# Medication-overuse headache: a perspective review

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**Maria Lurenda Westergaard, Signe Bruun Munksgaard, Lars Bendtsen and Rigmor Højland Jensen**

***Abstract***

Medication-overuse headache (MOH) is a debilitating condition in which frequent and prolonged use of medication for the acute treatment of pain results in the worsening of the headache. The purpose of this paper is to review the most recent literature on MOH and discuss future avenues for research. MOH accounts for a substantial share of the global burden of disease. Prevalence is often reported as 1–2% but can be as high as 7% overall, with higher proportions among women and in those with a low socioeconomic position. Management consists of withdrawing pain medication, focusing on prophylactic and nonmedical treatments, and limiting acute symptomatic medication. Stress reduction and lifestyle interventions may support the change towards rational pain medication use. Support, follow up, and education are needed to help patients through the detoxification period. There is fertile ground for research in MOH epidemiology, pathophysiology, and neuroimaging. Randomized and long-term follow-up studies on MOH treatment protocols are needed. Further focused research could be of major importance for global health.

***Keywords:*** medication-overuse headache, treatment, epidemiology, chronic headache

## Introduction

Headache is one of the most common health complaints. Of 301 acute and chronic diseases tracked by the Global Burden of Disease (GBD) studies, two headache forms are ranked among those with the highest prevalence: tension-type headache (TTH) and migraine [Global Burden of Disease Study 2013 Collaborators, 2015].

Medication-overuse headache (MOH) is another headache form that ranks high in the most recently published GBD report. It is a debilitating condition in which frequent and prolonged use of medication for the acute treatment of pain results in worsening of the headache. It is not as prevalent as TTH or migraine but it is very disabling. The GBD studies use a metric called years of life lived with disability (YLDs), which estimates years of life lived with any short-term or long-term health loss [Murray and Lopez, 2013; Institute for Health Metrics and Evaluation, 2013]. Among all causes of global YLDs, MOH ranks 18th [Global Burden of Disease Study 2013 Collaborators, 2015].

The personal impact of MOH has been shown to be greater than that of migraine or TTH in several European countries. Compared with those who have migraine or TTH, people with MOH are more likely to report adverse effects of headache on education, career, earnings, social acceptance, and feeling of control over their headaches. Those with MOH also report more lost days for productive work, housework, and social activities [Steiner *et al.* 2014]. MOH is among the most costly of neurologic diseases [Russell and Lundkvist, 2012] and is the most costly among headache disorders [Linde *et al.* 2012]. Very importantly, the high burden of MOH to the individual and to society is unnecessary because it is preventable and largely treatable.

Correspondence to:
**Maria Lurenda Westergaard, MD**
Danish Headache Center, Rigshospitalet - Glostrup, University of Copenhagen, Nordre Ringvej 67, Område Nord Bygning 14, 2600 Glostrup, Denmark

**Signe Bruun Munksgaard, MD, PhD**
**Lars Bendtsen, MD, PhD**
**Rigmor Højland Jensen, Prof**
Danish Headache Center, Rigshospitalet - Glostrup, University of Copenhagen, Glostrup, Denmark

**Table 1.** International Classification of Headache Disorders (ICHD-3 beta) diagnostic criteria for medication-overuse headache and its subtypes.

