ABSTRACT

Rebound headache occurs when patients are overusing medication to treat individual headache attacks; this overuse of medication causes an increase in headache frequency. A cardinal sign of rebound headache is progression from episodic to daily or near-daily headache. This continuum is important to recognize, for neurologists and primary care physicians, because it is preventable, treatable, and may herald the onset of a secondary headache disorder. The key to successful management of rebound headache is identifying the source of medication overuse through detailed history and patient diaries. Complete withdrawal from the offending agent is the first step in treatment but can be achieved only with the complete understanding and acceptance by the patient that headaches will get worse before they get better during this process. Numerous preventive therapies are available—the same as those for migraine prophylaxis. Neurologists should become more aware of the prevalence of rebound headache and actively look for it in patients who present with increasing headache frequency. This article provides a discussion of mediations that typically cause rebound headache, useful approaches to identifying the offending agents and preparing the patient for withdrawal, prescription and nonprescription preventive medications, and transition regimens that can be used during the withdrawal process.

nizing which drugs may signal rebound headache. Too often, it is easy to simply prescribe additional medication instead of carefully checking the patient’s medication history.

The International Headache Society (IHS) criteria for rebound headache (ie, headache induced by chronic substance use or exposure) state that the headaches occur after daily use of a substance (at a certain minimum dose) for at least 3 months, occur on 15 days or more per month, and disappear within 1 month of withdrawal from the substance.2 In my practice, I have found that patients are better able to follow a more general “rule of 2s”: 2 doses per day on 2 days per week for more than 1 month. Exceptions to this rule include opioids (more than 1 dose per day), simple analgesics (more than 3 days per week), and triptans (more than 2 weeks). Another strategy may be to ask the patient if they are ever unable to have 3 to 4 consecutive days without taking medication. Although it doesn’t strictly follow IHS criteria, it helps the patient to monitor their medication use and identify if and when they may be overusing their medications.

Headache diaries are also invaluable in a preventive program for rebound headaches. Patients must monitor number of headaches as well as medication use, with specific detail about type of medication, number of pills, and drug doses. This type of drug history should be part of the normal documentation of patient history. An example of a patient chart we have found to be useful is shown in the Figure. Review of these charts can offer surprising insights. For example, some patients may rate the severity of their headache as 0 or 1, but still take medication on those days. When asked why, they invariably respond that they were “afraid of getting a headache.” The acute medications are, in effect, used as preventive medications. This is not surprising—particularly with triptans—because recent studies have shown that taking medication early (ie, within 2 hours of pain onset) may render triptans more effective at achieving a pain-free state compared with waiting until pain reaches a moderate-to-severe intensity.3 As a result, patients may be confused about what appear to be mixed messages—take migraine medications early in headache onset, but do not overuse or use the drug as a preventive.

Patients may also overuse medications obtained through emergency department visits or at infusion clinics. Frequent visits to these settings should prompt an overall medication review. Table 2 lists the agents typically used in an emergency department setting to treat acute headache.

Progression from episodic to chronic headache, or attenuation of efficacy from normal headache treatments should prompt an evaluation for secondary causes of headache. Secondary causes

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**Table 1. Drugs Typically Causing Medication-Overuse/Rebound Headache**

- Opioids
- Butalbital-containing medications
- Caffeine-containing medications
- Triptans
- Ergots
- Nonsteroidal anti-inflammatory medications
- Isometheptene/acetaminophen/dichloralphenezone

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**Figure. Sample Headache and Medication Diary**

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<td>1. NSAIDs</td>
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NSAIDs = nonsteroidal anti-inflammatory drugs.
include, but are not limited to, sphenoid sinusitis, Arnold-Chiari malformation, abnormal cerebrospinal fluid pressure (high or low), tumor, unruptured intracranial aneurysm, hypertension, sleep apnea, thyroid dysfunction, and lupus.

Evaluation for comorbid conditions is also important and may be a contributing factor in change of headache status. Some of the more common comorbid conditions include depression, anxiety, fibromyalgia, and epilepsy. For epilepsy, my experience has been that improving the seizure control also reduces headache frequency, particularly as antiepileptic drugs are used for both disorders. Several medications are used to treat conditions comorbid with migraine as well as acting as a preventive for migraine itself. Accordingly, identification of comorbid or coexisting conditions can aid in optional medication selection.

**Prevention**

Preventive medications for rebound headache are typically the same as those used for prevention of migraine: antiepileptic drugs, tricyclic antidepressants, selective serotonin reuptake inhibitors, beta blockers, calcium channel blockers, nonsteroidal anti-inflammatory drugs (NSAIDs) including indomethacin, and botulinum toxin A.

