

A Review of the Ocular side effects of Topiramate

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Abstract

Acute angle closure glaucoma and visual blurring due to induced myopia have been reported with the use of the antiepileptic drug topiramate. Various hypotheses have been put forward to explain the mechanism of the aforementioned ocular side effects. These presumed ocular side effects of topiramate have included patients treated with other drugs such as serotonin reuptake inhibitors which are also reported to cause angle closure glaucoma and myopia. The review examines the available evidence on the mechanisms, the risk factors, patient characteristics and treatment of acute angle closure glaucoma associated with the use of topiramate.

Topiramate

Pharmacology: It is a sulfamate-substituted monosaccharide derived from D-fructose, which acts through a number of mechanisms which include inactivating the sodium gate channels, modulation of calcium dependant action potentials, hyperpolarising K⁺ currents, inhibition of kainate-mediated conductance and activating GABA postsynaptic receptors. In addition it also has some anti carbonic anhydrase activity. Topiramate is rapidly absorbed after oral administration and has a half life of 24 hours, being rapidly excreted in the urine(1, 2, 3).

Indications: Topiramate a new antiepileptic drug is used both as monotherapy and as an adjunct in the control of partial and primary generalised epilepsy in adults and children above the age of two(4-6). Effectiveness in migraine prophylaxis, trigeminal neuralgia, bipolar disorders, depression and eating disorders have also been reported(7-11). It has recently been reported to be effective in the management of idiopathic intracranial hypertension due to its anti carbonic anhydrase activity and its associated induction of weight loss (12-14)

Adverse ocular side effects.: Data collected from spontaneous reporting systems have identified one hundred and fifteen cases of ocular side effects which include acute-onset angle closure glaucoma, acute myopia, suprachoroidal effusions, peri-orbital oedema, scleritis, blepharospasm, oculogyric crisis, nystagmus and diplopia(15, 16).

Acute Angle Closure Glaucoma (AACG)(15-27)

The mean age of occurrence of secondary AACG is 34 years with a range between 3 years and 70 years. The condition has predominantly been reported in females (80%). It occurs within 2 weeks of initiation of treatment (range 1- 49 days) with doses ranging between 50mgs to more than 100mgs.

Patients present with blurred vision, headaches or nausea and vomiting with findings characteristic of an acute attack of angle closure glaucoma. Conventional and high frequency ultrasound demonstrated choroidal or cilio-choroidal detachments.

Refractive errors: The pre-existing refractive errors ranged from +4.00 dioptres to - 5.25 dioptres(18, 21-23). The refraction was reported in one child was + 4.00dioptres in an amblyopic eye and +1.50 dioptres in the other(22). In the majority of cases the visual acuity was reported as normal after the resolution of the attack of AACG which suggests no significant refractive error existed.

Mechanism of AACG. Ciliary body oedema or cilio-choroidal detachments causes a forward rotation of the ciliary body which displaces the iris forward to close the anterior chamber angle precipitating an attack of secondary AACG(28,29). Swelling of the lens may also contribute to the shallow anterior chamber(25). In patients on topiramate this was demonstrated by high frequency or standard ultrasound (17, 18, 21, 23, 30). A few patients were on SSRI's, in addition to topiramate, which are known to precipitate AACG in patients with pre-existing narrow angles(31, 32).

Though the configuration of the anterior chamber has not been mentioned it is possible that they may have contributed to the precipitation of an attack of AACG.

Treatment.: Topiramate should be discontinued and an alternative prescribed in discussion with the treating neurologist.

The initial treatment should include cycloplegia, in an attempt to displace the iris- lens plane posteriorly, topical and systemic ocular hypotensives and topical steroids.

Caution has been suggested with the use of acetazolamide, a sulfamated drug, concurrently with the continued use of topiramate for fear of inducing renal calculi and further ciliary body oedema. Laser peripheral iridotomy used in 23% of reported

cases has not been uniformly effective in relieving the secondary angle closure and should be reserved for cases where the above treatment fails. Rapid resolution of angle closure glaucoma associated with the use of topiramate has been reported in a 35 year female with the use of mannitol and methylprednisolone after failure to respond to acetazolamide, topical ocular hypotensives and atropine (33).

Screening: In a small study on Chinese patients treated with topiramate screening with clinical examination which included anterior chamber depth measurement, gonioscopy and ultrasound biomicroscopy failed to pick up any asymptomatic disease (34).

Screening patients on topiramate for asymptomatic disease is not recommended.

Acute Myopia (15, 16,20-22, 25, 36, 37)

Acute myopia between 2 to 8.75 dioptres, presents in adults(15,16, 20-22, 25, 26, 36) and children(37) with sudden bilateral blurring of vision. As topiramate is a sulphamated preparation, the mechanism of acute myopia is similar to that reported with sulphonamides(38, 39) and acetazolamide(40, 41). The severity of ciliary body oedema, cilio-choroidal detachment and forward movement of the iris lens diaphragm stopping short of an acute attack of glaucoma. Myopia may precede and persist after resolution AACG. Myopia on its own resolves following discontinuation of the drug.

Extra-ocular adverse effects (3, 11)

Diplopia and Nystagmus have been reported in 14% to 15% of those patients on high doses of topiramate.(3). Scleritis, including posterior scleritis has been reported in four cases, oculogyric crisis in two cases and single cases of blepharospasm , myokymia, periocular oedema, paresthesias and periocular pain(14). It is also reported to cause a significant weight loss when used to treat patients with idiopathic intracranial hypertension (13).

In summary Topiramate an antiepileptic drug, licensed for use in children above the age of 2 years and adults has been reported to be associated with blurring of vision which is due to acute myopia or acute secondary angle closure glaucoma. The underlying mechanisms of these adverse events are similar to sulphonamides and acetazolamide with ultrasonically demonstrable swelling of the ciliary body, cilio-choroidal detachment and forward

displacement of the iris lens diaphragm. Effective treatment includes topical and systemic ocular antihypertensive medications with discontinuation of topiramate. Though angle closure glaucoma occurs in eyes with no particular risk factors, a number of patients may be medicated with SSRI's which may aggravate the glaucoma by adding an element of pupil block.

Recommendations

1. Parents of children or patients initiated on topiramate should be warned of the possible ocular side affects.
2. In case of visual blurring or ocular pain initial advice from their local optometrist should be encouraged.
3. Patients referred to Ophthalmologists with acute myopia should consider drug replacement following advice from a neurologist
4. Acute angle closure glaucoma should be managed with 1.) Withdrawal or replacement of topiramate with an alternative drug. b) topical atropine drops and topical ocular hypotensives agents. c) Cautious use of oral acetazolamide
5. Pre symptomatic screening is not useful.

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