



Commentary

Anti-CGRP monoclonal antibodies in chronic cluster headache

Aline Turbino Neves Martins da Costa 

Federal University of São Paulo, São Paulo, Brazil.

 alineturbino@gmail.com

Cluster headache is known by excruciatingly painful side-locked headache attacks with ipsilateral cranial autonomic symptoms and restlessness, often usual several times a day. It has a prevalence of 0.1%, with male preponderance. Calcitonin gene-related peptide (CGRP) plays an important role in cluster headache pathophysiology as we know.

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Anti-CGRP monoclonal antibody galcanezumab was approved for the prophylactic treatment of cluster headache. Two randomized, placebo-controlled clinical studies showed positive results. In episodic cluster headache, a significant reduction of attack frequency was noticed, leading to approval by the US Federal Drug Administration (FDA) in June 2019, but the effect was not significant in chronic cluster headache (CCH).

Chronic cluster headache is refractory to other preventive therapies and severely affected by high frequencies of attacks happening for months, an individual treatment attempt with an anti-CGRP antibody appears to be a therapeutic option with a conclusive pathophysiological reason. It is a difficult condition to be treated with limited therapeutic options.

Galcanezumab trial was negative in chronic cluster headache, the results may be explained due to methodological limitations. It must be considered that the placebo effect may be larger during open-label treatment than in placebo-controlled studies. In this case, patients know they may receive placebo. Another consideration are the patients in randomized controlled trial (RCT) series showing patients who highly refractory to other preventive treatments, with a documented use of 2–11 preventive treatments previous to the anti-CGRP agent.

Real life data published in a recent article from Cephalalgia¹ may revert the idea that galcanezumab is ineffective for CCH. A significant reduction of attack frequency was noticed in a study, showing a 50% responder rate, moreover, 36% presented 75% reduction in headaches. Significant reduction of attack frequency started in one week. In the first month, a significant decrease during the use of acute headache medication and pain intensity during attacks, according to the numerical rating scale (NRS), was observed. Treatment attempts with anti-CGRP antibodies are successful in an important number of CCH patients with insufficient response to other treatments, providing reason to make these treatments accessible for highly disabled CCH patients on an individual basis.

The war is not over, further studies are necessary to test this hypothesis. Although evidence from RTC is lacking, galcanezumab may be worth in CCH considering severe pain and patients extremely refractory to previous treatments. Other MAbs should also be analyzed in CCH treatment, until patients responded to anti-CGRP treatment, experiencing a rapid and significant reduction of attack frequency and pain intensity.

Aline Turbino Neves Martins da Costa
<https://orcid.org/0000-0002-7947-8490>

Reference

Ruscheweyh R, et al. Effect of calcitonin gene-related peptide (-receptor) antibodies in chronic cluster headache: Results from a retrospective case series support individual treatment attempts. *Cephalalgia*. 2020;40(14):1574-84

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