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Medication-Overuse Headache: The Same Thing to Substance Abuse?

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Medication-Overuse Headache (MOH) is one of the most common chronic headache disorders characterized by overuse of kinds of acute headache medications. Many studies have found that MOH shares some common clinical and biological features with substance abuse, however, the complex pathophysiology behind MOH is still only partly known. In this article, the similarities between MOH and substance abuse and its role in the development of MOH was discussed.

MOH is a condition that can develop in headache patients after overuse of one or more drugs intended for acute and/or symptomatic treatment of headache. The population-based prevalence of MOH is reported as 1% in average, however, a relative high incidence has been found among chronic headache sufferer [1]. Our nationwide population-based study showed that MOH patients accounted for approximately 60% of these with headache occurring at least 15 days per month [2]. MOH is more disabling than other forms of headache and has become one of the major challenges in headache treatment. In the Global Burden of Disease Study 2013 [3], MOH was ranked the 18th high cause of YLDs (years lived with disability). The most important part of MOH therapy is drug discontinuation, while a relapse rate around one third after discontinuation has been reported [4]. According to the International Headache Society (IHS), MOH include two elements: Chronic headache and medication-overuse, and most researchers regard the association between overuse of medication and development of MOH as causal. However, the complex pathophysiology behind MOH is still only partly known.

As one of the most prevalent disorders associated with regular substance use, MOH has always been speculated to share some pathogenetic mechanisms with other drug addictions. MOH patients have been found to show some dependence-related behaviour according to behavioral diagnosis, but conflicting results are obtained in different studies [5]. Besides, some common gene polymorphisms were found in both MOH and substance abuse, which included the Brain-Derived Neurotrophic Factor (BDNF) polymorphism, the Serotonin Transporter (SERT) polymorphism and the dopamine transporter polymorphism [6], indicating the similarities between the two categories. Also, several recent imaging researches have proved the connection. In a PET study [7], persistent hypometabolism was found in orbitofrontal cortex of MOH patients, which is known to occur in drug dependence. Persistent dysfunctions in the

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midbrain dopamine circuit were also observed in MOH patients by functional MRI [8], suggesting that MOH may share some neurophysiological features with addiction.

Some drugs used by MOH patients, opioids for instance, are indeed addictive, but no evidence has been found for addiction to triptans or to simple analgesics. Moreover, MOH can only involve people with pre-existing headache. Consequently, we cannot simply divide MOH into the category of substance dependence. Moreover, episodic headache patients overusing analgesics even for reasons other than headache can also develop MOH [9], indicating that the pathogenesis behind the disease is specifically related to headache.

As one of the most common chronic headaches, MOH is also featured by series of neuroadaptive changes in headache chronification, such as increase of cortical spreading depression (CSD), brainstem dysfunction and the trigeminal hypersensitivity [5]. Both the recurring headache attacks and chronic analgesics exposure play a role in the development of peripheral and central sensitization. Our preclinical study [10] showed that

simply rizatriptan-overuse could not directly induce pain via the activation of nociceptive pathways but might aggravate the nociception-related behaviours induced by dural inflammatory stimulation via influencing the serotonin modulation system. These findings are in consistent with the clinical facts, indicating the pathophysiological mechanisms of MOH are specifically related to the migrainous or headache brain itself.

In summary, MOH do share some common clinical and biological features with substance abuse, but it is not reasonable to simply divide MOH into the category of substance abuse. From

our perspective, it is the headache brain itself that is prone to MOH, and these similarities between MOH and substance abuse mainly represent the physiological and ethological mechanisms of dependence. Medication-overuse promotes the process of headache chronification induced by recurring headache attacks and thus the pre-existing headache finally develops into MOH.

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