

## How should we treat chronic daily headache when conservative measures fail?

### ■ EVIDENCE-BASED ANSWER

For the purposes of this review, we considered conservative measures to include such therapies as nonsteroidal anti-inflammatory drugs (NSAIDs), physical therapy, and acetaminophen with codeine. Amitriptyline is the best-supported option for the treatment of chronic daily headaches for those patients who have not been treated by conservative measures (strength of recommendation [SOR]: **A**, based on a meta-analysis of randomized controlled trials [RCTs]).<sup>1</sup>

For patients who overuse symptomatic headache medications, medication withdrawal is effective (SOR: **B**, based on a systematic review of cohort and case-control studies).<sup>2</sup> Additional therapies include other tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and prophylactic treatments for migraine (SOR: **B**).<sup>3</sup>

### ■ EVIDENCE SUMMARY

Chronic daily headache is a heterogeneous primary headache disorder, often defined as a headache duration of more than 4 hours and a headache frequency of more than 15 per month; it affects less than 5% of the US population. Four headache subtypes included in the chronic daily headache definition are chronic (transformed) migraine, chronic tension-type headache, new daily persistent headache, and hemicrania continua. Each subtype may be associated with medication overuse.<sup>4</sup>

Chronic daily headache is challenging to categorize and difficult to manage, and scientific evidence to guide treatment is scant. Despite

this, a few studies do offer some hopeful alternatives to those patients who have had conservative measures fail (**Table**).

A meta-analysis from 2001 reviewed 38 RCTs of antidepressants as prophylaxis for chronic headache. Nineteen studies investigated TCAs, 18 examined serotonin blockers, and 7 focused on SSRIs. Patients taking antidepressants were twice as likely to report headache improvement (rate ratio [RR]=2.0; 95% confidence interval [CI], 1.6–2.4), with the average amount of improvement considered to be large (standard mean difference=0.94; 95% CI, 0.65–1.2). Serotonin blockers, most of which are not available or commonly used in the US, and TCAs were all effective in decreasing the headache burden, while the results for SSRIs were less clear. Dosages of amitriptyline ranged from 10 to 150 mg daily; most of the studies used 60 to 100 mg daily.<sup>1</sup>

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## What are Clinical Inquiries?

**Clinical Inquiries answer real questions** that family physicians submit to the Family Practice Inquiries Network (FPIN), a national, not-for-profit consortium of family practice departments, residency programs, academic health sciences libraries, primary care practice-based research networks, and other specialists.

**Questions chosen** for Clinical Inquiries are those that family physicians vote as most important through a web-based voting system.

**Answers are developed by a specific method:**

#### Type I answers

- FPIN medical librarians conduct systematic and standardized literature searches in collaboration with an FPIN clinician or clinicians.
- FPIN clinician authors select the research articles to include, critically appraise the research evidence, review the authoritative sources, and write the answers.
- Each Clinical Inquiry is reviewed by 4 or more peers and editors before publication in *JFP*.
- FPIN medical librarians coauthor Type I Clinical Inquiries that have required a systematic search.
- Finally, a practicing family physician writes an accompanying commentary.

TABLE

**Treatment options for chronic daily headache**

Treatment option	Study design, no. of studies	Total no. enrolled	Outcome
<b>Amitriptyline</b>	Double-blind, 7	257	↓ in headache severity, frequency and/or duration
<b>Fluoxetine</b>	Double-blind, 2	92	↑ in headache-free days, mood improvement; ↓ in headache severity
<b>Gabapentin</b>	Double-blind, 1	26	↓ in headache frequency
<b>Botulinum toxin A</b>	Double-blind, 1	16	↓ in headache intensity, frequency and duration
<b>Tizanidine</b>	Double-blind, 1	45	↓ in headache intensity, frequency and daily analgesic use
<b>Sumatriptan</b>	Double-blind, 1	42	No statistically significant change in headache intensity
<b>Valproate</b>	Open, 5	191	Mixed results

