

Migraine: diagnosis and pharmacologic treatment in Emergency Department

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Abstract. – Acute headache is a common chief complaint in the Emergency Department (ED), accounting for up to 4% of all ED visits. Migraine is a common, chronic, at times incapacitating disorder, characterized by attacks of severe headache, autonomic nervous system dysfunction, and in some patients, an aura characterized by various neurologic symptoms. It is the most common cause of severe, recurring headaches. Although most headaches in the ED are benign, one should be vigilant in searching for “red flags”, which may represent dangerous conditions. In addition to properly identifying important secondary causes of headache, the goal of acute therapy is to provide rapid, complete, and sustained relief of pain and associated symptoms without generating significant adverse effects. In many patients, migraine responds well to simple treatment at the time of an attack. In patients with substantial disability, it is appropriate to prescribe a triptan early in the course of treatment, in keeping with a stratified approach to care.

Key Words:

Headache, Migraine, Triptans, Diagnosis, Therapy.

17.6% in females and 5.7% in males⁵. Therefore, it is important for the emergency physician to be conversant with the diagnosis and treatment of migraine^{6,7}. The challenge of treating migraine in the ED is often increased by lack of resources available for follow-up care for patients, who consequently may resort to using the ED as their primary source of headache management. Other factors unique to the ED environment that may also contribute to unsatisfactory treatment response include limited physician contact time that may preclude a detailed history, overuse of the ED by patients with substance abuse problems, overuse of opioids for headaches by emergency physicians, the need for rapid triage, the competing distraction of patients with life-threatening conditions, and directives for care dictated by the referring physician. Concerning the pathogenesis of migraine, it is now well known that migraine is not a primary vascular phenomenon⁸⁻¹⁰. The perturbation of serotonergic circuitry in the brainstem leads to intracranial and extracranial vasoconstriction and dilation and activates pain receptors of the trigeminovascular system. This knowledge is important in comprehending the rationale behind migraine pharmacotherapy, particularly acute treatments discussed below.

Introduction

Acute headache is a common chief complaint in the Emergency Department (ED), accounting for 5 million visits annually and up to 4% of all ED visits¹⁻³. Migraine is the most common cause of severe, recurring headache. It is ranked by the World Health Organization as number 20 among all diseases world-wide causing disability⁴. Estimates of the American Migraine Study suggest that 23 million persons older than 12 years of age have migraine headaches, with a lifetime prevalence of

Diagnosis of Migraine in the ED

Clinical Criteria

Migraine is characterized by episodes of head pain that is often throbbing, frequently unilateral and often severe^{8,11,12}. The cornerstone to assessing the patient with a headache is the medical history (particularly the onset, severity, and quality of the headache and associated symptoms as well as presence or absence of prior episodes of headache) and physical examination. These ques-

tions should be asked and the responses documented for every patient with a headache. Migraine can be divided into two major sub-types: Migraine with or without aura.

Migraine without aura is a clinical syndrome characterized by headache with specific features and associated symptoms (Table I). In migraine without aura (previously known as common migraine), attacks are usually associated with nausea, vomiting, or sensitivity to light, sound, or movement. When untreated, these attacks typically last 4 to 72 hours.

Table I. Criteria for diagnosing migraine.

Migraine without aura

- A. At least five attacks fulfilling criteria B-D
- B. Headache attacks lasting four to 72 hours (untreated or unsuccessfully treated)
- C. Headache has at least two of the following characteristics:
 - 1. Unilateral location
 - 2. Pulsating quality
 - 3. Moderate or severe pain intensity
 - 4. Aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs)
- D. During headache at least one of the following:
 - 1. Nausea and/or vomiting
 - 2. Photophobia and phonophobia
- E. Not attributed to another disorder

Typical aura with migraine headache

- A. At least two attacks fulfilling criteria B-D
- B. Aura consisting of at least one of the following, but no motor weakness:
 - 1. Fully reversible visual symptoms including positive features (eg, flickering lights, spots, or lines) and/or negative features (ie, loss of vision)
 - 2. Fully reversible sensory symptoms including positive features (ie, pins and needles) and/or negative features (ie, numbness)
 - 3. Fully reversible dysphasic speech disturbance
- C. At least two of the following:
 - 1. Homonymous visual symptoms and/or unilateral sensory symptoms
 - 2. At least one aura symptom developing gradually over ≥ 5 minutes and/or different aura symptoms occurring in succession over ≥ 5 minutes
 - 3. Each symptom lasting ≥ 5 and ≤ 60 minutes
- D. Headache fulfilling criteria B-D for migraine without aura begins during the aura
- E. Not attributed to another disorder

Typical aura without headache is the same as typical aura with migraine headache, except that criterion D is replaced by "Headache does not occur during aura nor follows aura within 60 minutes."

