



Prophylaxis in Migraine Management

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ABSTRACT

A migraine is the most common cause of severe, recurring headache. With the recent advances in our understanding of migraine, it can be effectively treated and even prevented. Prophylactic treatment of migraines is indicated when patients have three or more severe migraine attacks a month that interfere with quality of life or when attacks are prolonged and symptomatic medication used alone is not satisfactory. The major objective of migraine prophylactic therapy is optimizing the patient's ability to function normally by reducing the frequency, duration, and intensity of attacks. The major migraine preventive therapies include β -blockers, calcium-channel blockers, and tricyclic medications. Preventive treatment should be tailored to individual patient needs. This requires that patient and healthcare professionals understand the rationale and participate actively in decisions regarding therapeutic intervention.

Key words: Migraine, migraine management, prophylaxis

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INTRODUCTION

Migraine is a chronic condition with episodic attacks, which are characterized by severe pulsating headache, usually associated with autonomic disturbances with freedom from symptoms between attacks. The most frequent types of migraine are those with aura and without aura. A migraine without aura is characterized by repeated attacks of headache lasting between 4 to 72 hours. In 60% of the attacks, the headache is restricted to one side.^[1] It is pulsating, of moderate to severe intensity, and aggravated by physical activity. In its typical form, it is accompanied by nausea, vomiting, photophobia, and phonophobia. Migraine with aura is characterized by neurological symptoms and deficits, which are generally localized in cortical areas or in the brain stem. These symptoms take 5-20 minutes to develop and they disappear completely in

less than 60 minutes. Within an hour after the cessation of the neurological symptoms, the typical headache starts. It is accompanied by autonomic disturbance. Some of the migraine subtypes are migraine with prolonged aura (>60 minutes), familial hemiplegic migraine, basilar migraine, ophthalmoplegic migraine, and retinal migraine. Its etiology is not yet fully understood, but it is believed that, in addition to a genetic predisposition, abnormal vascular reactivity such as dilation of cranial blood vessels is a major contributor, possibly in combination with sensitization of sensory nerve fibers and neurogenic inflammation.

During the last two decades, tremendous advances have evolved in our understanding of migraine pathophysiology. However, the effective management of this disorder often remains a challenge. The factors that predispose an individual to migraine, and the triggers that precipitate

migraine attacks in susceptible individuals, remain unknown. Traditionally, acute treatment and non pharmacological treatment such as behavioral and lifestyle changes including trigger avoidance, prevention, assurance, and patient follow-up have all been essential elements of migraine management.^[2]

Epidemiology

Migraines affects 10-12% of the general adult population. About 10% of migraineurs have attacks with aura while others have attacks without aura. It is found to be three times more common in females than males. It is more common among Whites than Blacks and Asians. The peak prevalence is encountered in the age group of 25–55 years old. Over 80% of migraineurs have a family history of migraines.^[3] The diagnosis of a migraine is generally made according to the criteria of the International Headache Society. In children, the diagnostic criteria do not differ from those in adults except for the duration of an attack, which normally lasts only 2 hours compared with 4 hours in adults. As there is evidence that the incidence of migraines is increasing in children, the availability of a clearly evaluated effective therapy seems to be more and more important.^[4]

Prophylactic treatment

Treatment for migraine attacks can be divided into symptomatic treatment and prophylactic. Symptomatic treatment should be started as early as possible for once the attack is fully developed, oral preparations become less effective. For many patients with mild-to-moderate migraine attack, simple oral analgesics such as aspirin, acetaminophen, ibuprofen, or analgesic combinations may be effective. The addition of metaclopramide/ domperidone shows a faster relief. For moderate-to-severe attacks, ergotamine, dihydro ergotamine, and the triptans are very effective. However, the current focus is shifted to prevention, which is being increasingly recognized as the ideal treatment in a majority of case.^[5]

