



National Headache Foundation

(NHF) is a non-profit organization established in 1970. NHF is the premier educational resource for headache sufferers, their families, and the healthcare professionals who treat them. Healthcare professional membership in the NHF provides the following benefits:

- *Standards of Care for the Diagnosis and Treatment of Headache*
- Listing in the NHF professional membership directory
- Copies of *NHF Head Lines* — a bi-monthly 12 page newsletter with in-depth articles on timely topics, medical forums, patient case studies, Kids Korner, and reader Q&A
- *NHF News to know* — a monthly e-newsletter containing up-to-the minute information on new drug approvals, and the latest in headache research.
- Access to a variety of useful patient aid booklets including: *A Patient's Guide to Migraine Prevention & Treatment*, *The Tyramine-Free Diet*, *Travel Tips for the Headache Sufferer*, *52 Proven Stress Reducers*, and others.
- Professional discount off registration at the Practicing Physician's Approach to the Difficult Headache Patient meeting held in February (Scottsdale AZ) and Headache Update in July (Orlando FL).
- An invitation to attend the NHF Annual Headache Research Summit.
- Inclusion in the online database of Physician Members (if desired)
- Web site access (www.headaches.org)
- Details on research grants available through the NHF
- Assistance in organizing local support groups, and more.

To join as a professional member or learn more about the services we offer, call 888-NHF-5552 or visit our Web site at www.headaches.org.

Recognizing Associated Symptoms With Migraine

Migraine is more than just a headache. Migraine is characterized by a constellation of symptoms that includes severe associated symptoms for many patients. In fact, migraine is defined as a recurrent headache disorder (with headache attacks of 4 to 72 hours characterized by unilateral location, pulsating quality, moderate-to-severe pain, and aggravation by or avoidance of routine physical activity) that is associated with at least one of the following: nausea and/or vomiting, phonophobia, or photophobia.¹ The prevalence of associated symptoms with migraine is so significant that a validated screening tool for migraine identifies the condition using the presence of 3 items (disability, nausea, and photophobia) with a sensitivity of 0.81 and a specificity of 0.75. In fact, sensitivity and specificity were not increased with additional screening items.²

The American Migraine Study II, a large study using self-administered questionnaires mailed to 20,000 US households, determined that associated symptoms are commonly experienced by patients with migraine. Photophobia and phonophobia are among the most common, experienced by 80% and 76% of patients, respectively. Nausea and vomiting are also common, experienced by 73% and 29% of patients, respectively. In addition, results showed that women were more likely to report these associated symptoms.³

Yet, the presence of debilitating nausea and vomiting with most or all of a

patient's migraine attacks may remain unrecognized and untreated. In addition, the impact of these symptoms on patient functioning and quality of life has rarely been studied. A recently completed patient survey by the NHF shows surprising results about the frequency and impact of associated symptoms with migraine (see sidebar).

NHF Patient Survey on Associated Symptoms

The NHF recently conducted an online survey of patients with migraine to determine the incidence and impact of associated symptoms. Results demonstrated that associated symptoms are very common and substantially impact a patient's daily life. A total of 513 patients with migraine (75% diagnosed by a healthcare provider) responded to the survey. Nearly all respondents (95%) use medication to treat their migraine, including prescription (31%) or over-the-counter medications (28%) or both (53%). Patients rated how often they experience various symptoms with headaches due to migraine (See symptoms Table on page 3).⁴

Of patients who experience nausea or vomiting, nearly half (48%) indicated that these symptoms had a moderate or major impact on when or how they take their migraine medication. Nine percent indicated they do not take medication to treat migraine if they have associated nausea or vomiting, and 30% indicated

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they delay taking their medication until the nausea subsides. Further, 31% take additional prescription medication specifically to manage their nausea.⁴

Migraine attacks were frequently debilitating and often recurred after acute treatment. When asked to rate the severity of their typical migraine pain on a scale of 1 to 10 (1 = somewhat manageable; 10 = unbearable), most patients (90%) rated their pain as ≥ 6 . Twenty-five percent rated their pain as 7, and 31% rated their pain as 8 on this scale. The majority of patients (78%) have missed time at work due to migraine headache or associated symptoms. Surprisingly, 42% of respondents stated that their migraine pain returned within 24 hours of taking medication.⁴

Despite the frequency of associated symptoms, more than half of respondents to the NHF survey (58%) stated that their healthcare provider does not inquire about these symptoms on a regular basis. Yet, the NHF results also suggest the patients rely heavily on their healthcare providers for guidance: 45% of respondents stated that discussion with their healthcare provider would prompt them to seek more information about migraine and associated symptoms.⁴

To learn more about the NHF, please call (888) NHF 5552 or visit our Web site at www.eadaches.org.

Impact of Associated Symptoms on Activities of Daily Living

The presence of associated symptoms can significantly affect patient functioning. A recent study of 232 migraine patients with ≥ 3 attacks per month demonstrated a significant ($P \leq .001$) correlation between severity of associated symptoms (photophobia, phonophobia, and nausea) and impaired functioning and quality of life. Surprisingly, severity of attack exhibited a smaller, though still significant, association with impaired function and quality of life. Multiple regression analysis revealed that severity of associated symptoms is

a strong and consistent determinant of impaired function and quality of life, and that this association is independent of migraine severity.⁵ A separate study showed correlation between headache intensity and the presence of associated symptoms, including nausea/vomiting, photophobia, and phonophobia.⁶ In addition, the presence of associated symptoms, specifically nausea and vomiting, complicates the treatment of migraine, as patients may be unable or unwilling to take their migraine medication during an attack for fear of vomiting.

