



## Be alert to the possibility of medication overuse headache

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**Edited by:**

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**Keywords:**

Medication-overuse

Chronic headache

Migraine

Management

### Abstract

Affecting 1-2% of the world's population and representing up to 40% of patients in specialist headache services, medication-overuse headache remains a challenge. Starting with the need to make professionals aware since basic care, through patient education and ending with adequate (and successful) management, there is still much to be done.

This literature review seeks to draw attention not only to the importance of recognizing the condition, but mainly to bring out the latest in the best management of patients who suffer from pain more than 14 days a month and who still see analgesics as the only way to manage their pain.

Submitted: June 13, 2023  
Accepted: June 19, 2023  
Published online: June 30, 2023



## Introduction

For a long time, it has been observed that the frequent use of analgesics can worsen an already established headache condition. The first description of this condition occurred in 1930 and was associated with the use of ergotamine. The possible explanation for this is a deterioration of a pre-existing headache, resulting from the frequent and continued use of analgesics. Medication-overuse headache (MOH), item 8.2 of the International Classification of Headache Disorders (ICHD-3<sup>1</sup>), occurs on 15 or more days per month in a patient with a pre-existing primary headache, because of regular overuse of symptomatic or acute headache medications (on 10 or more or 15 or more days per month, depending on the medication) for a period longer than three months. Overuse medications can be common analgesics, combined analgesics, ergotamine, triptans, or opioids, if taken regularly. Some patients overuse a specific class, others take combinations of them. It usually, but not invariably, disappears after excessive use is stopped.<sup>1,2</sup> The International Headache Society - IHS defined the diagnostic criteria for headache secondary to medication overuse.

### Diagnostic criteria

The main criteria are shown in Table 1.

**Table 1.** Diagnostic criteria for medication-overuse headache, according to the International Headache Society, 2018.<sup>1</sup>

#### Medication overuse headache, according to the ICHD-3<sup>1</sup>

- A. Headache occurring  $\geq 15$  days/month in a patient with a pre-existing headache.
- B. Regular overuse for more than 3 months of one or more drugs that may be taken for symptomatic and/or acute treatment of headache.
- C. Not better explained by another ICHD-3 diagnosis.

Depending on the medication or medications used excessively by the patient, the criteria vary. Excessive use is established for common analgesics and nonsteroidal anti-inflammatory drugs if equal to or greater than 15 days per month; for triptans, ergot derivatives, opioids, and combinations including carisoprodol and caffeine, the number is 10 or more days per month.

Drug overuse headache stems from an interaction between an overused therapeutic agent and a susceptible patient (person who has a primary headache). Among those previously diagnosed with a primary headache, most have migraine or tension-type headache (or both); only a small minority have other primary headaches such as chronic cluster headache or daily persistent headache since onset.<sup>1</sup>

### Epidemiology and Importance

Chronic headaches, those that occur 15 or more days

per month, affect 4-5% of the population. MOH is one of the most common chronic headaches, with a worldwide prevalence of 1-2%.<sup>3</sup> MOH is associated with frequent pain, medication side effects, and negative impact on quality of life. Clinical evidence shows that most patients with this disorder improve after they discontinue the medication in excessive use, as does their response to preventive treatment.

### Predisposing factors

Patients with high-frequency headache are more predisposed to develop MOH, as are those diagnosed with migraine and tension-type headache. Also, the type of abortive medication used seems to influence the risk of developing MOH, with opioids being the most associated with the condition, followed by combined analgesics and then triptans and ergotamines.<sup>4</sup> It should be noted that opioids, with rare exceptions, should not even be prescribed for primary headaches. Other associated conditions are use of anxiolytics, presence of musculoskeletal pain, high scores on anxiety and depression scales, smoking, and lack of physical activity.<sup>5</sup>

### Comorbidity

Comorbidity is the coexistence of two or more medical conditions. They can appear together only by chance, or more repeatedly in relation to the case. When they occur more frequently than expected, we tend to consider that the association is justified by causality, common etiological factors, or a common pathophysiology. The reason for the association is not yet understood for many factors in MOH, but several studies have shown that patients with MOH are more often found to have depression and anxiety at moderate to severe levels, overweight-obesity-metabolic syndrome, sleep disturbance, and physical inactivity. Recognizing these conditions and seeking to manage them can be useful in both the prevention and treatment of patients with MOH.

### Management

Headache due to excessive use of painkillers has its frequency reduced with withdrawal. Abrupt or gradual withdrawal is recommended to reduce both the side effects of the drugs and the frequency of crises. Patients with high headache frequency (>23 days of pain per month) seem to benefit especially from discontinuation of painkiller overuse.<sup>6</sup> The goals in managing MOH are to (1) discontinue the overused drug(s); (2) provide



non-pharmacological or pharmacological support to the patient; and (3) prevent recurrence.

