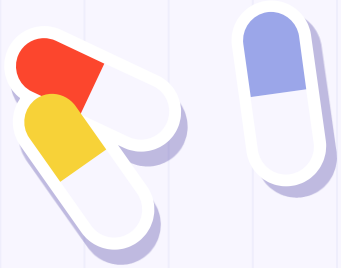
# Medication Overuse Headache (MOH)

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# HISTORY of MOH

**1930**

## Recognition

physicians observed **prolongation** of headaches associated with **ergotamine-overuse**

**1970s and 1980s**

## Evolutive migraine

physicians observed its association with analgesics such as **barbiturates**, **codeine**, and **combination analgesics** as well and also noticed a **reduction** in headache frequency **with stopping drugs**

**1988**

## ICHD-I

**first defined** the disorder calling it a **drug-induced headache** that was a “headache induced by chronic substance use or exposure

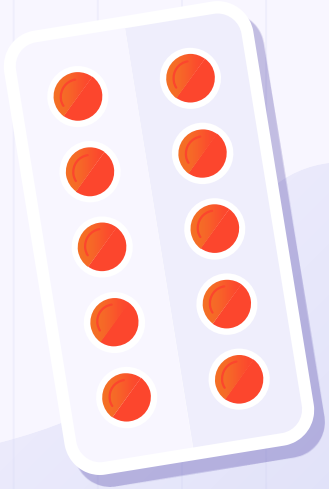
**2004**

## ICHD-II

MOH was first introduced in the second edition of ICHD (2004) with multiple **subtypes** dependent on offending medicine, such as **ergotamine**, **triptans**, **opioids**

# INTRODUCTION

- A **secondary** headache disorder (subsection 8.2 ICHD-III)
- Frequently **coexists** with primary and other secondary headache disorders and *complicates their management*
- Among the **top 20 causes of disability** worldwide
- Often **under-recognized**
- Significant **negative** impact on the patient's **quality of life**
- **Iran:** an **average** of **$2610 annually** for each MOH patient (55% indirect)



# DEFINITION & TERMINOLOGY

## Medication overuse headache (MOH)

analgesic rebound headache, drug-induced headache, medication-misuse headache

### Frequency?

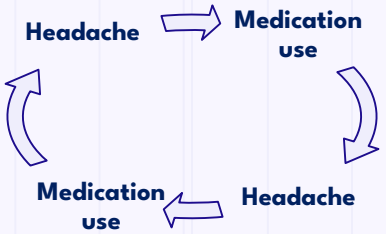
**≥15 days** per month
**>3 month** of use

### How?

a **consequence** of **regular overuse** of acute headache medication

### Course?

Usually **resolves after** the overuse is **stopped**



# EPIDEMIOLOGY

## Prevalence

**~1-2%**
in *general population*

**~50%**
in *headache centers* (11-70%)

**~4.6%**
in *general population* **Iran**

## Co-existing headache

65-80% **migraine**

27%tension-type

## Age

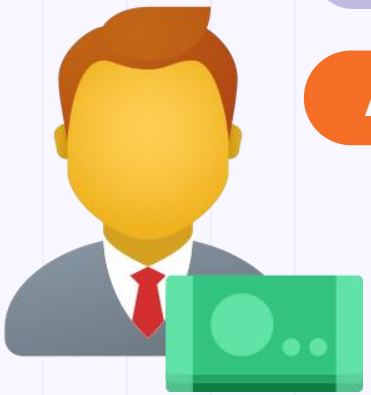
Aged **30 to 50 years**

## Sex

**Female** to male 3-4/1

# 3,120,000,000,000,000 IRR

Three Quadrillion One Hundred Twenty Trillion Iranian Rial



**Annual burden** of **MOH** in **Iran** (direct + indirect)

# PATHOPHYSIOLOGY

## Genetic predisposition

- have **underlying headache** disorder and does not develop **de novo**
- **migraine** > **tension** > cluster > hemicrania continua
- **33 genes** with 50 polymorphisms

