

California Rx MONITOR

CMA California Medical Association
Physicians dedicated to the health of California

Diagnosis and Treatment of Migraine Headache in Adult Patients

INTRODUCTION

California Medical Association is pleased to present the following therapeutic practice overview.

This working document is the first in a series of quarterly reviews that will provide primary care physicians with practice parameters in selected therapeutic categories. These reviews will serve as clinical context for personalized physician prescribing reports, which you can choose to receive in conjunction with and following each therapeutic review. The feedback reports will be provided for your use only, and are intended to support quality improvement through individual self-assessment and choice.

The goal of the program is to better align prescribing behavior with evidence-based guidelines. We envision a collaborative process and encourage your feedback in developing succinct, useful, clinically valid and relevant decision support tools that will enhance patient care as well as clinical and economic outcomes. Shortly after receiving this communication, we will request your input in the form of a brief questionnaire. Your feedback will be instrumental in developing future offerings and enhancements.

CMA has chosen migraine management as the subject of our initial review because despite numerous national initiatives, migraine remains underdiagnosed and undertreated leading to a tremendous burden of illness. According to a recent study presented at the 48th Annual Scientific Meeting of the American Headache Society, American employers pay \$24 billion annually in direct and indirect costs related to migraine headache. Direct costs, which include in-patient, out-patient, and emergency room care,

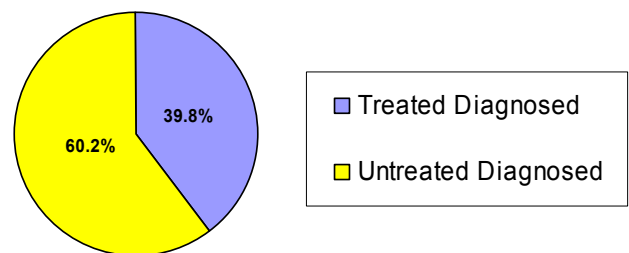
and prescription drugs, total \$12.7 billion; indirect costs related to absenteeism, short-term disability and workers' compensation total \$12 billion annually.

A recent analysis of nearly 6.2 million insured patients, published in *Headache and Pain: Diagnostic Challenges, Current Therapy*, showed that:

- While approximately 12% of people suffer from migraines, only 3% were diagnosed
- Of patients diagnosed with migraine, only 50% received a prescription
- Of those, 59% received narcotics/opioids, which are not FDA approved for migraine treatment, while only 41% received triptans, which are considered first-line treatment in the management of migraine

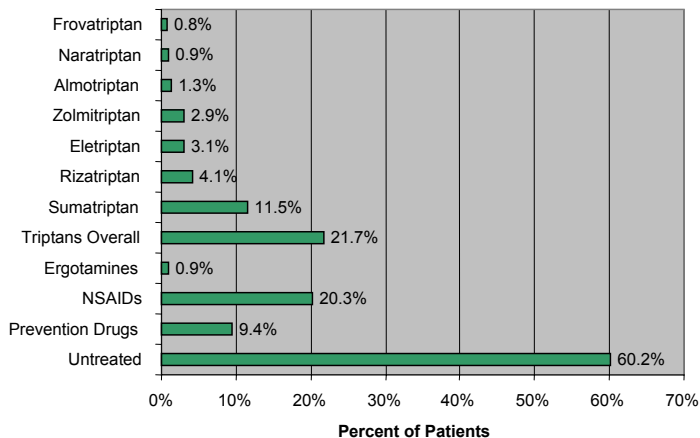
In comparison, an analysis of related practices using a national medical claims database shows consistent findings (Figures 1 and 2).

Figure 1: Patients with Migraine Diagnosed and Treated vs. Patients with Migraine Diagnosed and Untreated, April 2004 through March 2005 (Source: PharMetrics, a unit of IMS Health)



Clearly a need exists for greater education and awareness of consensus guidelines and best practices. The following recommendations are based to a great extent on the most current American Academy of Neurology guidelines and anticipate most changes in a revision of those guidelines, which is in development. Updates will be made as necessary.

Figure 2: Use of Indicated Medications in the Treatment of Migraine, April 2004 through March 2005
(Source: PharMetrics, a unit of IMS Health)



DIAGNOSIS

Finding an effective treatment requires accurate diagnosis. The most common type of a disabling headache seen by doctors is migraine. A quick and accurate way to make the diagnosis of migraine is to ask your patient three questions:

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

If the answer is yes to two of these questions then the diagnosis is migraine.

Please note that this is a screening tool and not a diagnostic test, so while you will correctly identify more than 90% of patients with migraine headaches, you should always keep in mind tumors, subdural hematomas, infections and other serious conditions, which can also cause these symptoms. Some features that should raise suspicion of a secondary headache include recent onset of headaches, sudden change in the character, frequency or severity of headaches, associated systemic symptoms or neurological signs and symptoms. Presence of these usually requires an imaging study and blood tests (TFTs, CBC, chemistry, etc).

