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TOPIRAMATE (TOPAMAX®) USE IN TREATING NEUROPATHIC PAIN

Topiramate is a second generation anti-epileptic drug with a mixed profile of GABAergic and anti-glutamnergic action. This drug has been available in the United States since 1997 and in parts of Europe since 1995. Presently, the drug is approved for monotherapy in European countries, but to date, only as an adjunctive therapy in the United States.

To this date, the US-FDA has approved Topiramate as an add-on treatment for partial onset seizures, primarily generalized tonic-clonic and those seizures seen in Lennox-Gastaut syndrome among those two years or older. Based on the outcomes of the company-sponsored RCT (Randomized Controlled Trial), Ortho-McNeil has applied to the FDA for a Supplemental New Drug Application of Topiramate as a prophylactic treatment for individuals with migrainous headaches.

There are a number of case-series reports regarding the use of Topiramate in the treatment of bipolar disorders and obesity as well. There is also a recent Cochrane review on Topiramate as an add-on treatment for drug-resistant partial epilepsy – This Cochrane review concluded that the drug has an efficacy as an add-on treatment. Note should be made that there was a short duration of follow-up in most of the studies reviewed.

Side effects

The drug manufacturer claims that among adult patients receiving Topiramate as an add-on therapy at a dose of 200 to 400 mg/day, 11% of the patients discontinued the medication due to adverse events versus 6% discontinuance rate for those taking various “baseline” anti-epileptic drugs along with placebo. There were other independent studies that show a drop out rate of up to 50%.

In combination with other traditional anti-seizure medications, the side effects observed in adults (once again at a dose of 200 to 400 mg/day) are: somnolence (29%), dizziness (25%), ataxia (16%), speech disorders and related problems (13%), psychomotor slowing (13%), abnormal vision (13%), difficulty with memory (12%), paresthesia (11%), and diplopia (10%).

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There have been recent reports of secondary open angle glaucoma and acute myopia while taking the medication. This has occurred bilaterally in a number of patients. The vast majority of these cases occurred in female adults. The adults had symptoms lasting between 5 and 26 days after the initiation of Topiramate. It was suggested that if this condition was detected early and medication was stopped immediately, symptoms subsided within twenty-four hours.

Other studies show that Topiramate had a detrimental effect on the performance of skilled tasks in patients and may cause sedation, confusion and cognitive impairment. This was observed in somewhat over 5% of patients receiving the drug. Use of Topiramate was occasionally associated with tinnitus, ataxia, auditory hallucination and nephrolithiasis.

Why Topiramate?

Primary medical research suggests that there are similar pathophysiological and biochemical mechanisms at play in epilepsy and neuropathic pain. Based on this association, it is hypothesized that anti-convulsant agents may be useful in the treatment of neuropathic pain.

Evidence on the efficacy and effectiveness of Topiramate on treating neuropathic pain

As of today, there are very few published reports (all small case series) on the application of Topiramate in treating neuropathic pain. These reports show that Topiramate is not effective in treating centrally-mediated pain or trigeminal neuralgia. One case report in a patient with intercostal neuralgia showed significantly reduced pain. Another study with 40 patients showed that both Amitriptyline and Topiramate were effective in controlling pain – all individuals had a diagnosis of diabetic peripheral neuropathy.

Conclusion

To date, there is no high level evidence to support the efficacy of Topiramate in treating neuropathic pain. There is low level anecdotal evidence that suggests this medication may be beneficial in treating diabetic peripheral neuropathy and intercostal neuralgia. It is also worthwhile mentioning that, in general, there is very little information on this medication. With that in mind, and recognizing that you may see increasing requests for “approval” of this medication, we would suggest that you take some of the above into account, recognizing what little evidence there is, and also recognizing that there is really little information on this subject. Certainly, clinical judgement in each individual case would be required here.

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