

# Medication Over Use Headache: Characteristic, Etiopathophysiology, Diagnosis and Emerging Treatment

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**ABSTRACT :Background:** Medication overuse headache (MOH), formerly known as drug-induced headache, which affects 1% of people worldwide, constitutes one of the most debilitating headache conditions. However, it's entirely different, the use of acute symptomatic medications for 10–15 days in a month (depending on the drug class, such as simple analgesics, triptans, and opioids) and the use of these medications for headache relief for three months or more in patients having a history of primary headache disorders.

**Objective:** With an emphasis on recent developments in the fields of pathophysiology, risk factors, clinical features, and treatment, the purpose of this article was to examine the subject of MOH and provide the specifics of this condition.

**Material and methods:** For the purpose of writing this review, a search of the literature was conducted using appropriate keywords in the PubMed/MEDLINE and Springer databases. We reviewed around 71 articles by using keyword like “MOH”, “pathophysiology of MOH”, “risk factors of MOH”, “CGRP”. Boolean operators “AND” and “OR” were employed.

**Results:** The idea of MOH has changed over time, despite one occurrence of grey matter disturbances, the distinct pathogenesis is still being contemplated. Modification in pain pathways, changes in areas of the brain associated with pain intensity, and neurotransmitter changes have all been related to genetic vulnerability. A detailed medical history is required to separate it from other secondary recurring daily headache disorders, focused testing, and information on medication usage. The most common forms of treatment for primary headache disorders in outpatient or inpatient settings include patient disease information, abstinence of the causative agent, and management through preventive medications are all approaches.

**Conclusions:** Any person with a chronic headache should be evaluated for MOH, a secondary headache disease. Its development is linked to a number of pathophysiological pathways and risk factors. Detoxification, preventive therapy, and education on the disorder are all part of management

**Index Terms -** migraine, medication overuse headache, headache disorder, triptans.

## INTRODUCTION

Headache disorders presents with highest morbidity worldwide and headache disorders are classified into primary and secondary headache. Recently concept of Medication Overuse Headache is being studied<sup>1</sup>. Medication overuse headache (MOH) is a secondary headache disease according to the revised third edition of the International Classification of Headache Disorders (ICHD-3). In MOH, a patient with a primary headache problem takes a medication intended to relieve the symptoms of their headache episodes. The two most prevalent major headache diseases worldwide are migraine and tension-type headache (TTH). Some patients who use medications for acute pain may paradoxically have an increase in their headache symptoms<sup>1</sup>. Depending on the medicine being abused, MOHs are defined as headaches that happen at least 15 days a month. Overusing a headache medication is described as using it on a regular basis (for more than three months) for more than 10 or more than 15 days a month. According to estimates, more than 50% of patients at headache clinics who experience chronic headaches abuse painkillers and develop MOH<sup>2</sup>. Chronic headache in a long run progresses to medication overuse headache.

Although the etiology of MOH is not fully understood, ideas involving gray matter atrophy have lately been linked to the disease's pathogenesis<sup>3</sup>. Various other pathophysiology related to neurophysiology like The dopaminergic, angiotensin-converting enzyme, and brain-derived neurotrophic factor pathways have been linked to genetic variables in the form of potential polymorphic variants. MOH could have a mechanism involving cortical neuronal hyper excitability brought by by excessive pharmaceutical use. Chronic acetaminophen administration in rat models led to an increase in the occurrence of cortical spreading depression (CSD) and cortical hyper excitability. The production of MOH may also be influenced by low serotonin (5-HT) levels. In animal studies, low 5-HT causes the pronociceptive 5 HT<sub>2A</sub> receptor to be upregulated

and CSD to occur more frequently<sup>1</sup>, have been studied using various neuroimaging techniques like Magnetic Resonance Imaging (MRI) and positron emission tomography (PET)<sup>2</sup>.

This article reviews and encapsulates the overall concept of MOH including history, epidemiology, risk factors, clinical features, pathophysiology, diagnosis, management, prognosis and role of pharmacists in MOH.

