

Review Article

Incidence, prevention and treatment of migraine

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ABSTRACT

Migraine is the second most common type of headache worldwide. It is estimated to affect about one sixth of population. Despite being a primary headache, it is severe, incapacitation, and disturbing normal daily life activity. Therefore, researchers and neuroscientists were and are still endeavouring to understand the basic mechanisms of migraine and its preventive strategies. Treatment of migraine is also a subject of continuous interest. Prevention of migraine is the cornerstone of migraine management. It is achieved by reducing exposure to risk factors, prophylactic treatment of recurrent migraines, and acute treatment prior to exposure to precipitating factors. Treatment of migraine refers to the acute management of headaches when they occur. Many medications are available for abortion or relief of headache, and the choice of which depends on many factors such as the patients' comorbidities, the headache characteristics and severity, the associated symptoms, the adverse events, and the patients' preferences. This article will review and discuss the incidence of migraine, its preventive measures, and treatment updates.

Keywords: Incidence, Migraine, Prevention, Treatment

INTRODUCTION

Migraine is the second most common type of headache and the third most common disease worldwide after tension headache and dental caries. It is estimated that about one sixth of the population (14.7%) have migraine.^{1,2} Despite being a primary type headache, migraine is always severe and debilitating, and migraine attacks have a significant impact on patients' quality of life. Migraine is diagnosed when a patient experiences at least five attacks of headache characterized by at least two of the four criteria: to be pulsatile in nature, to be unilateral, to be severe, or to be aggravated by physical

activity.³ These attacks must be associated with nausea and/or vomiting or photophobia and/or phonophobia. Each attack typically lasts for a couple of hours but may continue up to 72 hours if not properly treated.^{3,4}

Management of migraine requires a multidisciplinary approach that should put the patient at its centre. It is often recommended that the treatment plan is to be tailored according to each particular patient. This is because each patient has his own risk factors, comorbidities, drug preference, lifestyle, adverse events, and pain threshold. Successful treatment imposes putting all these factors into consideration during planning for management. Treatment of migraine is divided into

abortive (or acute) treatment to abort or ameliorate the migraine attacks and preventive (or prophylactic) treatment that aims at preventing the migraine from recurrence or at least reducing the frequency, severity, or duration of the migraine attacks.⁵ This article will discuss the incidence of migraine, its preventive, and its treatment.

INCIDENCE OF MIGRAINE

Migraine is a very common neurological disorder. It is the second most common type of headache after tension headache, and the most common headache seen by physicians at headache clinics.² Migraine is estimated to affect about 14.7% of population and, therefore, is considered the third most common disease worldwide.² It affects one in each seven individuals and is more common among women.⁶ Migraine affects from 4% to 9% of men and about 11% to 25% of women.⁷

In a study exploring the incidence of migraine among 2563 individuals in 2015, results showed that the average incidence of migraine was 2.38%. The incidence among women was slightly higher (2.98%) than men (1.93%).⁸

PREVENTION OF MIGRAINE

Because migraine attacks are always severe and last for hours, prevention of these attacks is more important than their treatment. When a migraineur experiences an episode of headache, he cannot continue his work or normal daily activity on that day.⁴ Migraine increases the percentage of work absenteeism and reduce the productivity. Thus, prevention of migraine is the cornerstone regimen of treatment. Prevention of migraine headaches includes avoidance of risk factors, early treatment of possible attacks during exposure to risk factors, and maintained preventive therapy.^{9,10}

The main aims of preventive migraine therapy are to reduce the frequency of migraine headache, to reduce the severity of the attack, to shorten the duration of the migraine episode, to enhance the response to abortive medications during headache episodes, to reduce the financial cost, and to improve the patients' quality of life.¹⁰ Prevention is not indicated to all patients with migraine. It is estimated that about 38.8% of migraineurs need prevention.¹¹ The indications for adopting preventive measures are frequent headaches occurring at least four times monthly, recurrent severe headaches interfering with quality of life, hemiplegic or basilar types of migraine, failure of abortive migraine therapy, development of adverse events of abortive medications, overuse of abortive drugs, and patient's preferences.¹² Patients who decide to take preventive treatment even if they experience just a single attack every few months but these attacks are severe enough to negatively impact their quality of life, their preference should be respected. Successful preventive therapy does not necessarily require complete negation of headaches. Instead,

successful prevention is defined as reduction of at least 50% of headache frequency, severity, or duration, or an increase in the headache response to abortive medications over a three months follow-up period.¹⁰

