

A Review of the Ocular side effects of Topiramate

Author: Patrick Watts

This manuscript was reviewed by Paediatric Ophthalmology Subcommittee, Royal College of Ophthalmologists

Address for Correspondence:
Mr Patrick Watts
Department of Ophthalmology
University Hospital of Wales
Cardiff CF14 4XW

Telephone: (+44) 2920748583
Fax: (+44) 2920748240

Keywords: Topiramate, Glaucoma

Abstract

Acute angle closure glaucoma and visual blurring due to induced myopia have been reported with the use of a new antiepileptic drug topiramate. Various hypotheses have been put forward to explain the mechanism of the aforementioned ocular side effects. Presumed ocular side effects with topiramate have included patients treated with serotonin reuptake inhibitors and other drugs associated with the induction of 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, which acts by predominantly by inactivating the sodium gate channels, hyperpolarising K⁺ currents 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).

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(3-5). Effectiveness in migraine prophylaxis, trigeminal neuralgia, bipolar disorders, depression and eating disorders have also been reported(6-10).

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(11).

Acute Angle Closure Glaucoma (AACG)(11-23)

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 dioptries to -5.25 dioptries(14, 17-19). The refraction was reported in one child was + 4.00dioptries in an amblyopic eye and +1.50 dioptries in the other(18). 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(24, 25). Swelling of the lens may also contribute to the shallow anterior chamber(21). In patients on topiramate this was demonstrated by high

frequency or standard ultrasound (13, 14, 17, 19, 26). A few patients were on SSRI's, in addition to topiramate, which are known to precipitate AACG in patients with pre-existing narrow angles(27, 28). 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. 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.

Acute Myopia (11, 15-17, 20, 29, 30)

Acute myopia between 2 to 8.75 dioptres, presents in adults(11, 15-17, 20, 21, 29) and children(30) with sudden bilateral blurring of vision. As topiramate is a sulphamated preparation, the mechanism of acute myopia is similar to that reported with sulphonamides(31, 32) and acetazolamide(33, 34). 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 (11, 35)

Diplopia and Nystagmus have been reported in 14% to 15% of those patients on high doses of topiramate.(35). Scleritis, including posterior scleritis has been reported in four cases, oculoogyric crisis in two cases and single cases of blepharospasm , myokymia, periocular oedema, paresthesias and periocular pain(11).

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 antihypotensive 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

Bibliography

1. McNamara J. Pharmacotherapy of Epilepsies. Goodman and Gilman's: The Pharmacological Basis of Therapeutics 2006; Chapter 19:519-520.
2. U.S. Food and Drug Administration. Topomax (topiramate) tablets prescribing information. Available at: <http://www.fda.gov/medwatch/SAFETY/2003/tpamax.pdf>. Accessed January 29, 2006 2003.
3. Rosenfeld WE, Sachdeo RC, Faught RE, Privitera M. Long-term experience with topiramate as adjunctive therapy and as monotherapy in patients with partial onset seizures: retrospective survey of open-label treatment. *Epilepsia* 1997; 38 Suppl 1:S34-6.
4. Privitera MD. Topiramate: a new antiepileptic drug. *Ann Pharmacother* 1997; 31(10):1164-73.
5. Privitera MD, Brodie MJ, Mattson RH, Chadwick DW, Neto W, Wang S. Topiramate, carbamazepine and valproate monotherapy: double-blind comparison in newly diagnosed epilepsy. *Acta Neurol Scand* 2003; 107(3):165-75.
6. Brandes JL, Saper JR, Diamond M, Couch JR, Lewis DW, Schmitt J, et al. Topiramate for migraine prevention: a randomized controlled trial. *Jama* 2004; 291(8):965-73.
7. D'Amico D, Grazi L, Usai S, Moschiano F, Bussone G. Topiramate in migraine prophylaxis. *Neurol Sci* 2005; 26 Suppl 2:s130-3.
8. Arnone D. Review of the use of Topiramate for treatment of psychiatric disorders. *Ann Gen Psychiatry* 2005; 4(1):5.
9. McIntyre RS, Riccardelli R, Binder C, Kusumakar V. Open-label adjunctive topiramate in the treatment of unstable bipolar disorder. *Can J Psychiatry* 2005; 50(7):415-22.
10. Nickel C, Lahmann C, Tritt K, Muehlbacher M, Kaplan P, Kettler C, et al. Topiramate in treatment of depressive and anger symptoms in female depressive patients: a randomized, double-blind, placebo-controlled study. *J Affect Disord* 2005; 87(2-3):243-52.
11. Fraunfelder FW, Fraunfelder FT, Keates EU. Topiramate-associated acute, bilateral, secondary angle-closure glaucoma. *Ophthalmology* 2004; 111(1):109-11.
12. Thambi L, Kapcala LP, Chambers W, Nourjah P, Beitz J, Chen M, et al. Topiramate-associated secondary angle-closure glaucoma: a case series. *Arch Ophthalmol* 2002; 120(8):1108.
13. Rhee DJ, Goldberg MJ, Parrish RK. Bilateral angle-closure glaucoma and ciliary body swelling from topiramate. *Arch Ophthalmol* 2001; 119(11):1721-3.
14. Banta JT, Hoffman K, Budenz DL, Ceballos E, Greenfield DS. Presumed topiramate-induced bilateral acute angle-closure glaucoma. *Am J Ophthalmol* 2001; 132(1):112-4.
15. Myopia and glaucoma with topiramate. *Prescribe Int* 2003; 12(64):61.
16. Boentert M, Aretz H, Ludemann P. Acute myopia and angle-closure glaucoma induced by topiramate. *Neurology* 2003; 61(9):1306.
17. Chen TC, Chao CW, Sorkin JA. Topiramate induced myopic shift and angle closure glaucoma. *Br J Ophthalmol* 2003; 87(5):648-9.
18. Lin J, Fosnot J, Edmond J. Bilateral angle closure glaucoma in a child receiving oral topiramate. *J Aapos* 2003; 7(1):66-8.

