Pharmacological Management of Acute Attacks of Migraine Headache: Clinical Practice Guideline

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Migraine headache is a common disorder seen in primary care. It affects 18% of women and 6% of men in the United States, almost half of who are undiagnosed and/or undertreated (1,2). This guideline, developed by the American College of Physicians-American Society of Internal Medicine and the American Academy of Family Practice (AAFP), with assistance from the American Headache Society (AHS), is based on the paper entitled, "Evidence-based Guidelines for Migraine Headache in the Primary Care Setting: Pharmacological Management of Acute Attacks," by Matchar, et al which can be found at www.aan.com/public/practiceguidelines/headache_gl.htm.[1] The target audience for this guideline is primary care physicians and it applies to patients with acute migraine attacks, with or without aura. Although this guideline is based on the above paper, our recommendations may differ based on differing thresholds of evidence needed to make a positive recommendation.

Diagnosis

Headache has many potential causes. The primary headache disorders, which include migraine, cluster, and tension-type headaches account for the majority of headaches. Secondary headaches, which are those with underlying pathology, are far less common. Migraine is a chronic condition with recurrent acute attacks, and its characteristics vary among patients, and often among attacks within a single patient. Migraine is a syndrome with a wide variety of neurologic and nonneurologic manifestations. The International Headache Society (IHS) has developed diagnostic criteria for migraine with and without aura. The IHS criteria (see appendix and for more detail visit their website at www.painforum.com/en/1/hcpmigihs.html) use both clinical features and laboratory tests to provide criteria of inclusion (features needed to establish a particular diagnosis) and exclusion (features that prevent assigning a particular diagnosis). This classification system serves to diagnose headache attacks, not patients. Thus, one patient could have more than one type of headache disorder. For example, it is not uncommon for migraine patients to also suffer from episodic tension-type headaches.

Treatment and Management

[1] In an effort to educate clinicians and patients about headache's impact, diagnosis, management, and prognosis, the US Headache Consortium was founded in 1996. The Consortium was made up of seven member organizations representing primary care, emergency medicine, neurology, and headache specialists. The objective of the US Headache Consortium was to develop scientifically sound, clinically relevant practice guidelines on chronic headache and particularly migraine, in the primary care setting. Five documents on headache and migraine were produced. These documents can be found on the American Academy of Neurology website (www.aan.com).

Effective long-term management of patients with migraine is challenging because of the complexity of the condition. Experts suggest several goals for successful treatment of acute attacks of migraine. These include treating attacks rapidly and consistently to avoid headache recurrence, in order to restore the patient's ability to function, and minimize the use of back-up and rescue medications.

Clinicians need to educate migraine sufferers about their condition and its treatment, and encourage them to participate in their own management. The physician must help the patient establish realistic expectations by discussing therapeutic options and their benefits and harms. Patient input can provide the best guide to treatment selection and helps the physician to better understand and accommodate patient treatment goals. Developing an effective acute migraine management strategy can be complex and an engaged patient is more likely to negotiate this process successfully. Encouraging patients to identify and avoid triggers and to be actively involved in their own management by tracking their own progress through daily flow sheets, etc. may be especially useful.

Once a diagnosis of migraine is established, patients and their health care providers should together decide how to treat acute attacks and whether the patient is a candidate for preventive medications *(see preventive treatment guideline)*. A wide range of acute treatments with varying efficacies is currently in use. A comprehensive review of the scientific literature, especially the data from randomized, controlled trials, provides a list of treatments that have been demonstrated to be effective in the management of acute migraine headache. It also provides a clear understanding of the adverse events associated with various agents.

The Headache Consortium's review of the evidence on antiemetics, barbiturate hypnotics, ergot alkaloids and derivatives, NSAID's, combination analgesics and non-opiate analgesics, opiate analgesics, triptans and others, found the there was good evidence of the efficacy of only a few agents in the treatment of acute migraine.

