

## CASE STUDY

### A 35-Year-Old Woman With Disabling Headache



#### Presentation

A 35-year-old woman seeks help from her primary care clinician for severe monthly headaches that she attributes to workplace stress. She knows when a headache is coming on because she feels queasy beforehand. The patient also notices that these headaches tend to occur after she has been working long hours—she is currently a chef at a trendy new restaurant—or missing sleep. She becomes tearful during her explanation and is especially distressed because the pain has caused her to miss work 4 times in the past 3 months, and to stay in bed for half the weekend twice.

She has been self-medicating with over-the-counter (OTC) nonsteroidal anti-inflammatory drugs (NSAIDs). These helped initially but have become less effective. She also says she has tried “everything on the shelf.” She is concerned that her manager will become intolerant of additional missed work days. She asks whether antianxiety or sleep medication might help.

#### Physical Examination and Laboratory Values

- Height 5 ft 7 in
- Weight 137 lb
- BMI 22.3 kg/m<sup>2</sup>
- BP 100/75 mm Hg
- Heart rate 73 bpm
- Lab tests Within normal range

BMI = body mass index; BP = blood pressure; bpm = beats per minute.

The patient appears healthy and has no evident physical abnormalities. She is tired but not excessively sleepy.

#### Clinical Decision Point

At this point, what action is indicated?

- Prescribe an antianxiety medication to reduce stress
- Prescribe a hypnotic to improve sleep
- Advise the patient to get more rest and to continue using OTC medication as needed
- Probe further into nature of headache
- Prescribe an acute migraine medication

#### Comment

While this patient may in fact be suffering from anxiety for any number of reasons, as well as the effects of disrupted sleep, her primary presenting symptom is an episodic headache severe enough to warrant a clinician's office visit. It is prudent to first understand the nature of the underlying headache rather than prescribe a “quick-fix” medication to treat her anxiety and/or fatigue. She has been treating her headaches for some time with OTC

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medications which are ineffective, so continued or escalated use of these medications will only put her at risk of medication overuse and progression of her headache.<sup>1</sup>

Although this patient's report of disability strongly suggests a migraine diagnosis, migraineurs frequently do not seek treatment, and for those who do, migraine is frequently missed or misdiagnosed.<sup>2-4</sup> Those who don't seek treatment may dismiss or incorrectly self-diagnose symptoms as "simple tension" headache, sinus headache, or a response to excessive stress that does not merit a clinician visit.<sup>4</sup> In the American Migraine Study, 56% of migraine sufferers never received a migraine diagnosis. Of these, 58% had not sought treatment but 42% had consulted a clinician and were not diagnosed.<sup>5</sup> The Landmark Study compared patient self-reports and clinician diagnoses of migraine made during a clinic screening with an expert review of longitudinal data from patient diaries kept by the same patients for 3 months or 6 attacks. Diary review was based on International Headache Society (IHS) guidelines.<sup>5</sup> Results of the study illustrate the prevalence of misdiagnosis. Of those diagnosed by a physician as having nonmigraine headache, 94% met

## Migraine: A Pressing Problem

Migraine headache is common in the United States, occurring in approximately 18% of women and 6% of men, or nearly 30 million Americans.<sup>1</sup> Of the households surveyed in the American Migraine Study II, 23% contained at least 1 migraineur, most of them adults between 25 and 55 years old.<sup>1,2</sup> Overall, 62% of survey respondents had at least 1 severe headache every month. Severe headache once a week was reported by 10.8%. The study investigators also found that migraine was more common in whites than in blacks, and among persons of lower socioeconomic status.<sup>1,3</sup>

There is significant pain and disability associated with migraine. Ninety-one percent of migraineurs reported being unable to function normally during an attack. In the American Migraine Study II, 35% of patients reported losing at least 1 day of normal activity, 51% reported being substantially (at least 50%) less productive than normal, 31% missed work or school, and 59% missed a family or social function over a 3-month period.<sup>1,3</sup> Not surprisingly, the cost of migraine and this lost productivity is significant, averaging \$13 billion annually.

Care is usually delivered in a primary care setting.<sup>2,4</sup> Despite the number of medical visits due to headache pain, migraine is still both underdiagnosed and undertreated. In the first American Migraine Study, 71% of men and 59% of women reported never being medically diagnosed with migraine.<sup>5</sup> The investigators call for increased public health initiatives to improve awareness and correct diagnosis of migraine to reduce the toll that this disorder extracts on the American public.<sup>5</sup>

### The Importance of Early Treatment

Early treatment of migraine produces the best outcomes regardless of medication used. The explanation for this phenomenon may lie in the way that the central nervous system (CNS) processes pain signals.

