(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 5, Issue 5 , Page No: 435-441
September-October 2022

IJMSCR

Medication Overuse Headache

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Type of Publication: Original Research Paper
Conflicts of Interest: Nil

Abstract

Medication overuse headaches, also known as MOHs, are a type of severe headache that can be brought on by abusing one or more drug groups that are classified as analgesics. MOH results from structural and functional changes to the brain brought on by excessive drug use. The most common medications that induce MOH are opiates, barbiturates, ergotamine derivatives, triptans, and simple analgesics. At this time, people who already suffer from migraines or other types of headaches, such as tension headaches or cluster headaches, are more likely to develop MOH than those who do not already have these types of headaches. As part of the treatment for MOH, the offending drug(s) must be discontinued, the withdrawal symptoms must be treated promptly, and patients can be educated on proper drug use and modifiable risk factors to prevent MOH.

Keywords: Medication-overuse headaches (MOH), ACE polymorphisms, neurotrophic factor (BDNF), migraine

Introduction

Medication-overuse headaches (MOH) are also defined as analgesic rebound headaches, drug-induced headaches, or medication-misuse headache, which are a frequent neurologic disease that can cause a great deal of pain and suffering, as well as play a key part in the transition from episodic to chronic headache [1]. These headaches are developed in patients with a history primary headache disorders who misuse drug to relieve the symptoms of their primary headache [2]. Excessive usage of drugs can result in an unsatisfying loop of increasing headache frequency, in which the medication used to treat the initial headache then becomes the cause of headaches [3, 4]. MOH can arise in patients who have a history of headaches and use painkillers for other reasons [5, 6]. The goal of this review is to go through the causes of medication overuse headache, and also its risk factors, prevention, and alternative treatments.

Etiology of Medication-overuse headaches

The most current version of ICHD-3 (2018) classifies medication overuse headache as a secondary headache that develops as a chronic headache condition after an initial headache syndrome [1, 3]. Which MOH subtype is present depends on the medication being taken [6]. The main criteria are that a patient with a history of headache disorder experiences a headache more than or equal to 15 days per month, that one or more medications that can be used to treat a headache's acute and/or symptoms have been misused for more than three months, and that the headache is not better accounted by another ICHD-3 diagnosis [7, 8]. All suitable/multiple codes should be provided if a number of drugs are being taken inappropriately [9]. No clinical characteristics are established since the headache is typically identical to the pre-existing headache condition. Once the medication is withdrawn, the MOH often disappears [10, 11]. The primary headache syndrome and the MOH are the two diagnosis in this situation [12]. The need that the headache pattern begin to alleviate two months after ceasing the offending

treatment is no longer necessary for the diagnosis [13, 14]. Each type of analgesics has a different risk profile, although the use of chronic medications, as the names indicate, is the main risk factor for the emergence of MOH [5, 15]. The lowest risk medications were triptans/ergotamine, single analgesics (NSAIDs, acetaminophen), and combinations of opiates or barbiturates.It has been demonstrated that combination analgesics, particularly those that include opioids and/or barbituates, have a twofold higher relative risk of MOH [16, 17]. NSAIDs may aid in preventing MOH in people who experience ten or fewer headache days per month [18].

Types of medications overused

Theoretically, any medication used to treat severe headaches may result in MOH (i.e., ergotamine derivatives, barbiturates, triptans, simple and combined analgesics, opioids, benzodiazepines, and possibly caffeine) [14]. It is unclear, nevertheless, if the clinical features of MOH brought on by various medications and the risks are different [14, 19]. Additionally, there is also discussion about whether dihydroergotamine and simple analgesics can result in MOH [5]. Up until the early 1980s, analgesics—especially combination analgesics—were thought to be the sole substances that might induce MOH [4]. The first case reports of MOH brought on by triptans were released in 1994 [20]. The significance of triptans was widely acknowledged as more research groups confirmed this discovery using larger samples [6]. Nowadays, triptans are the most often given medication for MOH patients, at least in high-income nations [9]. This used to be the case with ergotamine derivatives and later, briefly, barbiturates until the latter were withdrawn from the market (at least in European nations) as a migraine cure [21]. Ergotamine, however, continues to be the medicine that causes MOH the most frequently in India [22]. A new class of calcitonin gene-related peptide antagonists that is used to treat acute migraine episodes has been said not to induce MOH [12, 23]. However, given the history of the condition and the pathophysiological pathways that contribute to it, it is unlikely that these medications do not also induce MOH [24].

Currently, there is no epidemiological or scientific proof that medication combinations, particularly those including caffeine, are more likely to result in MOH than single drugs [1, 25]. Combination medications are often given and sold over the counter, as evidenced by the prevalence of these medications among all MOH patients [26]. Compared to simple analgesics, triptans and ergotamine derivatives are more likely to cause MOH [27]. Simple analgesics have been found to require more dose to cause MOH and a longer time to develop MOH than any other analgesics [15]. However, there are conflicting findings about whether triptans or ergotamine derivatives need a shorter induction period or whether smaller dosages of either compound are adequate to cause MOH [7, 16]. MOH headache symptoms are induced by ergotamine derivatives than by triptans. When triptans and analgesics are used excessively combined, headache frequency, severity, and related symptoms rise more than when triptans are used alone [28]. Patients with triptan induced MOH are more likely to mention a (daily) headache that is similar to a migraine or an increase in the frequency of migraine attacks than people who abuse ergotamine and analgesics [29]. In a population-based prospective investigation from the United States, only the use of barbiturates or opioids was substantially linked to the emergence of chronic headache, including MOH [30]. Due to the fact that up to 90% of MOH patients take many medications to treat acute attacks, it is hard to differentiate between the various MOH subtypes based on the overused drug [31, 32].

