucoma, anticholinergics, mental health, general practice, psychiatry

## Implications for Practice:

**1. What is known about this subject?**
Psychotropic medications are commonly associated with anticholinergic side effects. In susceptible patients, this can precipitate angle closure resulting in permanent vision loss.

**2. What new information is offered in this case study?**
Several psychotropic medications are of higher risk than others in susceptible patients. Patients can also remain asymptomatic until advanced glaucoma is present.

**3. What are the implications for research, policy, or practice?**
Identification of high risk patients and either having them formally assessed or managing them with a psychotropic medication with minimal anticholinergic effects can avoid this complication.

## Background

Angle closure secondary to psychotropic medications is a rare, but important, presentation which must be considered when prescribing psychotropic medications. Patients who develop angle closure may present symptomatically or asymptomatically. Both acute and chronic angle closure can lead to permanent visual dysfunction or loss due to glaucoma, if not managed appropriately.

With the increasing burden of mental health,[1] it is pertinent that all prescribing physicians are aware of this adverse effect that is related predominantly to the anticholinergic side-effects of psychotropic medications. Prescribing physicians should be able to identify patients in the highest risk groups and either have them formally assessed by an ophthalmologist or optometrist prior to prescribing or choose a psychotropic with minimal anticholinergic side-effects.

## Case details

A 35-year-old year Caucasian female was referred to an ophthalmologist with intermittent blurred vision associated with haloes in her left eye for one month. She had no history of spectacles and relevant medical history included postnatal depression of 13 years duration managed initially with fluvoxamine 50mg daily switched to quetiapine 100mg nightly for 3 months prior to her presentation.

Examination showed a visual acuity of 6/6 (right) and 6/12 (left) with mild corneal oedema on the left. She also demonstrated bilateral high intraocular pressures (IOP) by Goldmann applanation tonometry measuring 34mmHg (right) and 51mmHg (left) (normal 10–21mmHg).[2] Further examination showed shallow anterior chambers (AC) and gonioscopy confirmed no visible angle structures (angle closure) with no signs of synechiae or neovascularization. The left cup-to-disc ratio (CDR) of 0.95 (Figure 1) signified likely advanced left glaucomatous optic neuropathy (GON/glaucoma) secondary to angle closure (angle closure glaucoma). The right optic disc showed no significant cupping (CDR 0.3), representing high intraocular pressure related to angle closure which had not yet progressed to glaucoma.

Immediate management included oral acetazolamide, topical anti-glaucoma mediations and topical miotics (pilocarpine). Quetiapine was ceased in consultation with her general practitioner and she was switched onto agomelatine. Following IOP reduction and resolution corneal oedema successful bilateral Nd-YAG laser peripheral iridotomies were performed to alleviate a possible contributing pupil block mechanism. She also underwent Humphrey visual field testing (Figure 2) demonstrating a dense left inferior almost complete field defect and optical coherence tomography (OCT) (Figure 1) of the retinal nerve fibre layer (RNFL) showing superior, temporal and some inferior thinning of the RNFL. This confirmed the diagnosis of left GON. Following management her IOPs and mood remained stable and her anti-glaucoma medications were weaned.

## Discussion

This case demonstrates secondary angle closure glaucoma from systemic psychotropics. The presentation of blurred vision associated with haloes around lights is classic for a patient who has had an acute change in IOP. This results in corneal oedema which subsequently presents as haloes around lights. The eye is often painful, injected and has a fixed mid-dilated pupil that may be unresponsive to light however more commonly and as evidenced by the right eye, patients can be asymptomatic.[3]