Source: Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 2nd edition. Available at: www.ihs-classification.org/en/. Accessed September 15, 2010.

Migraine with aura (previously called classic migraine) is primarily characterized by the focal neurological symptoms that usually precede or sometimes accompany the headache. Occasionally, the aura can occur without the headache. Some patients also experience a premonitory phase, occurring hours or days before the headache, and a headache resolution phase. Premonitory and resolution symptoms include hyperactivity, hypoactivity, depression, craving for particular foods, repetitive yawning and other less typical symptoms reported by some patients. The recognition of migraine has been enhanced by the introduction of diagnostic criteria by the International Headache Society (IHS), listed in Table I.

In a large population-based study¹³, 64 percent of patients with migraine had only migraine without aura, 18 percent had only migraine with aura, and 13 percent had both types of migraine (the remaining 5 percent had aura without headache). Thus, up to 31 percent of patients with migraine have aura on some occasions, but clinicians who rely on the presence of aura for the diagnosis of migraine will miss many cases. It is important to note that individuals may experience more than one variety of migraine, or even different headache disorders¹⁰⁻¹⁵. Last, migraine frequently manifests initially in childhood with cyclic vomiting and abdominal pain, carsickness or headaches associated with nausea or vomiting after minor head trauma (e.g. "footballers migraine")^{16,17}.

Primary and Secondary Headaches in the ED

Distinguishing between primary and secondary headaches is essential for the safe and effective management of patients with headache. Although most headaches in the ED are benign, one should be vigilant in searching for "red flags", which may represent dangerous conditions such as subarachnoid hemorrhage, infectious or carcinomatous meningitis, encephalitis, raised intracranial pressure secondary to neoplasm, abscess, intracranial hemorrhage, temporal arteritis or other vasculitides¹⁸⁻²⁰. These are listed in Table II. Table III represents a list of red flags that should be assessed before discharge for any patient. Another important point is that a favorable response to analgesics including triptans should not be used to exclude a serious secondary cause of headache. In a recent review²¹, seven of the 18 studies found that 46/103 patients (44%) described a significant or complete resolution of secondary headaches from medications

Table II. Serious secondary causes of acute headache in the Emergency Department.

Subarachnoid hemorrhage
Meningitis or encephalitis
Cervical or cranial artery dissections
Temporal arteritis
Acute narrow angle closure glaucoma
Hypertensive emergencies
Carbon monoxide poisoning
Idiopathic intracranial hypertension (Pseudotumor cerebri)
Spontaneous intracranial hypotension
Cerebral venous and dural sinus thrombosis
Acute stroke (hemorrhagic or ischemic)
Pituitary apoplexy
Mass lesions
Tumor
Abscess
Parameningeal infection
Intracranial hematoma
Colloid cyst of third ventricle

such as anti-emetics and nonsteroidal anti-inflammatory drugs (NSAIDs). Eleven of the 18 articles including 25/25 patients (100%) described a significant or complete resolution of secondary headaches from sumatriptan, a serotonin 5HT agonist.

Neuroimaging and Lumbar Puncture for the Diagnosis of Migraine

A migraineur patient without any “red flags” (Table II), whose presentation conforms to one of the common migraine disorders, and with a normal physical examination, does not necessarily need any ancillary tests. The American College of Emergency Physicians on the evaluation and management of adult patients presenting to the Emergency Department with acute, nontraumatic headache recommends¹:

Table III. “Red flags” for patients presenting with a headache in Emergency Departments.