Adapted from Redillas and Solomon 2000.<sup>3</sup>

Medication withdrawal therapy is a treatment strategy for chronic daily headaches associated with the paradoxical induction of headaches by the frequent, long-term use of immediate relief medications such as aspirin, NSAIDs, acetaminophen, caffeine, codeine, ergotamine, and sumatriptan. A retrospective study tracked 101 men and women who underwent a controlled outpatient withdrawal of their overused medications. Headache diaries kept for 1 to 3 months reflected that 56% of the patients had at least a 50% reduction in headache days after removal of overused drugs. Twenty-two patients who had no success with withdrawal and continued to have headaches were treated with amitriptyline. Subsequently, 10 of these patients experienced a 50% reduction in headache frequency.<sup>5</sup>

A systematic review of the therapeutic approaches to medication-induced headache looked at 18 studies from 1966 to 1998. Although most were uncontrolled small trials,

medically monitored withdrawal of all symptomatic headache medications is recommended by the authors. No long-term outcome comparisons between withdrawal strategies are available.<sup>2</sup>

Other therapies for treating chronic daily headache include the skeletal muscle relaxant tizanidine (Zanaflex), which was studied in an industry-sponsored, double-blind, placebo-controlled trial of 92 patients. The medication was used as prophylaxis, titrating up to a dose of 8 mg 3 times daily. The overall headache index (a measure of headache intensity, frequency, and duration) significantly decreased. The headache index decreased in the tizanidine group from 2.6 to 1.2, and in the placebo group from 2.6 to 2.1 ( $P=.0025$ ). Decreases in headache frequency and headache intensity were less dramatic but still significant. This trial lasted only 12 weeks, so longer-term outcomes are not available.<sup>6</sup>

Stress management, acupuncture, botulinum toxin, behavioral therapy including relaxation ther-

apy, biofeedback, and even Internet-based self-help have all been studied, but most of these therapies do not have significant evidence-based support.

## ■ RECOMMENDATIONS FROM OTHERS

Our literature search and review of major textbooks found no formally organized guidelines or recommendations on the treatment of chronic daily headache.

*Jessie A. Junker, MD, MBA, Paul V. Aitken Jr., MD, MPH, New Hanover Regional Medical Center, Wilmington, NC; Donna Flake, MSLS, MSAS, Coastal AHEC Library, Wilmington, NC*

## ■ CLINICAL COMMENTARY

### A detailed history and assessment

#### of possible comorbid conditions is crucial

Obtaining a detailed history and the assessment of possible comorbid conditions such as psychiatric disorders, insomnia, and existing stressors is crucial to making the diagnosis of chronic daily headache and choosing therapy. A headache diary provides clinicians with helpful information such as the duration and frequency of the headaches, possible triggering factors, and the class, and numbers of analgesics used. Patients who have more than 2 episodes of migraine per week are appropriate candidates for preventive treatment.

The possibility of analgesic overuse must be considered for patients who use headache medications more than twice a week. Preventive headache medications do not work if analgesics are being overused. Once a diagnosis is made, detoxification needs to be discussed with the patient.

As a patient with chronic migraine, I have found stretching exercise, stress management, and dietary modifications very helpful. The most common foods to avoid are caffeine, chocolate, alcohol, aged or cured meat, bananas, and foods containing monosodium glutamate or tyramine.<sup>3</sup>

*Pouran Yousefi, MD, Baylor College of Medicine, Houston, Tex*

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## Should we screen for bacterial vaginosis in those at risk for preterm labor?

### ■ EVIDENCE-BASED ANSWER

Bacterial vaginosis (BV) is associated with preterm delivery (strength of recommendation [SOR]: **A**, meta-analysis). However, treating asymptomatic, low-risk women with BV does not always prevent preterm delivery (SOR: **A**, randomized controlled trials [RCTs]). There is some benefit to early screening by Gram stain using Nugent's criteria<sup>1</sup> (**Table**) and treating BV-positive women with a history of preterm delivery, premature rupture of membranes, low birth weight infants, or spontaneous abortion. In this group, treatment has been associated with decreased rates of preterm labor, preterm prelabor rupture of membranes, and low birth weight infants (SOR: **B**, conflicting RCTs).

Empirically treating high-risk women without documented infection has been associated with an increase in preterm deliveries and neonatal infections (SOR: **B**, single RCT).

### ■ EVIDENCE SUMMARY

Bacterial vaginosis in early pregnancy is a risk factor for preterm delivery.<sup>2</sup> The role of BV in

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