The mechanism by which this occurs is predominantly due to their anticholinergic effects, resulting in mydriasis, forward displacement of the lens-iris diaphragm and ciliary body swelling.[4,5] Combined, these anatomical changes can occlude the trabecular meshwork, blocking drainage of aqueous humour with a subsequent increase in IOP. The incidence of psychotropic induced angle closure however is likely very low. To our knowledge, no incidence rate has been reported in the literature. However, ophthalmic mydriatic agents have been shown to induce acute angle closure in 0.03 per cent of 6,760 patients in a Caucasian population from the Netherlands.[6] The observed baseline incidence of narrow angles (predisposing the patient to angle closure) was 2.2 per cent in that cohort. Other cohorts may have higher rates of narrow-angles. For example, in a Vietnamese study it was found to be 8.5 per cent.[7] With the increasing population of Asian migrants in Australia, it is likely that our prevalence of narrow angles will be higher than that observed in the Netherlands cohort. Furthermore, the use of psychotropic medications is increasing. A study from 2012 found a 58.2 per cent rise between 2000 and 2011,[1] so it is likely that we will see increasing presentations of psychotropic induced angle closure if this trend continues.

Typical medications associated with this phenomenon include medication classes: tricyclic antidepressants (TCAs), antipsychotics, selective-serotonin reuptake inhibitors (SSRIs), serotonin-noradrenaline reuptake inhibitors (SNRIs), monoamine oxidase inhibitors (MAOIs) and benzodiazepines.[4,8-12] The highest risk classes are the TCAs and some second generation antipsychotics (SGAs) as they have the greatest anticholinergic effects.[4,8,9] The risk profile of drugs in the other classes varies depending on their potency at the various receptors (Table 1).[4,9] Serotonergic effects implicated in angle closure occur as a result of lens-iris diaphragm displacement and relaxation of sphincter pupillae[4,9] and adrenergic effects implicated occur by direct action on dilator pupillae resulting in mydriasis.[4]

Medications alone are typically not enough to cause angle closure. Patients will often have other risk factors such as significant hypermetropia (long-sightedness), being of Asian descent, being female and having personal or family history of angle closure or angle closure glaucoma.[4,5,8,13] These patients are predisposed to narrow angles and shallow ACs and are at higher risk. In these patients it is recommended that screening be undertaken by an ophthalmologist or optometrist prior to commencement of such medications.

Peripheral iridotomies will minimise any pupil block and anterior bowing of the iris but will not prevent anterior displacement of the lens-iris diaphragm. In these patients psychotropics with the least anticholinergic effects (e.g., melatonergic antidepressants, as in this case) should be considered.

Patients identified as having an episode of acute angle closure require prompt assessment by an ophthalmologist as high IOPs can rapidly cause permanent vision-loss secondary to damage of the optic-nerve (GON). In this scenario management varies depending on the aetiology of the angle closure however typically includes acute-reduction of the IOP through means of topical anti-glaucoma eye-drops (e.g., beta-blockers, alpha-agonists), topical miotic agents where indicated, e.g., pilocarpine), systemic-medications (e.g., acetazolamide, mannitol) and interventional-procedures (e.g., indentation-gonioscopy, Nd:YAG-laser peripheral-iridotomies, AC-paracentesis).[3,14,15] If the symptoms are medication related the offending agent should be stopped where possible. Where medically necessary definitive ophthalmic intervention (e.g., lensectomy) could be considered and may facilitate continuation of the particular causative medication.

Aside from enquiring about risk factors one method to screen for these patients is an in-office screening test done by shining a penlight parallel to the iris from the temporal side can help identify patients at risk (Figure 3).[4,8,16] If the entire iris is illuminated the angle of the anterior chamber is likely open[4] and the patient at reduced risk. This method of screening was found to have a sensitivity of 94 per cent and specificity or 67 per cent from two non-ophthalmologist doctors in a study of 45 patients from Brazil.[16] However another study of 96 patients in India had a sensitivity of 45.5 per cent and a specificity of 82.7 per cent,[17] suggesting that reliability is operator dependent so judicious caution must be advised and the findings considered in context of the patient's history and risk factors. This recommendation was mirrored in a controlled Chinese study of 1,405 subjects in 2007.[18] Despite the utility and novelty of this test it should be noted that this is not a substitute for slit-lamp examination with gonioscopy performed by ophthalmologists or optometrists which remains the definitive method of risk assessment.