Migraine is a form of neurovascular headache in which brain-stem pathways that normally modulate sensory input become dysfunctional. Studies from nonhuman primates show that stimulation of vascular afferent fibers activates neurons in the superficial layers of the trigeminal nucleus caudalis in the region of the trigeminocervical complex. Peripheral trigeminal activation causes release of calcitonin-gene related peptide (CGRP), a vasodilator (Figure).<sup>6</sup>

criteria for IHS-defined migraine or probable migraine upon diary review by the expert panel, whose members were unaware of the clinic diagnosis.<sup>4</sup>

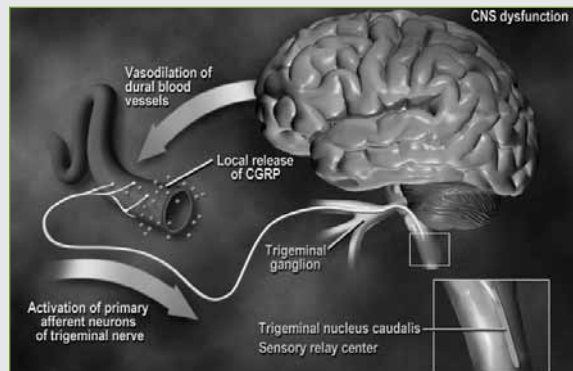
Reasons for the lack of clinical detection are numerous and include poor recall and incomplete information from the patient, limited consultation time and focus on a different presenting complaint, clinician distraction, poor communication between patient and clinician, and presence of other conditions or headaches that can obscure the diagnosis of migraine.<sup>4,6</sup>

Data from the Landmark Study showed that if a patient self-reported nonmigraine headaches, the IHS diagnosis was migraine or probable migraine 86% of the time.<sup>4</sup> The term probable migraine is used when a patient reports some, but not all, of the symptoms required for a strict diagnosis of migraine.<sup>7</sup> In the present case, more information is needed before a clinical decision is made.

### Decision: Probe further into the nature of the patient's headache.

The patient says that the headaches typically occur on one side of her head, producing throbbing pain. The pain intensity is 9 out of 10 on the visual analog scale. The headaches last 6 to 12 hours,

During the initial phases of a migraine attack, the first-order trigeminal nerve becomes sensitized, causing throbbing pain. If the attack goes untreated, this peripheral nerve activation leads to sensitization of the second-order neurons in the trigeminal nucleus caudalis of the midbrain. Eventually, third-order neurons in the thalamus become activated. These project onto the cortex, creating pain. Once the second- and third-order neurons are sensitized, they propagate nociceptive pain signals to the brain—regardless of peripheral nerve input. This concept is known as central sensitization. In this setting, triptans lose efficacy and rescue therapy might become necessary to combat rebound headache.<sup>7</sup>



**Figure.** Vasodilation and neurogenic inflammation occur during a migraine attack. CGRP = calcitonin gene-related peptide.

### References

1. Lipton RB, Stewart WF, Diamond S, et al. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache*. 2001;41:646-657.
2. Lipton RB, Bigal ME. The epidemiology of migraine. *Am J Med*. 2005;118(Suppl 1):3S-10S.
3. Lipton RB, Bigal ME, Diamond M, et al. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology*. 2007;68:343-349.
4. Sadosky R, Dodick DW. Identifying migraine in primary care settings. *Am J Med*. 2005;118(Suppl 1):11S-17S.
5. Lipton RB, Stewart WF, Simon D. Medical consultation for migraine: results from the American Migraine Study. *Headache*. 1998;38:87-96.
6. Goadsby PJ, Lipton RB, Ferrari MD. Migraine—current understanding and treatment. *N Engl J Med*. 2002;346:257-270.
7. Smith TR. The pharmacologic treatment of the acute migraine attack. *Clin Fam Pract*. 2005;7:423-444.

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and interfere with both her professional and social life. Importantly, she finally admits later during the history that the problem is not new—these headaches have recurred monthly, and sometimes more than once a month, for 10 years.