| | |
|---|---|
| Criterion A | Headache occurring on ⩾15 days/month in a patient with a pre-existing headache disorder |
| Criterion B | Regular overuse for >3 months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache.<br>*8.2.1. Ergotamine-overuse headache, 8.2.2. Triptan-overuse headache, 8.2.4. Opioid-overuse headache*<br>• Ergotamine, triptans, or opioids<br>• Regular intake on ⩾10 days/month for >3 months<br>*8.2.3. Simple analgesic-overuse headache*<br>• Paracetamol, ASA, or other NSAID<br>• Regular intake on ⩾15 days/month for >3 months<br>*8.2.5. Combination-analgesic-overuse headache*<br>• One or more combination-analgesic medications described as formulations combining drugs of two or more classes, each with analgesic effect or acting as adjuvants<br>• Most commonly combinations of simple analgesics with opioids, butalbital and/or caffeine<br>• Regular intake on ⩾10 days/month for >3 months<br>*8.2.6. Medication-overuse headache attributed to multiple drug classes not individually overused*<br>• Any combination of ergotamine, triptans, simple analgesics, NSAIDs and/or opioids<br>• Regular intake for a total of ⩾10 days/month for >3 months without overuse of any single drug or drug class alone.<br>*8.2.7. Medication-overuse headache attributed to unverified overuse of multiple drug classes*<br>• Any combination of ergotamine, triptans, simple analgesics, NSAIDs and/or opioids<br>• The identity, quantity and/or pattern of use or overuse of these classes of drug cannot be reliably established.<br>• Regular intake on ⩾10 days per month for >3 months |
| Criterion C | Not better accounted for by another ICHD-3 diagnosis. |

ASA, acetylsalicylic acid; NSAID, nonsteroidal anti-inflammatory drug.
(Summarized from: Headache Classification Committee of the International Headache Society [2013].)

The purpose of this perspective review is to discuss results of recent research and highlight important new areas of general interest to the study of MOH.

## Diagnosing MOH

MOH was first described in the 1950s [Boes and Capobianco, 2005]. There are as many as 40 different terms for MOH, including rebound headache, drug-induced headache, drug dependence headache, and medication-misuse headache [Westergaard *et al.* 2014b]. The current diagnostic criteria, arrived at by consensus among experts from the International Headache Society, are listed in the third edition of the International Classification of Headache Disorders (ICHD-3 beta) (Table 1) [Headache Classification Committee of the International Headache Society, 2013].

The specific characteristics of headache pain are important for the diagnosis of the primary underlying headache (e.g. migraine, TTH, cluster headache), but for the diagnosis of MOH, the most important parameter is number of headache days: 15 or more days per month.

The second criterion involves overuse of acute pain medication for more than a three-month period. 'Overuse' is assessed in terms of the number of medication days as opposed to doses. The cut-off levels for overuse are 10 or 15 medication days per month depending on the type of drug or combinations of different drugs.

It is important to ask patients about over-the-counter (OTC) pain medication use, often taken on top of prescribed pain medications. Patients may not report medication overuse when they believe their level of intake does not qualify as an 'overdose'.

The third criterion requires the exclusion of other headache diagnoses. This requires a thorough history, physical examination, and in some cases, ancillary tests.

The new ICHD-3 beta criteria do not require a trial of medication withdrawal and subsequent improvement in order to establish that medication overuse is the cause of the headache. It is possible for a patient to be diagnosed with more than one headache disorder. For example, a patient can be diagnosed as having chronic migraine, and when there is associated medication overuse, the diagnosis of MOH should also be applied [Headache Classification Committee of the International Headache Society, 2013].

For many people, daily use of medication for a chronic pain indication, for example arthritis, back pain, postoperative pain, or cancer, does not lead to headache. However, a person with a preexisting headache disorder who develops chronic headache with frequent intake of pain medication (for whatever indication) must be assessed for MOH. If a patient has MOH, increasing symptomatic pain medication will not help. In contrast, it could maintain a disabling chronic headache that is refractory to both pharmacological and nonpharmacological treatment.

## Population prevalence of MOH

The publication of GBD 2013 boosted efforts in studying MOH epidemiology. Prevalence was estimated for 188 countries based on best available data. It is estimated that 63 million people worldwide have MOH [GBD 2013 Collaborators, 2015].

MOH is difficult to study epidemiologically [Steiner, 2014]. Fortunately, there has been an increased focus on producing methodologically sound prevalence estimates for all headache disorders, including MOH [Steiner, 2004; Stovner *et al.* 2014; Ahmed *et al.* 2014]. In the last 10 years, there has been a remarkable increase in MOH population-based studies but there is still a lack of studies from many regions [Steiner *et al.* 2010].

