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REVIEW ARTICLE

Cluster headache: an invisible agony

Cefalea en racimos: una agonía invisible

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ABSTRACT

Introduction: Cluster headache is a primary disease that affects 1 in 1000 people. In Cuba, its prevalence is low. Migraine cases are often observed, approximately 6 % in men and 15 to 17 % in women. It is the most disabling headache that a human being can experience.

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Objective: to describe the pathophysiology, diagnosis and treatment of cluster headache.

Methodological Design: a bibliographic review of 34 references in Spanish and English was carried out between May and August 2024, in the SciELO, Pubmed and Google Scholar search engine databases. The most recent published literature in accordance with the novelty of this disease was considered as a selection criterion.

Development: Cluster headache causes pain in the frontal, orbital and temporal regions. Ipsilateral neurovegetative symptoms (ptosis, tearing, rhinorrhea, nasal congestion) involve activation of the trigeminovascular and parasympathetic systems and dysfunction of the cranial sympathetic system. Diagnosis is clinical. Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) studies show some areas related to pain activation. Oxygen treatment is the most commonly used method for attacks.

Conclusions: Cluster headaches do not have an exact etiology. Triggering factors have been identified, such as alcohol consumption, sleep changes, and exposure to toxic odors. When pharmacological treatment does not achieve the required results, some surgeries are performed that can considerably improve the spectacular symptoms.

Keywords: Trigeminal autonomic cephalalgias; Cluster headache; Diagnosis; Migraine disorders; Treatment

RESUMEN

Introducción: la cefalea en racimos es una enfermedad primaria que afecta a 1 de cada 1000 personas. En Cuba su prevalencia es escasa. A menudo se observan casos de migraña, aproximadamente el 6 % en hombres y de 15 a 17 % en mujeres. Constituye el dolor de cabeza más incapacitante que el ser humano puede experimentar.

Objetivo: describir la fisiopatología, diagnóstico y tratamiento de la cefalea en racimos.

Diseño Metodológico: se realizó una revisión bibliográfica de 34 referencias en español e inglés entre mayo y agosto del 2024, en las bases de datos SciELO, PubMed y el motor de búsqueda Google Académico. Se consideró como criterio de selección aquella literatura publicada con mayor actualidad en concordancia con lo novedoso de esta enfermedad.

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Desarrollo: la cefalea en racimos provoca dolor en las regiones frontal, orbitaria y temporal. Los síntomas neurovegetativos homolaterales (ptosis, lagrimeo, rinorrea, congestión nasal) involucran la activación del sistema trigémino vascular, parasimpático y disfunción del sistema simpático craneal. El diagnóstico es clínico. Los estudios de tomografía de emisión de positrones (PET) y resonancia magnética funcional (RMF), muestran algunas áreas relacionadas con la activación del dolor. El tratamiento con oxígeno es el método más aplicado para las crisis.

Conclusiones: la cefalea en racimos no presenta una etiología exacta. Se han identificado factores desencadenantes, como el consumo de alcohol, cambios en el sueño y exposición a olores tóxicos. Cuando el tratamiento farmacológico no logra los resultados requeridos, se realizan algunas cirugías que pueden mejorar de manera considerable la aparatosa sintomatología.

Palabras clave: Cefalalgia autónoma del trigémino; Cefalalgia histamínica; Diagnóstico; Trastornos migrañosos; Tratamiento

INTRODUCTION

Lindemann CR [(1)] points out that the nervous system is one of the most important and complex systems of the human organism. Disorders associated with this system are quite common in clinical practice, as is the case of headaches. It is estimated that around 90 % of patients have experienced this condition at some point in their life. Headaches are characterized by being extremely overwhelming and disabling, as well as generating significant economic losses. [(2)]

Cluster headache is a type of primary headache that causes pain in various areas of the head: frontal, orbital and temporal. It is not very common, affecting 1 in 1 000 people and is more common in men than in women. It is considered to be the most intense headache that exists. [(3)]

The first bibliographies on headaches were recorded as early as 3000 BC. From the point of view of Loreto Cid M [(4)] cluster headache is known by the namesake Horton according to the scientific contributions made by the American doctor Bayard Horton in the 20th century, related to its semiology.

It presents a variability of 0,05 % to 0,3 % with respect to female patients. It constitutes the most common episodic trigeminal-autonomic clinical entity

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suffered by just under 50 000 people worldwide, mostly men between 20 and 40 years of age. [4]

In Cuba its prevalence is low. Cases of migraine are often observed, approximately 6 % in men and 15 to 17 % in women. [5] In relation to Guantanamo, the references that address the subject on the incidence and prevalence of this condition are still insufficient.