NSAID's

Their demonstrated efficacy and favorable tolerability makes these agents a first-line treatment choice for all migraine attacks including severe attacks that have been responsive to NSAID's in the past. Among the NSAID's, the most consistent evidence exists for aspirin, ibuprofen, naproxen sodium, tolfemanic acid, and the combination agent acetaminophen plus aspirin plus caffeine for the acute treatment of migraine. There is no evidence for the efficacy of acetaminophen alone.

Serotonin$_{1B/1D}$ Agonists "Triptans"

There is good evidence for the effectiveness of the PO triptans naratriptan, rizatriptan, sumatriptan, and zolmitriptan. Additionally, there is good evidence for the effectiveness of SC and IN sumatriptan, making it an option for patients with nausea and vomiting. Adverse effects of the triptans include chest symptoms but post-marketing data indicate that true ischemic events are rare. They are contraindicated in patients with risk for heart disease, basilar or hemiplegic migraine, or uncontrolled hypertension. Sumatriptan SC is

associated with a very rapid onset of action and naratriptan is associated with a slower onset of action.

Ergotamines

For the ergotamines, there is good evidence for the efficacy and safety of intranasal DHE as monotherapy for acute migraine attacks. The evidence was inconsistent to support efficacy of ergotamine or ergotamine/caffeine and the studies documented frequent incidence of adverse events.

Opioids

While it is well recognized that opiates are good analgesics, there is good evidence only for the efficacy of butorphanol nasal spray. Although commonly used, there are surprisingly few studies of opioid use in headache pain documenting whether overuse and the development of dependence are as frequent as clinically perceived. Until there is further data available, they may be better reserved for use when other medications cannot be used, when sedation effects are not a concern, and/or the risk for abuse has been addressed.

Others

There is fair evidence that suggests that the antiemetic metoclopramide IV may be an appropriate choice as monotherapy for acute attacks, particularly in the patient with nausea/vomiting when its sedating side effect may also be useful. Other agents used in practice such as IV corticosteriods, isometheptene, isometheptene combinations, and IN lidocaine are not effective.

Since patient responses to these therapies are not always predictable, individualized management is important. The choice of treatment should be based on, among other characteristics, the frequency and severity of attacks, the presence and degree of temporary disability and the profile of associated symptoms such as nausea and vomiting. The patient's history of, response to, and tolerance for, specific medications must also be considered. Coexisting conditions (such as heart disease, pregnancy, and uncontrolled hypertension) may limit treatment choices.

There are no studies to document the effectiveness of specific treatment schedules but experts suggest that acute therapy should be limited to no more than two times a week in order to guard against medication-overuse headache (or drug-induced headache). Medication-overuse headache is thought to result from frequent use of acute medication and is a pattern of increasing headache frequency often resulting in daily headaches. In patients with suspected medication overuse or patients at risk of medication overuse, consider preventive migraine therapy.

Although some use the term rebound headache interchangeably with the medication-overuse headache, rebound headache is distinct from medication-overuse headache. Rebound headache is associated with withdrawal of analgesics or abortive migraine medication. There is no uniform agreement about which agents can cause rebound

headache, although ergotamine (not DHE), opiates, triptans, and simple and mixed analgesics containing butalbital, caffeine, or isometheptene are generally thought to do so. There is less uniform opinion about other antimigraine agents.

Another clinical consideration is the use of a self-administered rescue medication for patients with severe migraine attack that is not responding to (or failing) other treatments. A rescue medication is an agent such as an opioid, neuroleptic, or butalbital containing compound, that the patient can use at home when other treatments have failed. While rescue medications often do not completely eliminate pain and return patients to normal activities, they permit the patient to achieve relief without the discomfort and expense of a visit to the physician's office or emergency department. A cooperative arrangement between provider and patient may extend to the use of rescue medication in appropriate situations.

Summary

There is now a body of evidence that points to effective first and second line agents for acute treatment of migraine. Beyond the choice of agent lies the choice of management strategy. Recently there has been increased interest and research in the areas of step care versus stratified care. Step care refers to the initial use of safe, effective, and inexpensive medications as first line agents in acute attacks of any severity. If the initial agent fails, a second line, more expensive, migraine-specific medication is then used. The stratified care model initially stratifies migraine attacks by severity, advocating migraine-specific agents for moderate to severe attacks, regardless of previous response to or an unknown response to other agents. Which approach is more effective is still an open question (3).