## HISTORY

When doctors saw that headaches brought on by ergotamine usage lasted longer than usual, MOH was first identified in the 1930s<sup>4</sup>. The relationship between it and analgesics such as barbiturates, codeine, and combination analgesics was noted by doctors in the 1970s and 1980s. They also noted a decrease in headache frequency after ceasing the drugs. It was known for a brief period of time as transformed or evolutive migraine<sup>5</sup>. Drug-induced headache was initially described as a disorder in the first edition of the International Classification of Headache Disorders (ICHD) in 1988 as "headache characterized by chronic drug usage or exposure"<sup>6</sup>. MOH had first been mentioned in the second edition of ICHD (2004), where it was divided into a number of subgroups that depended on the offending drug, such as ergotamines, triptans, opioids, etc.<sup>6</sup>

## EPIDEMIOLOGY

The real prevalence of medication overuse headache is uncertain, in part because of numerous revisions assumptions in diagnostic standards, but for the general population fall between 0.5 and 2.6%. Russia (7.6%) and Iran (4.6%), two nations where it is assumed that drugs usage is more ubiquitous, have increased incidence.<sup>7</sup> The frequency of MOH in those who have persistent daily headaches has been observed in various studies from specialized headache centres to range from 11 to 70%, which is substantially superior to the average population. Most MOH patients (around 80%) have tension-type or post-traumatic headaches as their primary headache problem. MOH most frequently affects people between the ages of 30 and 50, with a 3 to 4 to 1 gender ratio. It's interesting to see that between 21 and 52% of paediatric patients and 35% of seniors over 64 matched the MOH requirements. First-generation migrants have been shown to have higher prevalence rates in some studies conducted in Europe, and it was thought that this could have a number of causes, including socioeconomic class, genetic predisposition, and cultural factors. Experts believe that the genesis of MOH involves a combination of economic, psychological, and physical incapacity because it is a global problem. Because MOH was thought to be an outgrowth of migraine and tension headache, migraine was classified as the second-leading cause of disability in the Global Burden of Disease (GBD) report from 2016<sup>8</sup>.

## RISK FACTORS

Among the various headache migraine and tension type headache poses greatest risk for development of MOH because of involvement of neurological manifestations. Regular use of tranquilizers, a mix of gastrointestinal issues, persistent musculoskeletal issues, and a Hospital Anxiety and Depression Scale (HADS) score  $\geq 11$  as well as smoking (daily vs. never). Age under 50, gender of women, and low education level were non-modifiable risk factors for MOH. However, smoking is not associated with chronic headache without the use of analgesics. The commonly used drug for management of this disorders are analgesics, triptans, opioids, ergotamine and gepants. Additionally, clinical data demonstrates that the majority of patients with cluster headaches do not progress to MOH, despite the fact that excessive usage of sumatriptan injections may increase the frequency of cluster attacks. A chronic headache does not appear to develop in individuals who abuse drugs prescribed for conditions other than cephalic pain, unless they have a history of a primary headache illness.<sup>9</sup> Risk factors for MOH with odds ratio are depicted in Table:1. Patients with MOH who abuse opioids and triptans more frequently exhibit dependency-like behaviour than those who abuse aspirin or ibuprofen. MOH can be linked to the spectrum of substance-related disorders since it is thought that their neurological mechanisms are similar<sup>12</sup>. The figure representing risk factors for MOH are shown in Figure: 1.

Table-1: Principal Risk Factors for MOH with Odds Ratios (OR) are: [5](#), [10](#), [11](#)

Population risk factors		Odds ratio
Population demographics	Population Age (under 50 years)	1.8
	Women	1.9
	Low educational attainment	1.9
Individual's symptoms	Long-term musculoskeletal discomfort	1.9
	Complaints about the stomach	1.6
	Anxiety or depression	4.7
Life style	Smoking	1.8
	Metabolic syndrome	5.3
	High daily caffeine intake (more than 540 mg versus less than 240 mg)	1.4
	Physical inactivity	2.7
	Metabolic syndrome	5.3
Medication	Tranquilizers	5.2
	Aspirin	0.5
	Ibuprofen	0.7
	Opioids	2.3