## Biobehavioral factors

- **compulsive drug seeking-taking behavior**
- **fear** of headache, **anticipatory anxiety**, psychologic drug **dependence**
- **opiates** or other drugs with sedative/anxiolytic effects to treat both pain and a coexistent anxiety
- **part of the addictive disorders spectrum**

## Central sensitization

- **facilitation of trigeminal pain processing**
  - the same process that occurs in migraine
  - primarily mediated at a supraspinal level

# PATHOPHYSIOLOGY

## Central sensitization

| | |
|---|---|
| **Chronic Exposure to Triptans and other Analgesics** | • **Downregulation** of **serotonin receptors**<br>• Impairment of antinociceptive activity<br>• Permanent feeling of head pain |
| **Sustained or Repeated Triptan Treatment** | • **Induces pro-nociceptive** neural adaptations<br>• Enhanced responses to **nitric oxide** (known trigger of migraine headache) |
| **Glucose Metabolism** | • *Reversible* metabolic change in pain processing structures<br>• *Persistent* orbitofrontal hypofunction |
| **Chronic Exposure to Opiates** | • **Peripherally;** increased calcitonin gene-related peptide expression in primary afferent neurons, activating of excitatory glutamate receptors, neurotoxicity manifested by neuronal apoptotic cell damage<br>• **Centrally;** increased descending facilitation from the *rostral ventromedial medulla* and increased excitatory neurotransmission at *dorsal horn* |

# PATHOPHYSIOLOGY

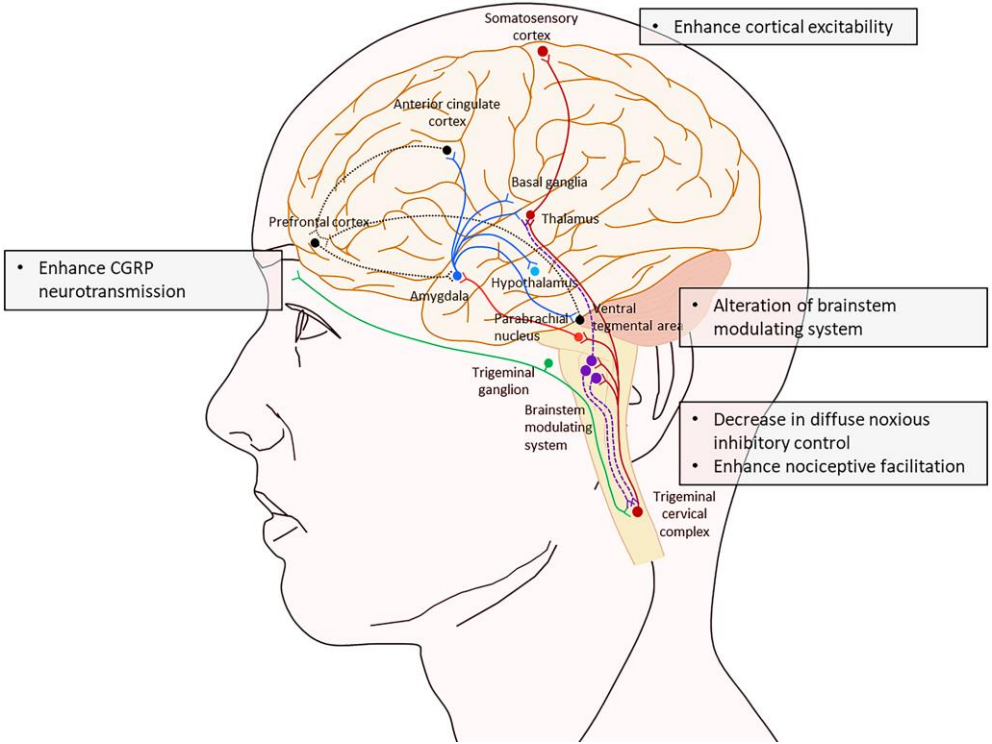



**Figure from:** *Sun-Edelstein C*, Rapoport AM, Rattanawong W, Srikiatkhachorn A. Possible pathogenesis of MOH. [Internet]. *The Evolution of Medication Overuse Headache: History, Pathophysiology and Clinical Update.* Springer International Publishing; 2021 [Access Date: 9/15/2022]. Available from: https://link.springer.com/article/10.1007/s40263-021-00818-9#Fig1

