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Waitemata District Health Board
Best Care for Everyone

TOPIRAMATE – TITRATE AND HYDRATE

- START AT A LOW DOSE AND TITRATE TO EFFECT
- WARN ABOUT OCULAR PAIN AND VISUAL IMPAIRMENT
- ENCOURAGE ADEQUATE FLUID INTAKE ESPECIALLY DURING EXERCISE OR WARM TEMPERATURES
- BE AWARE OF EMERGING OR WORSENING DEPRESSION OR SUICIDALITY
- PROVIDE EDUCATION ABOUT CONTRACEPTION

Topiramate is an antiepileptic medicine that can be given alone or as adjunct therapy. It is used for generalised tonic-clonic seizures and partial onset seizures. Topiramate is also indicated for migraine prophylaxis.[1]

START AT A LOW DOSE AND TITRATE TO EFFECT

For optimum benefit, it is recommended that topiramate should be initiated using a low dose, followed by slow titration to an effective dose. For all indications, dose titration should be guided by clinical outcome.[2]

The recommended starting dose for newly diagnosed epilepsy or migraine prophylaxis is 25mg at night for one week. The dose should then be gradually increased each week, as tolerated, in increments of 25mg until an effective dose is reached. This can take 4-6 weeks, but some people may require longer intervals between dose adjustments if side effects, such as drowsiness, become troublesome.[2]

For migraine prophylaxis, the recommended daily dose is 100mg per day in divided doses. Some people will experience relief at just 50mg per day; others may require up to 200mg per day.[2]

If topiramate is not helpful after 3-4 months at the maximum tolerated dose, slowly titrate off and try an alternative option.

People with epilepsy usually require higher doses; the optimal dose depends on whether topiramate is used as a monotherapy or add-on therapy. Refer to the datasheet for more detailed dosing information and for recommended doses in children.[2]

If there is hepatic impairment, a lower dose is generally required because the clearance of topiramate will be decreased. If there is renal impairment, it will take longer to reach plasma steady state levels, so it is recommended to use half the regular starting and maintenance dose.[2]

Note: If topiramate needs to be discontinued, withdrawal must be done gradually because there is an elevated risk of seizures following rapid withdrawal *regardless of whether there is a history of seizures or not.*[2]

WARN ABOUT OCULAR PAIN OR VISUAL IMPAIRMENT

Topiramate is associated with a syndrome that presents as acute myopia and can progress to secondary angle closure glaucoma; this applies to children as well as adults, and is not dose-related.

Visual symptoms can occur within one month of initiating topiramate,[2] and may present as blurred vision, headaches, nausea and vomiting. If ocular pain or visual impairment occurs, topiramate should be discontinued as soon as possible,[2] and refer to an ophthalmologist for advice. Elevated intraocular pressure can lead to permanent loss of vision if left untreated.[1]

ENCOURAGE ADEQUATE FLUID INTAKE ESPECIALLY DURING EXERCISE OR WARM TEMPERATURES

Decreased sweating and an increase in body temperature, especially after exposure to elevated environmental temperatures, have been reported with topiramate use.

Everyone taking topiramate should be informed about the likelihood of increased body temperature, especially during hot weather, and to ensure adequate hydration.[1] Take special care with children and people taking other medicines that predispose to dehydration and decreased sweating such as anticholinergic medicines.[1,2]

Note: Topiramate is associated with a risk of renal stone formation (nephrolithiasis), which can be increased if dehydrated or in hot climates.[1] This risk is further increased if other medicines that predispose to renal stone formation are used concurrently eg long-term corticosteroids.

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TOPIRAMATE

BE AWARE OF EMERGING OR WORSENING DEPRESSION OR SUICIDALITY

Although the overall risk is small, everyone taking antiepileptic medicines should be monitored for notable changes in behaviour that could indicate the emergence or worsening of suicidal thoughts or depression.[3,4] In clinical trials, suicide-related events occurred in 0.5% of people taking topiramate, compared with 0.2% with placebo.[2]

The risk appears to be similar with antiepileptic medicines used for any indication.[5] These thoughts and behaviours can occur as early as one week after starting the medicine.[3] Psychiatric and behavioural disturbances that have been observed with topiramate are generally dose-related.[2]

PROVIDE EDUCATION ABOUT CONTRACEPTION

Women using combined oral hormonal contraceptives and high-dose topiramate (greater than 200mg daily), may be at an increased risk of breakthrough bleeding and possible contraceptive failure because topiramate induces ethinylestradiol metabolism.[6,7] Contraceptive efficacy can be decreased even in the absence of breakthrough bleeding.[2] When prescribing an oral contraceptive with topiramate, consider a product with at least 35-50micrograms of ethinylestradiol.[6,7]

Topiramate is classified as pregnancy category D, so is considered to be teratogenic.[1] Although there are no studies using topiramate in pregnant women, data from pregnancy registries indicate that there is an increased risk of congenital malformation.[2]

All women of child bearing potential receiving antiepileptic medicines should receive pregnancy counselling,[8] and folic acid 5mg per day.[9] Women with epilepsy who are planning a pregnancy should be referred for specialist advice; the combined input of a neurologist and an obstetrician is usually required.[9]

Migraine

If migraine attacks are frequent, investigate potential provoking factors such as stress, sleep deprivation, alcohol use, or pharmacological triggers eg nitrates or combined oral contraceptives.[10]

Consider preventive treatment if there are:

- at least two attacks a month
- an increasing frequency of headaches
- significant disability despite receiving treatment for acute attacks, or if treatment options are not tolerated or unsuitable[10]

Explain that the goal is to reduce the frequency of acute attacks; they may still occur even with prophylaxis.[11] Options for prophylaxis include beta-blockers (such as propranolol, atenolol, metoprolol, nadolol, or timolol), or topiramate.

Unapproved options include sodium valproate, gabapentin, or tricyclic antidepressants such as amitriptyline.[10] The choice of therapy generally depends on individual factors such as comorbidities and tolerability.[11]

A Cochrane review of 17 studies concluded that topiramate (100mg per day) is effective for the prophylaxis of episodic migraine in adults, and was reasonably well tolerated.[12]

NICE recommends that either topiramate or propranolol can be offered for prophylactic treatment of migraine according individual preference, comorbidities and risk of adverse events.[13]

Note: The efficacy of topiramate for the acute treatment of migraine has not been evaluated.[2] Access to acute treatments will still be needed, even if prophylaxis is prescribed.[11]

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