

CE Credit - Topic Review

Bilateral Angle Closure Secondary to Topiramate

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ABSTRACT

Topiramate (Topamax) is an oral medication used for the treatment of migraines, seizure disorder, and alcohol dependence.^{1,2} In the United States, it is one of the most commonly prescribed medications and is taken by over ten million people.^{3,4} Despite this ubiquity, not all prescribers are aware that topiramate can cause angle closure, and even fewer health care providers are educating patients on this side effect. This case report describes a patient who presented with bilateral angle closure secondary to topiramate. It highlights the presentation, treatment, and management with an emphasis on pharmacology and interprofessionalism. Introduction

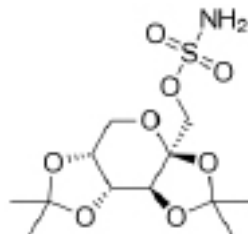
Background

Topiramate is a unique and popular medication that works through numerous channels in the body. It has a complex mechanism of action that provides potency across many different disease processes, and that causes several significant side effects. One such side effect that will be discussed in this case report is angle closure.

Pharmacology

Topiramate (Figure 1) was initially approved for patients with seizure disorder suffering from generalized tonic-clonic or complex partial seizures. The drug has an unusual sulfamate moiety (SO₂NH₂) that allows the molecule to penetrate the central nervous system more powerfully than other anticonvulsants. This structure also allows it to be classified as a neurostabilizer, meaning that it can “attenuate the excitability of brain neuronal pathways.”⁵ Neurostabilizers can be used to treat migraines, epilepsy, bipolar disorder, neuropathic pain, and diabetic retinopathy. Gabapentin is one other common neurostabilizer.⁵

Figure 1. The chemical structure of topiramate. Of note, the sulfamate moiety (SO₂NH₂, top of figure) gives the medication its uniqueness.⁶



Topiramate became such a successful anticonvulsant that additional clinical trials were done to find other useful indications for its use. Soon topiramate was approved for migraine prophylaxis and—when combined with phentermine—for the treatment of obesity.⁵

Adverse Effects

According to the U.S. Food and Drug Administration (FDA), the most common side effects of topiramate (>10% from placebo) are paresthesia, anorexia, weight decrease, speech disorder related speech problems, fatigue, dizziness, somnolence, nervousness, psychomotor slowing, abnormal vision, and fever. The U.S. FDA underscores abnormal vision as a possible adverse effect by listing decreased vision and ocular pain as the very first warning on the drug's label.¹ Other sources list the incidence of angle closure due to topiramate at three in 100,000 patients.⁷

Topiramate causes angle closure by ciliochoroidal effusion. The exact chemistry of this process is not known. However, many believe the medication increases blood flow, which creates edema in highly vascularized structures like the ciliary body and the choroid. The ciliary body swells with increased fluid, rotates anteriorly, and snaps the angle closed. The iris-lens apparatus is also displaced anteriorly.⁷

Patients will experience not only pain from elevated intraocular pressure, but also a myopic shift. This occurs due to the forward displacement of the iris-lens apparatus, which shortens the eye's axial length and increases its refractive power. Moreover, the zonular tension on the lens is reduced and this allows the lens to assume a more powerful spherical shape.

The range of symptoms associated with topiramate-induced angle closure varies. However, the most common presenting symptoms are ocular pain and blurred vision. Less often symptoms include nausea, vomiting, photophobia, and vision loss if the pressure remains elevated.

CASE REPORT

Emergency Room Visit

A 37-year-old white male presented to the emergency room in the middle of the night with complaints of headaches, blurry vision, and light sensitivity. The headaches were different than his usual headaches and migraines. They were more severe and had an unusual pattern. They affected his periorbital structures. They occurred throughout the day and night and did not improve with over-the-counter medication. He reported that his vision was blurry in both eyes at distance, but clear at near. He noted never previously needing glasses.

Ocular history was unremarkable. Medical history was positive for migraines with aura, post-traumatic stress disorder, anxiety, depression, insomnia, and adjustment disorder with anxiety. He had a family history of glaucoma and no known allergies. His medications included meloxicam and topiramate. He started topiramate two weeks ago for migraines and post-traumatic stress disorder (PTSD).

The emergency room physician assessed his pupils as equal, round, and reactive to light with no afferent pupillary defect and confrontation visual fields as full to finger counting. A basic blood panel and a CT scan were ordered to rule out an intracranial disease process, and the patient was sent to the eye clinic for further evaluation. The CT scan came back unremarkable.