# RISK FACTORS

Medication overuse

Anxiety & Depression

Socioeconomic status

Female Sex

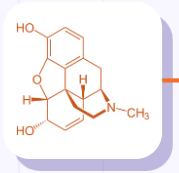
Cutaneous Allodynia

Migraine severity

Smoking

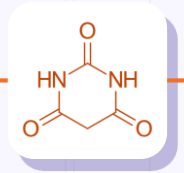
Age > 50

# CAUSAL MEDICATIONS



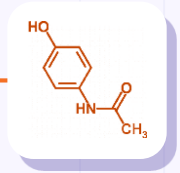

## Opioids

- More pronounced in **males**
- Critical dose of exposure was **~8 days/month**
- Approximate **doubled risk** of transformation from episodic to chronic migraine compared with patients taking acetaminophen




## Barbiturates

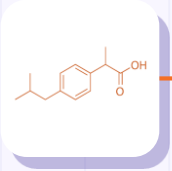
- More pronounced in **females**
- Critical dose of exposure was **~5 days/month**
- Approximate **doubled risk** of transformation from episodic to chronic migraine compared with patients taking acetaminophen




## Other Analgesics

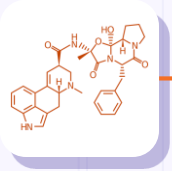
- With other combination analgesic medications, including acetaminophen-aspirin-caffeine
- Simple analgesic medications

# CAUSAL MEDICATIONS



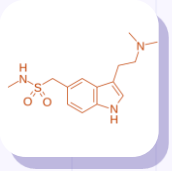
## NSAIDs

- **Conflicting** data
- **Low** in most but not all studies
- Some have suggested that NSAIDs are **protective** against the development of chronic migraine for patients who have less than 10 headache days per month



## Ergotamine

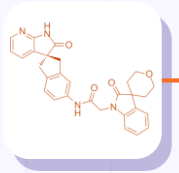
- **Decreasing** due to decreased use associated with the introduction of new acute headache medications since the mid-1990s



## Triptans

- Ranges **intermediate** to **low**
- Lead to MOH **sooner** than overuse of ergots or analgesics **at a lower frequency of use**
  - (1.7, 2.7, 4.8 years; resp.)

# CAUSAL MEDICATIONS



## Other medications

- **CGRP antagonists:**
  - Limited data
  - However; unlikely to cause
- **Ditans**
  - Selective serotonin 1F receptor
  - Uncertain, but may be similar to triptans risk

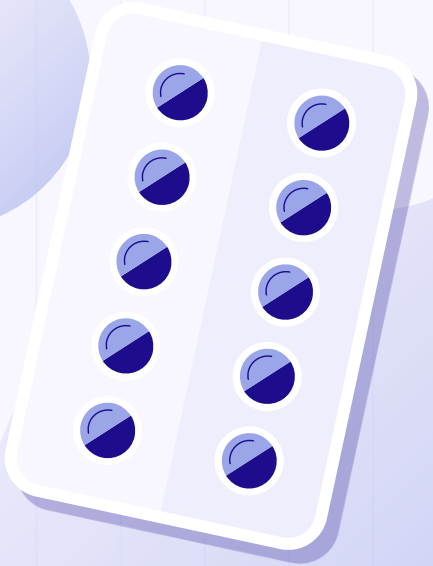
## Multiple medications

- It is **often difficult to identify a single causal substance** for MOH, since many patients are overusing more than one drug