While managing the acute attacks, the clinician must also take into account the possible need for preventive therapy. Generally accepted indications for preventive therapy include: 1. two or more attacks a month that produce disability that lasts three or more days, 2. contraindication to, or failure of, acute treatments, 3. use of abortive medication more than twice a week, and 4. the presence of uncommon migraine conditions, including hemiplegic migraine, migraine with prolonged aura, or migrainous infarction.

Recommendations

Recommendation 1: For most migraine sufferers NSAID's are first line therapy.

To date, the most consistent evidence exists for aspirin, ibuprofen, naproxen sodium, tolfenamic acid (not available in the US), and the combination agent acetaminophen plus aspirin plus caffeine. There is no evidence for the use of acetaminophen alone.

Recommendation 2: In patients whose migraine attack has not responded to NSAID's, use migraine-specific agents (triptans, DHE).

There is good evidence for the following triptans (IM, PO, IN): naratriptan, rizatriptan, sumatriptan, and zolmitriptan, and for DHE nasal spray. There is little literature that demonstrates which triptans are more effective. Oral opiate combinations and butorphanol may be considered in acute migraine when sedation side effects are not a concern and the risk for abuse has been addressed.

Recommendation 3: Select a non-oral route of administration for patients whose migraines present early with nausea or vomiting as a significant component of the symptom complex. Treat nausea and vomiting with an antiemetic.

Evidence is limited, but in some patients, concomitant treatment with an antiemetic and an oral migraine medication may be appropriate. Antiemetics should not be restricted to patients who are vomiting or likely to vomit. Nausea itself is one of the most aversive and disabling symptoms of a migraine attack and should be treated appropriately.

Recommendation 4: Educate migraine sufferers about the control of acute attacks and prevention as essential components of care.

There is strong consensus about the need for educating migraine sufferers. The physician must help the patient establish realistic expectations by discussing therapeutic options and their benefits and harms, such as medication-overuse headache. Patient input can provide the best guide to treatment selection. Many migraine sufferers are candidates for preventive therapy. Generally accepted indications for migraine prevention include: 1. two or more attacks a month that produce disability that lasts three or more days, 2. contraindication to, or failure of, acute treatments, 3. use of abortive medication more than twice a week, and 4. the presence of uncommon migraine conditions, including hemiplegic migraine, migraine with prolonged aura, or migrainous infarction.

APPENDIX

The IHS classification is as follows:

Migraine without aura

A. At least five attacks fulfilling B-D
B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated).
C. Headache with at least two of the following characteristics:
    Unilateral location
    Pulsating quality
    Moderate or severe intensity (inhibits or prohibits daily activities)
    Aggravation by walking stairs or similar routine physical activity
D. During headache at least one of the following:

Nausea and/or vomiting
Photophobia and phonophobia

E. At least one of the following:
    1. History and physical and neurologic examination do not suggest one of the disorders causing secondary headaches (appendix 1).
    2. History and/or physical and/or neurologic examinations do suggest such disorders, but it is ruled out by appropriate investigations.
    3. Such disorder is present, but migraine attacks do not occur for the first time in close temporal relation to the disorder.

Migraine with aura

A. At least two attacks fulfilling B
B. At least three of the following four characteristics:
    1. One or more fully reversible aura symptoms indicate focal cerebral cortical and/or brain stem dysfunction.
    2. At least one aura symptom develops gradually over more than 4 minutes or two or more symptoms occur in succession.
    3. No aura symptom lasts more than 60 minutes. If more than one aura symptom is present, accepted duration is proportionally increased.
    4. Headache follows aura with a free interval of less than 60 minutes. (It may also begin before or simultaneously with the aura.)
C. At least one of the following:
    1. History and physical and neurologic examinations do not suggest one of the disorders in appendix 1.
    2. History and/or physical and/or neurologic examinations do suggest such disorder, but it is ruled out by appropriate investigations.
    3. Such disorder is present, but migraine attacks do not occur for the first time in close temporal relation to the disorder.

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