Prevalence estimates based on nationally representative data from 16 countries (Brazil, China, Colombia, Georgia, Germany, Iran, Italy, Republic of Korea, Netherlands, Norway, Russian Federation, Spain, Sweden, Turkey, Taiwan and the United States) have been summarized in a systematic review [Westergaard *et al.* 2014b]. Preliminary data from the Republic of Korea reported at a headache congress by Chu and colleagues [Chu *et al.* 2011] have since been published [Park *et al.* 2014], and there are four additional studies from Denmark [Westergaard *et al.* 2014a], India [Kulkarni *et al.* 2015], Nepal [Manandhar *et al.* 2015] and Zambia [Mbewe *et al.* 2015].

Data from the USA [Scher *et al.* 2010] were derived from a case-control study of adults randomly selected for a telephone interview. Overall population prevalence was not estimated but authors described MOH prevalence as 32% among 206 cases with chronic headache. Results of all other nationally representative epidemiologic studies among adults are summarized in Table 2.

Studies with sex-specific data reported higher prevalence among women, with female:male ratios ranging from about 2:1 to 5:1. However, there was a notable exception in the study from Iran where the prevalence among females (4.8%) was slightly lower than the prevalence among males (5.1%) [Shahbeigi *et al.* 2013].

Studies from four countries in Europe (Denmark, Norway, Spain, Sweden) showed that MOH is most prevalent among middle-aged people in their 30s to 50s [Westergaard *et al.* 2014b; Aaseth *et al.* 2008; Zwart *et al.* 2004; Colás *et al.* 2004; Jonsson *et al.* 2011]. However, the study from India showed the opposite trend [Kulkarni *et al.* 2015]. In Nepal, the oldest age group (56–65 years) had the highest prevalence [Manandhar *et al.* 2015] while in Zambia, prevalence increased with age, going as high as 23.8% in the oldest age group [Mbewe *et al.* 2015].

The Zambian study showed a large difference in prevalence between rural and urban areas (2.1% and 14.5%, respectively) which the authors attributed to very limited access to OTC medication in rural areas [Mbewe *et al.* 2015]. However, there was a slight (nonsignificant) rural preponderance observed in India (1.5% rural *versus* 0.9 % urban) which could be explained by easy access to OTC analgesics in rural areas with difficult access to health care [Kulkarni *et al.* 2015].

Large Scandinavian studies from Norway and Sweden showed higher prevalence among those with lower socioeconomic position [Hagen *et al.*

**Table 2.** Prevalence of medication-overuse headache in adults based on nationally representative epidemiologic studies.