# CLINICAL FEATURES

## Headache – Characteristics

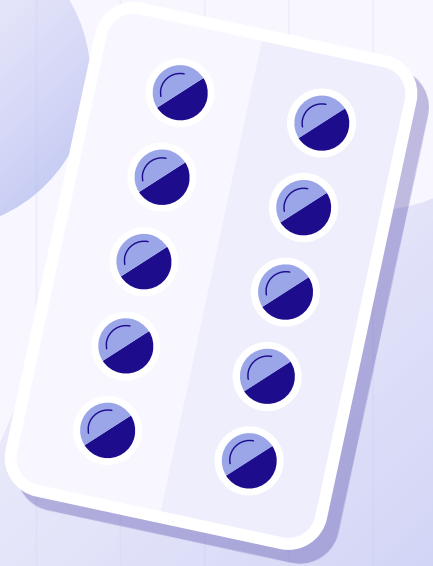
- **No typical clinical characteristics.**
- Preceded by an **episodic headache disorder**, treating with frequent and excessive **medications** amounts
- Present or develops **upon awakening** (nocturnal withdrawal)
- **A variety of** severity, location, and type of head pain
- Commonly occurs **daily or nearly daily**



# CLINICAL FEATURES

## Headache – Accompanying items

- **Neck pain,**
- **Autonomic** and **gastrointestinal** symptoms
  - **Runny nose,**
  - **Tearing,**
  - **Nausea,**
  - **Vomiting,**
  - **And diarrhea**
- **Asthenia,**
- Difficulty **concentrating,**
- **Memory** problems,
- **Irritability**

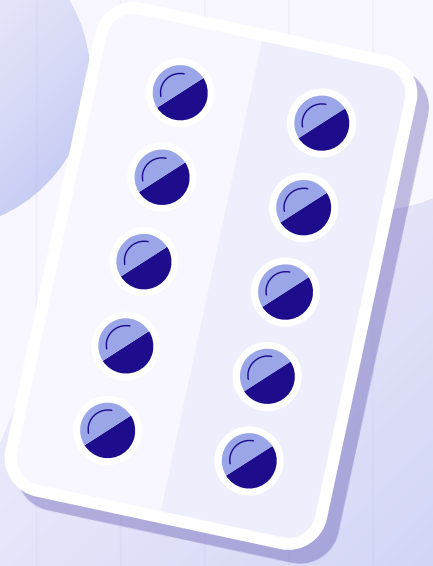


# CLINICAL FEATURES

## Headache – Medication Types

- Overusing **Ergots** and Analgesics (**Codeine, Barbiturates, Caffeine** Combinations):
  - Results in a daily **tension-type** headache phenotype

- **Triptan-induced** MOH:
  - Results in a daily **migraine-like** phenotype or an increase in migraine frequency



# DIAGNOSIS

## Clinical Impression

**01**

**Headache Disorder**

Course of an **Pre-existing headache** disorder

**02**

**Medications History**

History of **drug intake** With an intake **frequency** of **> 2-3 days per week**

**03**

**Secondary headaches**

Other disorders causing secondary headache **must be excluded**

Remember, it is the **frequency** of a headache and not the quality or intensity that makes the diagnosis of MOH

# DIAGNOSIS

## Diagnostic criteria: ICHD-3

**A** — occurring **≥15 days/month** in a patient with a **pre-existing headache disorder**

**Headache**

&

**B**

**Medication**

**Regular overuse** for **>3 months** of one or more drugs that can be taken for acute and/or symptomatic **treatment of headache**

&

**C** — Not better accounted for by **another ICHD-3 diagnosis.**

**Alternative Dx**

- **for ≥10 days** per month for >3 months: **ergotamines**, **triptans**, **opioids**, or **combination** analgesics, or any combination of ergotamines, triptans, simple analgesics, NSAIDs and/or opioids
- **for ≥15 days** per month for >3 months, of **simple** analgesics (ie, **acetaminophen**, **aspirin**, or **NSAID**)

# DIFFERENTIAL DIAGNOSIS

## Any form of chronic daily headache, whether primary or secondary!

- Chronic migraine

- Chronic tension-type

- Hemicrania continua

- Cluster headache

- Short-lasting Unilateral Neuralgiform Headache Attacks With Conjunctival Injection And Tearing (SUNCT)
- Hypnic Headache,
- Nummular Headache,
- Chronic Paroxysmal Hemicrania.

