Glaucoma Associated With Therapies for Psychiatric Disorders

Treatments for some mental illnesses can cause or exacerbate glaucoma.

BY JULIA SONG, MD

Approximately 26% of Americans over 18 years of age suffer from a mental disorder.[1] In patients 55 years or older, the prevalence of a mental illness is 20%.[2] The most common psychiatric conditions in the elderly are anxiety, severe cognitive impairment, and mood disorders (depression or bipolar disorder).[2] Unfortunately, some psychiatric treatments, both medical and electroconvulsive therapy (ECT), can cause glaucoma, and glaucoma therapy such as timolol, brimonidine, and pilocarpine can cause psychiatric symptoms.[2] This article provides an overview of the relationship between glaucoma and psychiatric treatments.

MEDICAL THERAPIES

Medications used to treat psychiatric conditions (psychotropic drugs) can be divided into two categories: (1) anticholinergic medications and (2) medications that result in swelling of the ciliary body and anterior rotation of the ciliary body (idiosyncratic reaction). Anticholinergic agents block the neurotransmitter acetylcholine in the central and the peripheral nervous system. Anticholinergics inhibit parasympathetic nerve impulses by selectively blocking the binding of the neurotransmitter acetylcholine to its receptor in nerve cells. This can cause glaucoma in individuals with narrow anterior chamber angles by dilating the pupil and causing pupillary block. Anticholinergic medications known to cause glaucoma include benzodiazepines (diazepam), tricyclic antidepressants (imipramine), and selective serotonin reuptake inhibitors (paroxetine, citalopram, escitalopram, fluoxetine, and fluvoxamine).[3,4]

The most notorious psychotropic medication that causes angle-closure glaucoma via ciliary body rotation is topiramate (Topamax; Ortho-McNeil Neurologics). Topiramate is a widely used psychiatric therapy indicated for epilepsy, migraine, alcohol addiction, nicotine addiction, peripheral neuropathy, radiculopathy, and posttraumatic stress disorders. The drug's mechanism involves the inhibition of carbonic anhydrase, glutamate receptors, and calcium channels; the blockage of sodium channels; and the enhancement of gamma-aminobutyric acid receptors.[5] Topiramate is a sulfa-based medication with a half-life of 24 hours, and it is excreted via urine.[6]

Figure 1. A shallow anterior chamber in the eye of a patient on topiramate. Reproduced with permission from Brandão MN et al.[8]

Glaucoma induced by topiramate is idiosyncratic and characterized by swelling of the ciliary body and lens due to the relaxation of the zonules, an anterior rotation of the lens-iris diaphragm, a shallow anterior

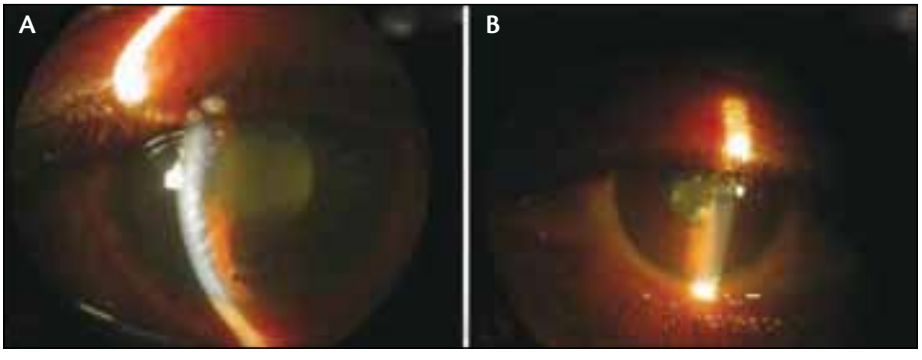

Figure 2. Nongranulomatous reaction (A) and fibrinous reaction (B) from topiramate-induced angle-closure glaucoma. Reproduced with permission from Acharya N et al.[7]

chamber (Figure 1), and bilateral angle-closure glaucoma (ACG).[7] Patients report blurry vision, headache, and photosensitivity. Physical examination typically reveals acute myopia (up to 8.75 D), choroidal effusion and detachment, nongranulomatous uveitis (Figure 2A and B), angle closure on gonioscopy, and prominent ciliary body processes on ultrasound biomicroscopy (Figure 3).[7]

