

Medication Overuse Headache (MOH): Best Practices in Management and Care

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DISCLOSURES:

- TEVA
- Abbvie
- Lundbeck Ltd
- Lilly/Organon
- Tillots Phrama
- Florence Nightingale Foundation

Some people say Paracetamol causes autism..... that's **FAKE NEWS!**



But what it really can cause is:
Medication Overuse Headache

OBJECTIVES:

- Definition and diagnostic features of medication overuse headache (MOH).
- Discuss the impacts of MOH on patients' health and quality of life.
- Identify key risk factors contributing to medication overuse in migraine.
- Explore the pathophysiology of MOH
- Evidence-based strategies for prevention and management of MOH in clinical practice.
- Demonstrate effective communication approaches to support patients

MIGRAINE¹

Headache has at least 2 of the following characteristics

- Nausea
- Vomiting
- Sensitivity to light (photophobia)
- Sensitivity to sound (phonophobia)
- Sensitivity to smell (osmophobia)
- Motion sensitivity
- Preference to stay still



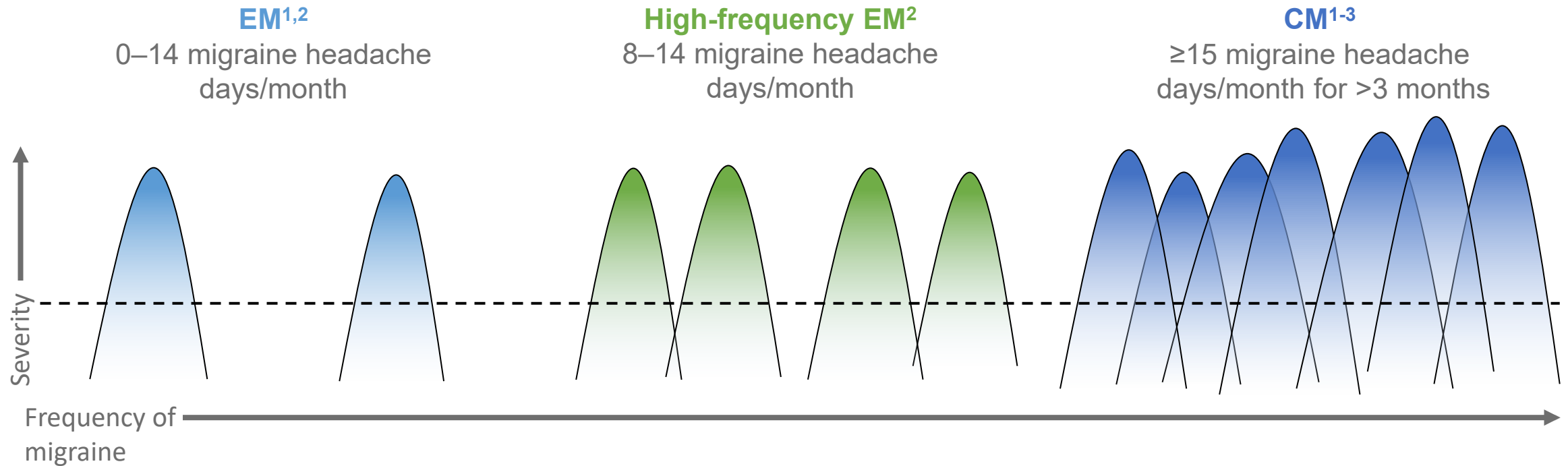
During headaches at least 1 of the following:

- Nausea and or vomiting
- Photophobia and phonophobia

Episodic – Headache on < 15 days/month

Chronic – Headache on >15 days/month

Some patients with EM will experience a transition into Chronic Migraine



EM, episodic migraine CM, chronic migraine

1. Blumenfeld AM et al. Cephalalgia 2011;31:301-15; 2. Buse DC et al. Headache 2020;60:2340-56;

3. Headache Classification Committee of the International Headache Society (IHS). Cephalalgia 2018;38:1-211; 4. Meletiche DM et al. Headache 2001;41:573-8