The approach to managing recurrent headache is highly dependent on correct classification. The International Classification of Headache Disorders (ICHD) was created by the IHS to provide structured criteria for clinical trials as well as to help clinicians make a differential diagnosis. The category of primary headache, into which migraine falls, also includes tension-type headache (TTH), cluster headache and other trigeminal autonomic cephalalgias (TACs), and other primary headaches.<sup>8</sup>

ICHD II differentiates migraines based on the presence of an aura. Migraines without aura last from 4 to 72 hours and are accompanied by 2 of these pain features: unilateral distribution, throbbing or pulsating pattern, aggravated by routine activity, moderate or severe intensity. Patients also have nausea or vomiting, and photophobia or phonophobia. The physical examination is typically normal. In the postdrome phase, once the headache ceases, patients may have cognitive and/or mood changes, muscle pain, fatigue, or gastrointestinal (GI) upset.<sup>8</sup>

ICHD II migraines with aura have all of these features plus an aura that develops over 5 minutes or more and consists of fully reversible visual and/or sensory symptoms and dysphasic speech. Patients have no motor weakness, and 2 or more of the following: homonymous visual symptoms, unilateral sensory symptoms, or symptoms that occur in succession and last 5 to 60 minutes.<sup>8</sup>

The ICHD II criteria for TTH differ from those for migraine in important ways (Table 1).<sup>7</sup> The patient must have had 10 or more attacks lasting 30 minutes to 7 days each, and pain must have at least 2 of the following qualities: bilateral distribution, nonpulsating nature, not aggravated by routine physical activity, mild to moderate intensity.<sup>8</sup> The most important differentiating factor is that TTH has only minimal impact on the person's function. Thus, patients with TTH do not commonly seek care. When patients with migraine have TTH it usually responds to treatment like a migraine.<sup>9</sup>

Headache experts have suggested that to improve migraine recognition, patients who present with a stable pattern of episodic, disabling headache and a normal physical examination should be

**Table 1. Key Features Distinguishing Migraine From Tension-Type Headache**

Feature	Migraine	Tension-Type
Location of pain	Unilateral	Bilateral
Intensity	Moderate-severe	Mild-moderate
Descriptor	Pulsating (50%)	Pressing or tightening
Physical activity	Aggravates pain	May improve or have no effect
Associated features	Nausea ± photophobia ± phonophobia	No nausea; rarely photo- or phonophobia
Duration	4-72 hours	Minutes to days

Sadovsky R et al.<sup>7</sup>

considered to have migraine, in the absence of contradictory evidence.<sup>4</sup> That evidence can be uncovered during a focused medical history conducted to differentiate migraine from secondary causes of headache.<sup>7</sup> Some of the most common causes of secondary headache are listed in Table 2.<sup>2</sup>

The etiology of secondary headaches is diverse and includes infection, head or neck trauma, cranial or cervical vascular disorders, nonvascular cranial disorders, substance use or withdrawal, disorder of homeostasis, disorder related to facial or cranial structure, or psychiatric disorders.<sup>7</sup> A simple mnemonic—SNOOP—can help clinicians probe indicators of possible secondary headaches during consultation for 1 particular headache<sup>7</sup>:

- **S:** Systemic involvement/signs
- **S:** Systemic disease (malignancy, AIDS)
- **N:** Neurologic symptoms/signs
- **O:** Onset sudden (thunderclap headache)
- **O:** Onset after age 40 years
- **P:** Pattern change
  - Progressive headache, fewer or shorter headache-free intervals
  - Change in type of headache

Once secondary headache is ruled out, clinical suspicion of migraine can be further screened with the simple but highly sensitive (81%) and specific (75%) ID Migraine™ screener. The tool's 3 questions address symptoms most highly correlated with migraine diagnosis and are easily incorporated into the clinical interview, a waiting room questionnaire, or office information management system.<sup>10</sup> It asks:

- Has a headache limited your activities for a day or more in the last 3 months?
- Are you nauseated or sick to your stomach when you have a headache?
- Does light bother you when you have a headache?

Affirmative answers to  $\geq 2$  of these queries indicate a likely diagnosis of migraine with a positive predictive value of 93.3%.<sup>10</sup>

The patient answers “yes” to the first 2 items on the ID Migraine™ questionnaire, which, when considered within the context of her clinical picture, points to a diagnosis of migraine.

### Clinical Decision Point

What would be the next course of action?