Migraines are often mistaken for tension headaches because many migraine patients lack many

Figure 3: Migraine Patient Distribution by Gender and Age, August 2005 through July 2006
(Source: IMS Health)

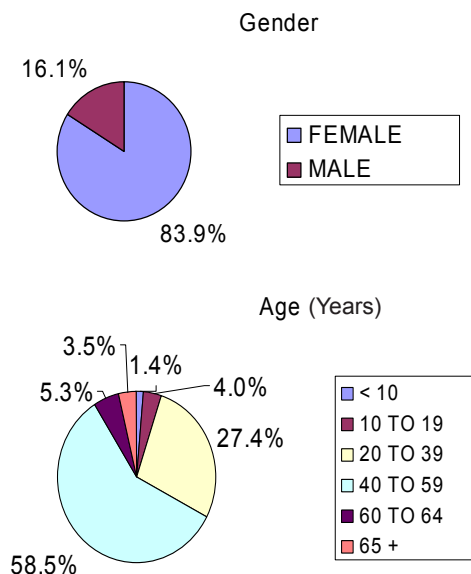
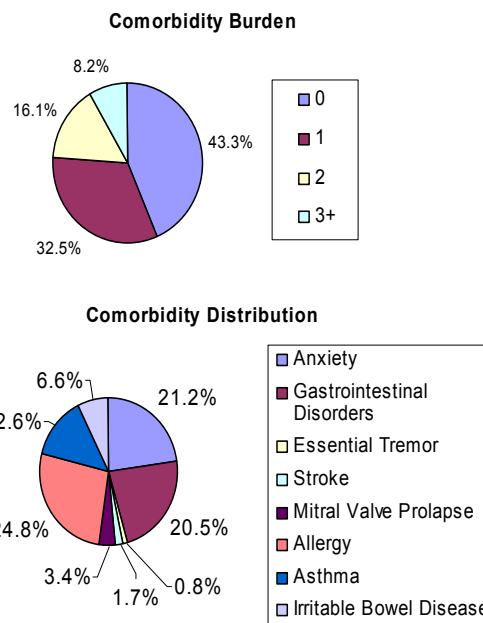


Figure 4: Migraine Patient Distribution by Comorbidity Burden, April 2004 through March 2005
(Source: PharMetrics, a unit of IMS Health)



typical features of migraines (aura, unilateral pain, nausea, photophobia, phonophobia, throbbing) and for sinus headaches because the pain is localized in the area of sinuses. Figures 3 and 4 detail demographic and clinical characteristics of migraine patient population.

In addition to establishing the diagnosis, it is important to determine the degree of potential disability because it may lead to a more appropriate

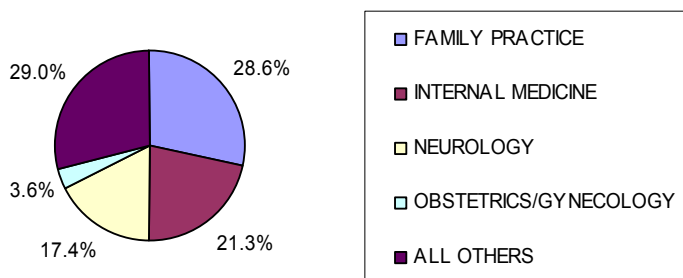
treatment. Physicians often underestimate the degree of disability caused by migraines and the impact on patients' quality of life. A simple validated questionnaire (Table 1) can give the physician an idea of how aggressively to approach treatment.

TREATMENT

Once the diagnosis is established the treatment, typically initiated by a primary care physician (Figure 5), should include three aspects:

1. Identification of triggers and lifestyle modification
2. Acute therapy
3. Prophylactic therapy

Figure 5: Treatment of Migraine by Provider Specialty, August 2005 through July 2006 (Source: IMS Health)



1. Identification of Triggers and Lifestyle Modification

Lack of sleep and skipping meals may appear obvious, but often needs to be pointed out to patients as common triggers. There are two effective strategies to counteract the effect of stress on headaches: frequent aerobic exercise (30 minutes, five days a week is ideal) and biofeedback or another form of relaxation training. Excessive caffeine intake is a major contributor to frequent or daily headaches and it usually makes all other therapies ineffective. Caffeine relieves headaches and is included in many drugs such as Excedrin®, Anacin®, Fioricet® and Esgic®, but it will cause rebound headaches if consumed on a daily basis. A daily limit of one caffeinated beverage and a monthly limit of 15-20 tablets of any caffeine-containing drug must be strictly adhered to.

2. Acute Therapy

In some patients mild migraines or attacks with very gradual escalation can be aborted with over-the-counter nonsteroidal antiinflammatory medications, such as ibuprofen, aspirin, naproxen and combination drugs, such as aspirin/acetaminophen/caffeine.