Abrupt onset of a new, severe headache
Onset with exertion, including sexual intercourse
Onset of headache during or after middle age
Progressive headache course
New abnormal findings in a neurologic examination (Decreased level of consciousness, meningeal signs...)
Headache associated with other significant physical findings (Fever, indurated temporal arteries...)
Postural features of the headache, including exacerbation supine and relief standing
History of cancer, immunocompromise, or infection
Significant worsening of headache with Valsalva maneuver

- Patients presenting to the ED with headache and new abnormal findings in a neurologic examination (eg, focal deficit, altered mental status, altered cognitive function) should undergo emergent noncontrast head computed tomography (CT).
- Patients presenting with new sudden-onset severe headache should undergo an emergent head CT.
- In patients presenting to the ED with sudden-onset, severe headache and a negative noncontrast head CT scan result, lumbar puncture should be performed to rule out subarachnoid hemorrhage.

Pharmacologic Treatment

Drugs for the treatment of migraine can be divided into drugs that are taken daily whether or not headache is present to reduce the frequency and severity of attacks and drugs that are taken to treat attacks as they arise.

Acute Migraine Therapy

The goal of acute therapy is to provide rapid, complete, and sustained relief of pain and associated symptoms without generating significant adverse effects^{8,22-24}. A wide range of medications with variable routes of administration may be used to abort migraine headaches. Treatments for attacks can be divided into nonspecific and migraine-specific treatments. Useful, acute migraine treatment principles include:

- Taking an abortive medication as early as possible after the onset of headache increases the likelihood of terminating it;
- Rest, and especially sleep, in a dark, quiet environment is helpful in decreasing the duration of the attack;
- The selection of initial treatment for acute attacks depends on the severity and frequency of the attacks, the associated symptoms, the preference of the patient, and the history of treatment (success or failure and presence or absence of significant adverse effects with prior headaches).
- In patients with little headache-related disability, it is usually appropriate to initiate treatment with one or more analgesic drugs and to escalate treatment as needed.
- Regular use of abortive medications, especially the combination drugs, can lead to chronic

daily headache (also known as analgesic-rebound headaches or transformed migraine).

- Avoid using opioids for acute migraines.

Non Specific Treatments

In many patients, migraine responds well to simple treatment at the time of an attack. This entails utilizing aspirin (900 mg), non-steroidal anti-inflammatory drugs (NSAIDs) in combination for acetaminophen (1000 mg) for mild to moderate headaches²⁵⁻²⁷. Several studies^{28,29} showed that both Naproxen 500 mg, ketorolac 30 mg and sumatriptan effectively reduce the pain associated with acute migraine headache, but intravenous ketorolac produces a greater reduction in pain than does nasal sumatriptan²⁸. Moreover, ketorolac is as effective as meperidine and hydroxyzine for the treatment of acute migraine headache³⁰. If this fails, selective serotonin agonists, ergot derivatives, combination drugs (e.g., an analgesic plus caffeine), and phenothiazines might be effective³¹. In patients with substantial disability, it is appropriate to prescribe a triptan early in the course of treatment, in keeping with a stratified approach to care³². Rarely, opioids or corticosteroids may be necessary³³. Opioids may be better reserved for use when other medications cannot be used, when sedation effects are not a concern, or the risk for abuse has been ad-

ressed. Clinicians should always consider alternatives to opioids when treating acute migraine³⁴. If nausea and vomiting are prominent an antiemetic, such as promethazine (orally or rectally) or metoclopramide^{34,35}, may be used along with the analgesic. Prochlorperazine 10 mg intravenously or as a 25-mg rectal suppository is also an efficacious treatment for ED patients with acute migraine³⁷⁻³⁹. The patient's co-morbidities and other medications are also important in the decision-making process.

Ergot Derivatives

The main advantages of the ergotamine and dihydroergotamine ergot derivatives are their low cost and the long experience with their use^{40,41}. The major disadvantages include their complex pharmacology, erratic pharmacokinetics, lack of evidence regarding effective doses, their potent and sustained generalized vasoconstrictor effects (which are associated with adverse vascular events), and the high risk of overuse syndromes and rebound headaches. However, if dihydroergotamine is not as effective as sumatriptan or phenothiazines as a single agent for treatment of acute migraine headache, some evidence suggests that, when administered with an antiemetic, dihydroergotamine appears to be as effective as opiates, ketorolac, or valproate⁴².

Table IV. Pharmacologic and clinical characteristics of triptans in comparison with 100 mg of sumatriptan, from^{34*}.