## NEWER GENERATION ANTIMIGRAINE MEDICINE AND ITS RELATION WITH MOH

As migraine is one of the main risk of developing MOH and traditional medicines used for treating migraine like triptans, opioids, NSAIDs also presents with higher risk for MOH. However, a new wave of targeted therapeutics for migraine has evolved, predicated on the idea that the calcitonin gene-related peptide (CGRP) is essential to the pathophysiology of the condition. Two of these treatments include lasmiditan and second-generation gepants (including rimegepant, ubrogepant,), which are small-molecule CGRP receptor antagonists. The connection between MOH and the new migraine treatments is being discussed<sup>13</sup>. Conclusions cannot be drawn since lasmiditan, ubrogepant, and rimegepant are recently developed substances from the currently conducted clinical trials, which are frequently of a short duration and do not consider their risk for MOH. Usually, before a prescription is administered, the safety and tolerability of excessive pharmaceutical use is not considered. The results from animal research may be worth taking into account when making assumptions about the situation. In order to understand how the brain changes as a result of excessive use of analgesics over time, animal models of MOH have been established<sup>14</sup>. These models display MOH-related traits as mechanical allodynia, hyperalgesia, and nociceptive behaviors. Preclinical MOH and elevated CGRP levels have been linked in several studies, and using an antibody to inhibit the CGRP pathway prevented cutaneous allodynia in mice sensitized to morphine and sumatriptan<sup>14-18</sup>. Additionally, in both clinical trials and real-world settings, the administration of monoclonal antibodies that block the CGRP pathway was successful in reducing headache in MOH patients.<sup>19-25</sup> A possible strategy to keep the risk of MOH development low may be to target CGRP signalling for the acute treatment of migraine. Ubrogepant and Olcegepant, when regularly administered, did not cause cutaneous allodynia in rats or neuroplastic alterations in trigeminal sensory afferents, but chronic Lasmiditan treatment in mice resulted in similar outcomes, including an enhanced expression of CGRP in trigeminal sensory afferents<sup>24, 26, 27</sup>. Triptans and lasmiditan may vary from second-generation gepants in their potential to cause MOH despite targeting several receptor subtypes and blocking postsynaptic adenosine 3',5'-cyclic monophosphate (cAMP) signalling cascades. However, caution is needed about our hypotheses. Preclinical models exclusively examine the effects brought on by medicines that elicit MOH, rather than assessing a rise in headache frequency. The precise MOH vulnerability that migraine patients may have is unknown in animal studies. Other investigations have questioned CGRP's function in the pathogenesis of MOH<sup>27, 28</sup>. There is currently no evidence that lasmiditan administration over an extended period of time causes MOH. If clinically shown, gepants may be very beneficial for patients with a history of MOH or who are at high risk of developing MOH, especially those who experience regular migraine attacks.

