www.nature.com/clinicalpractice/neuro

Is medication-overuse headache a distinct biological entity?

Peter J Goadsby

Medication overuse in the context of headache seems a very simple concept: the patient has frequent headache, uses some form of acute-attack medicine on many of the affected days, and the headache consequently becomes more difficult to control. The International Headache Society has provided guidelines to formalize this definition, giving rise to the term medication-overuse headache (MOH). Overuse of acute-attack medication is a significant problem in itself, but is MOH a distinct biological entity, or is medication overuse an elaborate trigger to the underlying biology of headache?

Medication overuse applies mainly to medicines such as acetaminophen (paracetamol), opioids, caffeine, ergotamine and triptans. Nonsteroidal anti-inflammatory drugs (NSAIDs) are often included, although aspirin is seldom cited. MOH is usually discussed in the context of frequent headache. The term chronic daily headache (CDH) is applied to patients with 15 or more headache days per month for more than 3 months, regardless of the headache type. MOH is often cited as a form of secondary CDH—that is, CDH caused by medication overuse.

Studies in several populations have converged on one clinical message: headache induced by analgesics and acute specific primary headache treatments seems to occur predominantly in patients with a personal or family history of migraine. For example, in a group of patients attending a rheumatology clinic and being treated with regular analgesics, 10% had CDH, and each had a personal or family history of migraine, or both (Bahra A *et al.* [2003] *Headache* 43: 179–190). Similarly, in a cohort of patients with bowel motility problems treated with daily opioids, only those with migraine developed CDH (Wilkinson SM *et al.* [2001] *Headache* 41: 303–309).

Pharmacologically, opioids, triptans and ergotamine are all receptor agonists, and, interestingly, the periaqueductal gray (PAG) is a potential site of action for each of these treatments. It is possible to speculate that an agonist action of each of these medicines, as well as of acetaminophen, specifically affecting the PAG, underlies the development of MOH. By contrast, NSAIDs are receptor antagonists, and on their own seem to be weak inducers of headache.

Headache induced by analgesics and acute specific primary headache treatments seems to occur predominantly in patients with a personal or family history of migraine

The International Classification of Headache Disorders currently recommends upper usage limits of 10 days for ergotamine, triptans, combined analgesics and opioids, and 15 days for simple analgesics, although it is emphasized that this conclusion is not evidence-driven. A simple approach would be to accept that 10 days' use per month of acute-attack medicine of any sort is excessive. If there is an upward trend in medication usage, intervention, such as treatment with a preventive medicine, is essential; if medication use is stable, the physician can work with the patient using effective acute-attack treatment strategies to try and contain the worsening headache problem.

The available evidence is compatible with a thesis that MOH is an expression of alteration of the underlying headache biology by the frequent use of acute-attack medicines. The approach of recording medication overuse as a complicating factor, along with other information about the patient's headache, frees one from the unwieldy position of diagnosing—in effect—'probable MOH' until the patient responds to medication withdrawal.

So in clinical practice, what do I tell my patients? A patient frequently using analgesics (whether simple or compound), triptans or ergotamine needs to reduce their intake, and might need preventive management strategies for their headache. It remains clear that medication overuse is unhelpful in terms of impending improvement of headache, and the implications for management are the same regardless of whether we define MOH as a separate entity.

PJ Goadsby is Professor of Clinical Neurology and Consultant Neurologist at the National Hospital for Neurology and Neurosurgery, Queen Square, London, UK, and an Advisory Board member of Nature Clinical Practice Neurology.

Competing interests
The author declared he has no competing interests.

www.nature.com/clinicalpractice
doi:10.1038/ncpneuro0236