



Chronic migraine and medication overuse: which strategy for a complex scenario

Licia Grazzi^{1,2} · Domenico D'Amico¹

Published online: 25 March 2019
© Fondazione Società Italiana di Neurologia 2019

The problem concerning treatment of chronic forms of migraine associated with medication overuse has been largely debated and discussed in the last years.

Chronic migraine (CM) (according to the ICHD-3; 2018) is a headache-form occurring on ≥ 15 days/month for > 3 months with features of migraine on ≥ 8 days/month; it is a disabling condition that affects 0.5 to 5% of the general population [1]. It is less common than episodic migraine (EM), but it is associated with greater and more significant disability, higher impact on physical, social, and occupational functioning, and worse health-related quality of life. About 3% of patients with EM progress to CM each year, even if there is a natural within-patient variation in headache-day frequency, meaning that patients can fluctuate between EM and CM [1, 2]. Possible factors inducing the chronicity of migraine have been identified: modifiable risk factors for progression from EM to CM include the frequency of headache attacks, their intensity, overuse of acute migraine medication, ineffective acute treatment, stressful life events, and obesity [1].

Medication-overuse (MO) is considered a complication rather than a cause of migraine; it can be associated to CM. All patients with CM need prophylactic treatment to reduce the frequency of pain attacks, severity, and associated disability and to reduce the risk of medication overuse. In the most part of cases, a simple pharmacological treatment is not enough to manage this category of patients so the opportunity to include non-pharmacological approaches to help patients during their therapeutic process have to be considered.

In the last decades, clinical experiences on chronic migraine with medication overuse have indicated the withdrawal as the first step to treat these patients: the withdrawal from overused medications can be helpful to make a preventive pharmacologic therapy more effective [2].

Patients can be educated to the correct use of symptomatic medications, and to the evaluation of their headache history, pharmacological treatments, and their habits: bad habits may induce the increase of headache attacks. Also a particular attention to mental stress and stressful life events has to be encouraged, as these aspects have a significant impact on clinical condition.

If a condition of overuse is present, the withdrawal is a reasonable step for helping patients to start their therapeutic process and, after withdrawal, a preventive treatment is needed to reduce the frequency of pain attacks. At the same time, it is convenient to support patients with non-pharmacological measures as behavioral approaches to manage their pain.

The rationale for using behavioral treatments for migraine treatment is based on new theories that have been developed about the nature of the migraine condition. Traditionally, headache has been considered from a limited perspective, both medically and psychologically. The new model that has been proposed explains how the migraine is a condition where an interaction of biological, psychological, and social variables may play a significant role. This clinical condition is not only a painful condition residing in an abnormality of receptor physiology; it is more aptly recognized as a condition wherein emotion and pain are strictly connected. Consequently, a multidisciplinary strategy of treatment that considers every aspect of individual life, social, and emotional components is needed [2].

Psychological and behavioral interventions assessing any tendency toward symptom exaggeration, or secondary gain associated to pain, that may lead to unconscious resistance to treatments have to be included in the therapeutic strategy for this category of patients [2]. The American Neurological Academy has recognized specific behavioral approaches as evidence-based for treatment of migraine and these approaches can be applied for patients with chronic forms of

✉ Licia Grazzi
licia.grazzi@istituto-besta.it

¹ Neuroalgology Unit, Headache Center, Neurological Institute “C. Besta” IRCCS Foundation, Via Celoria 11, 20133 Milan, Italy

² Headache and Neuroalgology Unit, Neurological Institute “C. Besta” IRCCS Foundation, Via Celoria 11, 20133 Milan, Italy

migraine in particular when they are associated to medication overuse, as complementary measures to enhance the clinical efficacy of pharmacological prophylaxis after withdrawal and to reduce the possibility of relapse of medication overuse.

In order to ensure that patients with EM do not develop an evolution in chronic forms, prevention of chronification by medication in patients with high-frequency EM would also help to limit the burden of CM and should be prioritized [3].