# TREATMENT

## Educate the patient

about the detrimental effects of medication overuse

## Wean the offending medication

- **Barbiturates, opioids, or benzodiazepines**
  - 100 mg **Butalbital** ➡ 30 mg **phenobarbital** taper
  - **Opioids** ➡ **Clonidine** transdermal patch
- **Other medications**
  - **Discontinue** the overused medication and **switch to an alternative** medication from a different class. Limit the use of acute medications to no more than two days per week, **or**
  - **Taper** the acute medication gradually as the headache frequency decreases in response to **effective preventive therapy**

# TREATMENT

## Bridge (transitional) therapy

suggested for patients who, in the clinician's opinion, are unlikely to be successful with a treatment plan consisting of discontinuing the overused medication along with rescue therapy and preventive therapy; including the short-term use of certain **oral** (**naproxen**, **tizanidine**, **glucocorticoids**) and **intravenous** (**dihydroergotamine**, **prochlorperazine**, **valproic acid**, **aspirin**) medications.

## Prophylaxis for co-existing headache disorder

starting preventive treatment at the same time as withdrawing the offending medication

# Prognosis

1101 patients with MOH

meta-analysis of 17 studies

**72%** Success

## Goal

treatment success was defined as either no headaches, or a reduction in headache days of >50 percent

## 1-6 months

success rate for withdrawal therapy

# Prognosis

240 patients with MOH

prospective data

withdrawal + preventive

**57%** Success

## Goal

absence of chronic headache and medication overuse

**1 year**

treatment success

**Independent predictors** of unfavorable treatment outcome at one year were a *higher frequency of primary headache*, *ergotamine* overuse, and a *greater degree of headache-related disability* at the time of MOH diagnosis

# Prognosis

96 patients with MOH

prospective study

**41%**

Success

## Goal

relapse rate at six months, one year, and four years

**6, 12, 24 month**

31, 41, 45 percent, respectively.

Patients with underlying **migraine headache had a lower relapse** rate than those with tension-type headache or combined migraine and tension-type headache, but small numbers prevent definitive conclusions.

# Prognosis

67 patients with MOH

retrospective report

multidisciplinary headache treatment

**50%** Tension-type

**72%** Migraine

## 🎯 Goal

reduction in total headache frequency

# Summary

| | |
|---|---|
| **INTRODUCTION** | Frequently coexists with primary chronic daily headache and other secondary headaches. |
| **DEFINITION** | ≥15 days/month, overuse of acute/symptomatic headache medication, for >3 months |
| **PATHOPHYSIOLOGY** | Uncertain; Genetic predisposition + Central sensitization + Biobehavioral factors |
| **EPIDEMIOLOGY** | ~ 1-2%; Female-to-Male ratio = 3-4:1; most associated with migraine, tension-type, mixed, and other |
| **RISK FACTORS** | Medication overuse, Age>50, Smoking, Female sex, Anxiety & Depression, Socioeconomic status, Cutaneous Allodynia, Migraine severity |
| **CAUSAL MEDICATIONS** | Opioids, Butalbital, Acetaminophen-aspirin-caffeine Combinations, Triptans (Int-low), NSAIDS (Low?-Protective?), Calcitonin Gene-related Peptide Antagonists (Uncertain-low), ... |
| **CLINICAL FEATURES** | preceded by an episodic headache disorder, usually migraine or tension-type headache, occurs daily or nearly daily |
| **DIAGNOSIS** | Clinical impression; suggestive: history of symptomatic medication use in association with Chronic daily headache (>2-3 d/w); diagnosis made: fulfilling the diagnostic criteria for MOH |

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# Thanks

Any questions? Get in touch:

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