Preventive medicines should be offered to patients whose quality of life is diminished by frequent migraine attacks. It has been observed that many patients who would benefit from preventive therapy do not receive it. Many might benefit from an earlier and more aggressive use of prophylactic treatment. The primary goal of preventive therapy is to minimize the disability caused by migraine pain and to potentially modulate the course of disease progression. Physicians have long recognized that the episodic migraines slowly evolved into chronic forms

with poor treatment outcomes.^[6] Timely use of preventive treatment limits this transformation. Prevention is a primary consideration in those patients whose migraines are not successfully treated by acute -care medications leading to overuse syndrome. Patients with contra indications or poor tolerance to acute treatment are also candidates for preventive therapy.^[7]

The major objectives of migraine prophylactic therapy are optimizing the patient's ability to function normally by reducing the frequency, duration, and intensity of migraine attacks and improving responsiveness to acute treatment and quality of life of migraine sufferers. Prophylactic treatment needs to be considered in conditions such as frequent headaches, significant interference with a patient's daily routine activities despite acute treatment, contraindication of acute therapies or failure to avoid their overuse, adverse events, and patient preference. Prophylactic treatment is also beneficial in the presence of uncommon migraine conditions, including hemiplegic migraine, migraine with prolonged aura or migraines infarction, and the patient's desire to reduce the frequency of acute attacks.^[8]

Methods to improve the efficacy of preventive medication are also suggested. Medications with high efficacy and low adverse effects are to be preferred. Co-existing conditions have to be considered while receiving treatment. Co-existent disease should not be contraindicated to the migraine treatment. A drug that treats more than one condition may be selected. The choice of preventive drug must be tailored to individual needs and influenced by drug interaction and the need to treat comorbidities such as asthma, tension type headache, depression, and insomnia. The treatment should start with a low dose and then gradually increase to an optimal dose over a period of 1 month and be maintained for 6 months. A long-acting formulation can improve compliance. The patient has to maintain a headache diary. If the headaches are controlled at 6 months, consider tapering or discontinuing the treatment.^[9]

Pharmacotherapy

A basic principle of preventive treatment is to start the drug at a low dose and increase the dose slowly. Patients should be involved in the treatment process and their preferences regarding cost, drug delivery, dosage schedule, and tolerability should be considered when choosing a course of action. In addition, educating patients about the goals, use, and appropriate expectations of migraine preventive therapies is crucial to maximizing the chances

for therapeutics success. In fact, preventive medications are considered effective if the frequency of attacks is reduced by more than 50%.

Treatment strategies

Prophylactic therapy strategies fall into three basic categories: episodic (pre-emptive), short term (mini-prophylactic), and chronic. Preventive episodic treatment should be considered if the headache trigger is known. For example, if exercise often leads to an attack, the patient can be instructed to take medication prior to the activity. Short-term prevention is used when exposure to the trigger is time limited, such as flying at high altitude or menstruation. For longer-term needs, chronic treatment can be used for months or years.

Pharmacological agents

The major classes of agents available for prophylactic treatment include calcium antagonists (flunarizine), serotonin receptor antagonists (methysergide, lisuride), beta-adrenergic blockers, antidepressants, antiepileptic (sodium valproate), non steroidal agents, and anticonvulsants. Among the drugs used for prophylaxis in migraine, flunarizine is found to be very effective in adults as well as in children. It is also recommended for the prevention of migraine variants such as cyclical vomiting migraine and abdominal migraine. It is the most preferred drug in cases of headache occurring at night causing disturbed sleep. Flunarizine is observed to be more effective than propranolol in prophylaxis of migraine without aura. A dose of 5-10 mg per day is recommended for migraine prophylaxis. Unlike β -blockers, it can be safely used by asthmatic as well as diabetic patients. It is contraindicated in atrioventricular block and sinus-sick syndrome. Among β -blockers, propranolol is the most preferred drug. β -blockers are chosen when the frequency of headache is low and intensity is high. They are contraindicated in sinus bradycardia, congestive heart failure, asthma, and diabetes mellitus.^[10]