- Initiate treatment with a prescription pain reliever
- Prescribe migraine-specific acute treatment
- Stratify patient's treatment needs with a disability questionnaire
- Advise behavioral/lifestyle measures

### Comment

Treatment for migraine headache generally follows either a step or stratified paradigm. In step therapy, treatment begins with a less intense, nonspecific agent (eg, NSAIDs). If attacks persist, treatment escalates to a migraine-specific agent,

**Table 2. Common Causes of Secondary Headache**

- Cranial or cervical vascular disorder
- Cranial, eye, neck, ear, nose, sinus, teeth, mouth disorders
- Cranial neuralgias
- Disorder of homeostasis
- Head and/or neck trauma
- Infection
- Nonvascular intracranial disorder
- Substance abuse or withdrawal
- Medication overuse
- Inflammation

Goadsby PJ.<sup>2</sup>

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such as a triptan. Patients treated via this gradual step protocol are at risk for prolonged symptoms, which discourages adherence and may lead to increasing disability.<sup>11</sup>

Stratified therapy is based on assessment of acute headache severity, which is most often expressed in terms of migraine-related disability.<sup>1,12</sup> The patient's immediate needs are evaluated with a tool such as the Migraine Disability Assessment (MIDAS) questionnaire (Figure 1), and treatment started with a medication targeted to the headache severity.<sup>3,13</sup> In the Disability in Strategies of Care (DISC) study, stratified and step-care treatment approaches were evaluated in migraine patients.<sup>14</sup> Stratified care improved outcomes (eg, headache response) and reduced migraine disability (measured as time missed from work, school, or leisure activities). Matching treatment to the level of illness increased the likelihood that patients would achieve relief and would be satisfied with the medical care.<sup>14</sup>

To determine the patient's headache severity, she is asked to complete the MIDAS questionnaire. Her score of 12 indicates moderate disability and high need for migraine-specific therapy.

#### Decision: Prescribe migraine-specific acute treatment.

People who have acute migraine overwhelmingly want complete pain relief. They also want a medication that prevents headache recurrence, works quickly, is tolerable, and eases symptoms.<sup>15</sup> These clinical attributes were used by the United States Headache Consortium (USHC)<sup>1,11,16</sup> to shape the guiding goals and principles of acute migraine therapy:

- Abort the acute attack
- Alleviate pain
- Control associated symptoms
- Reduce recurrence
- Minimize the use of rescue medications
- Preserve functionality, self-care
- Initiate treatment at first hint of migraine
- Prescribe adequate initial dose of medication for rapid, complete control
- Use medications as indicated to avoid medication overuse headache

Treatment that is consistently prompt and aggressive helps decrease the chance that acute migraine will progress to chronic headache, and maximizes therapeutic effect

#### In the last 3 months, because of your headache:

1. How many days did you miss work or school?
  2. How many days was your productivity at work or school reduced by half or more?
  3. How many days did you not do housework?
  4. How many days was your housework productivity reduced by half or more?
  5. How many days did you miss family, social, or leisure activities?
- A. On how many days did you have a headache?  
B. On a scale of 1 to 10, on average how painful are your headaches?

#### Total number of days:

Score	Disability	Grade
0-5	Minimal	1
6-10	Mild	2
11-20	Moderate	3
21+	Severe	4

**Figure 1. The MIDAS questionnaire allows the physician to assign treatment based on the patient's score or level of disability.** The MIDAS score is the sum of the number of days lost from school or paid work, housework/chores, and leisure activities. Patients with a score of 1-5 (grade 1) can receive a nonspecific agent as first-line treatment. A MIDAS score of 6-10 identifies the patient in moderate need of treatment (grade 2) with either a nonspecific or a migraine-specific medication. Persons with a MIDAS score of  $\geq 11$  are in high need of treatment (grade 3/4) with a migraine-specific medication. Lipton RB et al<sup>3</sup>; Stewart WF et al.<sup>13</sup>

(see *Migraine: A Pressing Problem*, page 52).<sup>11</sup> One study found that patients who took sumatriptan 50 mg in the early, or mild, stages of migraine had greater pain-free responses at 2 and 4 hours than persons who waited until pain was moderate to severe.<sup>17</sup> Five prospective early-intervention studies conducted since then found a greater percentage of patients were pain-free after early treatment with sumatriptan (50 or 100 mg) versus placebo, and that