19. Medeiros FA, Zhang XY, Bernd AS, Weinreb RN. Angle-closure glaucoma associated with ciliary body detachment in patients using topiramate. *Arch Ophthalmol* 2003; 121(2):282-5.
20. Blumenthal DT. Acute myopia and angle-closure glaucoma induced by topiramate. *Neurology* 2004;63(4):762; author reply 762.
21. Craig JE, Ong TJ, Louis DL, Wells JM. Mechanism of topiramate-induced acute-onset myopia and angle closure glaucoma. *Am J Ophthalmol* 2004;137(1):193-5.
22. Cereza G, Pedros C, Garcia N, Laporte JR. Topiramate in non-approved indications and acute myopia or angle closure glaucoma. *Br J Clin Pharmacol* 2005;60(5):578-9.
23. Mansoor Q, Jain S. Bilateral angle-closure glaucoma following oral topiramate therapy. *Acta Ophthalmol Scand* 2005;83(5):627-8.
24. Liebmann JM, Weinreb RN, Ritch R. Angle-closure glaucoma associated with occult annular ciliary body detachment. *Arch Ophthalmol* 1998;116(6):731-5.
25. Fourman S. Angle-closure glaucoma complicating ciliochoroidal detachment. *Ophthalmology* 1989;96(5):646-53.
26. Sankar PS, Pasquale LR, Grosskreutz CL. Uveal effusion and secondary angle-closure glaucoma associated with topiramate use. *Arch Ophthalmol* 2001;119(8):1210-1.
27. Kirwan JF, Subak-Sharpe I, Teimory M. Bilateral acute angle closure glaucoma after administration of paroxetine. *Br J Ophthalmol* 1997;81(3):252.
28. Eke T, Carr S. Acute glaucoma, chronic glaucoma, and serotonergic drugs. *Br J Ophthalmol* 1998;82(8):976-8.
29. Bhattacharyya KB, Basu S. Acute myopia induced by topiramate: report of a case and review of the literature. *Neurol India* 2005;53(1):108-9.
30. Coats DK. Bilateral angle closure glaucoma in a child receiving oral topiramate. *J Aapos* 2003;7(4):303.
31. Bovino JA, Marcus DF. The mechanism of transient myopia induced by sulfonamide therapy. *Am J Ophthalmol* 1982;94(1):99-102.
32. Hook SR, Holladay JT, Prager TC, Goosey JD. Transient myopia induced by sulfonamides. *Am J Ophthalmol* 1986;101(4):495-6.
33. Garland MA, Sholk A, Guenter KE. Acetazolamide-induced myopia. *Am J Obstet Gynecol* 1962;84:69-71.
34. Fan JT, Johnson DH, Burk RR. Transient myopia, angle-closure glaucoma, and choroidal detachment after oral acetazolamide. *Am J Ophthalmol* 1993;115(6):813-4.
35. Langtry HD, Gillis JC, Davis R. Topiramate. A review of its pharmacodynamic and pharmacokinetic properties and clinical efficacy in the management of epilepsy. *Drugs* 1997;54(5):752-73.