Medication Overuse (MO) vs Medication Overuse Headache (MOH)

Medication overuse⁵

- Using medication for the acute treatment of migraine for
 - ≥10 days/month (opioids, ergotamine, triptans)
 - ≥15 days/month (non-opioid analgesics, NSAIDs)

MOH

- **MOH is a secondary headache disorder** occurring in **1–2%** of the global population⁶
- Up to **70% of patients with CM** may develop MOH⁷

Medication overuse and CM

- Medication overuse is a **risk factor** in the development of CM¹
- **~65–80%** of patients with CM have medication overuse²⁻⁴

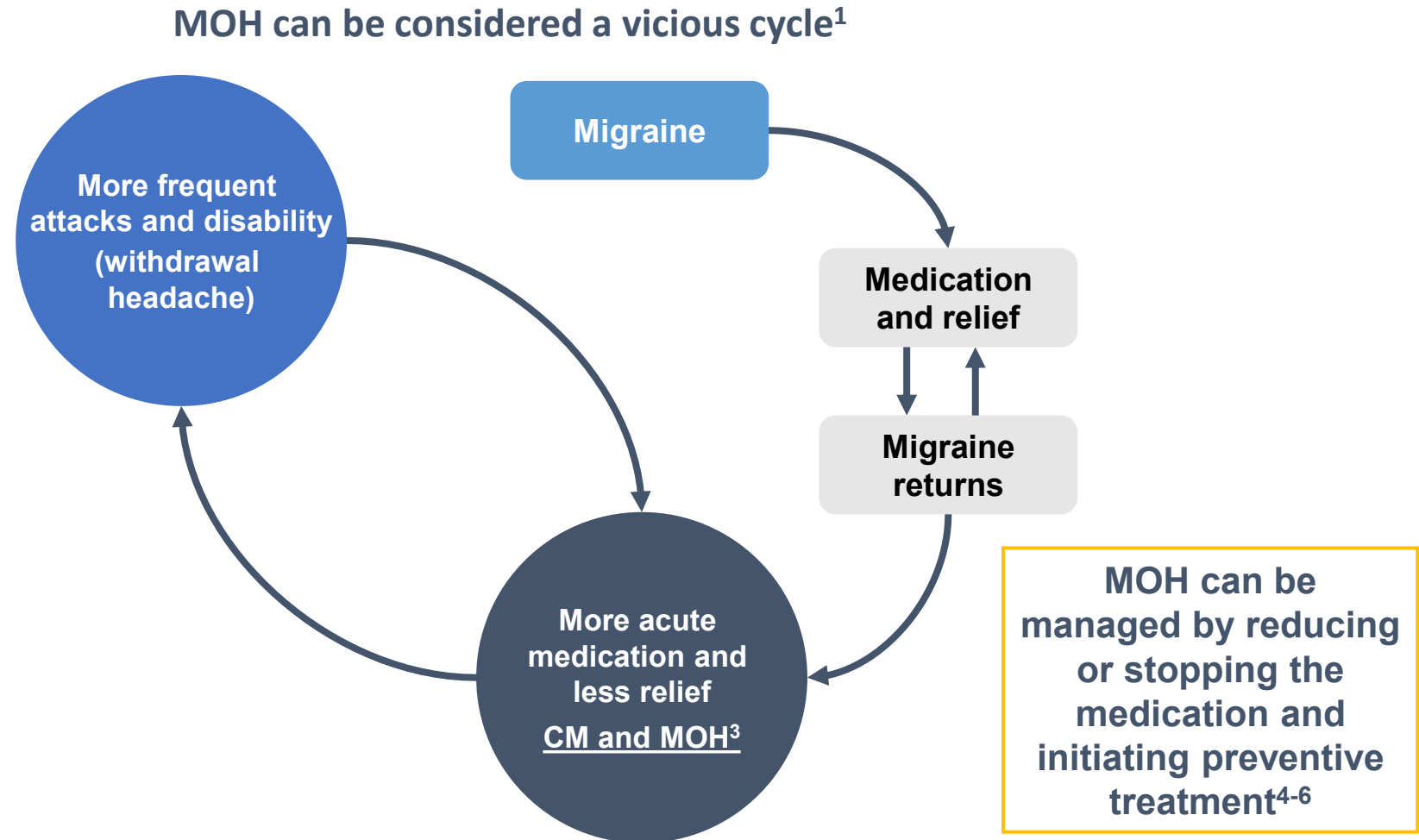
ICHD-3 criteria for MOH²

- ≥15 headache days/month
- Pre-existing primary headache disorder (eg migraine, tension-type headache)
- Regular overuse for >3 months of acute anti-headache medication
 - Triptans / combinations, ≥10 days/month
 - Simple analgesics only, ≥15 days/month
- Not better accounted for by another ICHD-3 diagnosis

MOH is a Secondary Headache Disorder

Patients with MOH may be categorised **depending on the medicine** involved²

- **Uncomplicated / simple:** patients with no history of opioid or barbiturate overuse and no behavioural impairment
- **Complicated / complex:** patients who chronically use opioids and / or barbiturates and / or have significant psychological issues



1. Fischer MA, Jan A. StatPearls [Internet]. 2022. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK538150/>. Last accessed October 2022;
2. Alstadhaug KB et al. Pain Rep 2017;2:e612; 3. Headache Classification Committee of the International Headache Society (IHS). Cephalgia 2018;38:1-211;
4. Evers S, Jensen R. Eur J Neurol 2011;18:1115-21; 5. Carlsen LN et al. JAMA Neurol 2020;77:1069-78; 6. Diener HC et al. Lancet Neurol 2019;18:891-902

Risk factors for MOH^a

Presented with odds ratios



Demographic^{a,1}

- 1.9** Female