It is a disease that lacks sources of research, since its etiology is still not well discerned. This review article will provide a valid level of information for future research where updated knowledge on cluster headache is appropriate. For this reason, the objective of this review is to describe the pathophysiology, diagnosis and treatment of cluster headache.

MATERIALS AND METHODS

A qualitative, documentary review article was conducted of 40 bibliographic references between May and August 2024 in Spanish and English in the SciELO, PubMed and Google Scholar search engine databases. The Health Sciences Descriptors (DeCS) thesaurus was used to delimit the keywords, which were included in the search terms. The search terms included: Trigeminal autonomic cephalalgia; Histamine cephalalgia; Diagnosis; Migraine disorders; Treatment, as well as their translation into English.

Inclusion criteria: articles published in the last five years (2020-2024) because they are the most up-to-date and those that merit it due to their importance, language of the articles published in Spanish or English, freely published articles or those that can be accessed through the Cuban Telematic Health Network INFOMED, documents that provide relevant information on low birth weight. Exclusion criteria: articles for which the full text could not be accessed, editorial articles.

DEVELOPMENT

Cluster headache is a disease with a very damaging potential. It can be classified as episodic or chronic, depending on whether the remission periods between events occurring in a year are greater or less than 60 days. [6]

Suri H [7] states that cluster headache is characterized by producing very intense unilateral periorbital or temporal pain, with ptosis, tearing, rhinorrhea and/or homolateral nasal congestion, criteria with which the authors of the present review agree as well as Ray JC. [8]

According to Diener HC [9], different areas related to pain contribute to the emergence of this disease, the activation of the trigeminovascular system and the secretion of vasodilation-inducing neuropeptides, such as vasoactive intestinal peptide, the peptide related to the calcitonin gene and the pituitary adenylate cyclase-activating peptide.

The opinion that its origin lies in the autonomic nervous system is shared according to Domínguez Garcia [10] which agrees with the arguments cited by Dikmen PY et al. [11] and Guillart Larduet. [12]

The events usually occur daily for several weeks, a condition that is related to episodic cluster headaches, separated by a headache-free interval that lasts several weeks, months or even years 10 % of episodic cases become chronic and 30 % of these become episodic according to Houts CR et al. [13]

During the crisis, the concentration of some neurotransmitters in the endings of the C fibers of the V cranial nerve pair increases considerably. The activation of the hypothalamic nuclei is of utmost importance, a condition justified by the cyclical appearance of the crises and the results of the functional neuroimaging tests. [14,15]

The typical pain is located in the ipsilateral orbital and frontotemporal region. During crises, the patient is noisy, hyperactive, sometimes aggressive, restless, agitated, and may even threaten suicide. [16] Therefore, the criteria of Diener HC et al. [17] are justified, who also corroborate that the pain can be unilateral and radiate to other regions of the face, neck, and even the shoulders.

This condition appears suddenly, although nausea and symptoms and signs similar to migraine may first appear. The pain usually ends suddenly, with an intensity that decreases rapidly. After the events, most people do not experience pain, but report being exhausted due to Padilla del Rey. [18]

Although one of the symptoms of cluster headaches is to manifest intense pain, the authors agree that there is no type of injury or tumor as an etiology that can condition its appearance.

It has a marked genetic component. Autosomal dominant could be the mechanism. The affected gene or genes can express the disease when only one of the parents has the disease in their genome. [19]

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In the opinion of Luz Roja [20], there is a possible relationship between cluster headaches and head traumas because epidemiological studies have shown a higher incidence in groups with previous head traumas, which contradicts the criteria of other authors who ratify it as an entity of primary causes.

The diagnosis of trigeminal-autonomic headache is based on the presence of autonomic disorders. Secondary neuralgias account for 5 to 10 % of cases, with the majority presenting uncommon characteristics and disorders on physical examination of the neurological system. [21]

The diagnosis is made based on the clinical method by evaluating the entire symptomatic cortege that the patient may report, which includes pain, location and intensity of the headaches, and associated symptoms. The frequency and duration of the headaches are also important factors. [22,23]

A neurological examination can help the doctor detect physical signs of a neurological disorder. The doctor must use a series of procedures to evaluate brain function, including tests of the senses, reflexes, and nerves. [24]