The treatment for ACG induced by topiramate is the immediate discontinuation of the drug. Supportive measures include maximal glaucoma medications, topical cycloplegics (atropine t.i.d.), and steroids (prednisolone acetate q.i.d. [Pred Forte 1%; Allergan, Inc.]), intravenous methylprednisolone (Medrol; Pfizer, Inc.) 250 mg, and intravenous mannitol 20% (100 mL b.i.d.). The glaucoma usually resolves within 1 week of treatment.[8] Unlike in traditional ACG (or angle closure induced by anticholinergic medications), pilocarpine is contraindicated, because it can further narrow the anterior chamber angle and cause the ciliary muscle to spasm. A laser iridotomy is not a helpful treatment, because the mechanism of topiramate-induced ACG does not involve pupillary block. If a patient has a severe fibrinous reaction that results in secondary pupillary block, following the resolution of ciliary body swelling, however, a laser iridotomy can then be performed. Argon laser peripheral iridoplasty (200-mm spot size, 0.7 sec, 280 mW) can also be used to help open the angle if performed within 24 hours of a glaucoma attack. If there are severe peripheral synechiae with elevated IOP, a trabeculectomy may be indicated. Drainage of the suprachoroidal fluid has been reported but is not recommended.[9]

Sequelae after ACG caused by topiramate can occur; these include pupillary membranes, synechiae, cataracts, visual field defects, blindness, decreased endothelial cell density (polymegathism, pleomorphism), periorbital edema, diplopia, and nystagmus.[10,11] These side effects can be avoided if the glaucoma is diagnosed early.

ELECTROCONVULSIVE THERAPY

ECT, formerly known as *electroshock*, was invented in 1977 for the treatment of depression and bipolar disorder and is associated with significant systemic side effects, including circulatory failure, cardiac arrest/arrhythmia, coronary occlusion, apnea, and death.[12]

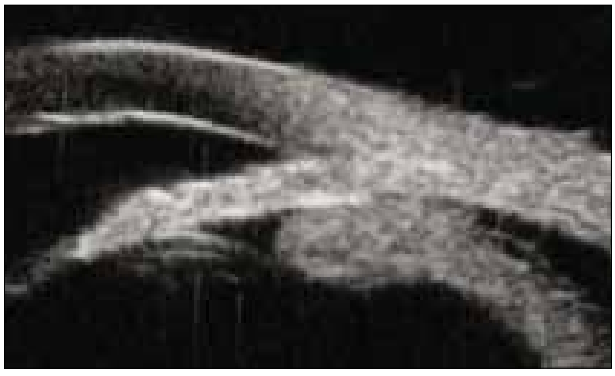

Figure 3. Ultrasound biomicroscopy shows swelling of the ciliary body and anterior rotation of the lens-iris diaphragm. Reproduced with permission from Acharya N et al.[7]

ECT can increase IOP (range, 25-68 mm Hg).[13-15] The mechanism of elevated IOP includes an increase in cerebral blood flow by 100% to 400%, also resulting in greater intracranial and venous pressure. The electrical stimulus to the cerebrum results in muscle spasms, but the blepharospasm's effects on IOP is minimal. Similarly, the extraocular muscle spasm does not increase IOP above that of suxamethonium.

Medications used during anesthesia for ECT can have variable effects on IOP. Succinylcholine, a depolarizing muscle relaxant, can raise IOP, whereas other agents (barbiturates, benzodiazepine, propofol) can lower it.[16] Intramuscular glycopyrrolate can result in pupillary dilatation and subsequent ACG in susceptible individuals, specifically those with narrow angles or large cataracts and in Asians and women.[13] Blood pressure can vary during anesthesia, and sudden increases in blood pressure can elevate IOP, despite choroidal autoregulation.

Patients should not undergo ECT within 3 weeks of intraocular surgery, and a visual field test should be performed

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TABLE. IOP SPIKES DURING ECT IN AN EYE WITH AND WITHOUT A GLAUCOMA TUBE IMPLANT

	IOP before ECT	IOP 1 minute after ECT	Δ IOP	IOP 2 minutes after ECT	Δ IOP	IOP 4 minutes after ECT	Δ IOP
No tube	14	20	+6	24	+10	25	+11
Tube	10	14	+4	16	+6	11	+8

Abbreviations: ECT, electroconvulsive therapy; Δ, change.
Note: All measurements in mm Hg.

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after a patient's first ECT treatment. Caution should be exercised in patients with advanced or end-stage glaucoma. During anesthesia, nondepolarizing muscle relaxants (such as mivacurium, d-tubocurarine, gallamine, pancuronium) can be used. Adequate oxygenation should be used to minimize cerebral vasodilatation, and hyperventilation can be implemented to minimize hypercarbia.

Song et al reported spikes in IOP in a patient undergoing ECT.[17] Interestingly, in the same patient, the IOP did not spike as dramatically in the eye with a glaucoma tube implant (Table). The presence of the implant helped to prevent excessive diurnal fluctuations from a Valsalva maneuver.

CONCLUSION

There is a high association between psychiatric disorders and glaucoma. Both medical therapy (anticholinergic agents and agents that cause ciliary body rotation) and ECT for psychiatric treatment can exacerbate or cause glaucoma. In the interest of early diagnosis and treatment, ophthalmologists need to be aware of how psychiatric conditions and medications can affect glaucoma. ■

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