- 1.9** Low educational level
- 1.8** Age (<50 years)



Self-reported complaints^{a,1}

- 2.6** Depression
- 2.0** Anxiety
- 1.9** Chronic musculoskeletal complaints
- 1.6** Gastrointestinal complaints



Lifestyle^{a,b,1,2}

- 12.7** Metabolic syndrome
- 2.7** Physical inactivity
- 1.8** Smoking
- 1.4** High daily caffeine intake (>540 vs <240 mg)



Medication^{a,c,1,3}

- 5.2** Tranquilisers
- 2.3** Opioids
- Triptans
- 0.7** Ibuprofen
- 0.5** Aspirin

1. Hagen K et al. Pain 2012;153:56-61;
2. He Z et al. Eur J Neurol 2015;22:1228-34;
3. Scher AI et al. Cephalalgia 2010;30:321-8

^aResults from 2 longitudinal cohort studies of adults with or without CM (n=41,766); ^bresults from a cross-sectional observational study of women with migraine (n=142); ^cresults from observational population surveys of adults with EM or CM (n=713)
MOH, medication-overuse headache; EM, episodic migraine; CM, chronic migraine

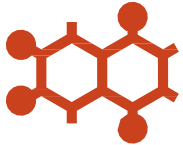
The pathophysiology behind MOH is complex and partially understood

MOH may cause network changes in the central nervous system¹⁻³



Cortical-spreading depression^{1,2}

- Vulnerability to headache attacks



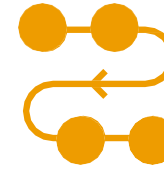
Dependence networks³

- Disturbances in normal brain pathway neurotransmitters



Pain medication can cause

- **Altered neurotransmitter metabolism** (serotonergic / cannabinoid pathway)³
- **Up-regulation of vasoactive and pro-inflammatory mediators¹** (eg CGRP)



Pain processing pathways¹

- Up-regulation of pronociceptive systems



Grey matter volume⁴

- Thalamus and the ventral striatum
- Orbitofrontal cortex
- Anterior cingulate cortex



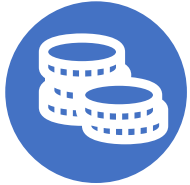
Polymorphic variants in genes³

- Angiotensin-converting enzyme
- Catechol-O-methyltransferase
- Brain-derived neurotrophic factor
- Serotonin transporter