**Table 3. Medications Used in Acute Migraine Therapy**

Treatment	Specific (S)/ Nonspecific (N)	Agents	Pro	Con
Triptans	S	Almotriptan Eletriptan Frovatriptan Naratriptan Rizatriptan Sumatriptan Zolmitriptan	Selective effect Evidence-based dosing, efficacy, safety Adaptive formulations Simple pharmacokinetics	Relative cost Restricted in persons with CVD
Ergots	S	Dihydroergotamine Ergotamine + caffeine	Long history Inexpensive Adaptive formulations Dihydroergotamine has fewer side effects	Erratic pharmacokinetics No evidence of dose-efficacy Vasoconstriction Risk of overuse, rebound headache Dihydroergotamine not available as oral formulation
Combination: Triptan/NSAID	S	Sumatriptan + naproxen	Reduces recurrence Reduces need for rescue medication	NSAIDs can cause GI effects Triptan is restricted in persons with CVD
NSAIDs	N	ASA, ibuprofen, naproxen	Effective if taken in adequate dose	Risk of overuse Risk of GI complications
Butalbital compounds	N	Butalbital + ASA + caffeine	Commonly prescribed for treating migraine and other headaches	Risk of overuse, medication-induced headache, withdrawal
Compounds	N	ASA + acetaminophen + caffeine	Effective if taken in adequate dose	Risk of overuse Risk of GI complications
Opioids	N	Butorphanol, acetaminophen + codeine	Rescue use	Do not address pathophysiology Negative cognitive effects Risk of habituation dependency, rebound
D <sub>2</sub> antagonists	N	Metoclopramide, prochlorperazine	Antiemetic effect	Risk of extrapyramidal symptoms

ASA = acetylsalicylic acid; CVD = cardiovascular disease; GI = gastrointestinal.  
Goadsby PJ<sup>2</sup>; Goadsby PJ et al<sup>16</sup>; Smith TR.<sup>11</sup>

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the higher dose was more effective than the lower.<sup>1</sup> The research supports both the goals and principles of the USHC, demonstrating that early use of an adequate dose of a migraine-specific medication provides both the quality and quantity of relief that patients want.

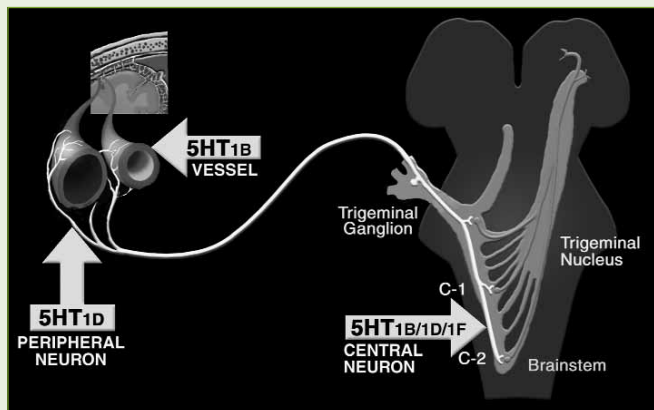
Headache medications are categorized as migraine-specific or nonspecific (Table 3, page 57).<sup>11</sup> Nonspecific agents, such as aspirin, acetaminophen, and NSAIDs, are used to treat pain caused by a wide range of disorders and injuries<sup>16</sup> and may also work well for patients with mild, nondisabling migraines.<sup>11</sup> Specific agents are effective for treating migraine and other neurovascular headaches that cause disability.<sup>9,16</sup> In the class of migraine-specific drugs, triptans are generally preferred over ergots because of their selective pharmacology, established dosing, greater tolerability, and safety record.<sup>16</sup>

The triptans are selective serotonin 5-HT<sub>1B/1D</sub> receptor agonists. Three potential mechanisms of action are proposed: cranial vasoconstriction, peripheral neuronal inhibition, and inhibition of transmission through second-order neurons of the trigeminocervical complex. Which of these exerts greatest influence is still unclear. The 5-HT<sub>1B/1D</sub> receptor agonist activity counters the effects of activated nociceptive trigeminal afferent fibers to abort an acute attack of migraine (Figure 2).<sup>16</sup>

The 7 available triptans differ in tolerability, dosage forms, and half-life, and all are proven safe for migraineurs (Table 4).<sup>16</sup> Combining triptans with selective serotonin reuptake inhibitors might cause CNS effects, but this seldom occurs.<sup>11</sup> Rare reports of myocardial infarction contraindicate the use of triptans in persons with ischemic heart disease, uncontrolled hypertension, coronary vascular disease, or peripheral arterial disease.<sup>16</sup>