Most patients seeing a physician for their headaches require prescription migraine drugs. Presence of disability (on MIDAS or by history) is a clear indicator of the need for a triptan. Triptans often have a dramatic impact on the quality of life of migraine sufferers. This group of drugs includes the first seven medications listed in Table 2. Naratriptan and frovatriptan have a longer half-life, but a relatively slow onset of action and should be reserved for patients with prolonged attacks or those who do not respond to the other five drugs. Zolmitriptan and sumatriptan are available in a nasal spray formulation, which is useful for patients with severe nausea. Sumatriptan can be self-injected by the patient and can save a trip to an emergency department. It provides excellent relief and has a surprisingly high acceptance rate by patients, but physicians often fail to offer this approach. Many patients have a significantly different response to different triptans and trials of many are occasionally required before an effective and tolerable choice is found. Major contraindications for triptans include uncontrolled hypertension and coronary artery disease.

Figures 6 and 7 show triptan utilization in the management of migraine as dispensed at retail pharmacies in California and nationally.

If nausea is not relieved by the acute therapy or if vomiting is present, antiemetics are indicated. Prochlorperazine (Compazine®) is available in a suppository form and in addition to its antiemetic properties can contribute to the relief of pain. Other antiemetics, such as trimethobenzamide (Tigan®) and promethazine (Phenergan®) are also available in a suppository form.

Migranal® (dihydroergotamine) Nasal Spray provides quick relief for some patients but can

Table 1. Validated Migraine Disability Assessment (MIDAS) Questionnaire

INSTRUCTIONS: Please answer the following questions about ALL your headaches you have had over the last 3 months. Write your answer in the box next to each question. Write zero if you did not do the activity in the last 3 months.

1.	On how many days in the last 3 months did you miss work or school because of your headaches?		days
2.	How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches? (Do not include days you counted in question 1 where you missed work or school)		days
3.	On how many days in the last 3 months did you not do household work because of your headaches?		days
4.	How many days in the last 3 months was your productivity in household work reduced by half or more because of your headaches? (Do not include days you counted in question 3 where you did not do household work)		days
5.	On how many days in the last 3 months did you miss family, social, or leisure activities because of your headaches?		days
	TOTAL		days
A.	On how many days in the last 3 months did you have a headache? (If a headache lasted more than 1 day, count each day)		days
B.	On a scale of 0-10, on average how painful were these headaches? (0=no pain at all; 10=pain as bad as it can be)		
Once you have filled in the questionnaire, add up the total number of days from questions 1-5 (ignore A and B).			

Treatment Recommendations Based on MIDAS Score

Score	Grade	Definition	Recommendations
0-5	I	Little or No Disability	<ul style="list-style-type: none"> ⊙ OTC analgesics may be effective in acute treatment ⊙ Impact of lost days on lifestyle should be assessed ⊙ Patients with infrequent but severe migraine may benefit from first-line treatment with triptan ⊙ Patients who have failed to achieve effective relief with OTC analgesics should also be considered for triptan therapy
6-10	II	Mild Disability	<p>Acute prescription medication may be necessary if</p> <ul style="list-style-type: none"> ⊙ headaches are severe ⊙ headaches are causing severe disruption in patients' lives ⊙ patients have failed to achieve relief with OTC analgesics
11-20	III	Moderate Disability	<ul style="list-style-type: none"> ⊙ Specific acute therapy is usually most appropriate ⊙ Prophylactic treatment should also be considered
21+	IV	Severe Disability	<ul style="list-style-type: none"> ⊙ Please note: very high MIDAS score may indicate a high frequency of non-migraine headache and these patients should be managed accordingly

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Figure 6: Distribution of Triptans Dispensed at Retail Pharmacies in California, August 2005 through July 2006
(Source: IMS Health)

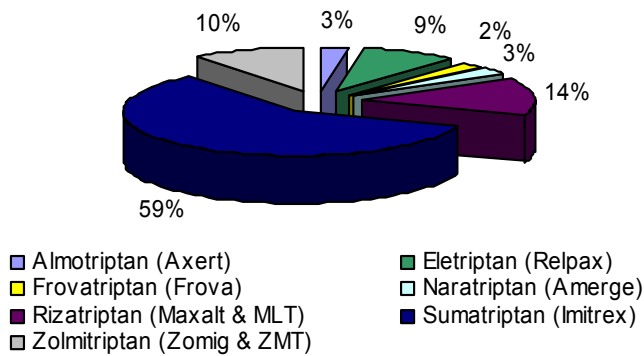
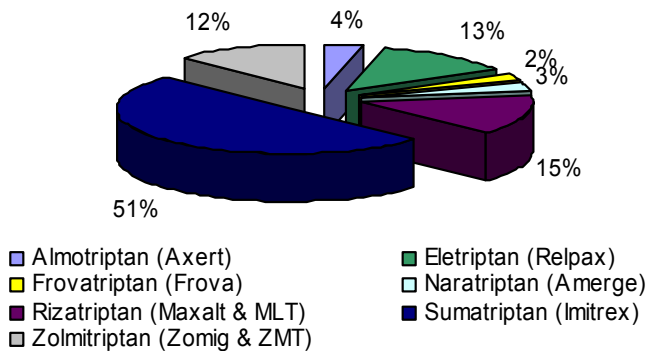


