

from DR M

A SPECIAL REPORT

Management of analgesic overuse headaches

Fred D. Sheftell, MD

Preview

Many patients with recurrent headaches take too many analgesics too often in an effort to relieve their pain. Ironically, this overuse contributes to the problem through "analgesic rebound headaches," and not until patients are weaned off medications do their headaches improve. This article describes the issues surrounding analgesic rebound headache and offers a strategy for treating patients who are enmeshed in this syndrome. Although the approach described may seem time-consuming, it is advocated when dealing with patients who have refractory headaches. It may prove to be more effective than the numerous failed attempts and the potential for substance addiction that are associated with less focused approaches.

■ Overuse of analgesics can be a significant obstacle to successful management of headaches, because as clinical studies have shown, it may actually exacerbate the problem.^{1,2} This paradox, known as analgesic rebound headache, occurs in patients who regularly take any of a wide

variety of pain-killing drugs or agents for migraine.

Clinical studies of drug-induced headache

A study of 200 patients with recurrent tension headaches confirmed the relationship between analgesic overuse and refractory pain.³ In the 4-week study, patients were divided into two groups of 100: Group 1 received the tricyclic antidepressant amitriptyline hydrochloride (25 mg/day for 1 week and 50 mg/day thereafter) as a preventive

medication; group 2 did not. Patients were further divided into subgroups. Half of those in group 1 and half of those in group 2 were permitted to continue taking analgesics without restriction; the remaining subjects were instructed to discontinue use of analgesics.

Weekly headache frequency was calculated for each group using a headache index and headache index ratio. Comparing analgesic-using and analgesic-restricted subgroups (table 1), investigators found significant improvement, as measured by headache frequency and graded pain severity, in the patients who abstained from analgesic use. Moreover, the study suggested that analgesic use may have interfered with responsiveness to amitriptyline.

Using a similar study design, Mathew et al⁴ attempted to define key clinical features and management strategies in patients with drug-induced headaches. Their study involved patients who were taking daily symptomatic or immediate-relief medications, often in excessive quantities, yet continued to have daily or near-daily severe headaches. Of the 200 patients studied, 86 (43%) were taking two analgesic preparations, and 44 (22%) were taking three or more.

Patients were divided into two groups: Group 1 used only symptomatic medications, and group 2 used symptomatic and prophylactic medications. The groups were further stratified. Group 1 was divided into three subgroups: those who were allowed to

Fred D. Sheftell, MD

Dr Sheftell is founder and director, The New England Center for Headache, Stamford, Connecticut, and clinical associate professor, New York Medical College, Valhalla.

Table 1. Improvement in tension headaches after 4 weeks of amitriptyline hydrochloride therapy with and without analgesics

Subgroup	No. patients	Headache index*	Headache index ratio†	Improvement (%)‡
Receiving analgesics	93	5.33	0.76	24
Not receiving analgesics	45	2.85	0.40	60§

* Weekly headache frequency × graded severity.

† Posttreatment + pretreatment headache index.

‡ Calculated as follows: $1 - \text{headache index ratio} \times 100$.

§ $P < 0.01$.

Adapted from Kudrow.³

Table 2. The migraine funnel

Level 1 (majority of patients with migraine)

- Episodes are moderate and intermittent
- Headaches respond well to self-care and over-the-counter medications
- Patients do not abuse or overuse medications

Level 2 (more intense headaches)

- Headaches are unresponsive to over-the-counter medications
- Patients seek help from their primary care physician
- Headaches may respond to a butalbital compound or simple narcotic
- Patients use prescribed drugs intermittently
- Patients rarely abuse or overuse medication

Level 3 (less response to simple interventions)

- Low-intensity interictal phenomenon may develop
- Patients seek preventive and abortive medication from secondary care physician

Level 4 (daily headaches from overuse syndromes)

- Hospitalization may be required to provide aggressive therapy
- Headaches are refractory, increasing medical and psychiatric comorbidity

continue taking symptomatic medication, those who discontinued symptomatic medication, and those who discontinued symptomatic medication and began prophylactic medication. Group 2 was divided into two subgroups: those who discontinued symptomatic medication but continued prophylactic medication, and

those who discontinued symptomatic medication and altered, either in dosage or in combination, prophylactic medication.

All patients received dietary instructions and biofeedback training, and they were assessed for changes in headache indexes for 3 months. Effects of continuing and discontinu-

ing symptomatic medications and of adding or changing prophylactic medications were studied in the various groups, and investigators reached the following conclusions:

- Daily use of symptomatic or immediate-relief medications resulted in recurrent daily headaches.
- In itself, discontinuation of daily symptomatic medications resulted in abatement of headaches.
- Concomitant use of symptomatic medications nullified the effect of prophylactic medications.
- Discontinuation of daily symptomatic medications enhanced the beneficial effect of prophylactic medications.

The transformed migraine model

A review by Mathew⁵ of several migraine studies suggests that most patients with recurrent headaches have "transformed migraines" and exhibit a mixture of migraine and tension-headache features.