The patient receives a prescription for a triptan, to be taken at the first sign of an attack.<sup>11</sup> She supplements this with recommended behavioral strategies, including regular exercise and working toward more regular sleeping habits. Clinical experience suggests that these and other types of lifestyle modifications—limiting caffeine intake, moderating alcohol intake, avoiding smoking, observing regular mealtimes, and practicing relaxation techniques—are beneficial for migraineurs.<sup>18</sup> Keeping a headache diary can also help patients learn to identify and manage common migraine triggers, such as skipping meals, changing sleeping patterns, or excessive exposure to light.<sup>2</sup>

At her 3-month follow-up the patient is feeling well and reports that the triptan



**Figure 2.** The triptans control migraine by behaving like a serotonin, exerting an agonist effect at 5-HT<sub>1B/1D</sub> receptors in the brain stem and trigeminovascular pain pathways. This causes reduction of CGRP-mediated vasodilation, cranial vasoconstriction, reduced neurogenic inflammation of the dura and meningeal vessels, and blunting of pain signal transmission in the trigeminal nucleus caudus of the midbrain. Goadsby PJ et al.<sup>16</sup>

stopped all but 1 of 7 headaches. She obtained relief with a single dose and the headaches, once aborted, did not return or require subsequent treatment. She is exercising daily and maintaining a regular sleep schedule. She is thrilled that she is getting back to reliably “showing up for life”—she has missed no work or social engagements since starting triptan therapy.

### Clinical Decision Point

Given the frequency of the patient’s attacks and her response to acute therapy, which of the following seems to be the best long-term strategy?

- Continue lifestyle measures along with triptan therapy to stop acute attacks
- Initiate prophylactic medication regimen
- Continue triptan and recommend daily use of OTC analgesic for prophylaxis
- Continue lifestyle measures and switch to a fixed-combination triptan/NSAID

### Comment

The USHC guidelines for preventive migraine therapy state that the decision to initiate prophylaxis should be guided by one or more of the following: recurring migraines, that, in the patient’s opinion, significantly interfere with daily routines, despite acute treatment; frequent headaches; contraindication to, failure or overuse of acute therapies; adverse events with acute therapies; the cost of both acute and preventive therapies; patient preference; and the presence of uncommon migraine conditions, including hemiplegic migraine, basilar migraine, migraine with prolonged aura, or migrainous infarction (to prevent neurologic damage—as based on expert opinion).<sup>19</sup> The patient has responded very well to triptan therapy, experiencing many fewer headaches and reduced disability. There would be no reason to initiate preventive treatment at this time or to combine her current regimen with prophylaxis. She has also been able to modify her daily habits and lifestyle to help reduce potential triggers. Moreover, daily use of OTC analgesics as preventive treatment is a risk factor for developing chronic daily headache (CDH).<sup>13</sup>

**Table 4. Triptans Used to Control Acute Migraine**

Name	Optimum/Maximum Dose (mg)	Forms	Half-life (h)
Sumatriptan <sup>a</sup>	50 or 100/200	Tablet, NS, SC, S	1.5-2.25
Sumatriptan + naproxen	85 sumatriptan + 500 naproxen	Tablet	2/19
Rizatriptan	10/30	Tablet, ODT	2-3
Zolmitriptan	2.5 or 5/10	Tablet, ODT, NS	3
Almotriptan	12.5/25	Tablet	3-4
Eletriptan	40/80	Tablet	4
Naratriptan	2.5/5	Tablet	6
Frovatriptan	2.5/7.5	Tablet	26

NS = nasal spray; ODT = orally dissolving tablet; S = suppository; SC = subcutaneous injection.

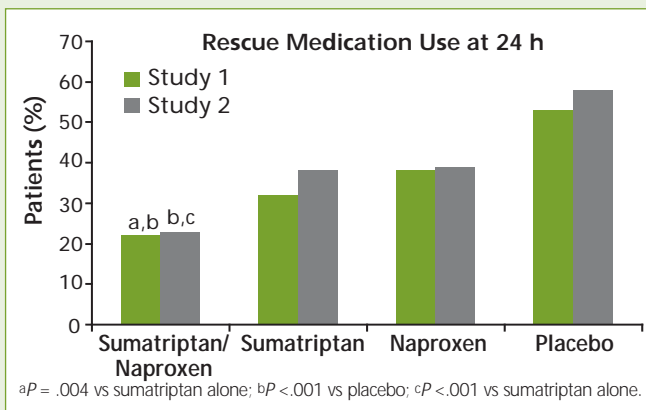
<sup>a</sup>Nasal spray and injection forms of medication provide faster, more complete relief of symptoms than oral preparations.

