



# Fueling the Migraine Fire

Overuse of narcotics and barbiturates may worsen migraine headache.

BY STEPHANIE STEPHENS

However they spell “relief,” it can’t come quickly enough for millions of migraine sufferers. To ease their excruciating pain and other symptoms, migraineurs are sometimes prescribed medications that contain barbiturates or narcotics. While providing welcome short-term respite, these drugs may worsen migraine if overused, according to a recent study published in the medical journal *Headache* in 2008.

Migraine occurs in two forms that are distinguished by headache frequency: episodic and transformed (or chronic). In episodic migraine, attacks occur fewer than 15 days per month. In transformed migraine, attacks occur 15 or more days per month.

The *Headache* study of more than 8,000 patients with episodic migraine revealed that 2.5 percent of them developed transformed migraine over the course of one year of follow-up—and that the risk of doing so depended in part on how they treated their attacks.

Researchers at the Albert Einstein College of Medicine in New York, NY, were led by principal investigator and senior author Richard B. Lipton, M.D., a longtime headache specialist. Dr. Lipton is professor and vice chair of neurology at the university and directs the Montefiore Headache Center in the Bronx, NY.

“Part of what’s striking is that it wasn’t all drugs that made things worse,” Dr. Lipton reports. “Our findings are very specific to two classes of drugs that were ‘major bad actors.’” Those two classes were barbiturates and narcotics.

The results of the study may well affect the way physicians treat the 35 million people that suffer from migraine headaches and the additional 5 million that experience transformed migraine. As the most common of neurological disorders, migraine causes staggering lost labor and productivity costs of more than \$13 billion each year.



Migraineurs experience moderate to severe headaches that last from four to 72 hours, typically with throbbing pain, often on one side of the head. They may also experience increased pain after exercise or movement, nausea or vomiting, and sensitivity to bright light, sound, and odors. Not surprisingly, many migraine sufferers are tempted to rely on pain relievers such as narcotics and barbiturates. And doctors may prescribe these drugs out of habit or because they relieve pain of all kinds and not just migraine, Dr. Lipton says.

However, he adds, “Because these medications may cause medication headache, they are a trap. The drugs you use to relieve headaches make you feel better on a short-term basis but may make you feel worse on a long-term basis. They actually add fuel to the migraine fire.”

## PRACTICE PERFECTS PAIN

Migraine medications include two broad classes: acute and preventive. When a headache starts, so-called acute medications are used to relieve pain and restore function. Acute therapies include narcotics, barbiturates, triptans, nonsteroidal anti-inflammatory drugs (NSAIDs), and combination products, which combine two drug classes into one. Triptans, available since the early 1990s, include seven different marketed drugs—for example, sumatriptan (Imitrex), zolmitriptan (Zomig), and rizatriptan (Maxalt). NSAIDs are anti-inflammatory drugs available by prescription or over the counter, such as ibuprofen (Advil, Motrin) and naproxen (Aleve). Recently a triptan/nonsteroidal combination drug marketed under the name Treximet was approved by the FDA.

## Narcotics and barbiturates may increase brain sensitivity to the pain they temporarily relieve.

Beta-blockers, anti-depressants, and calcium channel blockers are preventive therapies. These drugs prevent and reduce the frequency of headaches. They may also

keep headaches from worsening over time.

Unfortunately, the frequent end stage of medication overuse is transformed migraine, according to Dr. Lipton. The precise mechanics and progression of transformed migraine aren't completely understood, but Dr. Lipton offers this analogy: "Whatever the brain does repeatedly it gets better at doing, whether it's reading, playing the piano, or experiencing pain."

Researchers confirmed that long-term use of certain narcotics and barbiturates may actually increase brain sensitivity to the pain that they temporarily relieve, prompting the sufferer to require more medications. In turn, this results in an increasing number of episodic attacks. In addition, both classes of drugs are addictive and can cause withdrawal when discontinued.

### WHAT'S SAFE, WHAT'S NOT?

In the Einstein study, increased risk for transformed migraine was associated with commonly prescribed narcotics such as acetaminophen with oxycodone (Percocet) and commonly prescribed barbiturates such as butalbital with aspirin and caffeine (Fiorinal) and butalbital with acetaminophen and caffeine (Fioricet, Esgic).

"With narcotics and barbiturates, the higher the attack frequency and the more days drugs were taken, the greater the likelihood of headache progression. It was a pretty clean finding," Dr. Lipton says.

Narcotics relieve pain but may induce sleep. In excessive doses, they may cause stupor, coma, or even death. For episodic migraine pain, Dr. Lipton might cautiously prescribe their use no more than once or twice a month.

Barbiturates, which slow the senses and can depress the nervous system, are used for mild sedation and anesthesia, or as anticonvulsants. Barbiturate combination prod-

ucts, although widely used in the United States, are actually off-market in a number of countries including Germany. Dr. Lipton prescribes those combos infrequently, and not as the first line of headache defense.

What then are safe and effective options for the migraine sufferer? The Einstein study found that for those experiencing less than 10 headaches per month, triptans were very safe and did not increase the risk of transformed migraines. NSAIDs protected well against transformed migraine for people who had fewer than 10 headache days per month, but for those who experienced high levels of monthly headache days, NSAIDs also increased the risk of developing transformed migraine.

### USE WITH CARE

Many doctors believe that combination medications are more likely to cause an increase in headaches than single-ingredient drugs, according to J. D. Bartleson, M. D., associate professor of neurology at Mayo Clinic College of Medicine in Rochester, MN, whose specialties include migraine and other headaches.

Butalbital, for example, is usually coupled with aspirin or acetaminophen

(with or without caffeine) in the prescription drugs Fiorinal, Fioricet, and Esgic. All of these were looked at in the Einstein study. Opioids are commonly coupled with acetaminophen or less commonly aspirin (as in Percodan).

"Is it combination drugs that are to blame?" asks Dr. Bartleson. "Or is it the barbiturate alone, as in butalbital, or the opioid alone, such as codeine, oxycodone, or hydrocodone? Patients are very rarely prescribed butalbital, codeine, hydrocodone, or oxycodone alone. Perhaps it is the combination of one of these drugs with another analgesic that promotes an increase in headache frequency."

This question remains to be answered. But Dr. Lipton confidently encourages physicians to avoid use of narcotic or barbiturate medications that may exacerbate migraine. He also recommends that if these drugs are prescribed out of necessity, doctors should not only apply dose limits but advise patients of the risks of overuse.

"I believe in relieving headache pain and not leaving people in agony," Dr. Lipton emphasizes. "I also believe in not trading off feeling better in an hour if the price is a long-term increase in headache frequency. Proper treatment with the appropriate medicines can bring relief to most people with migraine." NN

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## WHAT IS A NARCOTIC?

The term "narcotic" originally referred to any pain-relieving drug derived from opium or opium-like compounds, which is why some doctors prefer the term "opioids." More recently, however, the term narcotic has expanded to include any drug—synthetic or naturally occurring—with effects similar to opium and opium derivatives, including meperidine and fentanyl and its derivatives. Like opioids, these drugs can make you drowsy and have a risk of dependence.