## Conclusion

In conclusion, it is prudent that prescribers of the above medications are aware for potential angle closure and symptoms associated with this including decreased visual acuity, haloes around lights, intermittent pain, photophobia and visual field changes. Patients with these symptoms require urgent ophthalmological assessment and management to prevent permanent vision-loss. Patients at increased risk of angle closure especially those with hypermetropia (long-sightedness) or a personal/family history of angle closure, or patients with another visual risk factor such as only one good eye, should be referred to an ophthalmologist or optometrist for assessment of their risk prior to commencing treatment. Alternatively these patients could be considered for treatment with medications with reduced ocular side-effects however we acknowledge that this may not always be easy and that the use of a particular psychotropic can be very necessary and even life-saving. For patients on higher risk medications we recommend regular discussion with patients at follow-up visits about any visual symptoms they may have experienced and education on the symptoms to be vigilant of, such as blurred vision, haloes, ocular pain and photophobia.

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## PEER REVIEW

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## CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

## FUNDING

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## PATIENT CONSENT

The authors, *Rocke JR, O'Day RFJ, Roydhouse TC,* declare that:

1. They have obtained written, informed consent for the publication of the details relating to the patient(s) in this report.
2. All possible steps have been taken to safeguard the identity of the patient(s).
3. This submission is compliant with the requirements of local research ethics committees.

**Figure 1: The left image of left optic disc which shows a cupped optic disc (CDR 0.95) and the image on the right shows the OCT of the left eye demonstrating reduction in the thickness of the RNFL in the superior, temporal and inferior regions**

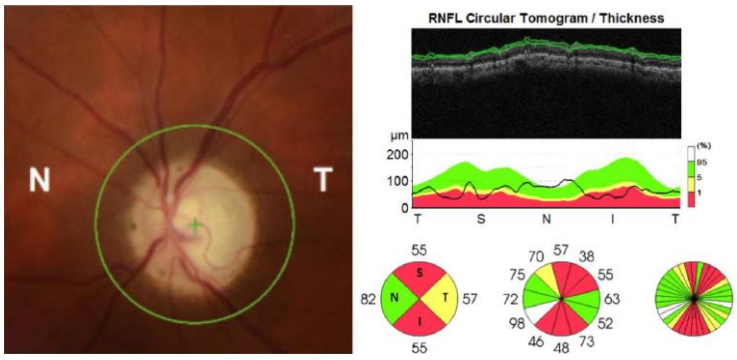


**Figure 2: This figure shows the 24-2 Humphrey visual fields left eye (left) and right eye (right). The left eye demonstrates marked inferior field and paracentral losses consistent with advanced glaucoma. The right visual field demonstrates only non-specific changes which may represent early arcuate scotomas**