| Country | Authors | Year of publication | Age group included (years) | Number of participants | Prevalence |
|---|---|---|---|---|---|
| Brazil | Da Silva *et al.* | 2010 | 10 to 93 | 1605[a] | 1.6[b]<br>0.9[c] |
| China | Yu *et al.* | 2012 | 18 to 65 | 5041 | 0.6 |
| Colombia | Rueda-Sánchez *et al.* | 2008 | 16 to 65 | 1505 | 4.6[a] |
| Denmark | Westergaard *et al.* | 2014a | 16 and older | 68,518 | 1.8[d] |
| Georgia | Katsarava *et al.* | 2009 | 16 and older | 1145 | 0.9 |
| Germany | Straube *et al.* | 2010 | 45 to 75 | 6536 | 1.1[a] |
| India | Kulkarni *et al.* | 2015 | 18 to 65 | 2329 | 1.2[d] |
| Iran | Shahbeigi *et al.* | 2013 | Over 10 | 3655 | 4.9 |
| Italy | Prencipe *et al.* | 2001 | 65 and older | 833 | 1.7 |
| Nepal | Manandhar *et al.* | 2015 | 18 to 65 | 2091 | 2.1[d] |
| Netherlands | Wiendels *et al.* | 2006 | 25 to 55 | 16,232 | 2.6[a] |
| Norway | Zwart *et al.* | 2004 | 14 and older | 49,064[a] | 1.0[e]<br>0.9[f] |
| | Aaseth *et al.* | 2008 | 30 to 44 | 20,598 | 1.7[d] |
| | Linde *et al.* | 2011 | 20 and older | 39,690 | 1.0[d] |
| Republic of Korea | Park *et al.* | 2014 | 19 to 69 | 1507 | 0.5[a] |
| Russian Federation | Ayzenberg *et al.* | 2012 | 18 to 65 | 2025 | 7.2 |
| Spain | Castillo *et al.* | 1999 | 14 and older | 1883 | 1.2 |
| | Colás *et al.* | 2004 | 14 and older | 4855 | 1.4 |
| Sweden | Jonsson *et al.* | 2011 | 15 and older | 44,300 | 1.8[d] |
| Taiwan | Wang *et al.* | 2000 | 65 and older | 1533 | 1.0 |
| | Lu *et al.* | 2001 | 15 and older | 3377 | 1.1 |
| Turkey | Ertas *et al.* | 2012 | 18 to 65 | 5323 | 2.1 |
| Zambia | Mbewe *et al.* | 2015 | 18 to 65 | 1085 | 7.1[d] |

Note: The studies used recall periods of 1 month to 1 year.
[a]Extracted from published data.
[b]All MOH prior to detoxification.
[c]MOH diagnosed 2 months after drug withdrawal.
[d]Adjusted according to demographic data.
[e]1 month of medication overuse.
[f]3 months of medication overuse.

2012; Jonsson *et al.* 2011]. Danish data showed highest prevalence among those on social welfare (11.0%), early pensioners (7.5%) and people receiving sickness benefits (6.0%) [Westergaard *et al.* 2014a].

There are differences among ethnic groups within several European countries, with migrants having a higher prevalence in Denmark [Westergaard *et al.* 2014a], Germany [Kavuk *et al.* 2006], the Netherlands [Wiendels *et al.* 2006], and Sweden [Jonsson *et al.* 2011]. The reasons for these differences are not known and may be genetic, cultural, or socioeconomic; or possibly related to differences in accessing health care, the stress of migration, and communication difficulties.

Chiappedi and Balottin [Chiappedi and Balottin, 2014], and Gelfand and Goadsby [Gelfand and Goadsby, 2014] recently reviewed the literature on MOH in children and adolescents and showed that population-based epidemiologic studies are sparse (with data available only from Norway, Taiwan, and the US) but MOH is commonly encountered in the clinical setting.

## Commonly overused medications

OTC analgesics are the most overused headache medications in both population- and clinic-based studies. In specialist care settings, a larger proportion of patients overuse centrally acting drugs [Kristoffersen and Lundqvist, 2014].

Paracetamol is the single most commonly overused drug. This does not necessarily mean that it has a greater propensity to cause MOH; rather it could simply reflect how it is the most often purchased analgesic for headache.

There are country/regional differences for ergotamine. Its use has declined in the US and Europe, but it remains among the most overused medications in Latin America [Shand *et al.* 2015].

In the US, data from 1990 to 2005 showed a decrease in overuse of ergot compounds, acetylsalicylic acid, paracetamol, butalbital, and opioids, but an increase in overuse of triptans and nonsteroidal anti-inflammatory drugs [Meskunas *et al.* 2006]. A more recent study in US emergency departments spanning 2001 to 2010 noted an increase in use of several opioids [Mazer-Amirshahi *et al.* 2014].

Danish registry data showed that one in three people with MOH were dispensed an opioid at least once in a year. There were no significant differences in the prevalence of self-reported cancer among those with and without chronic headache, suggesting that opioids were likely being taken for noncancer pain [Westergaard *et al.* 2015].

