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Medication Overuse Headache (MOH): Prevention and Treatment

Medication overuse headache, previously known as rebound headache or medication-induced headache, may be caused by the frequent or excessive use of various acute care medications. When these medications are used too frequently, they can cause headaches rather than relieving them. (Some headache specialists feel that MOH is the result of recurring severe headaches, and the patients' overuse of medications to relieve them.) These medications, some of which are painkillers or analgesics, include over-the-counter products such as acetaminophen, aspirin, and anti-inflammatories, as well as prescription medications such as triptans, ergots opioids, opioids, and barbiturates. The one category of acute care medication that does not seem to cause MOH is the gepants, such as rimegepant and ubrogepant.

MOH is the fourth most common headache disorder. It is defined by the International Classification of Headache Disorders (ICHD-3) as a headache present 15 days per month, evolving from regular use of strong acute medication (10 or more days of triptans, ergotamines, butalbital medications, opioids, or combination medications or 15 or more days per month of simple analgesics such as aspirin, acetaminophen, or nonsteroidal anti-inflammatories) for 3 months.

Patients are usually not aware they have MOH, and this is the most problematic aspect of the condition. Patients do not realize that the medicine they are taking is making their headaches worse. It can be difficult to explain to the patient exactly what is going on with MOH, and why they are doing the wrong thing by taking the very medication that was prescribed by their doctor to stop a migraine attack. Many doctors do not fully understand MOH either, which can make it difficult to treat patients with this type of headache; therefore, it is imperative to educate both doctors and patients on the causes and treatments of MOH.

One of the most important facets of treating MOH traditionally has been the process of detoxifying patients from their overused medication by gradually or precipitously withdrawing the offending medication. There is variability in how detoxification can be accomplished. Some of my patients stopped medications abruptly and experienced very bad headaches. Others tried reducing dosages on their own and reported experiencing the worst headaches of their lives—some of which lasted for a few weeks. I have found

that if patients can endure 2 to 3 weeks of detox, they start to feel better. But because the headaches can worsen before they get better, patients understandably try to avoid the detoxification process.

I start patients on preventive medicine, then slowly increase it to an effective dose, and have them come back in a month for an evaluation. I then have them gradually reduce, but not completely stop, the pain medication before they return. Once I feel their preventive medication is at a therapeutic level, I have them begin a slow detox. After a month of preventive medication, there is a reasonable chance that headaches will start to decrease and be less severe. I tell them that if their headache is less severe try to avoid taking the medicine that they were overusing to prevent perpetuating the MOH.

One plausible physiologic mechanism behind MOH is that chronic exposure to acute care migraine treatment leads to suppression of the serotonergic/norepinephrinergic endogenous antinociceptive system in the upper brain stem, with facilitation of the trigeminal nociceptive process via up-regulation of calcitonin gene-related peptide (CGRP).This increase in CGRP at the end of peripheral nerve terminals in the trigeminovascular system may facilitate pain transmission. An increase in cortical CGRP may cause cortical spreading depression: a wave of excitement traveling through the cortex, followed by a wave of electrical depression seems to cause headache.

Good, effective prevention often helps avoid MOH; medications such as topiramate, nortriptyline, gabapentin, onabotulinumtoxinA, and CGRP monoclonal antibodies or some type of local nerve block have improved MOH in patients, but detoxification is usually necessary is some patients.

Monoclonal antibodies targeting CGRP or its receptor (CGRP-R), given by subcutaneous or intravenous injection or small molecule CGRP receptor antagonists given orally (gepants), seem to be able to treat MOH in some patients without a detoxification. This has been best demonstrated in the monoclonal antibody group, but there is some evidence showing that it may also occur with gepants. These treatments seem to work even when patients are overusing acute care medications; this helps some patients to self-detoxify at their own pace, which is easier for both the patient and the doctor.

Currently, there are 4 monoclonal antibodies against CGRP or the CGRP-R. Erenumab is the only completely human one and the only antibody that blocks the CGRP receptor to prevent the CGRP ligand from docking and exerting its effect. The other 3 (fremanezumab, galcanezumab, and eptinezumab) are humanized monoclonal antibodies that selectively bind to the CGRP ligand, preventing it from docking on its receptor. Patients started on the monoclonal antibodies against CGRP or its receptor

usually have fewer headaches in the first week or two of therapy, and this helps make the self-detox easier for the patient.

Further, substantial data have shown that onabotulinumtoxinA reduces the number/frequency of headaches and reduces the need for patients to take acute medication. OnabotulinumtoxinA is currently the only medication approved for preventive treatment of chronic migraine; it has long-term safety data available and has reported efficacy lasting for up to 3 years when given in multiple injection sites every 3 months. Interestingly, although topiramate is used as a preventive medication, a recent study comparing erenumab vs topiramate for reducing monthly migraine days (MMD) showed that erenumab outperformed topiramate with a 50% reduction in MMD, and with fewer reported adverse events.

We are just starting to learn about some other potential cellular mechanisms that could be causing MOH in patients; these data could help create new and improved therapies for treating and possibly preventing MOH in the future. Patient outcomes could also be improved by encouraging the inclusion of MOH as part of a continuing education program for physicians who could potentially be treating new patients presenting with MOH.