Initial Presentation

The patient's uncorrected vision was 20/150 in the right eye and 20/200 in the left eye with pinhole acuity of 20/20 in each eye. Pupils were equal, round, and reactive to light with no afferent pupillary defect. Confrontation visual fields were full to finger counting and extraocular motilities were full and smooth. Manifest refraction was -3.00sph with vision correctable to 20/20.

Slit lamp examination revealed diffuse conjunctival injection with corneal haze and microcystic edema. The anterior chamber was shallow and quiet. Intraocular pressure was measured at 37 mmHg in the right eye and 42 mmHg in the left eye by Goldmann applanation tonometry at 8:00am. Gonioscopy revealed no structures in any quadrant of either eye with a bowed iris approach and no frank neovascularization, angle recession, or posterior anterior synechiae.

At this point, several differential diagnoses were considered given the elevated intraocular pressures alone. These differentials included: primary open angle glaucoma, primary angle closure glaucoma, secondary angle closure glaucoma, bilateral Posner-Schlossman, and bilateral Fuch's heterochromic iridocyclitis. The leading differentials were primary and secondary angle closure glaucoma because the angles were occludable on gonioscopy and the anterior chambers showed no signs of inflammation. The bilateral, simultaneous presentation in an otherwise healthy, young male with recent history of topiramate use made the eye clinic ultimately choose secondary angle closure as the diagnosis.

First, the intraocular pressure was lowered with one drop of brimonidine and one drop of Cosopt into each eye. Thirty minutes later, intraocular pressure decreased to 33 mmHg in the right eye and 35 mmHg in the left eye. Then, the patient was dilated with one drop of cyclopentolate 1% into each eye and the pressure was checked again thirty minutes later at 30 mmHg right eye and left eye. The anterior chamber already showed signs of deepening. Dilated fundus examination did not show signs of glaucomatous optic neuropathy and RNFL/GCC/Macula OCTs were unremarkable.

At this point, the eye clinic felt the patient's pressure had decreased sufficiently to release him from the hospital. He was diagnosed with bilateral angle closure secondary to topiramate. He was prescribed cyclopentolate 1% twice a day in each eye and asked to return to the eye clinic the next day. He was told to stop topiramate. The psychiatrist who prescribed topiramate was notified.

Follow-Up #1: Day 2

The following day, the patient reported that his symptoms had already improved. He explained that he was off topiramate and compliant with cyclopentolate as prescribed. His uncorrected vision was 20/200 in each eye with pinhole acuity of 20/20 in each eye. His pressure by Goldmann was 22 mmHg in each eye at 8:00am. The anterior chamber was now deep and gonioscopy was unoccludable with a flat iris approach and no peripheral anterior synechiae. The patient was told to continue cyclopentolate 1% twice a day in both eyes and to return in two days.

Follow-Up #2: Day 4

Two days later, the patient reported complete resolution of all symptoms. He no longer experienced headaches, blurry vision, or light sensitivity. He was still compliant with the eye drops. His uncorrected vision was 20/20 in each eye, pressure by Goldmann was normotensive at 14 mmHg in the right eye and 13 mmHg in the left eye with gonioscopy open to ciliary body in all quadrants and a flat approach. Small areas of peripheral anterior synechiae were seen.

The patient was told to discontinue cyclopentolate 1% and to return in one month. He was told to return sooner if he ever became symptomatic again. The patient was lost to follow up. Table 1 shows a summary of all findings and measurements.

	Day 1	Day 2	Day 4
VA: OD	20/200	20/200	20/20
OS	20/200	20/200	20/20
IOP: OD	37 mmHg	22 mmHg	14 mmHg
OS	42 mmHg	22 mmHg	13 mmHg
Gonio: OD	NS 360°	pTM 180° aTM 180°	CB 360° (+) PAS @ 1-2
OS	NS 360°	pTM 180° aTM 180°	CB 360° (+) PAS @ 6-7

Table 1. A summary of clinician findings and measurement across multiple visits.

Differential Diagnoses

Primary Angle Closure

The most important differential to exclude is primary angle closure. This can be due to either anatomically narrow angles or plateau iris syndrome. They both present with shallow anterior chambers, elevated intraocular pressure, and corneal edema. Treatment includes peripheral iridotomies. Primary angle closure can be differentiated from topiramate angle closure in that, unlike topiramate angle closure, primary angle closure is generally unilateral, exacerbated by dim illumination, and more common in hyperopic patients.