The first type of preventive therapy is to prophylactically treat potential impending migraine attacks when exposure to a known trigger is expected. For instance, patients who have history of exercise-induced migraine or migraine exacerbated with sexual activity should be given a single dose of abortive medications (such as indomethacin) prior to exposure to these established triggers.¹³ Abortive medications may also be given on a short-term basis for patients who are exposed to longer-lasting migraine triggers such as menstruation and ascending to high altitudes.¹⁴ Those patients would benefit taking daily triptans or non-steroidal anti-inflammatory drugs (NSAIDs) all through the menstrual period or during the duration of stay on high altitudes.¹⁵ Control of other risk factors is also essential for migraine prevention e.g. weight loss and avoidance of psychological stress.¹⁶

The second type of preventive therapy is to maintain the patient on long-term medications to abort future attacks, reduce their frequency, shorten their duration, or ameliorate their severity. This is indicated specifically for patients with recurrent severe headaches, frequent headaches (more than four episodes per month), failure of acute treatment, or certain types of migraine (e.g. basilar migraine or hemiplegic migraine).¹⁰ Many medications were approved for long-term prevention of migraine. Those medications include beta-blockers, antiepileptic drugs, antidepressants, calcium channel blockers, botulinum injections, and others.¹⁷ The choice of medication depends on the patient age, gender, comorbidities, previous response to similar medications, adverse events profile, and patients' preference. The general rule in using any migraine-preventive drug is to start low, with the lowest possible effective dose, and to go slow, raising the dose slowly over time to maximize the benefit.¹¹ Adequate time to monitor the response to any given medication should be given (from 2 to 6 months) before judging its effectiveness.¹⁸ Monotherapy is generally preferred to combination therapy, and success is considered when the medication reduces the headache frequency, duration, or severity at least 50% of the presenting condition. Preventive therapy should be continued for at least six to nine months to prevent relapse.¹⁰

Tricyclic antidepressants (e.g. amitriptyline) are the treatment of choice in young-aged migraineurs with depression or insomnia.¹⁹ However, they should be avoided in elderly, cardiac, or epileptic patients. Tricyclic antidepressants can result in confusion, mouth dryness, and excessive sedation in elderly, can exacerbate arrhythmias in cardiac patients, and can reduce seizure threshold in patients with epilepsy. Antiepileptic drugs (particularly topiramate, valproate, and lamotrigine) are the second most preferred migraine-preventive agents.

They suit elderly patients, cardiac patients, epileptic patients, and those with bipolar disorder.²⁰ Topiramate is preferred in obese females because it helps weight loss. However, the resulting cognitive impairment and numbness limit their use among young females. Valproate is the best choice in patients with concomitant bipolar disorder because it acts as a mood stabilizer as well. Beta-blockers (e.g. propranolol) are highly effective medications, commonly prescribed to young men with migraine.²¹ The main adverse events associated are hypotension and bradycardia. Therefore, they are better to be avoided in most females (because their blood pressure readings are often low), in cardiac patients, and in patients with depression (because they may aggravate depressive symptoms). Calcium channel blockers (e.g. verapamil) are less often used because of the resulting constipation and cardiac conduction abnormalities.²² Other preventive medications include magnesium, riboflavin, and angiotensin converting enzyme inhibitors (ACEI).¹⁰

Invasive and non-invasive strategies can also be used in migraine prophylaxis such as botulinum injection and neuromodulation.²³ The approved neuromodulatory techniques for migraine prevention include greater occipital nerve blockage, occipital nerve stimulation, electric supraorbital nerve stimulation, vagal nerve stimulation, and trans-magnetic stimulation.²⁴

