COMMENTARY



"Triaging" Chronic Migraine Patients in Need of CGRP(r) Monoclonal Antibodies

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Key Summary Points

Chronic migraine is a neurological disorder associated with a highly disabling and burdensome form of pain.

The management of chronic migraine must be allocated to the appropriate healthcare professionals.

Monoclonal antibodies against CGRP(r) should initially be reserved for the treatment of patients with pre-chronic migraine in order to reduce the economic impact to healthcare systems.

The social relevance of headache and headacherelated disability is evidenced by the enormity of the impact of this group of non-

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communicable diseases on epidemiology, progressive disability to the patient, and the direct and indirect costs that must be borne by both healthcare systems and patients [1–8].

Chronic migraine patients, in particular, are not always correctly diagnosed within an acceptable time frame or adequately treated. Thus, the patient, who may not be properly informed on the use of medications and the correct pharmalogical treatment, may opt for an uncontrolled self-medication regimen, often ending up in an Emergency Department with a completely different life-threatening condition [9-12].

The need to involve general practitioners in the management of low-frequency migraine is a clear priority in healthcare systems and would free tertiary-level headache centers from treating progressive and complicated forms of medication overuse [13]. This change in the approach to the treatment of low-frequency migraine is particularly important now that sufferers of high-frequency or chronic migraine need hospital access to be treated with a new pharmacological class of medications-monoclonal antibodies to calcitonin gene-related peptide (CGRP) or its receptor (CGRPr). Studies conducted on this pharmacological class of medications report clear evidence of a high efficacy, as well as associated high treatment costs [14–16].

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However, just how to identify those migraine patients in need of these new therapies with monoclonal antibodies is a matter still being debated and prioritized. The parameters for selecting these patients need to be very precise and based on a uniformity applied by all specialists treating chronic migraine, neurologists, pain physicians, Emergency Room specialists, and internal medicine specialists. An explicit aim, hopefully applicable on a large scale, is to identify early in the treatment trajectory those patients with a frequency of migraine crisis rapidly progressing towards chronicity that may, in the future, evolve into chronic forms and represent the hard core of refractoriness [17]. These are the patients who show fluctuations in the pre-chronic phase, with a high frequency of migraine crises, but who have not progressed to the stable chronic stage [18]. At the same time, it is very important to resolutely limit the creeping trend of expanding the targets of this new pharmacological class of medications by also including patients with highfrequency migraine in the definition of chronicity [19]. Such an inclusion would rapidly stress the spending sustainability of national health systems in general and also specifically penalize patients with chronic and pre-chronic migraine who have failed previous preventive therapies and who need priority access to these new treatments.

Through redefining the progression of the disease into chronicity with this new class of drugs, defined as *disease-modifying migraine drugs* (DMMDs), a significant reduction in public healthcare system expenditures can be achieved [20]. This highlights the importance of appropriately "triaging" migraine patients, with interventional priority on the interception of high-frequency patients who fluctuate in and out of the chronic migraine phase.

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REFERENCES

1. Steiner TJ, Stovner LJ, Vos T, Jensen R, Katsarava Z. Migraine is first cause of disability in under 50s: will health politicians now take notice? J Headache Pain. 2018;19:17.

- Yao C, Wang Y, Wang L, et al. Burden of headache disorders in China, 1990–2017: findings from the global burden of disease study 2017. J Headache Pain. 2019;20:102.
- 3. Hester RB, Rohrer SD, Liu PI, Coggin JH Jr. Prevalence and burden of headache in children and adolescents in Austria—A nationwide study in a representative sample of pupils aged 10–18 years. J Headache Pain. 2019;20:101.
- 4. Martelletti P, Schwedt TJ, Lanteri-Minet M, et al. My migraine voice survey: a global study of disease burden among individuals with migraine for whom preventive treatments have failed. J Headache Pain. 2018;19:115.
- 5. Martelletti P. Migraine disability complicated by medication overuse. Eur J Neurol. 2018;25:1193–4.
- 6. Peck J, Urits I, Zeien J, et al. A Comprehensive Review of Over-the-counter Treatment for Chronic Migraine Headaches. Curr Pain Headache Rep. 2020;24:19.
- Lublóy Á. Economic burden of migraine in Latvia and Lithuania: direct and indirect costs. BMC Public Health. 2019;19:1242.
- Negro A, Sciattella P, Rossi D, Guglielmetti M, Martelletti P, Mennini FS. Cost of chronic and episodic migraine patients in continuous treatment for two years in a tertiary level headache Centre. J Headache Pain. 2019;20:120.
- Giamberardino MA, Affaitati G, Costantini R, Guglielmetti M, Martelletti P. Acute headache management in emergency department. A narrative review. Intern Emerg Med. 2020;15:109–17.
- Sipilä JOT, Ruuskanen JO, Rautava P, Kytö V. Adult migraine hospital admission trends in Finland: a nationwide registry study. J Clin Med. 2020;9:E320.
- 11. Doretti A, Shestaritc I, Ungaro D, Lee JI, et al. Headaches in the emergency department—a survey of patients' characteristics facts and needs. J Headache Pain. 2019;20:100.

- 12. Peres MFP, Swerts DB, de Oliveira AB, Silva-Neto RP. Migraine patients' journey until a tertiary headache center: an observational study. J Headache Pain. 2019;20:88.
- 13. Steiner TJ, Jensen R, Katsarava Z, Linde M, et al. Aids to management of headache disorders in primary care (2nd edition). J Headache Pain. 2019;20: 57.
- 14. Urits I, Clark G, An D, et al. An Evidence-based review of fremanezumab for the treatment of migraine. Pain Ther. 2020. https://doi.org/10.1007/ s40122-020-00159-3.
- 15. Urits I, Jones MR, Gress K, et al. CGRP antagonists for the treatment of chronic migraines: a comprehensive review. Curr Pain Headache Rep. 2019;23: 29.
- 16. Sacco S, Bendtsen L, Ashina M, et al. European Headache Federation guideline on the use of monoclonal antibodies acting on the calcitonin gene related peptide or its receptor for migraine prevention. J Headache Pain. 2019;20:6.
- 17. Martelletti P. The application of CGRP(r) monoclonal antibodies in migraine spectrum: needs and priorities. BioDrugs. 2017;31:483–5.
- 18. Serrano D, Lipton RB, Scher AI, et al. Fluctuations in episodic and chronic migraine status over the course of 1 year: implications for diagnosis, treatment and clinical trial design. J Headache Pain. 2017;18:101.
- 19. Guglielmetti M, Raggi A, Ornello R, et al. The clinical and public health implications and risks of widening the definition of chronic migraine. Cephalalgia. 2020;40(4):407–10.
- 20. Martelletti P, Edvinsson L, Ashina M. Shaping the future of migraine targeting calcitonin-gene-related-peptide with the disease-modifying migraine drugs (DMMDs). J Headache Pain. 2019;20:60.