Cerebrovascular malformations of the occipital region and the territory of the cerebral artery, as well as aneurysms or dissection of basilar and vertebral arteries, carotid arteries and anterior communicating arteries are associated with intense and recurrent headaches, because they constitute one of the main symptoms of various cerebrovascular diseases of hemorrhagic etiology, to cite just one example. [24]

Positron emission tomography (PET) and functional magnetic resonance imaging (FMR) examinations show some areas related to pain activation in the cingulate, frontal and insular cortex and the ventral posterolateral nucleus of the thalamus. The most important finding that can be observed is the activation of the hypothalamic-psilateral nuclei and the intracavernous carotid artery, which all authors on the subject agree on. [25-27]

Oxygen treatment is the most widely used method for crises. Normobaric is used at ambient pressure, hyperbaric is less commonly used, and is used at pressures above ambient pressure, and is only used when normobaric fails [27], a statement that also corresponds to that proposed by Landín E. [28]

Subcutaneous sumatriptan is the most effective single acute treatment according to data from patient surveys. Faster forms of administration of triptans are preferred, starting with subcutaneous sumatriptan, followed by nasal zolmitriptan and nasal sumatriptan, followed by oral zolmitriptan. [29]

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Triptans cause vasoconstriction through activation of the 5HT receptor and are not recommended in patients with vascular disorders such as myocardial infarction, stroke, and uncontrolled hypertension. (29)

Octreotide (Sandostatin), is a synthetic injectable version of the brain hormone somatostatin. It acts at a less effective rate to relieve pain than triptans. The anesthetic effect of lidocaine may be beneficial against cluster headaches in some people when administered nasally (intranasally). (30)

The injectable form of dihydroergotamine (D.H.E. 45) may be an effective analgesic for some people with cluster headaches. This medication is also available in inhaled (intranasal) form, but this form has not been shown to be good for treating the condition. Verapamil is considered the most useful preventive treatment for cluster headaches in both chronic and episodic forms. Corticosteroids are considered as a transitional prophylactic treatment, due to their short latency and duration of effect. (30) Other authors such as Padilla del Rey et al. (18) argue that these are ineffective for prescription.

In cases that are resistant to standard treatment, ketamine is an effective drug as it blocks the glutamatergic N-methyl-d-aspartate (NMDA) receptor. In addition, this analgesic effect could be enhanced by the combination with magnesium sulphate, which acts by blocking the same pathway. (31)

Lithium carbonate (Lithobid), used to treat bipolar disorder, may be effective in preventing chronic cluster headaches if other medications have been used for that purpose without success. (32)

When drug treatment has not achieved the required results, it is possible to perform some surgeries that can considerably improve the spectacular symptoms.

Deep brain stimulation consists of performing stereotactic surgery with implantation of a stimulating electrode in the ventral tegmental area / posterior part of the hypothalamus, and subsequently stimulating this area continuously. It is used only in very severe cases of chronic cluster headaches, totally resistant to other less invasive therapeutic methods, which corresponds to the information proposed by Cavarra M et al. (34)

Radiofrequency of the sphenopalatine ganglion is a simple technique, performed under local anesthesia and minimal sedation, in which the ganglion

of the same name is injured. Complications are very rare. The chances of improvement with this technique are 60 %. [33]

CONCLUSIONS

Cluster headache is one of the most intense and debilitating forms of headache. Although the exact etiology of this condition is not yet fully understood, several triggering factors have been identified, such as alcohol consumption, sleep changes, and exposure to toxic odors. When drug treatment has not achieved the required results, it is possible to perform some surgeries that can significantly improve the burdensome symptoms.

BIBLIOGRAPHIC REFERENCES

1-Lindemann CR. Cluster headache. JAAPA [Internet] 2022 [cited 30/06/2024]; 35(8):15-9. Available in: https://pubmed.ncbi.nlm.nih.gov/35881711/

2-MedlinePlus. Bethesda (MD): Biblioteca Nacional de Medicina. Cefalea en racimos. [Internet] 2021 [cited 30/06/2024]. Available in: https://medlineplus.gov/spanish/

3-Ocampo SB, Carrillo PRA. Tratamiento de las cefaleas con acupuntura. Acta Med Cent. [Internet] 2018 [cited 30/06/2024]; 12(4):496-505. Available in: https://www.medigraphic.com/cgi-bin/new/resumenI.cgi?IDARTICULO=83424

4-Loreto Cid M. Cefaleas, evaluación y manejo inicial. Rev Médica Clínica Las Condes [Internet] 2014 [cited 30/06/2024]; 25(4):651-657. Available in: https://www.davila.cl/que-es-la-cefalea-tipos-de-dolores-de-cabeza

