

Medication-Overuse Headache

Questions and answers from Nina Tsakadze, MD, PhD;
Natasha Antonovich, PharmD; and Fabian Rossi, MD

Rebound headache, or what we now refer to as medication-overuse headache (MOH), is an important to recognize secondary headache because it diminishes the efficacy of preventive headache medicines, is associated with migraine chronification, and is treatable. Yet patients and clinicians alike are all too often unaware of MOH, hampering effective treatment. Fabian Rossi and colleagues, in question and answer format, present a comprehensive and practical overview of all things MOH.

What Is Medication-Overuse Headache?

Medication-overuse headache (MOH) is a pattern of chronic daily headaches, in a patient with a pre-existing headache condition, caused by regular and excessive use of symptomatic and acute headache medications for 3 months or more. It is a secondary disorder in that it is caused by the very medications a patient uses to treat his or her headaches.¹ For acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs), overuse is defined as taking the medications on 15 or more days per month. For triptans, ergotamines, opioids, and combination analgesics, medication overuse is defined as taking the medication on 10 or more days per month.¹ MOH may also occur when multiple drugs are used on 10 or more days per month, even though no single one of the medications is used on more than 10 days per month.

What Is the Epidemiology of Medication-Overuse Headache?

Approximately 50% of patients with chronic headache have MOH and the overall prevalence is 1% to 2%.^{2,3} The condition is more common in midlife, and less so among children and elderly. It is more than 3 times more common in women than in men and is thought to be one of the costliest headache disorders, with the majority of the cost being indirect from lost productivity and absenteeism from work.



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Risk factors for MOH include low socioeconomic status, higher body mass index, and anxiety and depression. The condition is more common in midlife, and less so among children and elderly.

Which Drugs Cause Medication-Overuse Headache?

Although virtually all drugs used for acute or symptomatic treatment of headache can cause MOH,⁴ and over-the-counter NSAIDs, acetaminophen, and combination analgesics are most frequently used, patients requiring secondary or tertiary care are more likely to be taking centrally acting drugs such as opioids, triptans, butalbital-containing combination pills, and over-the-counter combination products such as Excedrin (acetaminophen/aspirin/caffeine). The

most likely medications causing MOH varies geographically and over time.

Does Medication-Overuse Headache Occur in Isolation From Other Types of Headache?

MOH, by definition, occurs only in individuals who already have a headache disorder.¹ It does not occur de novo without history of headache. The majority of patients with MOH also have migraines or tension-type headache. Some will have cluster-type headache, and only a few will have newly diagnosed daily headaches.

How Is Medication-Overuse Headache Diagnosed?

The table below provides the diagnostic criteria for MOH from the International Classification of Headache Disorders, 3rd edition (beta).¹

The diagnosis is made clinically by taking a careful and thorough history of the frequency of headaches and the medications used to treat them. As symptoms of location, severity, and character of the headache may vary considerably, it is the quantity, not the quality of headache in a patient with pre-existing headache that should make one suspect MOH. In any patient experiencing chronic headache, the pattern and frequency of medication use should be assessed to confirm or rule out MOH.

MOH is usually worse in the morning after awakening and is often associated with neck pain, autonomic features, and anxiety and depression. Acute symptomatic treatment provides only transient relief, leading to continued and gradually escalating overuse of abortive medications.

The clinician must carefully ask what medications the

TABLE: DIAGNOSTIC CRITERIA FOR MEDICATION OVERUSE HEADACHE¹

1. Headache occurring on 15 or more days per month in a patient with a pre-existing headache disorder
2. Regular overuse for more than 3 months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache:
 - Regular intake for ≥ 10 days per month for > 3 months, of ergotamines, triptans, opioids, or combination analgesics, or any combination of ergotamines, triptans, or simple analgesics, or NSAIDs and/or opioids without overuse of any single drug or drug class alone or when the pattern of overuse cannot be reliably established
 - Regular intake for ≥ 15 days per month for > 3 months of simple analgesics (ie, acetaminophen, aspirin, or NSAIDs)
3. Not better accounted for by another ICHD-3 diagnosis

patient took for each headache and then patiently ask again if they took anything else as patients may not remember to state taking more than one medication. Clinicians should also carefully assess whether medications not specific to headache that may contain acetaminophen were also used, such as cold remedies. A headache diary that the patient keeps and uses to carefully document what medications he or she takes and when, can be very helpful in making the diagnosis of MOH. Patient education about medication overuse also plays a critical role in prevention and treatment of MOH and can be done during the clinical visit.