Figure 7: Distribution of Triptans Dispensed Nationally at Retail Pharmacies, August 2005 through July 2006
(Source: IMS Health)



cause nausea. Ergotamine/caffeine combinations may also be effective for some patients with moderate-to-severe migraines.

3. Prophylactic Therapy

Prophylactic pharmacotherapy is indicated when acute therapy is not effective, contraindicated or not tolerated. Agents used for migraine prophylaxis, including anticonvulsants, antidepressants, antihypertensives and several complementary therapies, are listed in Table 3. The general principles include escalation of the dose to the point of relief or unacceptable side effects and giving a sufficient trial of at least a month at the highest dose. The most effective drugs are divalproex sodium, topiramate, propranolol, timolol and amitriptyline. The second tier includes atenolol, metoprolol, nadolol, verapamil, NSAIDs, gabapentin, fluoxetine, magnesium, riboflavin

Table 2. Agents Used for Acute Therapy of Migraine

Generic (Brand)	Dosage Forms	Weight of Evidence
Sumatriptan (Imitrex®)	25, 50, 100 mg tabs 5, 20 mg nasal spray 4, 6 mg auto-injection 6 mg vial	A
Zolmitriptan (Zomig®)	2.5, 5 mg tabs 2.5, 5 mg ODT* 5 mg nasal spray	A
Rizatriptan (Maxalt®)	5, 10 mg tabs 5, 10 mg ODT*	A
Naratriptan (Amerge®)	1, 2.5 mg tabs	A
Almotriptan (Axert®)	6.25, 12.5 mg tabs	A**
Frovatriptan (Frova®)	2.5 mg tab	A**
Eletriptan (Relpax®)	20, 40 mg tabs	A**
Dihydroergotamine mesylate (Migranal® Nasal Spray)	4 mg/mL in glass vial	A
Ergotamine/caffeine (Cafergot®, Wigraine®)	1 mg ergotamine, 100 mg caffeine tabs Cafergot suppositories: 2 mg ergotamine, 100 mg caffeine	B

Silberstein SD. Neurology 2000;55:754-762.

Highest available tablet strength is the starting dose for all triptans for most adults.

*ODT – orally disintegrating tablet (offers no advantage in the speed of onset; can be taken without water when water is not available or if hard to swallow because of nausea)

**Almotriptan, frovatriptan, and eletriptan were approved for acute migraine treatment after publication of AAN guidelines.

and feverfew. Comorbidities, such as anxiety, depression, hypertension and epilepsy as well as potential side effects should be considered when choosing a drug. Divalproex sodium should not be used if a risk of pregnancy is high (Category D). Another disadvantage is its potential to cause weight gain. Lowering of blood pressure and impaired exercise tolerance limit the usefulness of beta-blockers. Amitriptyline can cause sedation and weight gain. Magnesium can be given to most patients. Diarrhea and stomach pains are usually the only side effects.

Patients who do not respond to several abortive or prophylactic agents should be referred to a neurologist.

Table 3.
Agents Used for Migraine Prophylaxis

Generic (Brand)	Dose Range (mg)/Day	Weight of Evidence
Propranolol (Inderal®)	60-480	A
Atenolol (Tenormin®)	25-100	B
Metoprolol (Lopressor®)	100-400	B
Timolol (Blocadren®)	20-30	A
Nadolol (Corgard®)	40-240	B
Verapamil (Calan®)	240-960	B
Amitriptyline (Elavil®)	10-150	A
Fluoxetine (Prozac®)	20-80	B
Topiramate (Topamax®)	25-800	A*
Divalproex (Depakote®)	500-1500	A
Gabapentin (Neurontin®)	600-3600	B
Naproxen (Naprosyn®)	375-1000	B
Magnesium	400-800	B
Riboflavin (vitamin B ₂)	200-400	B
Feverfew	100-400	B

Silberstein SD. *Neurology* 2000;55:754-762.

*Topiramate was approved for migraine prophylaxis after publication of AAN guidelines.

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FOR MORE INFORMATION

Links for patients

<http://www.migraines.org>

<http://headaches.org>

<http://www.achenet.org>

Links for physicians

<http://headaches.org>

<http://www.ahsnet.org>

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