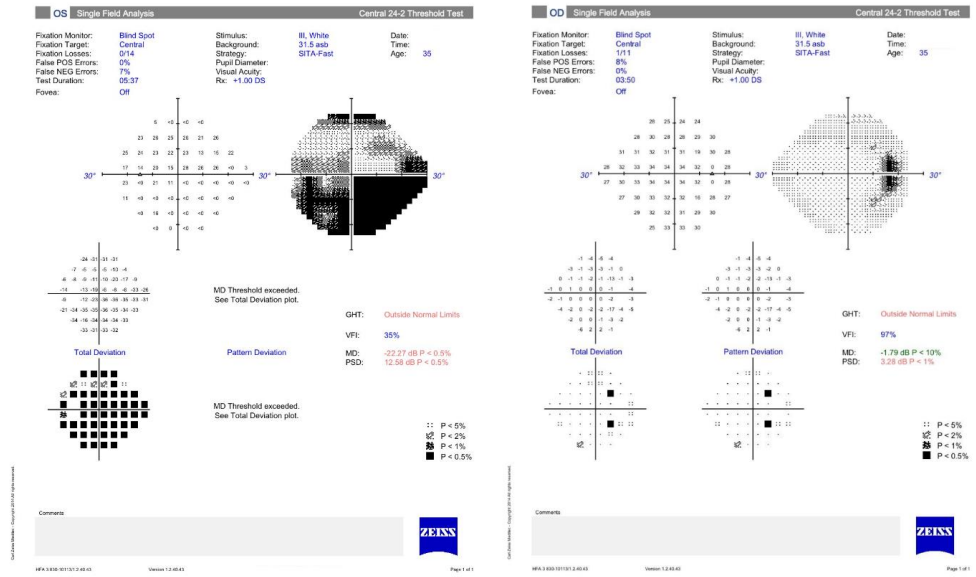


**Figure 3: This demonstrates a bedside test (Flash Light Test[19]) that can be done to assess the anterior chamber depth of patients. In deep anterior chambers, by shining a light source across the iris plane you can observe diffuse and uniform illumination of the iris whereas in shallow anterior chambers where often the iris plane is more convex (right image), irregular illumination of the iris is observed.[4,8] It should be noted that this is not a substitute for formal examination by an ophthalmologist or optometrist**

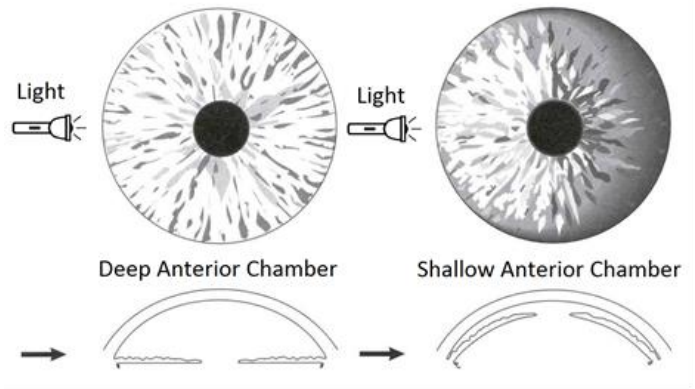

**Table 1: This table lists medications and their associated anticholinergic side effect risk ranging from 0 to +++++ in order of increasing magnitude of effect[10,20,21]**

| Drug | Anticholinergic effect |
|---|---|
| **First generation antipsychotics (FGAs)** | |
| Haloperidol | + |
| Fluphenazine | + |
| Thiothixene | + |
| Trifluoperazine | + |
| **Second generation antipsychotics (SGAs)** | |
| Chlorpromazine | ++++ |
| Clozapine | +++++ |
| Olanzapine | + |
| Quetiapine | + |
| Risperidone | + |
| Aripiprazole | + |
| Ziprasidone | ++ |
| **Tricyclic Antidepressants (TCAs)** | |
| Amitriptyline | +++ |
| Imipramine | ++ |
| Desipramine | + |
| Nortriptyline | ++ |
| Protriptyline | ++ |
| Trimipramine | ++ |
| Doxepin | ++ |
| Clomipramine | +++ |
| **Selective Serotonin Reuptake Inhibitors (SSRIs)** | |
| Fluoxetine | + |
| Sertraline | 0 |
| Escitalopram | 0 |
| Citalopram | 0 |
| Paroxetine | + |
| Fluvoxamine | + |
| **Seretonin-Noradrenaline Reuptake Inhibitors (SNRIs)** | |
| Venlafaxine | 0 |
| Desvenlafaxine | 0 |
| Duloxetine | + |
| Mirtazapine | ++ |
| **MAO Inhibitors (MAOIs)** | |
| Phenelzine | 0 |
| Tranylcypromine | 0 |
| Selegiline | 0 |
| **Other** | |
| Bupropione | 0 |
| Atomexatine | + |