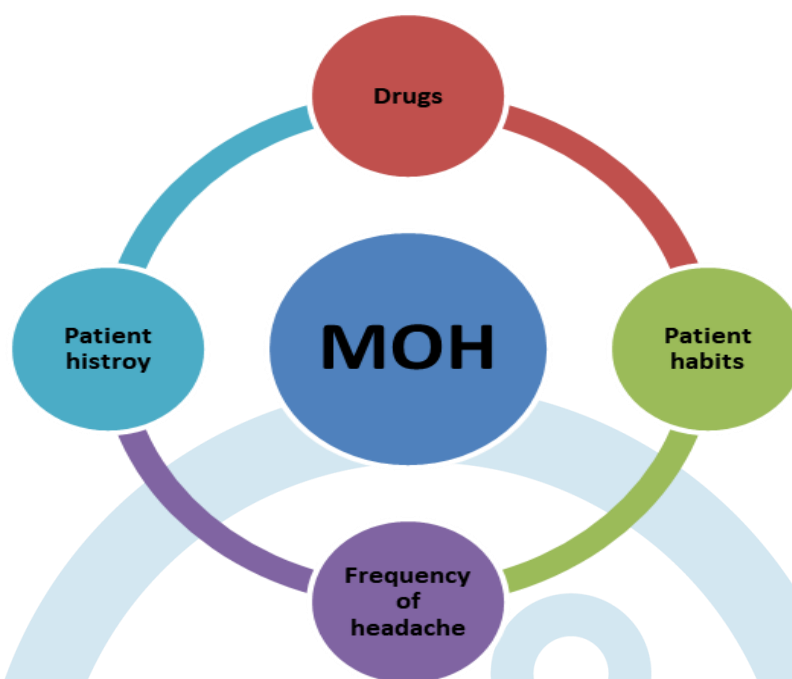


Figure: 1 Risk Factors associated with Medication Overuse Headache

## **PATHOPHYSIOLOGY**

There is still a lack of knowledge on the pathophysiology of MOH various theories have been stated and various research have been carried out to identify the correct pathophysiology. Even if the clinical components of MOH appear to be conflicted, there is evidence that certain neurobiological aspects of MOH-models exist<sup>29,30</sup>. The main concept responsible for development of MOH is desensitization or down-regulation of receptors thus, it is expected that agonist therapy will result in receptor desensitization and/or down-regulation, whereas receptor antagonist therapy would result in receptor overexpression<sup>13</sup>. However, animal studies has demonstrated elaborated pathophysiology of MOH. Due to a lower threshold, prolonged chronic sumatriptan administration increases susceptibility to evoked cortical spreading depression (CSD). Trigeminal ganglia were shown to have upregulated levels of vasoactive and nitric oxide synthase, substance P, and calcitonin gene-related peptide (CGRP), which are pro-inflammatory mediators<sup>15, 31-35</sup>. Additionally, it was discovered that long-term analgesic use increased the excitability of the neurons in the central amygdala, which could theoretically explain how anxiety or depression might develop in MOH patients<sup>35</sup>.

Although there is currently a paucity of credible evidence supporting hereditary features, genetic investigations have been conducted in MOH. Cargnin et al presumed polymorphic variations in the dopaminergic gene system (DRD4, DRD2, SLC6A3) and genes associated with drug-dependence pathways in a recent systematic review (WSF1, BDNF, ACE, HDAC3). According to the authors' findings, these traits may work as risk factors for MOH genetic predisposition or as markers of monthly drug usage.<sup>36</sup>

Additionally, research on animals have shown that taking painkillers by itself can change how neurotransmitters, particularly those in the serotonergic and endocannabinoid systems, are metabolized.<sup>14</sup> It has been suggested that people with MOH have their brains "frozen" in a pre-excitation state by a number of human investigations that have demonstrated hypersensitization and hyperresponsiveness of the cerebral cortex. Actually, after stimulation, the somatosensory evoked potential (SEP) amplitude was higher in all MOH patients. In addition to a lack of habituation after additional stimulation.<sup>37</sup> Following drug withdrawal, the majority of patients and the majority of brain regions showed a gradual return to normal sensory processing. Long-term use of painkillers appears to be the main factor contributing to anatomical and functional brain characteristics linked to MOH. All painkillers may result in MOH, however other types of drugs may not cause it more quickly or with less repeated use. As a result, it is assumed based on data from numerous research that MOH affects specifically the central nervous system in networks that process pain and depend on them, as well as in sensitization and receptor abundance, all of which have a role in the clinical characteristics of the illness.

A recent research describing pathophysiology of MOH related to gray matter changes was performed which shown alteration in various system. Increased gray matter in the bilateral ventral striatum and ventral tegmental area (VTA) of MOH patients with reward system change shows that addiction brought on by an abnormal reward system plays a crucial role in the etiology of MOH. It is well acknowledged that drugs, on which a patient depends for various reasons, can stimulate the -aminobutyric acid A receptors, inducing dopamine release from the VTA. The nucleus accumbens's dopaminergic receptors activated the reward system after receiving the signal from the VTA, and the patient thereafter took medications repeatedly. Both physically and functionally, the VTA and the nucleus accumbens are interconnected. Changes in the orbital frontal gyrus, as well as the orbitofrontal cortex (OFC), superior frontal gyrus, middle frontal gyrus, and inferior frontal gyrus, are present in patients with MOH. A FWE correction was passed on the orbital gyrus' gray matter atrophy.