In the transformed-migraine model, distinct episodes of migraine in the initial years give way over time to daily headaches. In the early years, episodes of migraine can be debilitating. As patients ma-

continued

Headache provides patients with calendars that include detailed information about their medication. Patients are carefully instructed in documentation of names and amounts of medications they are taking and intervals prescribed. Patients also record the relief they receive, using a scale from 0 to 3. Furthermore, patients note potential triggers to their headaches.^{9,10} Headache calendars also can reveal side effects and other problems.

AVOIDING REBOUND PHENOMENON—Management of headache relief should focus on avoiding rebound headaches by judicious use of medication (table 3). Often, as patients' headaches become more frequent, they begin to overuse analgesics to get relief. They may use a combination of aspirin or acetaminophen and a barbiturate² or a mixed analgesic and ergotamine. Intake of agents may range from 5 to 20 tablets a day,² but still headaches seem to worsen because this usage interferes with the effectiveness of the prophylactic medication.³

Rebound effect can occur if analgesics are taken more than 4 days a week.¹¹ Thus, attempts should be made to wean patients off excessive medications that may be interfering with their mainstay agents, and they should be instructed to avoid self-medicating for mild and, if possible, moderate headaches. Patients should be fully informed about the nature of analgesic rebound phenomenon, with emphasis on the following key concepts:

Table 3. Strategies to help patients relieve headache, but avoid rebound effects

Clearly define safe maximum or alternative therapy of agents being used

Determine whether several analgesics are being used, and if so, amounts of each

Evaluate that overuse of analgesics can block prophylactic effects of daily medications, thus promoting headaches

Wean off nonessential use of over-the-counter medications (eg, acetaminophen, aspirin, caffeine)

Encourage limiting self-medication whenever possible (eg, for mild headaches)

Limit supply of prescription drugs, except for rescue amounts that are sometimes needed

Provide educational materials

- Continued use of symptomatic medications maintains the cycle of headaches.
- Pharmacologic as well as nonpharmacologic therapy is less likely to relieve pain in the face of ongoing analgesic overuse.
- Short-term discomfort will lead to an improved long-term outcome.
- Some time is needed before full benefits are seen from discontinuation of analgesic overuse.

WITHDRAWING NONPRESCRIPTION DRUGS—Initially, patients should terminate use of all nonprescription medications.⁹ They will be less apprehensive about continuing the treatment plan if they receive appropriate support for their

most severe headaches. Support may include a variety of nonsteroidal anti-inflammatory drugs (NSAIDs), such as naproxen sodium or meclizolam sodium, or a vasoactive drug, such as isometheptene mucate, given three or four times a day and tapered down over a period of several weeks.

Taking patients off a daily regimen of 10 to 20 tablets of a high-caffeine over-the-counter agent can be a significant problem. In combination-analgesic overuse, calculate the amount of caffeine from both medicinal sources and beverages. Reduce intake of caffeinated beverages slowly, by one 5-oz cup or half a mug of coffee every 5 to 7 days. Reduce the intake of combination analgesics, using the schedule described in table 4.

WITHDRAWING PRESCRIPTION DRUGS—Prescription medications must be withdrawn carefully (table 5).⁹ Of greatest concern is the increased risk of seizures associated with rapid tapering or abrupt cessation of butalbital medications.⁵ Sudden removal of butalbital can be life-threatening.¹¹ For these patients, switching to phenobarbital during the tapering process may be necessary.⁹ The recommended conversion schedule is 100 mg of short-acting butalbital to 30 mg of long-acting phenobarbital, reducing by 10% to 15% every 2 to 4 days. Patients must be closely monitored for sedation and signs of central nervous system irritability. Caffeine intake and possible interactions with

continued

tion medication is increasing.

- Severe pain is likely on withdrawal of medications.
- Frequency of visits to the emergency room is increasing.
- Underlying medical disorders (eg, coronary disease, hypertension, ulcers) complicate outpatient intervention.
- Moderately serious psychiatric difficulties accompany headaches.

WITHDRAWAL OF MEDICATIONS—In the hospital, non-prescription medications are discontinued and prescription drugs are tapered off. Narcotics are tapered in a manner similar to that described for outpatient care. Intravenous dihydroergotamine mesylate, which acts both peripherally and centrally, is ideal for use in the hospital setting. Patients using ergots respond well to dihydroergotamine and usually have an excellent long-term prognosis. In these patients, ergots are gradually decreased 0.5 to 1 mg daily. For withdrawal of benzodiazepines, use of carbamazepine may decrease withdrawal time.⁸

INTERVENTION—Break-through headaches are managed with a high-intervention plan. Nonpharmacologic measures are instituted first, and if necessary, NSAIDs are given. Corticosteroids may be administered to patients who do not respond to dihydroergotamine. Essentially, as-needed administration of analgesics is avoided. Often, severe break-through headaches require use of hydroxyzine hydrochloride, intramuscular ketorolac tromethamine, or intravenous chlorpromazine hydrochloride.

