

Are Headaches Preventable? New Ideas in Migraine Prophylaxis (2000)

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Options in the acute therapies of migraine have and will continue to increase exponentially. Unfortunately similar rates of expansion in prophylactic therapies have not as yet occurred. Fortunately, a number of pharmacological and non-pharmacological strategies are available, with several new promising areas of investigation.

Indications for prophylactic treatment include: frequent headaches, severe impact of headache on lifestyle, failure of acute treatment, and complications of migraine such as prolonged aura or migraine stroke. Goals of prophylactic therapy must be determined early in treatment and should focus on reduction of headache frequency, severity, and duration which result in improved function and quality of life. The use of headache calendars which monitor headache frequency, intensity, duration, trigger factors, intake of medication is absolutely essential to monitor progress. In general, medications should be started at low dose and titrated slowly, allowing adequate treatment duration, before adding or replacing medications.

The choice of which agent or agents to use is based on a number of factors. There are only four approved preventive medications for migraine. These are methysergide, propranolol, timolol, and divalproex sodium. These are the only agents subjected to rigorous double-blind placebo controlled studies and approved for use by the FDA for migraine. Other beta blockers, heterocyclic antidepressants, and calcium channel blockers have been used extensively, as well. Other agents have been successful in a number of cases however, including monoamine oxidase inhibitors, such as phenelzine and tranylcypromine, and the SSRI antidepressants. The newer antiepileptic drugs gabapentin, lamotrigine, topiramate, and tiagabine are also viable alternatives that need further study.

Adverse event profiles are important in choosing medication and include considerations of life-style (e.g. exercise intolerance with beta-blocker, potential sexual dysfunction and weight gain with antidepressants, etc.) Comorbidity is likely one of the most important factors in choosing which agent to use. Be aware of comorbid medical problems which may contraindicate a given preventive medication such as asthma and beta blockers, NSAIDs and hyperacidity syndromes or renal disease, etc. At the same time be aware of therapeutic opportunities such as beta blockers with migraine and hypertension or mitral valve prolapse, anti-depressants with migraine and comorbid depression or anxiety disorders, and valproate in migraine and epilepsy or bipolar disease.

Botulinum toxin A injected prophylactically in facial musculature has produced significant improvement in a cohort of migraineurs studied in a recent multi-center trial, and further study may be very productive.

Recently the use of long-acting opioids has been shown to be beneficial in a limited segment of the chronic population who fail to respond to aggressive traditional therapies for a sufficient period of time including hospitalization and who do not have histories of substance abuse or other contra-indications to opiate maintenance. Choices include methadone, long-acting morphine sulfate, and long-acting oxycodone.

Non-steroidal anti-inflammatory agents have been used widely in the treatment of migraine. Another class of anti-inflammatory agents, known as leukotriene modifiers has not been studied to date in regard to their possible role in the treatment of migraine. The name, "leukotriene", is derived from the parent molecule having been originally isolated from leukocytes and its 3 double bond carbon backbone, in series, constituting a triene, in their structure. Both prostaglandins and leukotrienes are derived from the metabolism of arachidonic acid, with prostaglandins coming off the cyclooxygenase pathway and leukotrienes derived via the enzyme, 5-lipoxygenase. Both prostaglandins and leukotrienes mediate inflammatory responses. The latter have been studied in regard to their role in the pathophysiology of asthma. Clinical observation of a decrease in migraine frequency in patients with comorbid asthma, on montelukast or zafirlukast prompted us to explore a possible role for leukotriene modifiers in the treatment of migraine. A prospective, open label study, evaluating the efficacy of 10 or 20mg of montelukast in the prophylaxis of migraine in 17 patients resulted in 53% showing a greater than 50% reduction ($p < .025$) in the frequency of severe attacks, with 41% showing a greater than 60% reduction. Responders, including modest responders, rated the drug as excellent.

Non-pharmacologic regimens are essential in migraine prophylaxis. Education of the patient is likely the major non-pharmacologic measure that we all employ. It is essential for patients to understand the origins of their disorder, factors contributing to exacerbations such as triggers and life-style, rationale for therapy, and what they can and can't expect from you and treatment.

Non-pharmacologic measures may include, diet modification, vitamins such as riboflavin, supplements such as magnesium, herbs such as feverfew, and lifestyle changes including stress management, proper nutrition, cognitive behavioral therapy, biofeedback, relaxation training, exercise, and the like. Where significant psychiatric co-morbidity exists such as Axis I and II disorders appropriate referral needs to be considered, hopefully to a colleague that is knowledgeable in regard to the neurobiological origins of migraine.

CONCLUSION:

Increased options for migraine prophylaxis in the hands of knowledgeable health care professionals will improve the quality of life for migraine patients around the world. Principles of management of the acute headache and a grasp of the concepts of prophylactic care are essential in successful treatment and better outcome. The combined uses of pharmacologic prophylactic agents, non-pharmacologic techniques, and complimentary therapies can make improved control and quality of life a reality for sufferers.

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