It has been suggested that the risk of progression may potentially be reduced combining acute treatment to reduce migraine severity and prophylactic treatments to reduce migraine frequency [3].

Concerning specific prophylaxis for chronic migraine, up to now, the two available evidence-based prophylactic treatments for CM are topiramate and onabotulinum toxin A. Innovative prophylactic therapies are needed to reduce the high burden of CM in particular when Medication Overuse is a condition associated to chronic migraine: this last aspect complicates the clinical feature and makes the treatment of this condition more difficult and problematic.

Recently, monoclonal antibodies that target the calcitonin gene-related peptide (CGRP) pathway of migraine pathogenesis, have been specifically developed for the prophylactic treatment of different forms of migraine. These new molecules have demonstrated good efficacy and excellent tolerability in phase II and III clinical trials. They are a new and interesting option for patients who reported failures from different prophylactic therapies.

Anti-CGRP monoclonal antibodies may also prove to be useful in this regard, as suggested by the results of a phase II clinical trial in which fremanezumab significantly reduced migraine days versus placebo in patients with high-frequency migraine [3].

This innovative treatments can be considered a “revolution” in the history of migraine therapies: this is the first preventive therapy specifically addressed to the treatment of migraine: the medications used in the past for migraine prophylaxis were, in the most part of cases, used for treating other clinical conditions and their use for migraine was not specific.

For all these implications, it is necessary that patients with CM are managed at headache centers, where they can receive specific treatment for their condition and a high level of multidisciplinary care: this can help to reduce the risk of diagnostic error and to avoid incorrect treatment practices with different therapies, as topiramate, OBT-A and anti-CGRP monoclonal antibodies.

Moreover, patient education, lifestyle factors, overuse of acute medication, and comorbidities will be evaluated in a multidisciplinary treatment strategy to ensure optimal management of CM. Patients have to be informed about CM and the treatment they are prescribed, and supported to take an active role in managing their condition by adopting positive lifestyle behaviors (e.g., regular sleep, meals, and exercise

routines), avoiding triggering and aggravating factors, and collaborating with their neurologist on a long-term treatment strategy which can include different kinds of approaches, pharmacological, and non-pharmacological [2].

More accurate diagnosis and more individualized treatment approach including pharmacological and non-pharmacological options have to be considered in order to develop a culture of prevention and a solid partnership between patients and their physicians in order to build a good medical alliance and improve adherence to treatments. When patients become more conscious about their clinical condition and more informed about how to manage pain, the response to treatment is more effective.

The significant progress currently being made in the prophylactic treatment of CM will open a new and promising scenario in CM management. Progress toward a common, shared clinical and scientific management strategy will improve CM definition, by determining biological markers, in order to be more specific in tailoring therapy. The new emerging treatment options, such as OBT-A and the new anti-CGRP monoclonal antibodies, have to be used to their best effect; if they will be combined with other therapeutic non-pharmacological measures, it will be possible to significantly reduce the personal, social, and economic impact of this problematic clinical condition and to do the best for helping our patients to manage this problematic and so common clinical condition [3].

Compliance with ethical standards

Conflict of interest We certify that there is no actual or potential conflict of interest in relation to this article.

Ethical standards All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

References

1. Bigal ME, Lipton RB (2006) Modifiable risk factors for migraine progression. *Headache* 46(9):1334–1343
2. Andrasik F, Flor H, Turk DC (2005) An expanded view of psychological aspects in head pain: the biopsychosocial model. *Neurol Sci* 26:S87–S91
3. Bigal ME, Dodick DW, Rapoport AM, Silberstein SD, Ma Y, Yang R, Loupe PS, Burstein R, Newman LC, Lipton RB (2015) Safety, tolerability, and efficacy of TEV-48125 for preventive treatment of high-frequency episodic migraine: a multicentre, randomised, double-blind, placebo-controlled, phase 2b study. *Lancet Neurol* 14(11):1081–1090

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.