Table 5. Guidelines for terminating use of prescription analgesics

Mixed butalbital compounds

- Calculate average daily butalbital dose at 50 mg/tablet
- Reduce by 1 tablet q3-5d
- or
- Convert 100-mg (short-acting) butalbital to long-acting phenobarbital (100 mg butalbital = 30 mg phenobarbital)
- Give in divided doses
- Taper 10% to 15% q2-4d
- Adjust caffeine content when appropriate
- Monitor for sedation or central nervous system irritability
- Monitor for potential interactions with preventive medications

Mixed butalbital compounds with codeine

- For butalbital, follow procedure above
- Reduce codeine by 30 mg qd
- Consider use of clonidine HCl, given orally (0.05 or 0.1 mg tid) or in transdermal patches (2.5 or 5 mg total clonidine content)
- Consider use of naltrexone HCl*, 50 mg qd (or tid for faster withdrawal)

Narcotics

- Reduce by 1 tablet or spray qd or q3-4d
- Consider use of clonidine or naltrexone*
- Treat sleep disturbance with tricyclic antidepressant, trazodone HCl, or hydroxyzine

Benzodiazepines

- Reduce slowly, by ½ tablet q7d
- Differentiate among withdrawal, recurrence of original symptoms, and rebound
- Consider use of carbamazepine to speed tapering

Ergotamine tartrate

- Reduce by 0.5 to 1 mg qd
- Consider use of clonidine

*Naltrexone is an opioid antagonist that may cause withdrawal in patients dependent on opioids.

PATIENT OUTCOME—Most patients respond well to hospitalization. Appropriate discharge planning is very important. Use of a model of relapse prevention similar to that of Alcoholics Anonymous is recommended.⁸

Follow-up data are excellent. As part of an inpatient pain-treatment program with the Commission on Accreditation of Rehabilitation Facilities, Lake et al⁸ measured outcome data for 100 pa-

tients with chronic, intractable migraine who were evaluated at Chelsea Community Hospital in Michigan (mean hospital stay, 8.5 days). Among the parameters assessed were headache, depression, sleep disturbance, performance of responsibilities, medication use, and work status. Assessments taken before hospitalization, at discharge, and at long-term follow-up (mean, 8.3 months) revealed significant

continued

DISCUSSION

Dr Portenoy: My understanding is that there is minimal evidence of rebound to drugs other than caffeine and ergots.

Dr Rapoport: While we don't have double-blind, placebo-controlled studies, we do have the expert opinion of headache specialists throughout the world. Clinical experience indicates that a significant percentage of patients with refractory headaches are taking too much medication. Many of our patients begin their day by taking a handful of analgesics, and they continue popping pills every 3 to 4 hours throughout the day. When you break the cycle by taking patients off the medication, they do much better. That's the evidence.

Dr Portenoy: The problem we face with opioids is the predisposed population. We don't want to say this therapy isn't good based on a subgroup of patients. We run this same risk when we say that nobody should take more than two doses of acetaminophen a day, or more than two times a week. That's a big leap. Is there any scientific support of that leap?

Dr Solomon: We see a very skewed population; a large part of our practice is patients with daily headache. But epidemiologic studies done in this country and in Denmark have shown that chronic tension-type headache, the International Headache Society's

term for chronic daily headaches, occurs in only 3% of the population. We admonish patients who have been overusing acute-pain medication not to take these drugs more than 2 days a week after they have been withdrawn from them for 1 or 2 months.

Dr Sheftell: We must have a sense of precaution in our recommendations. There are patients who don't escalate their use of prescribed medications. It's difficult for the nonspecialist to identify those who do. Of course, we don't see those who are doing well on what their physicians are prescribing.

Dr Portenoy: I would be comfortable saying that there is a possibility, based on the literature and to be confirmed, that frequent use of short-acting analgesics may lead to a syndrome of chronic daily headache that may require withdrawal to treat. After giving a patient access to a prescription for short-acting analgesics, I would closely monitor that patient. If there were indications of abuse or overuse, I would intervene early and aggressively.

Dr Solomon: I think that's a very logical approach.

Dr Portenoy: I use a similar approach with opioids. I call it a therapeutic opioid trial for noncancer-related pain. That's how I would incorporate it. You don't know how patients will respond. They have never had regular access to a drug in conjunction with good moni-

toring and concurrent therapies directed toward functionality. You enter into a contract with the patient: "I'm going to prescribe this. I'm going to watch to make sure you don't cross into a danger zone, and if you do, I'm going to tell you it's not appropriate."

Dr Sheftell: We have been trained that addiction is a physiologic dependence. Certainly, patients who require maintenance opioid therapy may be physiologically dependent. However, we must also consider addiction as a behavioral phenomenon, a compulsion for ongoing use in spite of destructive events. These behaviors also include non-compliance, such as using multiple prescribers and multiple pharmacies. Patients who require opiate maintenance should adhere to guidelines specified in a "contract." ■