Smith TR<sup>11</sup>; Physicians’ Desk Reference. 61st ed. Montvale, NJ: Thomson PDR; 2007.

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**Figure 3. Combination therapy can be more effective than monotherapy for controlling migraine and reducing the need for rescue medication.** In this 2-study comparison, about 20% of patients taking sumatriptan plus naproxen needed rescue medication at 24 hours, compared with an average of 37% of patients taking sumatriptan and 40% of persons taking naproxen. Brandes JL et al.<sup>12</sup>



Fixed-dose combination therapy, which combines 2 drugs with differing mechanisms of action to inhibit migraine, is an option for patients who experience frequent recurrence of headaches using triptan monotherapy.<sup>11</sup> This approach is also used as initial treatment for some patients, as it can reduce the need for rescue medication and blunt the symptoms associated with migraine more effectively than monotherapy in the 24-hour post-dose interval as well as at the standard assessment point 2 hours after dosing.<sup>11,12</sup> In 2 replicate, randomized, double-blind, single attack, parallel-group trials, fixed-dose sumatriptan/naproxen was compared to placebo (study 1) and to each drug as monotherapy (study 2), each in cohorts of more than 1000 patients.

The fixed-dose combination was better than placebo and either agent alone at producing a sustained pain-free response in the 2- to 24-hour post-dose period.<sup>12</sup> The incidence of pain-free response in the first study was 25% for combination therapy compared with 16% for sumatriptan monotherapy ( $P < .01$ ), 10% for naproxen monotherapy ( $P < .001$ ), and 8% with placebo ( $P < .001$ ). Responses were similar in the second study with an incidence of pain-free response for combination therapy of 23% compared with 14% for sumatriptan monotherapy ( $P < .001$ ), 10% for naproxen monotherapy ( $P < .001$ ), and 7% for placebo ( $P < .001$ ).<sup>12</sup> Fixed-dose combination therapy also reduced the incidence of migraine recurrence as well as the need for rescue medication at 24 hours (Figure 3).<sup>12</sup>

The most common combination is a triptan with an NSAID. Promising results have also been found with other fixed combinations—rizatriptan plus tolfenamate and rizatriptan plus rofecoxib (currently unavailable in the United States).<sup>11</sup> Other fixed-combination agents include aspirin plus metoclopramide, triptans plus antiemetics, and ergotamine plus caffeine.

Given the patient's current migraine presentation, a fixed-dose combination is not indicated. Importantly, she reports her pain subsides within 2 to 4 hours of taking the prescribed triptan monotherapy, she has not required rescue medication, and symptoms do not return once the pain is aborted. A dual-action agent may prove beneficial in the future, however, should the profile of her headaches change.

**Decision: Continue lifestyle measures along with triptan therapy to stop acute attacks.**

During the 3-month follow-up visit the patient is encouraged to maintain the changes she is making in her life to better balance rest and activity, be more consistent with mealtimes, and continue regular exercise and relaxation. She says she noticed recently that she wakes up with “the beginnings of a headache” if she consumes more than 2 glasses of wine when out with friends and has decided to eliminate alcohol for the time being.

The clinician suggests that she make an appointment for a 6-month check-in to evaluate the efficacy of her medication and stresses that she should call immediately if she notices any change in the nature of her headaches, including frequency, intensity, or duration. If she has a headache that does not respond to her current medication or that is different in any way from her regular pattern, she is instructed to go to her local emergency department. She leaves feeling very satisfied with the care she is receiving.

It should be noted that, while this patient responded well to the clinician's plan, patients with acute migraine can progress to headaches that occur daily, or almost daily, and that are superimposed with migraine headaches. When incidence has progressed to >180 headache days/year, the patient is considered to have CDH. Risk factors for CDH include<sup>3</sup>:

- Chronic migraine (>15 days/month)
- Obesity
- Life stress
- Sleep apnea/snoring
- Medication overuse
- Female gender
- Previous head injury

Since CDH frequently is associated with medication overuse, not every migraineur is a candidate for pharmacologic prophylaxis. This is best reserved for patients who:

- Are intolerant of or unresponsive to acute medications
- Have migraine on  $\geq 3$  days/month
- Have disabling headaches despite taking specific antimigraine medication

While some risk factors for CDH are not readily modifiable—migraine as a disorder, female gender, lower socioeconomic status, head injury—others are amenable to change through heightened attention to the disorder and alterations in lifestyle. Attack frequency may be reduced by avoiding known triggers, using preventive medication, or intervening in an attack as early as possible with an appropriate migraine-specific medication. At the same time, patients should be monitored to avoid continued overuse of medication if that has been an instigating factor. Weight loss and developing a regular exercise routine can both help improve overall health and lower risk. Restricting or eliminating caffeine from all sources, including beverages and medications, is also recommended.