Opioids are not recommended for headache treatment [Bendtsen *et al.* 2012]. Canadian and US-based reviews showed that there is weak evidence for tramadol efficacy in migraine [Orr *et al.* 2015; Kelley and Tepper, 2012] and it is not indicated for TTH. Prolonged opioid use is associated with progression or transformation from episodic to chronic migraine [Bigal *et al.* 2008]. Opioid overuse headache, a subclass of MOH, is very difficult to treat and often requires hospital admission. It is possible that MOH and opioid-induced hyperalgesia share the same pathophysiology and mechanism [Johnson *et al.* 2013].

There are several prescription drug registry studies on triptan overuse from European countries. The earliest was done only 2 years after the release of sumatriptan [Gaist *et al.* 1996]. The most recent studies are from the Netherlands [Dekker *et al.* 2011], Sweden [Von Euler *et al.* 2014], Denmark [Westergaard *et al.* 2015], and France [Braunstein *et al.* 2015]. These studies are consistent in showing how a small number of people account for a large share of triptan purchases. In France, for example, 2.3% of users purchased 20% of the total volume dispensed.

In 2008, triptans became available OTC in Sweden. Analysis of data on triptan purchases from 1991 to 2011 showed that the amount of dispensed prescriptions remained stable while OTC sales increased slowly to 11% of total expenditure [Von Euler *et al.* 2014]. There are no data on whether OTC availability of triptans increase MOH prevalence, but it is a legitimate concern [Tfelt-Hansen and Steiner, 2007] and could be a focus for future pharmacoepidemiologic studies.

## MOH, perceived stress, and lifestyle

There are surprisingly few studies on the relationship between perceived stress and MOH despite the clear relationship between stress and headache [Yokoyama *et al.* 2009; Stensland *et al.* 2013; Lipton *et al.* 2014; Schramm *et al.* 2015].

Danish studies showed that young adults (aged 25–44 years) with headache who have limited coping resources are more likely to use analgesics when faced with stress [Koushede *et al.* 2011, 2012]. Population-based data confirmed the graded association between MOH and increasing levels of perceived stress [Westergaard *et al.* 2016].

There appears to be a relationship between lifestyle factors (smoking, obesity, physical inactivity) and MOH [Wiendels *et al.* 2006; Straube *et al.* 2010; Hagen *et al.* 2012; Westergaard *et al.* 2016]. Cross-sectional studies cannot show causation, and it is not possible to say whether an unhealthy lifestyle somehow leads to the development of MOH. However, it is important to screen for lifestyle factors among people with MOH, and it is possible that change in these modifiable factors could support change towards rational pain medication use.

## Treatment goals and dilemmas

It can be argued that increasing medication use could be a patient's response to increasing pain, and that the medication is not the cause of the worsening headache. Patients themselves might be averse to hearing that the 'indispensable medication' [Jonsson *et al.* 2013] could be the reason for their pain. However, near-daily use of acute pain medication without relief of headache suggests that the treatment is ineffective, if not harmful, and a new approach is indicated.