Secondary Angle Closure

Topiramate is one kind of secondary angle closure. However, it still needs to be distinguished from other kinds of secondary angle closure, including: phacomorphic, and neovascular. Phacomorphic angle closure occurs after a large intraocular lens creates irido-trabecular touch, and neovascular angle closure is a result of blood vessel proliferation that zips the angle closed. These secondary etiologies can be differentiated by gonioscopic evaluation.

Other differential diagnoses considered in this case included bilateral Posner-Schlossman syndrome and bilateral Fuchs' heterochromic iridocyclitis. Posner-Schlossman syndrome typically presents with unilateral episodes of markedly elevated intraocular pressure associated with mild anterior chamber inflammation, whereas our patient presented with bilateral involvement, no anterior chamber reaction, and a recent medication trigger. Similarly, Fuchs' heterochromic iridocyclitis often presents with low-grade inflammation, iris heterochromia, and secondary open-angle glaucoma, none of which were observed.

Similar Medications

Studies suggest that angle closure can be induced by sulfa-drugs other than topiramate. These include acetazolamide, hydrochlorothiazide, and cotrimoxazole. The proposed pathophysiology is similar in that edema creates swelling and rotation of the ciliary body.⁸ Therefore, all patients who present with bilateral angle closure after recently starting a sulfa-drug should be considered to have a medication induced angle closure.

DISCUSSION

This case report describes a patient who presented with bilateral angle closure secondary to topiramate. Angle closure was diagnosed by intraocular pressure, gonioscopic evaluation, and corneal haze. It was attributed to topiramate because it was bilateral and had the appropriate timeframe. Topiramate is most likely to cause angle closure within two weeks of initiation.

This case presented classically and made diagnosis straightforward. However, diagnosis may be complicated in patients who have concomitant phacomorphic changes or pathological angles. B-scan can prove helpful in these situations. Remember that topiramate causes effusion of not just the ciliary body, but also of the choroid. B-scan will show thickening of both these structures. Skilled clinicians may also be able to identify a rotated appearance to ciliary body on gonioscopy. Anterior OCT may provide a helpful, quantitative analysis of how the angle improves throughout treatment.

The etiology of an angle closure is critical because treatment of primary and secondary angle closures differ dramatically. Whereas cycloplegia of primary angle closure is contraindicated, cycloplegia of secondary topiramate angle closure is warranted. This allows the ciliary body to relax, and it returns the ciliary body and iris-lens apparatus to their proper configurations.

CONCLUSION

A patient with bilateral angle closure secondary to topiramate is reported. The patient's condition improves after treatment with cycloplegia and discontinuation of topiramate. All prescribers need to educate patients taking topiramate on angle closure as a potential side effect, and all eyecare providers need to be wary of bilateral, simultaneous angle closure.

REFERENCES

1. FDA. *Highlights of Prescribing Information: Topamax*. Accessed May 30, 2020. www.fda.gov/medwatch.
2. Johnson BA, Ait-Daoud N, Bowden CL, et al. Oral topiramate for treatment of alcohol dependence: A randomised controlled trial. *Lancet*. 2003;361(9370):1677-1685. doi:10.1016/S0140-6736(03)13370-3
3. The Top 300 of 2020. Accessed May 30, 2020. <https://clincalc.com/DrugStats/Top300Drugs.aspx>
4. Topiramate - Drug Usage Statistics, ClinCalc DrugStats Database. Accessed May 30, 2020. <https://clincalc.com/DrugStats/Drugs/Topiramate>
5. Maryanoff BE. Phenotypic Assessment and the Discovery of Topiramate. *ACS Med Chem Lett*. 2016;7(7):662-665. doi:10.1021/acsmedchemlett.6b00176
6. Topiramate - Wikipedia. Accessed May 30, 2020. <https://en.wikipedia.org/wiki/Topiramate>
7. Topiramate-Induced Angle Closure. Accessed May 30, 2020. <https://webeye.ophth.uiowa.edu/eyeforum/cases/283-topiramate-induced-angle-closure.htm>
8. Case Report: Bilateral acute angle closure glaucoma associated with hydrochlorothiazide-induced hyponatremia. Accessed May 30, 2020. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4256597/>