



Ocular side effects of Topiramate- Frequently asked questions

1. What is Topiramate and when is it indicated clinically?

Topiramate is a sulfamate-substituted monosaccharide derived from D-fructose. Its is used mainly as an antiepileptic drug both as mono-therapy and as an adjunct in the control of partial and primary generalised epilepsy in adults and children above the age of two¹⁻³. Effectiveness in migraine prophylaxis, trigeminal neuralgia, bipolar disorders, depression and eating disorders has also been reported⁴⁻⁸. Recently it is been used to treat idiopathic intracranial hypertension^{9, 10}. In an open label study it has been show to be as effective as acetazolamide in the treatment of intracranial hypertension¹¹.

2. How does topiramate work?

It, acts predominantly by inactivating the sodium and or calcium gate channels, hyperpolarising K⁺ currents, inhibition of kainate-mediated conductance and activating GABA postsynaptic receptors¹². 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^{13, 14}. Its possible mechanism of reduction of intracranial pressure is related to its inhibition of carbonic anhydrase activity¹⁵ and perhaps its induction of weight loss¹¹.

3. What are the reported ocular side affects of topiramate?

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 diplopia¹⁶.

4. Which patients develop Acute Angle Closure Glaucoma? (AACG)

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%). A number of these patients may be medicated with SSRI's (selective serotonin reuptake inhibitors) in addition to topiramate, which may aggravate the glaucoma by adding an element of pupil block¹⁶⁻²⁸

5. How soon is angle closure glaucoma seen after initiation of topiramate?

It occurs within 2 weeks of initiation of treatment (range 1- 49 days)¹⁶⁻²⁸.

6. Is the onset of AACG dose related?

No. AACG occurs with doses ranging between 50mgs to more than 100mgs¹⁶.

7. How do patients present clinically?

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 detachments¹⁶⁻²⁸.

8. Is pre-existing hypermetropia necessary for patients started on topiramate to develop AACG?

No.

The pre-existing refractive errors ranged from +4.00 dioptres to -5.25 dioptres. The refraction was reported in one child was + 4.00dioptres in an amblyopic eye and +1.50 dioptres in the other. 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. Hence pre-existing hypermetropia is not a prerequisite for development of AACG secondary to topiramate therapy^{19, 23-24}.

9. What is the mechanism of development 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. Swelling of the lens may also contribute to the shallow anterior chamber. In patients on topiramate this was demonstrated by high frequency or standard ultrasound. A few patients were on SSRI's, in addition to topiramate, which are known to precipitate AACG in patients with pre-existing narrow angles. 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^{29, 30}.

10. What treatment should be initiated in AACG secondary to topiramate?

Topiramate should be discontinued and an alternative prescribed in discussion with the primary physician. 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 fails¹⁶⁻²⁸. Rapid resolution of an attack has been reported with the use of intravenous methylprednisolone and mannitol³¹.

11. Can blurring of vision be associated with the development of Acute Myopia?

Acute myopia between 2 to 8.75 dioptres, presents in adults and children with sudden bilateral blurring of vision^{16, 20-22, 24, 32-35}. As topiramate is a sulphamated preparation, the mechanism of acute myopia is similar to that reported with sulphonamides^{36, 37} and acetazolamide^{38,39}. 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 causes myopia. Myopia may precede and persist after resolution AACG. Myopia on its own resolves following discontinuation of the drug.

12. What are the Extra-ocular adverse effects of topiramate?

Diplopia and Nystagmus have been reported in 14% to 15% of those patients on high doses of topiramate. 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^{16, 40}. Weight loss has been reported in a group of patients treated with topiramate for idiopathic intracranial hypertension¹¹.

13. What advice can be given to patients or parents of children started on topiramate?

Parents of children or patients initiated on topiramate should be warned of the possible ocular side effects. In case of visual blurring or ocular pain initial advice from their local ophthalmologist should be encouraged.

14. What should an ophthalmologist do when dealing with side effects associated with topiramate?

Patients referred to Ophthalmologists with blurring of vision or acute myopia should consider drug replacement following advice from a neurologist. Acute angle closure glaucoma should be managed with

- Withdrawal or replacement of topiramate with an alternative drug
- topical atropine drops and topical ocular hypotensives agents
- intravenous mannitol

15. Is routine screening for asymptomatic disease warranted?

No. The incidence or prevalence of AACG in the population of patients treated with topiramate is not known. A prospective pilot study using an ultrasound biomicroscope failed to show angle narrowing in a group of patients aged 18 years to 75 years over a four week period⁴¹. Routine screening for possible ocular side effects hence cannot be recommended.

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