

MIGRAINE HEADACHES

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This talk will encompass the following topics:

1. What are the new ICHD-III β criteria for episodic and chronic migraine?
2. Acute treatment strategies for migraine
3. Preventive treatment guidelines for migraine
4. Treatment strategies for challenging clinical sub-types of migraine:
 - a. Migraine with nausea
 - b. Menstrual migraine
 - c. Chronic migraine

The ICHD-III β criteria for migraine without and with aura are listed below.

1.1 Migraine without aura

Description:

Recurrent headache disorder manifesting in attacks lasting 4-72 hours. Typical characteristics of the headache are unilateral location, pulsating quality, moderate or severe intensity, aggravation by routine physical activity and association with nausea and/or photophobia and phonophobia.

Diagnostic criteria:

- A. At least five attacks¹ fulfilling criteria B–D
- B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)^{2,3}
- C. Headache has at least two of the following four characteristics:
 1. unilateral location
 2. pulsating quality
 3. moderate or severe pain intensity
 4. aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs)
- D. During headache at least one of the following:
 1. nausea and/or vomiting
 2. photophobia and phonophobia
- E. Not better accounted for by another ICHD-3 diagnosis.

1.2 Migraine with aura

Description:

Recurrent attacks, lasting minutes, of unilateral fully reversible visual, sensory or other central nervous system symptoms that usually develop gradually and are usually followed by headache and associated migraine symptoms.

Diagnostic criteria:

- A. At least two attacks fulfilling criteria B and C
- B. One or more of the following fully reversible aura symptoms:
 1. visual
 2. sensory
 3. speech and/or language
 4. motor
 5. brainstem
 6. retinal

- C. At least two of the following four characteristics:
 1. at least one aura symptom spreads gradually over ≥ 5 minutes, and/or two or more symptoms occur in succession.
 2. each individual aura symptom lasts 5-60 minutes
 3. at least one aura symptom is unilateral
 4. the aura is accompanied, or followed within 60 minutes, by headache
- D. Not better accounted for by another ICHD-3 diagnosis, and transient ischemic attack has been excluded.

1.3 Chronic migraine

Description:

Headache occurring on 15 or more days per month for more than 3 months, which has the features of migraine headache on at least 8 days per month.

Diagnostic criteria:

- A. Headache (tension-type-like and/or migraine-like) on ≥ 15 days per month for >3 months and fulfilling criteria B and C
- B. Occurring in a patient who has had at least five attacks fulfilling criteria B-D for 1.1 Migraine without aura and/or criteria B and C for 1.2 Migraine with aura
- C. On ≥ 8 days per month for >3 months, fulfilling any of the following:
 1. criteria C and D for 1.1 Migraine without aura
 2. criteria B and C for 1.2 Migraine with aura
 3. believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative
- D. Not better accounted for by another ICHD-3 diagnosis.

A1.1 Migraine without aura

A1.1.1 Pure menstrual migraine without aura

Diagnostic criteria:

- A. Attacks, in a menstruating woman,¹ fulfilling criteria for 1.1 Migraine without aura and criterion B below
- B. Documented and prospectively recorded evidence over at least three consecutive cycles has confirmed that attacks occur exclusively on day 1 ± 2 (i.e. days -2 to $+3$)² of menstruation¹ in at least two out of three menstrual cycles and at no other times of the cycle.

Notes:

1. For the purposes of ICHD-3 beta, menstruation is considered to be endometrial bleeding resulting from either the normal menstrual cycle or from the withdrawal of exogenous progestogens, as in the use of combined oral contraceptives or cyclical hormone replacement therapy.
2. The first day of menstruation is day 1 and the preceding day is day -1; there is no day 0.

A1.1.2 Menstrually related migraine without aura

Diagnostic criteria:

- A. Attacks, in a menstruating woman,¹ fulfilling criteria for 1.1 Migraine without aura and criterion B below
- B. Documented and prospectively recorded evidence over at least three consecutive cycles has confirmed that attacks occur on day 1 ± 2 (i.e. days -2 to $+3$)² of menstruation¹ in at least two out of three menstrual cycles, and additionally at other times of the cycle.

Notes:

1. For the purposes of ICHD-3 beta, menstruation is considered to be endometrial bleeding resulting from either the normal menstrual cycle or from the withdrawal of exogenous progestogens, as in the use of combined oral contraceptives or cyclical hormone replacement therapy.
2. The first day of menstruation is day 1 and the preceding day is day -1; there is no day 0.

A1.1.3 Non-menstrual migraine without aura

Diagnostic criteria:

- A. Attacks, in a menstruating woman,¹ fulfilling criteria for 1.1 Migraine without aura and criterion B below
- B. Attacks do not fulfill criterion B for A1.1.1 Pure menstrual migraine without aura or A1.1.2

Knowing the different migraine criteria are important for many reasons, not the least of which is that proper management depends of accurate diagnosis. Once the diagnosis of migraine has been established, and prior to initiating therapy, it is imperative for the clinician and patient to establish a therapeutic partnership.

