Headache Medicine

Cluster Headache Syndrome: symptoms, pathophysiological mechanisms and treatment

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Introduction
Cluster headache is a rare type of primary headache and the most common of the trigeminal- autonomic headaches. It predominates in males (4:1) and usually begins in the third decade of life. In addition, although it has a low prevalence, cluster headache stands out for being a disabling condition due to the severe intensity of its symptoms. Although its pathophysiology is not fully explained, it is known to involve activation of the trigeminal autonomic reflex through stimulation of the trigeminovascular pathways.

Objective
To investigate and present a summary of cluster headache syndrome, highlighting its symptoms, pathophysiological mechanisms and treatment. This was done through a critical and up-to-date analysis of existing data in the literature.

Methods
This is an integrative literature review, searching for articles published between 2013 and 2023 in the PubMed and Scielo databases, using the DeCS/MeSH descriptors "Cluster headache", "Primary headaches", "Headache" and "Trigeminal autonomic cephalalgias". A total of 22,061 articles were found, according to the inclusion criteria used, in portuguese and english. A total of 13 articles were analyzed, 8 of which were selected for this review.

Results
Cluster headache is often diagnosed late due to the infrequency of the disease and the clinical picture, which can be similar to that of other headaches. There are, however, diagnostic criteria for this condition, defined by the International Classification of Headaches - 3rd edition, which include the manifestation of at least five intense unilateral, orbital, supraorbital and/or temporal crises, lasting between 15 and 180 minutes if left untreated. They must also be associated with at least one symptom/sign ipsilateral to the pain, including conjunctival injection and/or tearing, nasal congestion and/or rhinorrhea, eyelid edema, miosis and/or ptosis and a feeling of agitation and/or restlessness. Seizures usually occur between once every other day and 8 times a day, usually at night. Furthermore, the analysis of the articles provided a better understanding of the possible pathophysiological mechanisms behind cluster headache. Although there is no consensus on the exact pathological pathway, theories revolve around three structures: the trigeminocervical complex, the parasympathetic complex and the hypothalamus. The trigeminocervical complex connects the peripheral neurons of the trigeminal nerve to the central nervous system. Activation of the trigeminal system results in the release of various neuropeptides, including calcitonin gene-related peptide, a potent vasodilator. This neuropeptide may be involved in the pain of this headache. The hypothalamus, in turn, is involved in the circadian and circannual rhythmicity of cluster headache, linking this disease to sleep disorders. As for management, this can be divided into acute abortive and preventive therapies, with therapy in between using prednisone and lidocaine. Abortive treatment includes the use of triptans and 100% high-flow oxygen, while preventive treatment includes the use of verapamil, lithium and melatonin. The drugs used to treat cluster headaches are off-label, but supported by clinical evidence. Finally, new treatment techniques using monoclonal antibodies and neuromodulation devices can be used in both forms of therapy.

Conclusion
The underlying mechanisms of cluster headache have not yet been fully clarified, but it is known that there is a strong relationship with the transmission of trigeminal nociceptive stimuli. A better understanding of the pathophysiology of cluster headache will allow us to improve the treatment and control of this disease, and more studies are needed in this regard.

Keywords: Cluster headache; Primary headache; Trigeminal autonomic cephalalgias; Headache.