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Case Report

# Chronic Cluster Headache from the Beginning Successfully Treated with Verapamil and Lithium: A Case Report

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## Abstract

Cluster headache is a trigeminal-autonomic headache that predominantly affects young men. In its pathophysiology, it is believed that there is involvement of the ipsilateral trigeminal nociceptive pathways and activation of the cranial parasympathetic system. We report a case of a 23-year-old man presenting the chronic form of cluster headache from the beginning, according to ICHD-3 criteria. After effective prophylactic treatment, he evolved into an episodic form. To our knowledge, chronic form of cluster headache is uncommon and when it is successfully treated it evolves into the episodic form.

**Keywords**: Chronic Cluster Headache; Treatment; Verapamil; Lithium

## Introduction

Cluster headache (CH) is characterized by attacks of severe pain and strictly unilateral, in the regions orbital, supraorbital, temporal or in any combination of these sites. It lasts 15 to 180 minutes and occurs from once every other day to eight times a day. Pain is associated with the following ipsilateral cranial parasympathetic autonomic signs: conjunctival injection, lacrimation, nasal congestion, rhinorrhoea, forehead and facial sweating, miosis, ptosis and/or eyelid oedema, and/or with restlessness or agitation [1].

Pathophysiology of CH has not yet been clarified [2,3], but it is hypothesized that it is genetic (autosomal dominant) [4]. It is believed that there is involvement of the ipsilateral trigeminal nociceptive pathways and activation of the cranial parasympathetic system [5]. Based on clinical, anatomical and molecular data, it appears that trigeminovascular system, cranial autonomic system and hypothalamus are involved in the pathophysiology of CH [2]. A positron emission tomography study demonstrated that, during precipitated headache attacks, there is bilateral activation in the cavernous sinus with increased flow in the cavernous portion of the internal carotid artery, confirming yet another phenomenon associated with trigeminal activation [6].

There are two forms of CH, depending on the length of the headache-free period. CH will be episodic or chronic, if this interval without headache is, respectively, less than three months and greater than or equal to three months [7]. Chronic form of CH accounts for about 10% of cases [2,8], but a third of them may change from episodic to chronic or vice versa [2].

We report a case of chronic cluster headache (CCH) from the beginning that evolved to episodic form, after successful treatment with verapamil and lithium. This clinical report was authorized for publication by the patient who completed a signed informed consent form.

## Case Presentation

A 23-year-old man, medical student was seen at the neurology outpatient clinic of the Integrated Center for Medical Specialties (CIEM), in Parnaíba, Brazil, in February 2019 with a 12-months history of headache that fulfilled the diagnostic criteria for CCH.

Headache attacks were described as pulsating, localized to the right retro-orbital region, severe intensity, lasting 20 to 30 minutes, occurring every two days, always to 7 p.m. The pain was associated with tearing and nasal congestion on the same side of the pain, in addition to the sensation of agitation and restlessness. He remained asymptomatic for less than 90 days and had new headache attacks that disappeared after 10 days. During headache attacks, he used dipyrone and ketorolac, but without pain relief. He was unaware of triggering factors. There was no family member with similar headache.

The patient suffered from systemic arterial hypertension and was treated with hydrochlorothiazide 25 mg/day. He was obese, with a body mass index equal to 35.5 kg/m$^2$. Both neurologic and general examination results were normal. Brain MRI was normal. Routine blood tests (biochemical, haematological, liver, kidney and metabolic investigations) yielded normal results.

His diagnosis was CCH. During headache attacks, the patient was treated with inhalation of 100% oxygen or subcutaneous injection of 6 mg sumatriptan, at most twice daily. Prophylactic treatment was started with verapamil at a dose of 240 mg/day and lithium carbonate 450 mg/day. Immediately after the lithium prescription, the cardiologist was consulted. He suspended the use of diuretics and considered verapamil as a treatment for hypertension.

Abortive treatment was effective with sumatriptan. Pain relief occurred 8 minutes after sumatriptan, while with 100% oxygen inhalation only after 15 minutes. There was a significant improvement in the frequency, intensity and duration of headache attacks with prophylactic treatment. Lithium was discontinued, but maintains verapamil, now as an antihypertensive medication. In a follow-up of two years, there were only two episodes of cluster headache, of short duration and mild intensity. The patient has been asymptomatic for over a year.

## Discussion

CH is three times more common in men, with a typical age of onset between 20 and 40 years of age [2,9]. Our patient was a young man and fulfilled the diagnostic criteria for CCH, according to ICHD-3 [1].

In this case report, we describe an unusual evolution of CH in which the patient had a chronic form from the beginning. Usually, the chronic form arises from the episodic form [10], but rarely the episodic form is due to the chronic form [11]. Although both forms have the same clinical characteristics, CCH interferes much more in the patients' quality of life.

Treatment of CH is divided into abortive, transitional and preventive. Main abortion medications are oxygen administered 100% through a mask at a rate of 12 L/min for at least 20 minutes, and triptans, particularly sumatriptan and zolmitriptan [2,12-14]. Our patient was treated with 100% oxygen inhalation and subcutaneous injection of sumatriptan, with pain relief in a few minutes.

Stimulation of the sphenopalatine ganglion, a part of the cranial autonomic system that is involved in its pathophysiology, is another abortive treatment used in CH [2,15]. There is a study in which sphenopalatine ganglion stimulation as an acute therapy relieved pain in 67% of patients compared to 8% of control [16].

Transition medications are used for short periods of time in patients with short headache cycles or while preventive medication has not yet been effective. Most effective transitional treatment is occipital nerve stimulation, especially in the chronic form [17], but there are other options, such as high-dose prednisone or frovatriptan [13]. In our patient, we did not use any transitional treatment, as prophylactic medications had a rapid and effective effect.

CCH is usually refractory to prophylactic treatment [17]. Most used and first choice drugs are verapamil and lithium [18-20]. The second option includes topiramate, valproic acid and gabapentin [18]. Melatonin and clomiphene can be used, but with lower levels of evidence [21].

Galcanezumab has recently been made available as a new preventive treatment option, but its long-term effects are not yet

known [13] and its effectiveness is still not a consensus among researchers [5,19].

Our patient improved with low doses of verapamil and lithium. Although the daily maintenance dose of verapamil is 480mg, divided into three doses, he was followed up by a cardiologist and had no adverse effects. There are reports that high doses of verapamil can cause abnormalities in cardiac conduction, especially a prolongation of the PR interval [13,22].

## Conclusion

To our knowledge, chronic form of CH is uncommon and when it is successfully treated it evolves into the episodic form.

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## Authors' Contributions

RPSN was responsible for the conception and design. AGM, LGBC, CGFM, WPOS and RPSN carried out the acquisition of data. RPSN did the analysis and interpretation of data. AGM and RPSN did the drafting the manuscript. RPSN revised the intellectual content. All authors read and approved the final manuscript

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## Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request

## Consent for Publication

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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