Hospitalization is recommended for patients with previous failure of outpatient cessation attempts, for opioid and benzodiazepine users, and for those with associated psychiatric disorders. Different studies, with varying populations, have shown successful withdrawal from overuse in 48-95% of patients based solely on counseling about the condition. However, most patients experience withdrawal symptoms within 2-10 days of symptomatic medication withdrawal, making discontinuation difficult. The most common symptom is an initial worsening of headache, accompanied by varying degrees of nausea, vomiting, hypotension, tachycardia, sleep disturbances, restlessness, and anxiety. The duration of headache attributed to withdrawal varies with the different drugs, being shorter in patients using triptans and opioids in excess (about 4 days) than in those using ergotamine (7 days) or common analgesics (10 days).<sup>7</sup>

It is well established that educating the patient about the condition is the initial and fundamental step for the cessation of excessive use. This orientation can be done by different professionals and in different ways, depending on the patient's context: the assistant physician in the office, physician-nurse-psychologist in multiprofessional teams; verbal orientation (always indicated), provision of support material (folder, videos), insertion in support groups. Although there is no consensus on the best way to treat overuse, some protocols have been studied as a form of transition, helping in the withdrawal of analgesics: course with oral corticosteroids or with non-hormonal anti-inflammatory drugs (NSAIDs), anesthetic blockade of the occipital nerves, and fixed or symptomatic use of anti-emetics and antipsychotics with anti-emetic effect.<sup>2,8</sup>

### Protocols:

- (1) Oral corticosteroid course: the use of prednisone 0.5-1 mg/Kg/day for 5-7 days, or this initial dose for 3 days with subsequent de-escalation over up to 10 days, have been studied with positive effects.
- (2) Non-steroidal anti-inflammatory drug (NSAID) course: ibuprofen 600 mg every 12/12 hours or naproxen 550 mg every 12/12 hours for 5 days. This protocol is not indicated if the medication being overused is an NSAID.
- (3) Occipital nerve block anesthesia: major occipital block associated or not with minor occipital block with lidocaine 1-2% or bupivacaine 0.25-0.5%, 1-4 mL per point; weekly, biweekly, or monthly.<sup>9</sup>

- (4) Anti-emetics and antipsychotics: metoclopramide 10 mg orally (VO) 3 times daily, domperidone 10-20 mg VO 3 times daily, chlorpromazine 25-50 mg VO 1-3 times daily, chlorpromazine 25-50 mg 1-3 times daily; prochlorperazine 10 mg IM or VO 1-3 times daily; levomepromazine 6-25 mg VO 1-3 times daily. This protocol can be used alone or in combination with the medications in protocols (1) or (2).

To date, there is no definitive position on the best time to start prophylaxis in these patients. Detoxification prior to initiation of prophylaxis would allow identification of patients who may not need prophylaxis (patients converting from a chronic to infrequent episodic form of headache - occurring less than 3 days per week in the case of migraine); on the other hand, the time required for the prophylactic medication to take effect could favor recurrence of overuse in the case of initiating prophylaxis post-detoxification. There is greater consensus to start prophylaxis in conjunction with cessation counseling for symptomatic medication use, although this discussion is still open.<sup>10</sup> More recently, with the use of onabotulinum toxin type A<sup>11</sup> and monoclonal antibodies (galcanezumab<sup>12</sup>, fremanezumab<sup>13</sup> and erenumab<sup>14</sup>) as prophylactic agents, even patients who did not undergo painkiller withdrawal had a reduction in the number of days with pain and in the use of painkillers (primary endpoints of these studies); however, interestingly, to a lesser extent than the reduction observed in the COMOESTAS Consortium (multicenter, prospective, non-controlled, non-blinded study), which started with the withdrawal of excessive use as a form of management, associated with the use of oral prophylactics.<sup>2</sup>

The drugs used in prophylaxis are those indicated for the primary headache presented by the patient. When it comes to migraine, those with more evidence for the chronic form are: topiramate, onabotulinum toxin, and anti-CGRP monoclonal antibodies. With less evidence, but still widely prescribed in our environment due to availability in the public health system, we have amitriptyline and sodium valproate. In tension-type headache we use amitriptyline, nortriptyline, tizanidine and venlafaxine.<sup>8</sup>

### Prognosis

The recurrence rate of MOH after discontinuation of excessive analgesic use is 10-30% in 6 months. Factors favoring this recurrence are high frequency of headache, male gender, use of combined analgesics after withdrawal of medication in excessive use and associated psychiatric



conditions. Close monitoring of the patient, the support of a multidisciplinary team, and the maintenance of effective prophylaxis can help prevent recurrence.

### Prevention

Simple counseling on the causes and consequences of medication overuse headache is an essential part of its management and can be successfully provided in primary care. Prevention is especially important in the case of patients prone to frequent headache and is done by establishing adequate management with the use of prophylaxis (medicated or not) preferably even before the chronification of headache. The Brazilian Headache Society has been warning about the need to preventively diagnose and treat patients with migraine, since migraine is the primary headache most commonly seen among MOH patients, who have 3 or more days with pain per month, in the campaigns #3edemais and #maiobordo.

## Conclusion

Although not simple, the management of the MOH patient is feasible. It depends on the knowledge of the professional who sees the patient and on a piece of rather unavailable commodity: time. Educating the patient about their condition, discussing treatment alternatives that best fit the patient's routine: lifestyle modifications, types of prophylaxis (including discussing costs), types of bridging treatment (course of corticoid or NSAIDs, blocks, use of antipsychotics with anti-emetic effect - which in psychiatry are used to reduce cravings), bringing the patient into an active role in the management of this very limiting condition. Additionally, the literature review is an invitation to conduct studies with more subjects, which produce more robust evidence.

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**Funding:** None

**Conflict of interest:** None

**Declaration:** This manuscript was published in Portuguese as a chapter of the printed book "Cefaleia vol.1".

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