IDENTIFYING A RARE AND REVERSIBLE OCULAR SYNDROME IN TOPIRAMATE-TREATED PATIENTS: ACUTE MYOPIA AND SECONDARY ANGLE CLOSURE GLAUCOMA

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ABSTRACT

Topiramate has been used in more than 1.25 million patients worldwide for epilepsy, migraine, bipolar disorder, depression, neuropathic pain, psychosis, and obesity. A rare (n = 54 as of March 1, 2002) ocular syndrome has been observed: acute myopia and secondary angle closure glaucoma. Secondary angle closure glaucoma is usually recognized by the acute decrease in visual acuity and/or the presence of ocular pain. Important clinical points based on observation of these patients include: 1) the rapid onset (usually within 2 weeks of treatment initiation, up to 1 month); 2) the bilateral increase in pressure (up to 50 to 60 mm) and shallowing of anterior chambers; 3) no predictors or risk factors have been identified and pre-existing pathology (e.g., glaucoma, narrow angles) is not a contra-indication; 4) it is an acute event with no evidence of asymptomatic, chronic progression; 5) occurrence is easily identifiable by symptoms; 6) the myopia is detectable with an ophthalmoscope; and 7) the condition resolves with treatment discontinuation.

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Topiramate is an antiepileptic drug that is currently under investigation for the treatment of several disorders, including migraine. Its exact mechanism of action in migraine is not fully known. To date, topiramate has been used in more than 1.25 million patients worldwide to treat epilepsy, migraine, bipolar disorder, depression, neuropathic pain, psychosis, and obesity. Topiramate is an unusual antiepileptic agent in that it is the first in this class of drugs to be associated with weight loss; most antiepileptic drugs are associated with weight gain. From the broad clinical experience of this drug, a rare ocular syndrome has been observed: acute myopia and secondary angle closure glaucoma. Glaucoma is a group of diseases with the potential to produce optic nerve damage and visual field loss, primarily due to retinal ganglion cell/axon loss. It is characterized by elevated intraocular pressure and is classified by the open or closed state of the angle of the anterior chamber behind the lens of the eye.

Secondary angle closure glaucoma in topiramate treatment is usually recognized by the acute decrease in visual acuity and/or the presence of ocular pain. Ophthalmic examination shows a significant myopic shift of as much as 6 to 8 diopters, bilateral elevation of intraocular pressure, and bilateral shallowing of the anterior chambers. Pupil dilation is an inconsistent finding.

Of the more than 1 million people treated with topiramate, 75 cases of acute myopia and secondary angle closure glaucoma have been reported to the Food and Drug Administration and Johnson & Johnson. Of those 75, 54 cases (as of March 1, 2002) were due to
this ocular syndrome. The remaining 21 cases were associated with previous glaucoma or did not fit the syndrome. This form of ciliary block glaucoma secondary to drug treatment is not specific to topiramate. It has been observed and reported with several other drugs such as acetazolamide, dichlorphenamide, hydrochlorothiazide, quinine, sulfamethoxazole, sulfonamides, and tetracycline. Many of these reported cases were single-patient cases.

In the 54 topiramate-treated patients, the mean age was much younger than is typically seen in glaucoma patients: 34 years vs typical age of onset of 40 plus years. In fact, the ages ranged from 5 to 70 years, with almost one half occurring in those younger than 36 years (Figure 1). There was a high woman-to-man ratio of 9:1; this high ratio may be explained by the demographics of those who take topiramate. Migraine is more prevalent in women, and the potential weight-loss effects of the drug make it an appealing choice of therapy for many women.

The mean onset of symptoms was 7 days after treatment initiation, ranging from 1 day to 49 days. Sixty-six percent of the cases were observed by day 10, and 91% were observed by day 14 (Figure 2). The doses associated with onset of symptoms are of particular interest. The doses ranged from 25 mg to 150 mg (53-mg mean dose). Almost half (47%) of the cases were observed in patients taking low doses of topiramate (25 mg to 50 mg) (Figure 3).

The outcomes were positive: the signs and symptoms resolved when topiramate was discontinued; intraocular pressure fell within 24 hours. However, resolution of myopia occurred in 4 to 5 days, and in some cases it took up to 1 week. It is important to note that 1 case did not resolve and this patient did not stop topiramate treatment. Seventeen of the 54 patients were treated with laser iridotomy with no benefit.

Following is a list of key points in the clinical identification of acute myopia and secondary angle closure glaucoma in topiramate treated patients:
• The rapid onset can occur within 2 weeks of treatment initiation and it can continue up to 1 month.
• There is bilateral increase in pressure (up to 50 mm to 60 mm) and shallowing of anterior chambers.
• Predictors or risk factors have not been identified and pre-existing pathology (e.g., glaucoma, narrow angles) is not a contraindication.
• It is an acute event with no evidence of asymptomatic, chronic progression.

• Occurrence is easily identifiable by symptoms, even in young children and nonverbal patients.
• The myopia is detectable with an ophthalmoscope.

This rare syndrome is easily and quickly identifiable after topiramate treatment initiation, and it is reversible with drug discontinuation. Patient education can lead to early detection and, thus, appropriate medication adjustments. There are no predisposing risk factors.

REFERENCES


