

Topiramate for migraine prevention

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Topiramate is an option for migraine prevention in patients suffering from frequent migraines or when less frequent attacks are so severe in degree as to warrant prophylaxis.

What is topiramate?

Topiramate (Topamax) was introduced as an anticonvulsant in the early 1990s. It has several actions that may be relevant to its anticonvulsant effect, including sodium channel blockade and effects on gamma-aminobutyric acid (GABA) and alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors. As is often the case with migraine prophylactic agents, the basis for its effect in migraine is speculative.

When is it used?

Topiramate is an option for migraine prevention in patients suffering from frequent migraines or when less frequent attacks are so severe in degree as to warrant prophylaxis. There are many effective

prophylactic agents to choose from and few truly comparable studies of efficacy. Most neurologists would regard all the first-line prophylactic agents to have roughly similar efficacy, except for methysergide, which is probably more potent than the rest. The choice of agent, therefore, is often based on its side-effect profile and how the patient in question would be affected in each case (Table).

In practice, prior to its PBS listing, topiramate has been an attractive choice when other older agents have failed and especially if the patient is overweight. The PBS listing provides subsidised treatment for migraine prevention in patients who have experienced an average of three or more migraines per month over a period of at least six months and who:

- have a contraindication to beta blockers, as described in the relevant TGA-approved product information, or
- have experienced intolerance of a severity necessitating permanent withdrawal during treatment with a beta blocker, and
- have a contraindication to pizotifen because the weight gain associated with this drug poses an unacceptable risk, or
- have experienced intolerance of a severity necessitating permanent withdrawal during treatment with pizotifen.

Intolerance to two previous therapies (pizotifen and propranolol) is sufficient

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to qualify for PBS subsidy, however, inefficacy of previous other treatments is not. It seems that this PBS decision is based on there being insufficient scientific demonstration that topiramate is effective when other agents have failed, despite widespread anecdotal experience. Consequently, topiramate may be used according to the PBS guidelines or prescribed as a private script for suitable patients outside of the guidelines mentioned above.

How is it used?

Topiramate should be titrated gradually, beginning at 25 mg nightly for one week. The dosage can then be increased weekly in increments of 25 mg/day. If side effects such as drowsiness develop as the dose is increased, one can cut back to the previous dose and titrate more slowly.

The usual dose of topiramate for migraine is 50 mg twice a day. Some patients may respond sufficiently at a dose of 50 mg/day whereas others benefit from increasing the dose to 200 mg/day. Overall, titration and final daily dose should be guided by the individual patient's response to the drug and whether side effects are a problem.

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Table. Associated side effects of agents for migraine prevention

Agents	Typical problems
Older agents	
Amitriptyline	Dry mouth, drowsiness
Clonidine	Variable efficacy
Cyproheptadine	Weight gain
Methysergide	Retroperitoneal fibrosis
Pizotifen	Weight gain, drowsiness
Propranolol	Asthma, Raynaud's phenomenon
Sodium valproate	Weight gain
Verapamil	Variable efficacy, constipation, ankle oedema
Newer agents	
Botulinum toxin A	Expense, variable efficacy
Candesartan	Hypotension
Topiramate	Dysphasia, paraesthesiae, weight loss

What needs monitoring?

There is no requirement for routine blood tests in patients taking topiramate, but bicarbonate levels should be measured if there is suspicion of metabolic acidosis; serum topiramate levels are unhelpful. Clinical monitoring is generally sufficient with particular attention to recognised side effects.

Common side effects

Side effects of topiramate are mostly dose related and are less troublesome when it is used for migraine than epilepsy as the doses are typically lower. (The usual doses of topiramate for epilepsy are 200 to 400 mg/day.) There are four main types of side effects, as listed below.

- CNS effects may include drowsiness, dizziness, somnolence and an unusual problem with word-finding. There may also be an increased incidence of depression in patients taking this medication.
- Carbonic anhydrase inhibitor effect may result in metabolic acidosis. This

effect may also contribute to the following two problems, which are rare but important to recognise:

- aggravation or precipitation of renal calculus
- a syndrome consisting of acute myopia associated with secondary angle closure glaucoma.
- Paraesthesia in hands and feet is a common problem in patients taking topiramate for migraine. Most patients find this tolerable if they know it is reversible, not unexpected and does not indicate sinister pathology.
- Reduced appetite and weight loss may occur; occasionally there is anorexia of a more troublesome degree. As usual, there are a number of rare idiosyncratic effects, which are listed in the product information.

Important precautions

As for all anticonvulsants, abrupt withdrawal should be avoided to prevent provoking seizures even in nonepileptic

patients. Use of topiramate in pregnancy or during lactation is not recommended as safety has not been established. Patients with a history of nephrolithiasis, glaucoma or depression would not be ideal candidates for treatment with this medication.

Interactions

There are only minor interactions of topiramate with most other medications. These are listed in detail in the product information. There appear to be no important interactions with oral contraceptive agents. Of course, care is required when other agents producing similar side effects (especially drowsiness) are used with topiramate.

How will the availability of topiramate change migraine treatment?

Overweight patients, in particular, have until now faced substantial limitations in their options for migraine treatment. Overall, if migraine prophylaxis is required and the traditional drugs have been unsatisfactory, it is important to remember that there are usually other viable options; the introduction of topiramate highlights this point. MT

This article is for general information purposes only, and the full product information should be consulted before prescribing any of the mentioned medications.

COMPETING INTERESTS: Associate Professor Stark has acted as a consultant to Janssen-Cilag, Allergan and Pfizer. He has received speaker fees from Janssen-Cilag.

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