Other headache disorders, primary or secondary, also need to be considered in the differential diagnosis. Patients should undergo diagnostic testing, if appropriate, to rule out secondary causes of headache.

What Is the Pathophysiology of Medication-Overuse Headache?

It is unclear whether MOH is a consequence of living with chronic daily headache or the reverse, but it is clear that withdrawal of the overused drug(s) bring(s) relief to the majority of patients, suggesting a causative role for the medications. However, not everyone with medication overuse develops MOH. As the mechanism of action for the overused drugs differs from one another, it is unlikely that MOH is caused by a specific action of any of these drugs. As pre-existing headaches seem to be required for MOH to develop (daily use of these drugs for other conditions does not cause MOH), there seems to be a relationship between the pre-existing headache mechanism or pain pathway and MOH. However, the nature of those mechanisms for activating pain pathways is not yet fully understood.

Alteration of cortical activity, central sensitization of the nociceptive trigeminal system, and changes in serotonin and dopamine expression and cannabinoid and calcitonin gene-related peptide receptors have all been considered as potential pathways for MOH.⁵⁻⁷ Genetic predisposition, socioeconomic, and behavioral factors are also believed to play a role.⁷ MOH produces central sensitization with structural and functional changes in the trigeminal nucleus caudalis, resulting in a decrease in the pain threshold and an increase in receptive fields.⁶ Genetic predisposition and biobehavioral factors also play a role.⁷

What Is the Treatment for Medication-Overuse Headache?

The generally accepted treatment is detoxification through withdrawal of the overused medication(s) and the use of “bridge therapy” to help the patient through the period of withdrawal. This is followed by initiation or reinforcement of prophylactic therapy and is another time for patient education regarding MOH.

“... it is clear that withdrawal of the overused medications brings relief to the majority of patients.”

Triptans and NSAIDs can be stopped immediately without causing withdrawal effects; however, headache symptoms may worsen. Opioids, barbiturates, and caffeine should be tapered off slowly to avoid withdrawal symptoms. Withdrawal symptoms include worsening of headache symptoms, vomiting, nausea, tachycardia, hypotension, sleep disturbances, anxiety, and nervousness. Withdrawal varies with each drug and may take as long as 10 days depending on the drug that is being discontinued.

Bridge therapy is used to provide symptomatic relief for patients with MOH during withdrawal of the overused medications to create a bridge from the acute medications to prophylaxis. It can include counseling and education, antiemetics, tranquilizers, neuroleptics, rescue medication (NSAIDs, dihydroergotamine, triptans, tizanidine, lidocaine, and prochlorperazine), as long as the medication used is not in the same class as the overused drug.^{6,8} Steroids have been used; however, two double-blind, controlled, randomized studies showed that the steroid prednisolone was no more effective than placebo.^{9,10}

Most patients with MOH can be treated on an outpatient basis. Those using complex combinations of drugs or who have been overusing triptans, opioids, or barbiturates benefit from the in-patient detoxification and supportive care.^{8,9}

What Is the Prognosis for Medication-Overuse Headache?

Left untreated, MOH contributes to the development of a chronic and refractory character to headaches, which become less responsive to both preventive and acute medications.¹¹ This leads to profound disability and poor quality of life. Patients with MOH are also at risk of other, non-headache-related complications secondary to the frequent use of acute medications, such as gastrointestinal bleeding, renal and liver failure, and addiction and dependence.

With treatment, 72% of patients have at least 50% fewer headaches within 1 to 6 months. Relapse is relatively high at 31%, 41%, and 45% at 6 months, 1 year, and 4 years, respectively.¹²

How Can Medication-Overuse Headache Be Prevented?

The high rate of relapse and high cost of MOH makes prevention of great importance. Use of acute medications in patients with episodic and chronic migraine should be carefully limited. The rationale for restriction should be explained to the patient with serious warnings about the risk of developing MOH.¹³ The acute management schedule should be optimized by using highly effective and specific migraine medications, with the goal of sustained pain-free response, rather than using less effective, nonspecific medications, which give only partial relief, and therefore require multiple doses. The use of effective medication at an optimal dose as early in the attack as possible and while the pain is still mild to optimize response to treatment should be encouraged. ■

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Nina Tsakadze, MD, PhD

Director of the Comprehensive Headache Center
Orlando VA Medical Center
Orlando, FL

Natasha Antonovich, PharmD

Orlando VA Medical Center
Orlando, FL

Fabian Rossi, MD

Director of the Clinical Neurophysiology Laboratory
Orlando VA Medical Center
Orlando, FL