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Review

Low dose galcanezumab for treating trigeminal autonomic cephalalgias: clinical observation from Colombia and Mexico on behalf of ASOLAC

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Background
Although evidence exists regarding the efficacy of galcanezumab in treating cluster headaches and other trigeminal autonomic cephalalgias (TACs), data on its effectiveness at lower doses are still lacking.

Objective
To report the clinical outcomes of Latin American patients treated with galcanezumab (GNZ) at a dose approved for migraine.

Methods
This case series included patients with cluster headaches, hemicrania continua, and short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT-SUNA) who were treated with a 240 mg loading dose of GNZ followed by 120 mg monthly.

Results
A total of 18 subjects were included: 12 with cluster headaches, 4 with hemicrania continua, and 2 with SUNCT-SUNA who received 1 to 24 monthly cycles of GNZ. Among those with episodic cluster headaches, 7 of 8 patients experienced a reduction in attack frequency of more than 50%. In the chronic cluster headache group, this reduction was achieved in 2 of 4 patients. Additionally, 2 of the 4 patients with hemicrania continua became headache-free. In the SUNCT-SUNA group, 2 were included, both reduced their daily attack frequency from 120 to 30 and from 10 to 2, respectively.

Conclusions
These clinical observations suggest that lower doses of GNZ may be a viable option for treating Latin American patients with TACs.

Keywords:
Cluster headache
Hemicrania continua
SUNCT
SUNA
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Introduction

Cluster headache (CH), hemicrania continua (HC), paroxysmal hemicrania (PH), and short-lasting unilateral neuralgiform headache attacks (SUNCT-SUNA) are rare conditions categorized as trigeminal autonomic cephalalgias (TACs) and classified under the third group of the International Classification of Headache Disorders (ICHD-3) (1). A shared characteristic of these conditions is the lack of specific and highly effective treatments, leading to the exploration of therapeutic strategies derived from primary headache treatments (2,3). Galcanezumab (GNZ), a humanized monoclonal antibody recently approved in our region for the preventive treatment of episodic and chronic migraine, has also demonstrated efficacy at a dose of 300 mg monthly for CH patients, moreover, reports suggest favorable outcomes for HC patients treated with GNZ (4,5). Another case reported the efficacy of erenumab in a patient with refractory SUNCT (6).

Given the need for alternative treatments for patients who have failed other therapies and the unavailability of GNZ at 300 mg in Colombia and Mexico, we find it relevant to share our clinical experience with TACs patients treated with GNZ at a dose approved for migraine.

Methods

Data were collected from the medical records of patients treated at five headache centers in Colombia and Mexico between June 2023 and February 2024. All patients were diagnosed based on ICHD-3 criteria (1). Patients received a 240 mg subcutaneous loading dose of GNZ, followed by 120 mg monthly. Patients with episodic CH were included only if treatment was initiated in the first two weeks of the cluster bout. Demographic data and pre- and post-treatment clinical information, including headache frequency, HIT-6 score variation, global self-perception, and major side effects, were obtained.

Results

Eighteen patients were included (12 CH, 8 episodic and 4 chronic CH, 10 male, 2 female; median age 26.5, IQR 23.5–44.5; 4 HC, 1 male, 3 female; median age 45 years, IQR 38.5–52.5; 2 SUNCT-SUNA patients, aged 67 and 42 years, both female). All diagnoses were confirmed using the ICHD-3 criteria. Among the episodic CH patients, seven of eight experienced a >50% reduction in attack frequency, while two of four patients with chronic CH reached this threshold. In the HC group, two patients became headache-free, one remained pain-free 30% of the time, and one showed no change. Both SUNCT-SUNA patients reduced their daily attack frequency from 120 to 30 and from 10 to 2 and reported a lower probability of triggering attacks. All patients had previously failed at least one first-line therapy. No significant adverse effects were observed (Table 1).