MOH places a significant burden of disease on individuals and societies due to high costs and co-morbidities¹



MOH is considered a **major and growing** public health concern²



MOH is likely the **most costly** of all headache disorders³



Indirect costs due to **reduced productivity** and **absenteeism** accounting for **~90%** of the costs³



Associated with **poorer QoL** compared to episodic migraine⁴



MOH is the **most common** headache evaluated in tertiary headache centres⁵



People with MOH experience **increased disability** and are at higher risk of migraine **co-morbidities**⁵⁻⁷



MOH is associated with a higher risk of **suicide** and a higher prevalence of psychiatric disorders such as **anxiety, depression** and **substance-related disorder** spectrum^{1,8}

There are many unmet needs in the treatment of MOH

There is no universal consensus on how to treat MOH and there is a lack of evidence from sufficiently powered RCTs to recommend a specific treatment approach¹

Relapse to medication overuse can be high (28–31% within 6 months of withdrawal, increasing to 41% at 1 year and 45% at 4 years)^{a,2}

Standardised education approach to MOH is needed to enhance awareness and understanding for both patients and physicians³

Preventive treatments may play a role in breaking the vicious cycle of MOH⁴

1. Alstadhaug KB et al. Pain Rep 2017;2:e612; 2. Da Silva AN, Lake AE 3rd. Headache 2014;54:211-7;
2. 3. Diener HC et al. Eur J Neurol 2020;27:1102-16; 4. American Headache Society. Headache 2019;59:1-18

^aResults reported in a clinical review regarding MOH
MOH, medication-overuse headache; RCT, randomised controlled trial

MOH can be managed, though strategies vary

The goals for treating and managing MOH should be to reduce the frequency and / or severity of headache, reduce acute medication consumption, improve responsiveness to acute and preventive treatments, alleviate disability and improve QoL¹

Standard strategies for MOH management approach include:



Education and counselling to limit future acute medication use²



Withdrawal of the overused medication^{1,2}



Initiation of migraine-preventive therapy to treat the primary headache disorder^{1,2}

1. Rapoport AM. CNS Drugs 2008;22:995-1004;
2. Diener HC et al. Eur J Neurol 2020;27:1102-16

Preventive migraine treatments can also support patients with medication overuse / MOH

Results from RCTs in adults with CM

Topiramate^{1,2}

An RCT has shown reductions in the **mean number of MMDs^a** in patients with CM, including those with medication overuse (n=306)

OnabotulinumtoxinA^{3,4}

Post hoc analysis of 2 large RCTs (PREEMPT) showed significant reduction in **migraine days** for onabotulinumtoxinA vs placebo in patients with CM (~65% of whom were overusing acute medications (-8.2 vs -6.2; p<0.001),³ and **73.4%** of medication overuse patients with CM reduced their **acute medication intake** by ≥50%⁴

Anti-CGRP mAbs⁵⁻⁹

Eptinezumab: significant reduction in **MMDs**; reductions in **number of patients meeting CM and MOH criteria**, and **acute medication use** (n=431)^{5,9}

Fremanezumab: significant reduction in **headache days** and **medication overuse** in patients with baseline overuse (n=587)⁶

Erenumab: significant reduction in **MMDs** and **acute medication use** in patients with medication overuse (n=274)⁷

Galcanezumab: significant reduction in **MMDs** and **medication overuse** in patients with medication overuse (multiple trials, n=1042)⁸

None of the above are indicated for MOH

Efficacy of other preventive medications for medication overuse / MOH has not been shown in randomised, placebo-controlled trials¹⁰

1. Silberstein SD et al. Headache 2007;47:170-80; 2. Silberstein S et al. Headache 2009;49:1153-62; 3. Dodick DW et al. Headache 2010;50:921-36; 4. Caronna E et al. Front Neurol 2018;9:808; 5. Diener H-C et al. Headache 2021;61:125-36; 6. Silberstein SD et al. J Headache Pain 2020;21:114; 7. Tepper SJ et al. Neurology 2019;92:e2309-20; 8. Dodick DW et al. Cephalalgia 2021;41:340-52; 9. Marmura MJ et al. Headache 2021;61:1421-31; 10. Diener HC et al. Eur J Neurol 2020;27:1102-16