FDA-APPROVED ACUTE MIGRAINE MEDICATIONS

● (Oral) ● (Dissolving Tablet) ● (Suppository) ◀ (Nasal Spray) ⇄ (Injection)

Type of Medication	Trade Name (generic name)	Route of Administration (US)
Triptans	Amerge (naratriptan HCl)	●
	Axert (almotriptan)	●
	Frova (frovatriptan)	●
	Imitrex (sumatriptan succinate)	● ◀ ⇄
	Maxalt (rizatriptan benzoate)	● ●
	Relpax (eletriptan)	●
	Treximet (sumatriptan and naproxen sodium)	●
	Zomig (zolmitriptan)	● ● ◀
Ergotamine derivatives	DHE 45 (dihydroergotamine mesylate)	◀ ⇄
	Ergotamine/caffeine*	●† ●
Analgesics (over-the-counter)	Acetaminophen*	●
	Combination products (acetaminophen/aspirin/caffeine)	●
	Ibuprofen*	●
	Naproxen sodium*	●
Analgesics — (prescription, used infrequently)	Butalbital/caffeine with aspirin*	●
	Stadol NS (butorphanol)	◀
Other prescription medications	Combination isometheptene mucate/dichloralphenazone/acetaminophen*	●

FDA = Food and Drug Administration

* Marketed under one or more brand names

† Also available as a sublingual tablet containing ergotamine

Associated Symptoms and Treatment Choice: Optimizing Medication Use

The American Academy of Neurology and the US Headache Consortium recommend a non-oral route of administration in patients with migraine associated with severe nausea or vomiting. In addition, antiemetics are recommended for patients with nausea or vomiting. Antiemetic use should not be restricted to patients who are vomiting or likely to vomit, as nausea itself is one of the most aversive and disabling symptoms of migraine attack and requires appropriate treatment.^{7,8}

The table on page 2 summarizes FDA-approved acute medications for migraine and delivery routes available in the United States. Several agents are available in non-oral routes, including nasal

spray, injection, and suppository formulations. Some dissolving tablets can be taken orally and dissolve on the tongue, avoiding the need to swallow a pill or take liquid. In addition, a transdermal iontophoretic sumatriptan succinate delivery system, which uses electrical current to propel sumatriptan across intact skin and underlying tissue, is under investigation. A preclinical study demonstrated that this delivery system offers pharmacokinetics comparable to oral, nasal, or rectal administration.⁹ A recent phase I trial identified the current density targets for delivery of therapeutic drug levels,¹⁰ and clinical trials are ongoing, with the agent entering phase III trials.

Talking to your Patients About Migraine

Talking to your patients specifically about associated symptoms, including nausea and vomiting, is essential to effectively diagnose and treat these symptoms. A recent study of patients meeting IHS criteria for migraine or probable migraine determined that additional and more descriptive questions increase identification of the associated symptoms, such as photophobia and phonophobia. Nearly all patients who asserted that they did not experience these symptoms with a headache attack then identified photophobia (91%) or phonophobia (96%) with further questioning.¹¹

Because nausea and vomiting often accompany migraine attacks, be sure to ask your patient about these important symptoms with questions such as:

Do you experience nausea or vomiting when you have a migraine attack?

— If patients answer, “no,” follow up with a second question: During a headache attack, do you feel like eating or do you feel sick to your stomach?

Do you take extra medication to treat nausea or vomiting during a headache?

Do you delay or avoid taking your migraine medication due to nausea or vomiting?

Does nausea or vomiting affect your ability to function normally during a headache?

Patients who answer yes to any of these questions may be considered for a non-oral delivery route of medication.

FREQUENCY OF SYMPTOMS WITH MIGRAINE HEADACHES

Symptoms	Frequently Experience	Always Experience
Throbbing pain on one side	34% of Patients	50% of Patients
Aura	25	17
Nausea	36	19
Vomiting	13	6
Sensitivity to bright lights	29	54
Sensitivity to sounds	35	46
Sensitivity to smells	25	28
Blurry Vision	29	17
Neck pain	31	38
Nasal stiffness	28	16
Frequent urination	21	6
Pallor	26	14
Sweating	30	9

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Summary

The presence of one of the 3 key associated symptoms (nausea/vomiting, photophobia, or phonophobia) is a defining characteristic of migraine.¹ Yet, the effect of these associated symptoms on patient functioning and quality of life has not been adequately studied. Results suggest that the presence of associated symptoms significantly correlates with impaired function and quality of life.⁵ In addition, results of the American Migraine Study II demonstrate that associated symptoms are common; nausea and vomiting are experienced by 73% and 29% of patients, respectively.³ Non-oral route of administration of migraine medication, with antiemetic therapy as needed, is recommended for these patients.^{7,8} Several agents approved for migraine are available in non-oral routes. In addition, a novel transdermal iontophoretic delivery system for a triptan is under investigation. Physicians are encouraged to question patients specifically about associated symptoms with migraine at frequent intervals to identify those who require additional management of nausea/vomiting, including use of a non-oral agent.

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