5-Maya Entenza CM, Martín Labrador M, Monteagudo Torres M. Cefalea en racimos: Estudio prospectivo de 245 enfermos. Rev cubana med [Internet]. 2007 [cited 30/06/2024]; 46(1). Available in: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S0034-75232007000100004&lng=es

6- Cheema S, Matharu M. Cluster Headache: What's New?. Neurol India. [Internet] 2021 [cited 30/06/2024]; 69(Supplement):S124-S134. Available in: https://pubmed.ncbi.nlm.nih.gov/34003158/

7-Suri H, Ailani J. Cluster Headache: A Review and Update in Treatment. Curr Neurol Neurosci Rep. [Internet] 2021 [cited 30/06/2024]; 21(7):31. Available in: https://pubmed.ncbi.nlm.nih.gov/33948734/

8- Ray JC, Stark RJ, Hutton EJ. Cluster headache in adults. Aust Prescr. [Internet] 2022 [cited 30/06/2024]; 45(1):15-20. Available in: https://pubmed.ncbi.nlm.nih.gov/35233134/

9- Diener HC, May A. Drug Treatment of Cluster Headache. Drugs. [Internet] 2022 [cited 30/06/2024]; 82(1):33-42. Available in: https://pubmed.ncbi.nlm.nih.gov/34919214/

10-Domínguez Garcia IM. Hadjigeorgiou. Clínica y fisiopatología de la cefalea en racimos. Acercamiento a la indicación de neuroestimulación combinada occipital y supraorbitaria. Rev Med Esp Anes y Rean. [Internet] 2022 [cited 30/06/2024]. Available in: https://www.sciencedirect.com/science/article/abs/pii/S0034935621002978-

11-Dikmen PY, Bozdağ M, Güneş M, Koşak S, Taşdelen B, Uluduz D, et al. Reliability and Validity of Turkish Version of Headache Impact Test (HIT-6) in Patients with Migraine. Noro Psikiyatr Ars. [Internet] 2020 [cited 30/06/2024]; 58:300-307. Available in: https://pubmed.ncbi.nlm.nih.gov/34924791/

12-Guillart Larduet J. Efectividad de la acupuntura con microsistema de cara como tratamiento de pacientes con cefalea migrañosa. Rev Cub Enf [Internet] 2018 [cited 30/06/2024]; 34 (3): [aprox 16p]. Available in: http://www.revenfermeria.sld.cu/index.php/enf/rt/printerFriendly/1395/371

13-Houts CR, Wirth RJ, McGinley JS, Gwaltney C, Kassel E, Snapinn S, et al. Content Validity of HIT-6 as a Measure of Headache Impact in People with Migraine: A Narrative Review. Headache. [Internet] 2020 [cited 30/06/2024]; 60:28-39. Available in: https://pubmed.ncbi.nlm.nih.gov/31811654/

14-Díaz Jiménez MM. Evaluación clínica en Atención Primaria de Salud del paciente con cefalea. Rev Inf Cient [Internet] 2015 [cited 30/06/2024]; 92(4):894-908. Available in: http://www.revinfcientifica.sld.cu/index.php/ric/article/view/208/1380

15-Wei DY, Goadsby PJ. Cluster headache pathophysiology - insights from current and emerging treatments. Nat Rev Neurol. [Internet] 2021 [cited

30/06/2024]; 17(5):308-324. Available in: https://pubmed.ncbi.nlm.nih.gov/33782592/

16-Schindler EAD, Burish MJ. Recent advances in the diagnosis and management of cluster headache. BMJ. [Internet] 2022 [cited 30/06/2024]; 376:e059577. Available in: https://pubmed.ncbi.nlm.nih.gov/35296510/

17-Diener HC, May A. Drug Treatment of Cluster Headache. Drugs [Internet] 2022 [cited 30/06/2024]; 82(1):33. Available in: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8748342/

18-Padilla del Rey M L. Antagonismo NMDA en el tratamiento de la cefalea en racimos. SciELO. [Internet] 2019 [cited 30/06/2024]; 26 (4): [aprox 10p]. Available in: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S1134-80462019000400009

19-Malu OO, Bailey J, Hawks MK. Cluster Headache: Rapid Evidence Review. Am Fam Physician. [Internet] 2022 [cited 30/06/2024]; 105(1):24-32. Available in: https://pubmed.ncbi.nlm.nih.gov/35029932/