Numerous areas linked to the sense of pain are altered by alterations in the pain network. Gray matter was shown to have increased in the thalamus, cerebellum, trigeminal afferent region in the midbrain, and Periaqueductal Gray (PAG), while gray matter had decreased in the insula<sup>3</sup>.

## DIAGNOSIS

A headache's frequency, not its quality or strength, is what determines whether it is MOH. There are no mandatory laboratory, radiological, or other investigations needed to confirm the prognosis of MOH until the patient's history reveals noticeable clinical signs during the physical examination.

**Identification of Medication-Related Headache (MOH) requires compliance criteria A-C for the diagnosis of MOH as per International classification of headache disorders (ICHD-3)<sup>9</sup>**

- A) 15 or more days of monthly headaches AND a history of headache disorders.
- B) Overusing medications for acute and/or symptomatic headaches for more than three months (regular use of medications on at least 15 days per month for acetaminophen, ASA, and NSAIDs, and at least 10 days per month for ergotamine, triptans, opioids, and combination analgesics).
- C) No other ICHD-3 diagnosis offers a better justification.

### **Drug Class and Headache Duration in Medication Overuse Headaches<sup>38</sup>**

- 10 days / month for more than 3 months on ergotamine
- 10 days / month for more than 3 months on Triptan
- ASA: 15 days / month for more than 3 months.
- NSAIDs: >3 months, 15 days / month
- Acetaminophen / paracetamol: for more than three months, 15 days per month
- 10 days each month for more than 3 months on opioids combined analgesics.
- 10 days / month for more than three months various medication classes.

Early MOH diagnosis was shown to be quite difficult by Natalia A. Shnayder et al. They therefore conducted study on serum and urine proteomic indicators to aid in early MOH diagnosis. This study found 24 serum and 25 urine proteomic biomarkers related to MOH. The urine proteome biomarkers (uromodulin, alpha-1-microglobulin, zinc-alpha-2-glycoprotein, etc.) and serum biomarkers (vitamin D-binding protein, lipocalin-type prostaglandin D2 synthase, apolipoprotein E, etc.) of MOH were examined<sup>39</sup>.

The detection of patients with MOH development may be aided by the serum and urine proteomic indicators of MOH. Additional research into the MOH proteomic biomarkers in various ethnic and racial groupings of individuals with primary headache is required because of the importance of the topic. Additionally, it's critical to look into whether certain drug classes have an impact on the levels of serum and urine proteomic indicators<sup>39</sup>.

## TREATMENT

Although withdrawal has recently been touted as the major therapy of choice for MOH<sup>40</sup>, some studies have proposed withdrawal as the best course of action for MOH.<sup>41-43</sup> Withdrawal improves responsiveness to acute or preventative medications<sup>41, 44</sup>, in addition to reducing headache attacks. The most typical withdrawal symptoms include headache that first gets worse, nausea, vomiting, hypotension, tachycardia, sleep problems, restlessness, anxiety, and agitation<sup>44, 45</sup>. They seldom stay more than 4 weeks and often last 2 to 10 days<sup>44</sup>. To ensure therapeutic success, it's also critical to ensure that patients have realistic expectations for their care, i.e., that their primary headache won't be completely eliminated<sup>46</sup>.

### **Patient counselling**

MOH is frequently regarded as a condition that is avoidable. A key preventive intervention is to educate patients about the link between a propensity for overusing acute medicines and headache progression. Numerous research findings have revealed that the majority of MOH patients know very little to nothing about headache chronification caused by excessive medication use. Many patients did however, receive the right information, but frequently failed to recall or properly comprehend the message. MOH patients, like other patients with chronic pain disorders, appear to be most concerned about the adverse effects of the acute painkillers, including as gastrointestinal bleeding, renal damage, and liver impairment. They are frequently shocked to find that using acute pain medications excessively might increase headache frequency and cause MOH<sup>47-51</sup>.