Tricyclic medications are used when the frequency of headache is high but intensity is low. It is contraindicated in glaucoma, prostate hypertrophy, epilepsy, and cardiac disease. Other option blockers in the prevention of migraine are angiotensin Type II receptor blockers such as candesartan. Anticonvulsants such as valproic acid, topiramate, and gabapentin have been proven to be effective in the treatment of migraines in randomized, placebo-controlled trials. Lamotrigine has been proven to be effective in controlling migraine aura, but its

effectiveness in controlling migraine headaches is yet to be proved. The selection of a drug should be based primarily on efficacy, with due consideration of comorbid psychiatric or medical disease, patient preference, and patient compliance.^[11]

Newer prophylactic medications under development include botulinum toxin and tizanidine. Studies demonstrated that botulinum toxin A has the potential to reduce the frequency and severity of migraine attacks. The mechanism by which botulinum toxin A prevents headache is not clear. Tizanidine is an alpha-2 adrenergic agonist that is indicated for spasticity associated with multiple sclerosis and other diseases. Studies have indicated that tizanidine holds promise for the prophylaxis of chronic daily headache, migraine, chronic tension type headache, and in the detoxification from analgesic rebound headache.^[12]

Since glutamine is implicated in the genesis of aura, and possibly migraine pain, there has been growing interest in the use of memantine, the new N-methyl-D-aspartic acid (NMDA) receptor antagonist, in the prophylaxis of migraine and refractory headache. Phytotherapies have offered an alternative source of therapy for migraine and gained much importance in prophylactic treatment. The aqueous extract of *Sapindus trifoliatus* has exhibited significant 5-HT_{2B} receptor inhibition and moderate platelet serotonin release inhibition, thus interfering with the pathogenesis of a migraine. Acupuncture is another alternative form of therapy that claims to lead to persistent, clinically relevant benefits for patients with chronic headache, particularly migraine.^[12]

Patient Compliance

There are several factors that could explain poor adherence, the most importance being patient's expectation of complete eradication of migraine attacks. As with any daily medication, the degree of patient compliance can have an important impact on patient outcomes. This could explain the low therapeutics gain seen with migraine preventive medications. Patients should understand the rationale for their particular therapy and know what adverse events may occur. As noted above, patients should be educated to have reasonable expectations from their prophylactic medications and realize that it may take several months to achieve their full benefit. This information is very useful in assessing therapy outcomes.^[13]

Patient counseling

Once the decision to initiate prophylaxis has been made,

the patient must be educated about the nature and goals of prophylactic therapy. Patients need to understand that complete freedom from headaches is not generally an attainable goal. They also need to understand that all of the current prophylactic agents are associated with side effects, although many of these effects diminish over time. Many of the medications employed for migraine prophylaxis are associated with weight gain. Hence, the patients should be counseled to deal with the possibility of weight gain. Patients also need to be counseled that some prophylactic medications may take weeks or even months before they are fully effective. Some patients may need additional abortive medications to ease the transition from abortive to prophylactic therapy. Many patients have the mistaken idea that prophylaxis will last for the rest of their lives. They need to understand that the goals of prophylaxis is to stabilize the migraine mechanism; once the patient responds and patient is headache-free for several months to a years, the drug may be withdrawn. In many cases, patients will remain headache-free for an extended period, a phenomenon that suggests that prophylaxis may favorably alter migraines.^[14]

CONCLUSION

The primary aim of preventive therapy is to decrease the frequency of attacks of migraine headache. As few as two disabling attacks per month is an indication for starting preventive therapy in many patients. Preventive migraine treatment should be tailored to individual patient needs; this requires that the patient understand the rationale and participation activity in decisions regarding therapeutic intervention. The choice of the initial and subsequent preventives is based on the patient's physical and mental

condition and associated symptoms. One should start from the lowest dose of the drug and titrate up to the highest dose tolerable to receive the clinical effect.

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