

## What is the best treatment for analgesic rebound headaches?

### ■ EVIDENCE-BASED ANSWER

Abrupt discontinuation of the offending analgesic(s), and treating rebound headaches with dihydroergotamine (DHE) as needed, results in significant improvement for most patients (strength of recommendation [SOR]: **C**; based on case series). Amitriptyline does not affect the frequency or severity of rebound headaches, but it may improve quality of life (SOR: **B**, low-powered randomized controlled trial). Prednisone or naratriptan (Amerge) lessen acute withdrawal symptoms from analgesics and reduce the need for rescue medications during the first 6 days of treatment; however, they do not affect headache frequency or severity (SOR: **B**, low-quality randomized controlled trial).

### ■ EVIDENCE SUMMARY

Analgesic rebound headaches are seen in 1% of the population, mostly middle-aged women with underlying migraines.<sup>1,2</sup> Also termed analgesic-overuse headaches, they are defined by the International Headache Society guidelines as headaches occurring more than 15 days per month, mild to moderate in intensity, developing or worsening with analgesic overuse, and resolving or reverting to the prior underlying headache pattern within 2 months of discontinuing the analgesic(s).<sup>3</sup>

A case series studied 50 patients with rebound headaches for 5 or more days a week at baseline.<sup>4</sup> Patients were educated regarding analgesic overuse headaches, after which their analgesics were abruptly discontinued, and they were followed up to a year. Subcutaneous DHE was used as needed for symptomatic relief of excruciating headaches. At study completion, 78% of patients had adequately stopped analgesics. The goal of greater than 6 consecutive headache-free days was achieved in 74% patients in an average of 84 days.

A 9-week double-blind, placebo-controlled trial randomized 20 nondepressed patients with analgesic overuse headache to receive amitriptyline or active placebo (trihexyphenidyl).<sup>5</sup> Patients were admitted to the hospital for 1 week and withdrawn from all analgesics. The 2 groups had similar baseline characteristics. During the hospitalization, the amitriptyline treatment group received intravenous amitriptyline escalating from 25 to 75 mg. During the following month, oral study medications were continued, and patients took low doses of aspirin or acetaminophen, as needed. There was no significant difference between the 2 groups with regard to analgesic use. At completion of this low-powered study, no difference was found between the 2 groups in headache frequency or analgesic use, although certain components of a quality-of-life scale were better in the amitriptyline group.

An open-label trial of patients with chronic migraine and analgesic overuse in a headache subspecialty center abruptly withdrew 150 participants from analgesics and quasi-randomized them to 3 groups: prednisone (tapering from 60 to 20 mg over 6 days), naratriptan (Amerge) (2.5 mg twice daily for 6 days), or no prophylactic treatment.<sup>6</sup> Patients given the active substances were told it would reduce withdrawal symptoms; patients given placebo were not given this advice. All patients received education about the pathophysiology of rebound headaches, kept a headache diary, and were phoned weekly to ensure compliance. In addition, they all received capsules containing gradually increasing doses of atenolol, nortriptyline, and flunarazine (a calcium channel blocker not FDA-approved.) Indo-methacin and chlorpromazine were used as needed. Results from the first 6 days showed no difference in headaches between the 3 groups; however, significantly more patients used chlorpromazine in the “no pharmacologic treatment” group.

By the end of 5 weeks, headache frequency was significantly reduced in all groups from baseline; however, there were no differences between groups in headache frequency or intensity in this

small study. Of note, there were statistically fewer withdrawal symptoms and less use of rescue medications among patients who received the initial prophylactic treatments. The indomethacin rescue use was 24%, 18%, and 14% of patients for the no prophylactic treatment, prednisone, and naratriptan groups respectively, while chlorpromazine rescue use was 14%, 0%, and 0%, respectively. The number of patients needed to treat to prevent any withdrawal symptoms (nausea, vomiting, nervousness, dizziness, etc.) was 1 for every 3.5 for naratriptan, and 6.4 for prednisone.

### ■ RECOMMENDATIONS FROM OTHERS

The American Council for Headache Education recommends discontinuing all analgesics.<sup>7</sup> It notes some patients may need prophylactic medication (although no specific agent is recommended), and hospitalization may be indicated for withdrawal for patients who have abused narcotics.

A headache textbook recommends 1 of 2 approaches for patients undergoing outpatient treatment: (1) gradual tapering of the offending medication with substitution of a long-acting nonsteroidal anti-inflammatory drug (NSAID) and initiation of preventive therapy, or (2) abrupt discontinuation of the offending medication and initiation followed by gradual tapering of a “transitional” medication such as NSAIDs, DHE, corticosteroids, or triptans. The authors recommend an intravenous DHE protocol for treatment failures and patients requiring inpatient treatment.<sup>8</sup>

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### ■ CLINICAL COMMENTARY

#### Consider anxiety, depression, substance abuse, psychosocial stressors as triggers

Analgesic rebound headaches are clinically challenging. Patients are reluctant to believe that analgesic use is the cause, and good evidence for pharmacologic treatment of the problem is limited. Therefore, the family physician's unique skills in patient-centered care are invaluable for helping patients comply with the only proven remedy: long-term analgesic abstinence. Even with intense education and support, abstinence rates are low and headache improvement for abstinent patients is relatively slow and not universal.

In discussing options for assisting with detoxification, we must be honest about the limits of our knowledge and clarify that improvement, rather than cure, is the goal. Identification and treatment of concurrent anxiety, depression and substance use is important, as well as identification of psychosocial stressors that may have triggered increased headache frequency. As even moderate amounts of regular analgesic use can cause this difficult to treat syndrome, preventive counseling with migraine patients, particularly those with increasing headache frequency, is essential.

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