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Letter to the Editors

Topiramate in non-approved indications and acute myopia or angle closure glaucoma

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Topiramate is an antiepileptic drug with potentially serious adverse effects. In placebo-controlled trials, myopia was seen in 1% of children and abnormal vision in 13% of adults under the drug. In 2001, postmarketing experience led the US Food and Drug Administration to warn about a new syndrome consisting of acute myopia associated with secondary angle closure glaucoma, and this was added to its labelling.

Up to March 2004, the Spanish System of Pharmacovigilance has gathered six reports of myopia and two of glaucoma in eight patients treated with topiramate (see Table 1). In all cases the only suspect medicine was topiramate. Time to onset of symptoms was reported in seven cases; in five the reaction appeared within the first week. All cases of myopia recovered in less than 1 week after drug discontinuation. One patient with glaucoma was operated because initially the role of topiramate was not suspected as the cause. Alternative causes other than topiramate were excluded in most reports.

As in previous experiences, these complications occurred early in the course of therapy and they recovered shortly after drug discontinuation [1]. Strikingly, for the six patients for whom the indications for use were known, this was different from epilepsy, which was the only approved indication in Spain until April 2004.

The prevalence of epilepsy is low (4–10 per 1000) [2]. In more developed countries, where people are able to pay for new treatments, the prevalence is half that of less developed countries [3], and the majority of patients are already under treatment with one or more antiepileptic drugs. Thus, the market prospects for any pharmaceutical company developing a new antiepileptic drug are limited. Pharmaceutical companies, however, seek market expansion for their products by looking for

Table 1
Myopia or angle-closure glaucoma associated with topiramate

Sex/age	Reaction	Dose (mg day^{-1})	Induction period (days)	Recovery period (days)	Alternative cause	Indication for use
F/19	Myopia (7 diopters)	50	1	1	Excluded	Weight loss
F/34	Myopia (6 diopters)	25	≤6	≤7	Excluded	Unknown
F/40	Myopia (5 diopters)	100	≤30	3	Excluded	Anxiety and weight loss
M/42	Myopia	50	2	24	Excluded	Personality disorder
M/23	Myopia	25	1	1	Not excluded	Weight loss
F/15	Myopia	50	5	2	Excluded	Migraine
M/67	Glaucoma	25	30	Unknown	Not excluded	Neuropathic pain
M/–	Glaucoma	25	Unknown	Unknown	Not excluded	Unknown

regulatory approval of additional indications, by involving medical opinion leaders and others in clinical research in new indications, and even by illegally promoting off-label use [4]. Pressure to prescribe concentrates on patent protected medicines. Topiramate is one such drug. Its off-label use made up 14% of the US migraine prophylaxis market [5], before its recent approval for this indication.

Monitoring drug safety should not only focus on identifying adverse effects. Pharmacovigilance should be less drug-oriented and more patient-oriented. Had topiramate not been promoted and used for non-approved indications, the patients in the present series would not have developed such serious adverse effects, at the expense of uncertain or absent clinical efficacy in these indications.

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References

1 Thambi L, Kapcala LP, Chambers W, Nourjah P, Beltz J, Chen M, Lu S. Topiramate-associated secondary angle-closure glaucoma: a case series. Arch Opthalmol 2002; 120: 1106.

2 Shorron SD. Epidemiology, classification, natural history, and genetics of epilepsy. Lancet 1990; 336: 93–6.

3 Anonymous. In the shadow of epilepsy. Lancet 1997; 349: 1851.

4 Lenzer J. Pfizer pleads guilty, but drug sales continue to soar. BMJ 2004; 328: 1217.

5 Anonymous. Topiramate approvable in migraine prevention. Scrip 2004; 2904: 24.

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