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IM - COMMENTARY

An emerging problem in clinical practice: how to treat chronic headache patients

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In this issue, an interesting article by Farinelli and co-workers [1] debates an important emerging and not yet resolved problem: how to treat the chronic headaches complicated by medication overuse. Headache is the most common neurological disease in clinical practice. In Europe, this affects about 51% of the population, of which 31% are tension-type headache and 14% are migraine sufferers; 2% of these patients become chronic sufferers, more than 15/day/month, and chronic daily headache (CDH). 4–5% of general population suffers from a chronic form (CDH), with prevalence between 1.7 and 2.1% in men and between 2.8 and 6.8% in women [2]; within this group of patients in the US general population ranges around 1.3–2% of chronic migraine (CM).

A number of possible pathophysiological mechanisms for the transformation from episodic to chronic headache have been proposed including a progressive damage of the central nociceptive system. One physiopathological hypothesis is the activation of *N*-methyl-D-aspartate (NMDA) and non-NMDA receptors glutamate, released by central nociceptive terminations, induces calcium entry in dorsal horn neurons, as well as in the trigeminal nucleus caudalis. Calcium entry leads to the activation of nitric oxide (NO) synthetase causing NO synthesis. These neurotransmitters produce the release of sensory neuropeptides, such as CGRP and substance P, which support the development of hyperalgesia and maintain central sensitization [3–5].

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Medication near-daily use and subsequent medication overuse headache (MOH) have been described by the revised International Classification of Headache Disorders (ICHDs)-IIR criteria as the use of each drug for at least 3 months, for a certain number of days per month, and is one of the most critical parameters in the process of becoming chronic.

In the past few years, a lot of studies have shed light on potential risk factors for CM such as medication-overuse headache, temporomandibular disorders, obstructive sleep apnea and obesity. Recent clinical trials have started to focus on CM or CDH. Topiramate, onabotulinum toxin type A, gabapentin, pentasites and tizanidine are among the agents that appear to be effective in the treatment of CM. In the treatment of CM, preventive treatment and a better understanding of its risk factors will allow clinicians to better identify individuals at the greatest risk and prevent the development of CM [6].

The main problem remains how to treat these patients to avoid a relapse in the daily drug use because recurrence of headaches and the management of CM patients in re-prophylaxis after detoxification of abuses still appears complicated.

Regarding abusers, the first step always consists in drug interruption. Only after detoxification can a new prophylaxis therapy be commenced, which will otherwise be useless from the start.

Within the possible treatment strategies in the review of Farinelli are examined the use of topiramate and the onabotulinum toxin A, a substance obtained from the gram-positive anaerobic bacterium *Clostridium botulinum*.

The comparison between these treatments does not indicate a clear superiority between the two treatments, and studies report no particular differences among treatments in terms of efficacy, but there is a significant difference for

what concerns safety profiles, which is definitely in favour of onabotulinum toxin A. In fact, adverse events due to topiramate therapy result more often in abandoning the treatment itself [1, 7, 8].

The future in relapse prevention of CM complicated by MOH consists in considering how drugs currently used such as triptans and emerging therapies present responsivity profiles related to well-defined genetic polymorphisms.

The feasible diagnostic setting for tailored treatment of CM based on the application of pharmacogenomics will allow us to predetermine the efficacy of single old and new drugs by avoiding abuse due to non-responsivity of the abused drug [9].

Headache brought on by chronic overuse of headache drugs responds well to a regimen of withdrawal, fluid replacement and anxiolytics, as Trucco et al. [10] report in a recent article showing that there is a good toleration of steroids along with a large volume of intravenous fluids. Moreover, the oral administration of steroids is not effective, so they recommend the parenteral route of administration.

For acute treatment, new medications including an inhaled form of dihydroergotamine will soon be available, and electric and magnetic neuromodulatory procedures such as occipital nerve stimulation may be effective for the most disabled patients.

In conclusion withdrawal of drug daily use, physical procedures, life-style modifications and an economic evaluation need to be studied considering that chronic headache sufferers represent a diverse population that needs a specific treatment approach. In fact, population-based studies suggest that these patients do not seek medical care for their headaches, and do not use prescription drugs to treat them [11].

Conflict of interest None.

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