If sleep apnea and/or snoring is contributing to CDH, clinical assessment and treatment can help prevent migraine progression. Establishing regular mealtimes and sleep schedule can be helpful for some patients. Other important strategies include managing stress and anxiety through means suited best to the individual and assessing for and treating depression.<sup>3,18</sup>

This patient averaged only 1 headache in the 3 months of follow-up, was proactive about lifestyle modification, and did not meet the criteria for or show any evidence of developing CDH.

## References

1. Landy S. Migraine throughout the life cycle. Treatment through the ages. *Neurology*. 2004; 62(Suppl 2):S2-S8.
2. Goadsby PJ. Recent advances in the diagnosis and management of migraine. *BMJ*. 2006;332:25-29.
3. Lipton RB, Bigal ME. Ten lessons on the epidemiology of migraine. *Headache*. 2007;47(Suppl 1):S2-S9.
4. Tepper SJ, Dahlof CGH, Dowson A, et al. Prevalence and diagnosis of migraine in patients consulting their clinician with a complaint of headache: data from the Landmark Study. *Headache*. 2004;44:856-864.
5. Lipton RB, Stewart WF, Simon D. Medical consultation for migraine: results from the American Migraine Study. *Headache*. 1998;38:87-96.
6. Lipton RB, Diamond S, Reed M, et al. Migraine diagnosis and treatment: results from the American Migraine Study II. *Headache*. 2001;41:638-645.
7. Sadowsky R, Dodick DW. Identifying migraine in primary care settings. *Am J Med*. 2005;118 (Suppl 1):11S-17S.
8. IHS Classification ICHD-II. International Headache Society Web site. <http://www.ihs-classification.org/en>. Accessed November 5, 2008.
9. Lipton RB, Stewart WF, Cady R, et al. Sumatriptan for the range of headaches in migraine sufferers: results of the Spectrum Study. *Headache*. 2000;40:783-791.
10. Lipton RB, Dodick D, Sadowsky J, et al. A self-administered screener for migraine in primary care. The ID Migraine™ validation study. *Neurology*. 2003;61:375-382.
11. Smith TR. The pharmacologic treatment of the acute migraine attack. *Clin Fam Pract*. 2005;7:423-444.
12. Brandes JL, Kudrow D, Stark SR, et al. Sumatriptan-naproxen for acute treatment of migraine. A randomized trial. *JAMA*. 2007;297:1443-1454.
13. Stewart WF, Lipton RB, Kolodner K, et al. Reliability of the migraine disability assessment score in a population-based sample of headache sufferers. *Cephalalgia*. 1999;19:107-114.
14. Lipton RB, Stewart WF, Stone AM, et al. Disability in Strategies of Care Study Group. Stratified care vs step care strategies for migraine: the Disability in Strategies of Care (DISC): a randomized trial. *JAMA*. 2000;284:2599-2605.
15. Lipton RB, Stewart WF. Acute migraine therapy: do doctors understand what patients with migraine want from therapy? *Headache*. 1999;39(suppl 2):S20-S26.
16. Goadsby PJ, Lipton RB, Ferrari MD. Migraine—current understanding and treatment. *N Engl J Med*. 2002;346:257-270.
17. Cady RK, Lipton RB, Hall C, et al. Treatment of mild headache in disabled migraine sufferers: results of the Spectrum Study. *Headache*. 2000;40:792-797.
18. Dodick DW. Chronic daily headache. *N Engl J Med*. 2006;354:158-165.
19. Ramadan NH, Silberstein SD, Freitag FG, et al; US Headache Consortium. Evidence-based guidelines for migraine headache in the primary care setting: pharmacological management for prevention of migraine. <http://www.aan.com/professionals/practice/pdfs/gl0090.pdf>. Accessed November 6, 2008.