Drug and dose	Pharmacokinetic profile†	Relief at 2 hr	Sustained freedom from pain	Consistency of effect‡	Tolerability
Sumatriptan					
50 mg	=	=	=	= or -	=
25 mg	=	-	= or -	-	+
Zolmitriptan					
2.5 mg	+	=	=	=	=
5 mg	+	=	=	=	=
Naratriptan, 2.5 mg	+	-	-	-	++
Rizatriptan					
5 mg	+	=	=	=	=
10 mg	+	+	+	++	=
Eletriptan					
20 mg	+	-	-	-	=
40 mg	+	= or +	= or +	=	=
80 mg	+	+ (+)	+	=	-
Almotriptan, 12.5 mg	+	=	+	+	++

*An equals sign indicates a similar value to that associated with 100 mg of sumatriptan; a plus sign indicates superiority to 100 mg of sumatriptan (a double plus sign indicates considerable superiority). †Minus sign indicates inferiority to 100 mg of sumatriptan. ‡The pharmacokinetic profile includes bioavailability and the time to maximal concentration during attacks. §The unusual design of the study involving rizatriptan makes it difficult to compare the consistency of its effect with the consistency of the effects of the other drugs.

Triptans

The triptans are serotonin 5-HT_{1B/1D}-receptor agonists and, to a lesser extent, the 5-HT_{1A} or 5-HT_{1F} receptor⁴³. Triptans have three potential mechanisms of action: cranial vasoconstriction, peripheral neuronal inhibition, and inhibition of transmission through second-order neurons of the trigeminocervical complex. These actions inhibit the effects of activated nociceptive trigeminal afferents and, in this way, control acute attacks of migraine⁴⁴. In comparison with the ergot derivatives, the triptans have distinct advantages, selective pharmacology, simple and consistent pharmacokinetics, evidence-based prescription instructions, and established efficacy based on well-designed controlled trials. They also have a moderate side effect profile, and a well established safety record. The most important disadvantages of the triptans are their higher cost and the restrictions on their use in the presence of cardiovascular disease. There are five triptans in routine clinical use: sumatriptan, naratriptan, rizatriptan, zolmitriptan, and almotriptan. Sumatriptan and related selective serotonin receptor agonists are excellent for severe migraines or those that do not respond to NSAIDs or other non specific treatments⁴⁵. In a large multicenter study⁴⁶, 6 mg subcutaneous sumatriptan was effective in treating acute migraine in the ED and oral sumatriptan (100 mg) was effective in treating headache recurrence within 24 hours. In a meta-analysis⁴⁷, using data from 24,089 patients in 53 controlled clinical trials of triptans, the Authors compared the percentages of patients with sustained freedom from pain (defined as freedom from pain at 2 hours with no rescue medication and with no recurrence of headache within 24 hours) with triptans. The rates were higher with 10 mg of rizatriptan, 80 mg of eletriptan, and 12.5 mg of almotriptan than with 100 mg of sumatriptan, and lower with 20 mg of eletriptan than with 100 mg of sumatriptan (Table IV). Although the triptans represent an important advance, they are ineffective in 40% of patients²³.

Prophylactic Migraine Therapy

Initiating prophylactic therapy depends to a great extent on patient preference, but there are some useful, general guidelines^{8,22-24}. Prophylactic migraine medications are indicated if: attacks occur more than 2-3 times a month; attacks last more than 48 hours; migraines are so severe, that the patient is unable psychologically to cope with them; abortive therapies are inadequate or cause

significant side effects; attacks are associated with prolonged aura. This does not concern the emergency practitioners, and the patients experiencing severe recurrent migraine have to be referred to a migraine specialist at discharge.

Conclusions

Migraine is the most common cause of severe, recurring headache. It is a common, chronic, incapacitating disorder, characterized by attacks of severe headache, autonomic nervous system dysfunction, and in some patients, an aura characterized by neurologic symptoms. Despite advancement in migraine understanding and management, pain relief at discharge is still inadequate in some patients. It is important for the emergency physician to be conversant with the diagnosis, prevention and treatment of migraine because neither a particular abortive nor prophylactic migraine therapy is universally efficacious. Thus, combined treatment and prevention approaches are most likely to succeed.

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