Many patients ask for nonprescription prophylactic agents. Although the clinical studies to support their use are much more limited, we encourage patients to try them for 1 to 2 months if they express an interest in these types of drugs. If they are ineffective, a prescription medication is typically the next step. Whereas a neurologist may not need to promote these medications, it is important to be familiar with them, especially given their frequent coverage in the lay press. Nonprescription headache medications include magnesium, vitamin B$_2$ (riboflavin), feverfew, melatonin, and petasites (burterbur root).4-12

There are 4 important aspects of headache prevention. First, preventive regimens should be administered proactively. It is not necessary or helpful to wait until headaches have reached daily frequency. Second, prescribing preventive medication benefits from the “start low, go slow” strategy. This allows patients a chance to manage any side effects. Third, an adequate drug trial should be completed. Each drug should be taken at optional doses for at least 2 to 3 months to determine true efficacy. Finally, avoiding triggers is essential, especially in this behavior-based headache syndrome. Although it may be difficult to incorporate into an individual patient’s lifestyle, avoiding triggers can be an effective way to reduce medication needs.

**Management**

The first step in managing rebound headache is to discontinue the offending medication(s). This can be achieved through either tapering or abrupt withdrawal. Much of the choice will depend on patient preference, unless the agent is potentially dangerous. If, for example, the causative drug was high-dose butalbital, abrupt withdrawal can induce seizures and high temperatures; the withdrawal side-effect profile must be taken into account. Of utmost importance before discontinuation begins, however, is the patient’s understanding that headaches will get worse before they get better. If the patient is not prepared for this, and cannot or does not prepare and mobilize the necessary support and motivational structures to help them through it, success is not likely. This is true even for discontinuation of a common drug, such as caffeine. It is also useful to give the patient a time frame for the withdrawal process, which typically lasts 1 to several weeks. The rebound headache associated with discontinuation of triptan

<table>
<thead>
<tr>
<th>Table 2. Emergency Department Treatments for Headache</th>
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<tbody>
<tr>
<td>- DHE: 0.5–1.0 mg IV or IM, up to 3 mg</td>
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<td>- Valproate sodium: 500–1000 mg IV</td>
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<td>- Ketorolac: 30 mg IV or 60 mg IM</td>
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<tr>
<td>- Chlorpromazine: dilute 25 mg (1 mL) in 4 mL saline and inject IV in 5-mg increments q5min</td>
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<tr>
<td>- Magnesium sulfate: 1 g IV</td>
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<tr>
<td>- Solumedrol: 500 mg IV</td>
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<td>- Normal saline: 1 L IV</td>
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DHE = dihydroergotamine; IV = intravenously; IM = intramuscularly.
overuse may be shorter than with some other drugs. Overall, patients must be motivated to stop medication overuse; fortunately, most patients who see specialists, particularly in tertiary care facilities, are usually highly motivated.

A second, sometimes controversial option during discontinuation is to use a transition regimen. These regimens may include a prednisone burst and taper, daily long-acting triptan (eg, naratriptan, frovatriptan), tizanidine and long-acting NSAID, or dihydroergotamine (DHE; intramuscularly, subcutaneously, or intravenously [IV]) acutely or on a regular schedule over several days. The prednisone burst and taper may be performed several ways (eg, 60 mg for 2 days, 40 mg for 2 days, 20 mg for 2 days). The IV DHE protocol is mostly used in an inpatient setting (ie, DHE over several days to break the cycle), although it can be done on an outpatient basis. Other drugs may be used to minimize withdrawal symptoms, such as the clonidine patch (for 1 week) and hydroxyzine for abdominal cramps in the case of opiate withdrawal, and phenobarbital (30 mg for 3 days) in the case of butalbital withdrawal. Once discontinuation is completed, the patient is ready to begin a prophylactic regimen. However, no prophylactic regimen will be successful unless the offending agent is completely discontinued.

The prognosis for success is high: 50% to 80% chance of sustained improvement with detoxification. Most relapses occur within the first 2 years. Katsarava et al recently reported a 14-day hospitalization plan for detoxification in which patients received only NSAIDs for severe headaches. Despite a very high reported success rate, insurance coverage and the time commitment for the patient may make this level of detoxification unfeasible. Overall, predictors for long-term success have not been identified.

**Conclusion**

Rebound headache is more common than most neurologists realize. The key to successful management is identifying the source of medication overuse through detailed history and patient diaries. Complete withdrawal from the offending agent is the first step in treatment but can be achieved only with the complete understanding and acceptance by the patient that headaches will get worse before they get better during this process. Numerous preventive therapies are available—the same as for migraine prophylaxis. Neurologists should become more aware of the prevalence of rebound headache and actively look for it in their patients who present with increasing headache frequency.

**REFERENCES**