MOH, medication-overuse headache; RCT, randomised controlled trial; CM, chronic migraine; MMD, monthly migraine day; CGRP, calcitonin gene-related peptide; mAb, monoclonal antibody; EM, episodic migraine

gepants and MOH

- No signal of MOH reported in clinical trials or real-world studies¹
- Long-term use does not increase headache frequency¹

Expert Consensus²

- No known risk of MOH with gepants
- Can be used frequently without triggering rebound headaches

Real-World Impact

- Rimegepant use linked to reduced reliance on opioids and barbiturates³

1. Johnston K., et al. *Journal of Headache and Pain*. 2022;23:10. 2. Koonalintip, P., Phillips, K., & Wakerley, B. R. (2024). *Life*, 14(9), 1146.

2. 3. Rosen Net.al Headache. 2025 Jul 12. doi: 10.1111/head.15004. Epub ahead of print. PMID: 40650461.

MOH, medication overuse headache

MOH is preventable and requires increased awareness¹

Emphasis should be on EDUCATING PATIENTS



Increased awareness in the **general population** and among **health-care professionals** of the relationship between frequent use of pain medications and the transition from EM to CM **may be effective in preventing MOH** in at-risk patients with migraine



Only 8% of patients demonstrated knowledge that overuse of all types of headache medication could lead to the development of MOH²



Risk of potential development of CM with excessive medication use



The importance of appropriate medication administration and the risk of side effects

Communication and Patient Education Strategies in MOH

- Empathetic, non-blaming explanation of MOH
 - ✓ Explain 'rebound cycle', avoid patient blame, use simple terms.
- Headache diaries & education tools (leaflets)
 - ✓ Improve awareness, track medication use.
- Clear withdrawal plan & symptom prep¹
 - ✓ Set timelines, plan to manage rebound headaches.
- Follow-up & relapse prevention
 - ✓ Safety netting, regular check-ins, reinforce limits, adjust preventives.
(Relapse risk 20–35% in first year; early intervention key³)
- Shared decision-making & motivational interviewing
 - ✓ Increase patient buy-in; tailor withdrawal plans (BIMOH¹ trial – 50% reverted to episodic headache)

Based on speaker's clinical experience

1. Kristoffersen ES et al., BMJ 2015 (BIMOH trial). 3. Diener HC et al., Lancet Neurol 2019

Summary

- EM can progress to CM;¹ such progression is associated with a variety of risk factors²
- Overuse of acute medications is considered a risk factor for migraine progression¹ and can also lead to MOH⁶
- MOH is a secondary headache occurring on ≥ 15 days/month in a patient with a pre-existing primary headache disorder⁷
- MOH places a significant burden of disease on individuals and societies⁸ and is associated with a poorer QoL compared to EM⁹
- While MOH can be effectively managed by using strategies such as patient education, withdrawal of the overused medication and initiation of migraine-preventive therapy,¹⁰ the best strategy is still under debate

1. May A, Schulte LH. Nat Rev Neurol 2016;12:455-64; 2. Buse DC et al. J Neurol Neurosurg Psychiatry 2010;81:428-32;
3. Delussi M et al. BMC Neurol 2020;20:256; 4. Blumenfeld AM et al. Headache 2013;53:644-55; 5. Hepp Z et al. Cephalalgia 2017;37:470-85;
6. Scher AI et al. Cephalalgia 2010;30:321-8; 7. Headache Classification Committee of the International Headache Society (IHS). Cephalalgia 2018;38:1-211;
8. Linde M et al. Eur J Neurol 2012;19:703-11; 9. Da Silva AN, Lake AE 3rd. Headache 2014;54:211-7; 10. Diener HC et al. Eur J Neurol 2020;27:1102-16



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