TREATMENT OF MIGRAINE HEADACHE

Acute treatment of migraine headache depends mainly on the severity of headache. The medications of choice in patients with mild headaches include acetaminophen or NSAIDs, whilst triptans and dihydroergotamines are preferred in patients with moderate to severe headaches.²⁵ Other less commonly used medications are codeine, tramadol, or opioids for analgesia.²⁶ If the associated nausea and vomiting were debilitating, an antiemetic should be offered. Metoclopramide is considered the most potent antiemetic drug approved for relief of migraine-associated nausea.²⁷ The main adverse events of this drug are QT interval prolongation and extrapyramidal side effects. Trials of Diphenhydramine failed to prove its efficacy in reducing migraine-associated nausea.²⁵

In migraineurs with mild headaches, paracetamol is often the first line of therapy preferred by most patients because of its low adverse events on gastric irritation.²⁸ The initial dose should be 1000 mg and it can be repeated after 2 hours if the migraine was not resolved. The maximum daily dose should be kept below 4 grams to avoid hepatotoxicity.²⁵ Despite being the first line of therapy, paracetamol is less effective than NSAIDs. The most commonly prescribed NSAID is ibuprofen because of its lowest gastric adverse events. Ibuprofen is administered in 400 mg doses and higher doses were not shown to be more effective.²⁸ Acetyl salicylic acid is as effective as sumatriptan and has a longer half-life than many other NSAIDs (about 6 hours), but can result in

severe gastric upset.²⁶ Naproxen is considered a potent NSAID with the longest half-life (14 hours), but it has a relatively slow onset of action (around 2 hours) making it less likely to be described.²⁵ Diclofenac potassium has the advantage of being available in powdered formulation that acts very rapidly within 15 minutes of administration. It also has a lower adverse events profile and a half-life of 2 hours. Diclofenac potassium is given in 50 mg doses, and the maximum daily dose is 150 mg.²⁹

For patients with moderate to severe migraines, triptans are the treatment of choice. Seven triptans are available in the market for treatment of migraine namely sumatriptan, eletriptan, rizatriptan, zolmitriptan, almotriptan, naratriptan, and frovatriptan.³⁰ No single triptan is more efficacious than another. Therefore, the choice of triptan depends on the patients' preference, the drug formulation available, the adverse events profile, and the patients' comorbidities. Generally, all triptans are contraindicated for patients with vascular diseases.³¹ Four triptans have a sulfa group in their structure and, therefore, they are contraindicated in patients who are sensitive to sulfa.²⁵ These four sulfa-containing triptans are sumatriptan, eletriptan, almotriptan, and naratriptan. If a patient developed an allergic reaction after taking one of these four agents, another non-sulfa containing triptan should be offered such as rizatriptan, zolmitriptan, or frovatriptan.²⁵ Sumatriptan is preferred by many physicians because it is available in subcutaneous formulation with a very rapid onset and low adverse events. Because water intake with oral triptans often exacerbates the nausea, triptans available in oral dissolving tablets formulation (e.g. rizatriptan and zolmitriptan) are preferred in patients with nausea and vomiting.³⁰ Some studies showed that naratriptan and frovatriptan are less effective. They also have a slower onset of action. This, they are the least commonly used triptans.³¹

Dihydroergotamine are the least used abortive migraine medications.³² They cause notable gastric upset and exacerbate nausea, and in a number of the patients, result in intolerable leg cramps and coldness.³³ If this occurred, they must be stopped immediately to avoid peripheral vascular ischemia. Codeine, tramadol, and opioids were studied in cases of migraine and were shown to be efficacious.²⁵ However, they should not be used to avoid substance use.

CONCLUSION

Migraine is a common and debilitating neurological disorder affecting a large proportion of population. Because of its disabling episodes, prevention is considered more important than acute management. Prevention strategies are various. They include control of the migraine risk factors, administration of analgesics prior to exposure to inevitable precipitating factors, and prescription of maintenance long-term prophylactic

agents in cases of recurrent or frequent headaches. The main medications available for migraine prophylaxis include beta-blockers, antidepressants, antiepileptic agents, calcium channel blockers, and vitamins. Abortive medications are used at the onset of the headache or aura. They include acetaminophen, NSAIDs, triptans, dihydroergotamines, and other analgesics. The choice of abortive therapy depends on the headache characters (e.g. severity and association), the patients' characteristics (e.g. age, co-morbidities, life style, history of allergy, and preference), and drug characteristics (e.g. adverse events, formulations, onset of action, and half-life). Each medication should be tailored to each patient.

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