### **Drug withdrawal**

Different headache clinics have different procedures for stopping drugs. No studies have compared the abrupt interruption of the overused drugs to the gradual cessation of use, but it is generally accepted that the abrupt withdrawal is the preferred treatment for NSAIDs, combination analgesics, simple analgesics, triptans, and ergots due to the lack of significant withdrawal symptoms these medications elicit. In contrast, when it comes to opioids, benzodiazepines, and barbiturates, a progressive drug reduction is the recommended course of action. The duration of withdrawal symptoms, which include headaches, nausea, vomiting, tachycardia, arterial hypotension, and sleep difficulties, is typically between two and ten days.

Even among patients who abuse barbiturates, seizures and hallucinations are uncommon. Subjects with a high triptan intake experience a shorter withdrawal phase<sup>46, 52</sup>.

### **The use of the particular offending substance must be stopped during treatment:**

Other than opioids, barbiturates, and benzodiazepines, the following medicines should be stopped using:

- Launch or improve preventive therapy: A different drug from a different class should be used in place of the overused one. Not more than two days per week should be allowed for the use of acute medications. OR
- As the incidence of headaches declines in response to preventative therapy, reduce the acute medicine gradually. A long-acting NSAID or steroid should be added to bridge therapy for patients who continue to have headaches.
- Benzodiazepines, barbiturates, and opioids should all be stopped using: If using greater<sup>9</sup> dosages of a drug, it is progressively tapered (in 2-4 weeks). If smaller doses are administered, they could be quickly stopped using a transdermal clonidine patch once per week as treatment.

### **Prophylaxis**

An important therapeutic step in preventing the development of persistent episodic headache is the beginning of preventative therapy. But it's still unclear which strategy is more efficient: initiating preventative therapy as soon as withdrawal symptoms appear or waiting until detoxification takes effect. Some publications advise delaying the choice to begin preventative care for two to three months after discontinuation in patients with non-complicated MOH. On the other hand, patients who have a history of several preventative treatments and who already get headaches frequently before medication misuse may benefit from early prevention<sup>53</sup>.

Other medical professionals think that detoxification can work without immediate prophylaxis. There is currently no prophylactic medication that has demonstrated prominence to other therapies in an exploratory studies with suitable design, as shown by a recent meta-analysis of randomised controlled studies on the effectiveness of preventative treatments (i.e. valproate, nabilone, onabotulinumtoxin A, topiramate, amitriptyline)<sup>51, 54</sup>. The administration of onabotulinumtoxinA and topiramate without an immediate break is recommended by the findings of randomized controlled studies with individuals who had MOH and chronic migraine. The data's reliance on post hoc analysis however, limits the quality of the information<sup>55</sup>. Monoclonal antibodies that target the CGRP pathway may have a future application. In the end, the clinical history, comorbidities, contraindications, and side effects of the potential medications should be taken into consideration while determining the correct prophylactic<sup>51, 56</sup>.

A study by Louise Ninett Carlsen, MD et.al stated that a three therapeutic interventions were examined in a randomised controlled trial: (1) withdrawal including preventive treatment, (2) preventive treatment without withdrawal, or (3) withdrawal with an additional preventive treatment that could be initiated two months following withdrawal. Which concluded that, all 3 treatment approaches were successful for MOH and did not differ in their ability to reduce the number of monthly headache days. In addition, we expected that there wouldn't be a substantial difference in the number of monthly headache days between the withdrawal plus prevention and withdrawal techniques, and we were proven to be wrong. In spite of this, the withdrawal plus preventative group experienced the greatest numerical decreases days requiring short-term drug usage, days with migraines, and days with headaches, and days with higher pain. Additionally, the chance of curing MOH was much greater for patients in the withdrawal with preventative group than it was for those only undergoing preventive care. Additionally, in contrast to the withdrawal group, a disproportionately higher percentage of patients in the withdrawal with preventative group relapsed to episodic headache<sup>57</sup>.