Patients have the expectation as well as the right to participate in their own care, and their input should be considered when designing a treatment protocol. After an initial clinical assessment it is often quite useful to provide the patient with educational materials and strategies for identifying and avoiding triggers, behavioral interventions, and non-pharmacologic therapies.

The pharmacologic treatment of migraine may be acute or preventive. Acute therapies attempt to reverse or prevent the progression of the headache already in progress. Preventive therapies are given on a daily basis even when the headache is not present in an attempt to reduce both the frequency and severity of future attacks. Throughout this talk, the putative mechanisms of action of the preventive agents will be discussed. It is important to recognize that although only a handful of agents have received an FDA approval for these purposes, in clinical practice, non-FDA approved medications are frequently employed. Medications used in the prevention of migraine include antidepressants, β -adrenergic blockers, calcium channel antagonists, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), non-steroidal anti-inflammatory drugs (NSAIDs), onabotulinum toxin type A, serotonin antagonists, and various vitamins, minerals, and herbal preparations. Non-pharmacological treatment strategies (biofeedback, relaxation therapy, cognitive behavioral therapy, acupuncture) are also occasionally useful as adjunctive or primary therapies, but are beyond the scope of this talk. Suggestions will be given, when possible, based on the Report of the Quality Standards Subcommittee of the AAN and AHS, the American Headache Society Evidence Assessment of migraine pharmacotherapies, the US Headache Consortium Guidelines.

Special Situations:

Migraine with nausea:

Nausea accompanies migraine in 70-90% of patients, and is consistently present in more than 30% of migraine sufferers. More than half of migraineurs vomit during acute attacks. Almost 1/3 of patients who experience nausea, and about 40% of those who vomit, report that these symptoms interfere with their ability to use the oral medications they have been prescribed. For this situation, treatment should be tailored to treatments that circumvent the gut- injectable, intra-nasal, suppositories, and when available, iontophoretic patches and oral inhalers.

Menstrual migraine:

Menstrual migraine (MM) is the term used for migraines occurring during menstruation, which is noted in ICHDIII β may be endometrial bleeding resulting from either the normal menstrual cycle or from the withdrawal of exogenous progestogens, as in the use of combined oral contraceptives or cyclical hormone replacement therapy.

Pure MM is characterized by migraines that occur exclusively during the menses, whereas menstrually related migraines (MRM) refer to headaches that occur during menstruation and sporadically throughout the month as well. In general MM are migraines without auras. In clinical practice these headaches usually occur on days -2 to +5, and are more severe, longer lasting, less responsive to treatment.

In general, agents typically used in the acute treatment for migraine (triptans, DHE, NSAIDs) should be employed as first line therapy. For women with predictable, disabling MM, strategies using short-term prevention should be utilized. Agents useful in short-term prevention include magnesium, naproxen, estradiol, frovatriptan, and naratriptan.

Perimenopause and Menopause:

There is an increased risk of developing high frequency headaches (≥ 10 headache days per month) during the transition phase into menopause, with the risk being the highest in the "late" stage. Physicians need to be aware of this increased risk so they can proactively offer prevention.

Selected References:

1. Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: Pharmacologic treatment for episodic migraine prevention in adults. Report of the Quality Standards Sub-committee of the American Academy of Neurology and the American Headache Society. *Neurology* 2012; 78: 1337-1345.
2. Marmura MJ, Silberstein SD, Schwedt TJ. The acute treatment of migraine in adults: The American Headache Society Evidence Assessment of migraine pharmacotherapies. *Headache* 2015; 55: 3-20.

3. Lipton RB, Bigal ME, Diamond M, et al. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology*. 2007;68(5):343-349
4. Martin VT. Menstrual migraine: a review of prophylactic therapies. *Curr Pain Headache Rep* 2004;8: 292-237.
5. Sullivan E, Bushnell C. Management of menstrual migraine: A review of current abortive and prophylactic therapies. *Curr Pain Headache Rep* 2010; 14: 376-384.
6. Hu Y, Guan X, Fan L, Jin L. Triptans in prevention of menstrual migraine: a systemic review with meta-analysis. *J Headache Pain* 2013; 14: 7.
7. Silberstein, SD. Practice parameter-evidence-based guidelines for migraine headache (an evidence-based review): Report of the Quality Standards Sub-committee of the American Academy of Neurology for the United States Headache Consortium. *Neurology* 2006, 55: 754-762
8. Gladstone JP, Eross E, Tepper DW. Migraine in special populations: Treatment strategies for children and adolescents, pregnant women, and the elderly. *Postgrad Med*. 2004;115: 39-44.
9. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (Beta version). *Cephalalgia* 2012; 33: 629-808.
10. MacGregor EA. Migraine management during menstruation and menopause. *Continuum* 2015;21 (4):990-1003
11. Martin VT, Pavlovic J, Fanning KM, et al. Perimenopause and menopause are associated with high frequency headache in women with migraine: Results of the American Migraine Prevalence and Prevention (AMPP) Study. Epub. Ahead of print January 2016