**Table 3.** Key points in the treatment of medication-overuse headache.

| | |
|---|---|
| Setting | Most cases of MOH can be managed in primary care through patient education and advice to cut down on medication use for headache [Kristoffersen *et al.* 2015]. |
| | Complex cases (characterized by long periods of overuse, intake of opioids or other psychoactive drugs, comorbid psychiatric or somatic disorders, or previous unsuccessful attempts at detoxification [Saper and Lake, 2006]) and those who failed detoxification in primary care should be referred for specialist care. |
| In-patient vs. outpatient | Both regimens are effective in the hospital setting, although the drop-out rate may be higher in the out-patient approach [Tassorelli *et al.* 2014]. |
| Patient education | Patient education and constant support are needed to limit pain medication use and to prevent relapse [Munksgaard *et al.* 2011; Tassorelli *et al.* 2014]. Patients should be informed that even after MOH is resolved, their primary headache has not been cured. The difference is that there is a shift in the focus of management from acute treatment of pain to prevention of headache. |
| Treatment protocol | The best treatment involves discontinuation of the overused medication with the addition of preventive medication [Chiang *et al.* 2016]. There is disagreement on how to discontinue medication (gradual reduction *versus* complete withdrawal); and when to use preventive medication (early in the treatment period or after medication reduction). |
| | There is sparse data on best practice for the treatment of MOH in children [Gelfand and Goadsby, 2014]. |
| Comorbidity | MOH has been linked to comorbid psychiatric disorders [Atasoy *et al.* 2012; Fuh and Wang, 2012; Radat and Lanteri-Minet, 2012]. Successful treatment of MOH appears to considerably reduce comorbid anxiety and depression [Bendtsen *et al.* 2014]. |
| Team approach | Multidisciplinary treatment involving physicians, nurses, physiotherapists, and psychologists can make a difference [Munksgaard *et al.* 2012a; Pijpers *et al.* 2016] especially for the most treatment refractory patients [Munksgaard *et al.* 2012b]. |
| Costs | Medication costs are substantially reduced after treatment [Shah *et al.* 2013]. |

Several key points in MOH treatment are outlined in Table 3. Most cases of MOH can be managed in primary care. A follow-up study in the primary care setting in Norway compared two groups of patients: one group with MOH received brief intervention (BI), essentially simple advice and education on MOH; the other group did not. The BI group, whose headache days were reduced from 25 to 17, on average, was able to cut down medication intake from 24 to 13 days. The control group did not experience any change in headache days or medication days (25 and 22 days, respectively) at follow up [Kristoffersen *et al.* 2015].

In specialist care, detoxification can be carried out through outpatient or inpatient programs. The results of a multicenter study conducted in Europe and South America, are promising: 62% were no longer overusers and 46% reverted back to an episodic pattern of headache after 6 months [Tassorelli *et al.* 2014].

MOH management protocols differ in two important ways: (1) the pace of detoxification (complete withdrawal *versus* slow reduction); and (2) the timing of the introduction of preventive medication. A systematic review of studies on MOH treatment published between 2004 and 2014 discussed various treatment strategies implemented internationally, and suggested that the best treatment involves discontinuation of the overused medication with the addition of preventive medication [Chiang *et al.* 2016]. Comparative studies with and without preventive medication are lacking.

The Danish Headache Center currently advocates starting prophylactics after detoxification. Up to half of the patients may not even need migraine prophylactics if headache days are few [Munksgaard and Jensen, 2014].

TTH benefits from targeting the sources of stress and strengthening coping mechanisms, rather than reacting to the symptom of headache with an analgesic. For migraine, the focus shifts to optimizing acute treatment (for example, with triptans), and use of preventive medications: antiepileptics (e.g. topiramate, valproic acid), tricyclic antidepressants (e.g. amitriptyline), and antihypertensive agents (e.g. beta-blockers).

There is an increasing role for psychological interventions for the management of chronic pain [Kaiser *et al.* 2015]. It is important to address psychiatric disorders (most commonly anxiety and depression) that are often comorbid with chronic headache and specifically MOH [Atasoy *et al.* 2012; Fuh and Wang, 2012; Radat and Lanteri-Minet, 2012]. Physiotherapy can reduce intensity, frequency and duration of migraine, TTH and cervicogenic headache [Luedtke *et al.* 2016].

There is no evidence on the effectiveness of occipital nerve stimulation and occipital nerve block for the treatment of MOH. Randomized control trials are needed to evaluate the usefulness of onabotulinumtoxinA alone or with early discontinuation [Chiang *et al.* 2016]. Neuromodulation is not recommended [Martelletti *et al.* 2013].

## Current research

Current research on MOH ranges from basic science to clinic-based and population-based studies.