Table 1 Demographic and clinical characteristics

Diagnosis ICHD 3 criteria	Gender	Age (years)	Time of evolution (months)	Past medical history	Previous treatments	Anti CGRP cycles-months	Adherence to treatment	Constipation After GNZ	Improvement trigeminal autonomic symptoms	HITS 6 score reduction	Frequency headache reduction	Global self-perception scale
Hemicrania continua	Female	50	26	None	Indomethacin, Celecoxib, Botulinum Toxin, Melatonin	2	Yes	No	Yes	NA	97%	Very Much better
Hemicrania continua	Female	34	120	Migraine, Gastritis	Indomethacin, Celecoxib, Verapamil, Topiramate, Botulinum Toxin, Pericranial Blocks, Facet Block, Valproate	6	Yes	No	Yes	14	33%	Much better
Hemicrania continua	Male	60	120	Migraine, Esophagitis	Indomethacin, Celecoxib, Verapamil, Topiramate, Botulinum Toxin, Lithium, Pericranial Blocks	12	Yes	No	Yes	NA	93%	Very Much better
Hemicrania continua	Female	40	18	Anxiety, hypertension, SLE	Indomethacin, Celecoxib, Verapamil, Topiramate, Botulinum Toxin, Gabapentin, Pericranial Blocks, Lidocaine infusion	6	Yes	No	No	NA	0%	No change
SUNCT – SUNA	Female	72	14	Hypertension, Stroke	Indomethacin, Topiramate, Botulinum toxin, Lamotrigine, Pericranial blocks, Carbamazepine, sphenopalatine blockade	2	Yes	No	Yes	16	73%	Very Much better
SUNCT – SUNA	Female	43	12	Discopathy	Pregabalin, Phenytoin, Amitriptyline	1	NA	No	Yes	NA	83%	A little better
Chronic cluster headache	Male	20	48	None	Verapamil, Topiramate, Valproate	6	No	No	Yes	16	73%	Very Much better
Chronic cluster headache	Male	45	3	Smoking	Indomethacin, Celecoxib, Verapamil, Topiramate, Botulinum toxin, Lamotrigine, Gabapentin, Lithium, Pericranial blocks, Valproate, Melatonin	12	Yes	No	Yes	NA	67%	Very Much better
Chronic cluster headache	Male	35	12	Anxiety, Smoking	Indomethacin, Celecoxib, Verapamil, Topiramate, Botulinum Toxin, Lamotrigine, Gabapentin, Lithium, Pericranial Blockades, Lidocaine Infusion, Melatonin	6	Yes	Yes	No	NA	0%	A little better
Chronic cluster headache	Female	50	48	Depression, Anxiety, hypertension, Smoking, Alcoholism	Topiramate, Lithium	24	Yes	No	Yes	23	0%	Very Much better
Episodic cluster headache	Male	33	48	Smoking	No	3	Yes	No	Yes	28	100%	Very Much better

Continued Table 1 Demographic and clinical characteristics

Diagnosis ICHD 3 criteria	Gender	Age (years)	Time of evolution (months)	Past medical history	Previous treatments	Anti CGRP cycles-months	Adherence to treatment	Constipation After GNZ	Improvement trigeminal autonomic symptoms	HITS 6 score reduction	Frequency headache reduction	Global self-perception scale
Episodic cluster headache	Male	21	36	Anxiety	Indomethacin, Verapamil, Pericranial Block0s	3	Yes	No	Yes	24	75%	Very Much better
Episodic cluster headache	Male	23	48	Anxiety	Verapamil, Lidocaine infusion	3	Yes	No	Yes	20	87%	Very Much better
Episodic cluster headache	Male	31	6	Alcoholism	Valproate	4	Yes	No	Yes	30	81%	Very Much better
Episodic cluster headache	Female	43	12	Anxiety, Migraine	Topiramate	3	Yes	No	Yes	20	100%	Very Much better
Episodic cluster headache	Male	60	60	Anxiety	Melatonin	4	Yes	No	Yes	20	100%	Very Much better
Episodic cluster headache	Male	25	48	Anxiety, Smoking	Verapamil, Topiramate, Zolmitriptan	6	Yes	No	Yes	28	50%	Very Much better
Episodic cluster headache	Male	30	60	Depression, Anxiety, Anxiety, Hypertension, Smoking	Indomethacin, Verapamil, Topiramate, Pericranial blocks, Amitriptyline	8	No	No	Yes	18	73%	Very Much better

Discussion

In this report, GNZ at the standard migraine dose demonstrated efficacy in treating patients with TACs, as shown by a reduction in headache episodes, improvements in self-perception, and lower HIT-6 scores with no significant side effects, including constipation. For episodic CH, seven out of eight patients (87.5%) achieved a reduction of 50% or more in attack frequency, a result comparable to findings from an observational study where 86% of episodic CH patients treated with 240 mg GNZ monthly showed similar reductions (7). Among chronic CH patients, 50% or more improvement was observed in two of the four cases, although all reported positive changes in self-perception, likely due to improved HIT-6 scores and reduced attack intensity, which is in contrast with a previous report where 83% of chronic CH patients achieved a 50% reduction at a GNZ dose of 240 mg monthly (8). These findings suggest a possible dose-dependent effect of CH subtypes, with higher doses potentially being more effective in chronic cases. The results in the HC and SUNCT groups align with other reports in which anti-Calcitonin Gene-Related Peptide Receptor (CGRP) therapies were effective even after the failure of first-line treatment (5,6). The efficacy of lower-dose GNZ in Latin American populations, as demonstrated here, is consistent with observations in migraine prevention using amitriptyline, topiramate, and propranolol, which are often prescribed and effective at lower doses than Anglo-Saxon populations (9). This clinical response could be explained by genetic variations in drug metabolism, lower body weight, environmental and lifestyle factors, heightened patient expectations, placebo effects, and differences in CGRP pathway sensitivity (10).

Exploring lower doses in a real-world clinical setting for a specific population is the key strength of this study. However, the use of retrospective data and variable follow-up periods have limitations.

Conclusions

These results suggest that lower doses of galcanezumab may be a viable option for treating Latin American patients with TACs, because it´s use reduces frequency, severity and its negative impact in patients functionality, measured by the HIT-6 score variation, and enhances global self-perception.

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