20-Luz Roja I. Cuidados de enfermería a paciente con cefalea en racimos basado en el modelo de promoción de la salud de Nola Pender. Rev Cient Soc Esp Enferm Neurol [Internet] 2021 [cited 30/06/2024]; 57 (36-42). Available in: https://www.sciencedirect.com/science/article/abs/pii/S2013524621000179

21- Peng KP, Burish MJ. Management of cluster headache: Treatments and their mechanisms. Cephalalgia. [Internet] 2023 [cited 30/06/2024]; 43(8). Available in: https://pubmed.ncbi.nlm.nih.gov/37652457/

22- Leone M, Ferraro S, Proietti Cecchini A. The neurobiology of cluster headache. Handb Clin Neurol. [Internet] 2021 [cited 30/06/2024]; 182:401-414. Available in: https://pubmed.ncbi.nlm.nih.gov/34266608/

23- Belin AC, Barloese MC. The genetics and chronobiology of cluster headache. Cephalalgia. [Internet] 2023 [cited 30/06/2024]; 43(10). Available in: https://pubmed.ncbi.nlm.nih.gov/37851671/

24-Membrilla JA, Roa J, Díaz-de-Terán J. Preventive treatment of refractory chronic cluster headache: systematic review and meta-analysis. J Neurol. [Internet] 2023 [cited 30/06/2024]; 270(2):689-710. Available in: https://pubmed.ncbi.nlm.nih.gov/36310189/

25-Irimia P, Garrido Cumbrera M, Santos Lasaosa S, Aguirre Vazquez M, Correa-Fernández J, Colomina I, et al. Impact of monthly headache days on anxiety, depression and disability in migraine patients: results from the Spanish Atlas. Scientific Reports. [Internet] 2021 [cited 30/06/2024]; 11:1-9. Available in: https://www.nature.com/articles/s41598-021-87352-2

26- Grinberg AS, Best RD, Min KM, et al. Cluster Headache: Clinical Characteristics and Opportunities to Enhance Quality of Life. Curr Pain Headache Rep. [Internet] 2021 [cited 30/06/2024]; 25(10):65. Available in: https://pubmed.ncbi.nlm.nih.gov/34668084/

27- Lund NLT, Petersen AS, Fronczek R, Tfelt-Hansen J, Belin AC, Meisingset T, et al. Current treatment options for cluster headache: limitations and the unmet need for better and specific treatments—a consensus article. J Headache Pain. [Internet] 2023 [cited 30/06/2024]; 24(1):121. Available in: https://pubmed.ncbi.nlm.nih.gov/37667192/

28-Landín E. Cefalea en racimos: cómo reconocerla y tratarla. elPlural [Internet] 2021 [cited 30/06/2024]. Available in: https://www.elplural.com/sociedad/cefalea-en-racimos-como-reconocerla-tratarla_279055102_amp

29-Hans A, Stonnington CM, Zhang N, Butterfield R, Friedman DI. The impact of resilience on headache disability as measured by the Migraine Disability Assessment (MIDAS). Headache. [Internet] 2023 [cited 30/06/2024]; 63: 743-750. Available in: https://pubmed.ncbi.nlm.nih.gov/37218745/

30- Burish MJ, Lipton RB. Cluster Headache: Worse in Female Patients. Neurology. [Internet] 2023 [citado 30/06/2024]; 100(12):547-548. Available in: https://pubmed.ncbi.nlm.nih.gov/36543573/

31-Ray JC, Stark RJ, Hutton EJ. Cluster headache in adults. Aust Prescr [Internet] 2022 [citado 30/06/2024]; 45(1):15. Available in: https://pubmed.ncbi.nlm.nih.gov/35233134/

32-Gribbin C, Dani K, Tyagi A. Chronic Migraine: An Update on Diagnosis and Management. Neurol India [Internet] 2021 [citado 30/06/2024]; 69(7):67. Available in: https://pubmed.ncbi.nlm.nih.gov/34003150/

33-Drescher J, Khouri A, Amann TK, Gaul C, Kropp P, Siebenhaar Y, et al. Effectiveness of medication in cluster headache. BMC Neurol [Internet] 2021

[citado 30/06/2024]; 21(1):1-8. Available in: https://bmcneurol.biomedcentral.com/articles/10.1186/s12883-021-02195-8

34-Cavarra M, Mason NL, Kuypers KPC, Bonnelle V, Smith WJ, Feilding A, et al. Potential analgesic effects of psychedelicson select chronic pain conditions: A survey study. Eur J Pain. [Internet] 2024 [citado 30/06/2024]; 28(1):153–65. Available in: https://pubmed.ncbi.nlm.nih.gov/37599279/

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

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