### **Prognosis:**

A chronic headache's prognosis can be bad and its quality of life can be reduced by overusing acute therapy. Patient motivation is crucial to the treatment of MOH.<sup>58, 59</sup> It has been reported in numerous research that there is a well established response rate of more than 50% take a hit from baseline headache frequency for MOH patients weaning from acute medication abuse. After a year, 50 to 70 percent of MOH patients were reported to have successfully withdrawn.<sup>60</sup> Retaining withdrawal after a year is an excellent indicator of long-term success.<sup>61, 62</sup> After six years, there is a 40–50% relapse rate.<sup>63</sup> Even in patients whose headache frequency does not significantly improve after a successful withdrawal phase, preventative therapy has a better effect.<sup>64</sup> several indicators of relapses have been linked to symptoms like tension-type headaches, prolonged regular usage, a large number of emergency treatments, no recovery after two months of withdrawal, drinking and smoking, and resumption of abuse of previously used medications.<sup>65-67</sup> While consolidated medication treatment has a higher rate of relapse, triptan abuse has a reduced recurrence rate.<sup>68</sup> In addition, patients' reports of poor sleep quality and significant levels of bodily discomfort are likely indicators of poor 1-year outcomes.<sup>69</sup> The relapse rates for MOH can be significantly decreased by include behavioral therapy in the treatment plan. In this study, only 12.5% of patients experienced a headache relapse after receiving behavioural therapy, compared to 42% of patients without it.<sup>70</sup>

### **Patient Education and Deterrence:**

If concomitant conditions like Obesity, smoking, inactivity, and mental problems are all treated, and continuing assistance is given through counselling and patient monitoring, and behavioural therapy, patients with MOH will fare better. A 2014 study found that 77% of undergraduate students were unaware that MOH existed. 83% of students were interested in

learning more about MOH agreed that MOH warnings should be placed on pharmaceutical bottles, and 80% said they would use less analgesics as a result of their new found knowledge<sup>71</sup>.

## THE IMPROVEMENT OF HEALTHCARE TEAM RESULTS AND ROLE OF PHARMACISTS

MOH is a prevalent condition that affects people all over the world. It has a occurrence of 1% in the overall population, but it causes 11 to 70% of chronic daily headache sufferers. Sadly, they frequently go unrecognized and have a profoundly severe effect on the patient's quality of life. It is important to acknowledge the elevated risk for MOH associated with opiates and combination analgesics. Some of the many MOH advancement risk factors can be changed and must be paid attention to. Up to 50% of patients who have anxiety and depression also exhibit dependence-like behaviors, such as tolerance or an inability to limit the use of painkillers.

The most efficacious evidence-based strategy for assisting these people in breaking the cycle of headaches will still necessitate treatment trials, but approaches will include patient counselling services, detoxification, and mitigative therapy. MOH must be made more widely known to the general public, and patients and clinicians must be taught basic mitigation techniques. When MOH is speculated, effective communication between the primary care physician, nurse practitioner, pharmacist, internist, and neurologist is critical for treatment effectiveness.

The pharmacy staff lacks significant awareness about MOH, but with the right information, they would be well-equipped to prevent MOH in both its main and secondary forms. We advocate for both stepping up MOH education initiatives within pharmacy programs and providing all employees with ongoing training in pharmacies. Additionally, it's critical to educate pharmacy customers.

## CONCLUSION

Medication overuse headache is the most debilitating disorder where much information about its cause, pathophysiology, diagnosis and treatment is not available and is been discovered. Differential diagnosis of MOH and non-MOH but chronic headache patient should be screened properly by healthcare provider by inquiring detailed patient history, drug use pattern, disease pattern, frequency of headache and symptoms. It is an disorder which if neglected and treated as normal pain then the patient will be more prone to experience adverse effects and no efficacy.

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