The Global Burden of Disease studies provide MOH prevalence estimates based on best available data, but representative studies are lacking in many areas of the world and there is hardly any research on children and adolescents. There are still many knowledge gaps in MOH epidemiology but an interesting and important avenue for prevention of chronic headache has been paved.

The pathophysiology of MOH is still unclear, with recent work pointing towards alterations in pain-related and reward-related systems: central serotonin (5-HT) or endocannabinoid-dependent modulating systems [Srikiatkhachorn *et al.* 2014, Kristoffersen and Lundqvist 2014]. Understanding the pathophysiology of opioid-induced hyperalgesia might also lead to an understanding of opioid-overuse headache [Johnson *et al.* 2013].

Different methods of measuring pain perception in patients with MOH all show alterations in pain perception between MOH patients and healthy controls. These findings indicate central sensitization [Ayzenberg *et al.* 2006; Coppola *et al.* 2010; Munksgaard *et al.* 2013; Perrotta *et al.* 2010, 2012; Zappaterra *et al.* 2011]. Patients with MOH appear to be more sensitive to pressure pain than patients with chronic TTH and chronic migraine [Zappaterra *et al.* 2011].

There are very few imaging studies on MOH. Studies have reported orbitofrontal hypometabolism [Fumal *et al.* 2006], reversible dysfunction in the ventromedial prefrontal cortex [Ferraro *et al.* 2012], changes in gray matter volumes in several brain areas including the midbrain and orbitofrontal cortex [Riederer *et al.* 2013; Chanraud *et al.* 2014], and changes in resting functional connectivity [Chanraud *et al.* 2014]. It is not known whether changes in the brain structure and function of people with MOH are the result or the cause of medication overuse.

In coherence with the changes seen in the fMRI scans of patients before and after detoxification [Grazzi *et al.* 2010], Perrotta and colleagues [Perrotta *et al.* 2010, 2012] found decreased thresholds for eliciting nociceptive withdrawal reflexes in MOH patients before detoxification compared with healthy volunteers. Furthermore, they found that the stimulation needed to elicit the reflexes increased after detoxification (after 10 days and after 2 months), indicating a decrease in sensitization after withdrawal. Munksgaard and colleagues [Munksgaard *et al.* 2013] showed that the pain intensity for pressure above the pain threshold is significantly higher in MOH patients before withdrawal, but continued to decrease during the first year after detoxification. After 12 months without overuse, these levels were similar to the pain intensity of healthy volunteers.

These findings in patients parallel data from animal studies which suggest that pre-exposure to acute medication decreases the electrical stimulation threshold to generate a cortical spreading depression, which increases activation of the trigeminal nucleus caudalis, thereby precipitating headache [Green *et al.* 2013].

The demonstration of central sensitization that decreases after withdrawal of overused medication shows how MOH is a condition that is treatable, and more importantly, preventable.

Randomized and follow-up studies on MOH treatment are needed. There are many unanswered questions: Is complete withdrawal of acute pain medication necessary, or is it enough to reduce medication days? Is abrupt cessation more effective than gradual reduction of an overused medication? Which types of patients benefit

from prophylactics and when should these be introduced (before, during, or after detoxification)? Which types of patients are best managed by in-patient treatment? What are the best medical treatments for children? Can behavioral interventions help prevent headaches and reduce medication days? Do interventions such as physiotherapy and acupuncture improve outcomes? What are the protective factors in patients who do not relapse?

## Conclusion

In summary, MOH is a debilitating condition of public health importance that has been included among the 20 most debilitating diseases in the GBD studies. It is the focus of increasing research activity. Prevalence is often reported as 1–2% but new country reports go as high as 7%. These data call for increased awareness of this unique chronic pain disorder that in principle is both preventable and treatable. Effective protocols for treatment have been developed but additional randomized and long-term follow-up studies are needed. A dedicated and international information campaign for prevention of MOH may reduce the burden of this costly and highly disabling type of headache. Further focused research could be of major importance for global health.

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