Pathology

Some research has hypothesised that a potential hereditary predisposition may be the cause of MOH [33, 34]. One such model is the renin-angiotensin system, which is known to regulate brain plasticity actively [33, 34]. A new study has linked gene variation in the angiotensin-converting enzyme (ACE) gene to an increased risk of MOH [35]. ACE is a critical enzyme in regulating blood pressure, but it interacts with the monoaminergic synaptic transmission in the brain, contributing to dependence development [17]. It has been shown that ACE polymorphisms in MOH patients alter sensitisation and habituation patterns. Brain-derived neurotrophic factor (BDNF), catechol-O—methyltransferase (COMT), and serotonin transporter are further possible polymorphisms (SERT) [13]. All of these cause disruptions in the normal neurotransmitter

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pathways in the brain, rendering patients more vulnerable to dependency, behavioural disorders, substance misuse, pain disorders, and a variety of neuropsychiatric illnesses [36, 37]. Studies on animals have also shown that pain medicines can change neurotransmitter metabolism, particularly in the serotonergic and endocannabinoid systems [38, 39]. Multiple human studies have demonstrated hypersensitisation and hyperresponsiveness of the cerebral cortex, suggesting that the brains of people with MOH are "locked" in a state of pre-excitation [4]. All MOH patients displayed an increase in the amplitude of the somatosensory evoked potential (SEP) in response to stimulation and a lack of habituation in response to additional stimulation [10, 30]. Most patients and most brain regions observed a gradual return to normal sensory processing. Long-term exposure to pain drugs appears to be the critical factor influencing MOH's anatomical and functional brain changes [40]. All pain drugs are capable of causing MOH, but certain drug types can cause it more quickly or with less misuse [6, 41]. Based on evidence from several studies, it is believed that MOH induces changes in the central nervous system, notably in pain processing and reliance networks, sensitisation, and receptor density, all of which serve to explain the disease's clinical manifestations [1, 3, 42].

Risk factors

Chronic primary headaches have been linked to heavy pharmaceutical usage, which is a substantial risk factor [9, 43]. The results of this systematic review, which included the analysis of 29 studies, revealed that the risk of MOH varied depending on the drug being taken [19]. Compared to combined analgesics, the risk was lowest for triptans (0.65 relative risk) and ergotamine (0.41 relative risk) [44]. Compared to opioids, triptans and ergotamine-containing drugs were deemed more desirable. NSAIDs reduced the risk of chronic headache in patients with a low to a moderate number of monthly headache days in those with a high number of monthly headaches (more than 10 days per month) [45]. Pre-existing headache disorder: migraine is the most prevalent type of headache that MOH exacerbates [46]. MOH can also exacerbate other pre-existing headache disorders, such as tension-type headaches and cluster headaches [18]. As an underlying biological trait, predisposition to migraine or tension-type headache is a significant risk factor for MOH development [47].

Treatment

An essential component of effective headache prevention is educating patients about the connection between prolonged use of acute pain relievers and the development of chronic pain [1]. MOH is commonly regarded as a preventable condition [1]. Multiple studies have shown that most MOH patients know little to nothing about the chronification of excessive drug intake headaches [1, 48]. However, many patients frequently fail to recall or fully comprehend the message despite receiving accurate information [49]. Like other patients suffering from chronic pain conditions, patients with MOH appear to be primarily concerned about the adverse effects associated with the acute pain medications, such as bleeding in the gastrointestinal tract, damage to the kidneys, and liver impairment [50]. They are frequently surprised to learn that excessive acute pain medications can increase headache frequency and lead to MOH [50]. For many MOH patients, symptomatic medications are the only way to alleviate the impact of the disease on their lives and are therefore the only drugs they require to relieve their pain [4, 50].

Evidence suggests that headache medicine should focus on educating patients at risk, preferably prior to MOH development, to improve outcomes [51]. Migraine sufferers who also take much medication found that a brochure on medication overuse kept MOH at bay with the help of these headache centres in Germany [20]. The best setting for prevention and initial treatment of MOH is primary care since most MOH patients visit their general practitioner (GP) for headaches (80%) [17]. General practitioners have the potential to play a pivotal role in educating patients about the appropriate use of medication and modifiable risk factors such as stress, daily smoking, lack of physical activity, and obesity [17]. When necessary, general practitioners can also prescribe first-line headache prophylaxis to episodic patients [12]. Using over-the-counter medication, MOH patients frequently bypass medical advice [52]. A study of patients recruited from pharmacies revealed that only 14.5% were ever advised to limit the frequency of acute headache medication consumption. In a recent study conducted in Sweden, 326 pharmacists were quizzed about their knowledge

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regarding the treatment of headaches [52]. Of those pharmacists, only 8.6% demonstrated knowledge that excessive use of any acute headache medication could lead to MOH development [53].

In 2016, the Danish national MOH awareness campaign targeted the general public, general practitioners, and pharmacists [52, 53]. The survey revealed an increase in the public's awareness of the MOH [53]. The dissemination of critical messages such as pain medication overuse can worsen headaches, the pain medication should be used sparingly, and medication overuse headaches can be treated through online resources, print media, radio interviews, and television broadcasts [21, 37, 54].

Conclusion

Research in medicine is advancing and uncovering the mechanisms underlying headache progression and excessive medication use. This aspect of research strives to help physicians construct more favourable decisions for patients with severe headaches and other comorbidities by gathering more evidence. Whether MOH is a distinct entity, a pathophysiological complication of primary headache disorders or an epiphenomenon of the natural progression of headache disorders is still debatable. It is abundantly clear that high-quality research will assist us in resolving several issues brought up in the preceding questions because the methodology is getting better, and people from all over the world are working together to form collaborative efforts.

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