Alodinia in cluster headache: a review
Alodinia na cefaleia em salvas: uma revisão

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INTRODUCTION
Cluster headache (CH) is defined as the primary cephalalgia which lasts 15 to 180 minutes, sited around the orbit (periorbital, temporal and in frontal areas), usually afflicting the same side of the head cluster after cluster, obsessively, with autonomic trigeminal dysfunction (tearing, conjunctival injection, rhinorrhea, localized sweating, eyelid edema, and ptosis). These symptoms and signs occur commonly up to eight times a day. In episodic forms of CH the patients may experience periods of weeks, months or even years without symptoms. The clusters recur periodically, usually on the same season, or yet at the same time of day. These characteristics are gathered by the classification proposed by the International Headache Society.(1)

Allodinia is the phenomenon which the subject feels pain due to non-painful stimulus.(2) Thus, it is possible that the descending pain modulating paths are involved, as the hypothalamus, trigeminal paths and autonomic structures. According to several authors, the prevalence of allodynia in CH patients is still a theme for debate. A particular study shows a relevant prevalence, up to 49%, and others consider this association a rare entity.(3)

METHODOLOGY
To bring light to this yet blurry matter, a review was made using the terms "allodynia" and "cluster headache" through the CAPES periodicals, accessing the most relevant studies regarding to this association.

Keywords: Allodynia; Cluster headache

Descritores: Alodinia; cefaleia em salvas
through the CAPES periodics, accessing the most relevant studies regarding to this association. The scrutiny used in this review developed a methodological assessment as follows: 1 – to observe the number of patients involved in each of the studies; 2 – to analyze the method of allodynia detection; 3 – to describe the skin areas put to test; 4 – to analyze the gender distribution of patients for each study; 5 – to describe the type of cluster headache (episodic or chronic) in each study; 6 – to describe the mean duration of disease; 7 – to analyze the prevalence results.

**REVIEW**

This primary headache also might be divided in two major subtypes: episodic CH and chronic CH. The criteria for this separation are well established, and when the attacks occur for more than one year without remission, or with remissions that last less than 14 days, then it fulfills the features for the chronic form. Otherwise, when the remissions last 14 days or more, and the attacks last seven days to one year, it is defined as the episodic form.

In addition to these major subtypes, there is another subdivision applied to the chronic cluster headache, which defines the ones having a temporal pattern typical of chronic forms since the onset as chronic CH unremitting form. And the others that evolve from an initial episodic pattern into the chronic features are named secondary chronic forms. There is also the CH which has a chronic pattern by the onset, and then evolves into an episodic one, namely secondary episodic pattern, even though it is the rarest form, it seems relevant to mention.

Concerning the clinical characteristics of this primary headache, it is imperative to mention that unlikely most headaches, CH are far more common in males. There are studies form 1979 and 1982 describing a ratio of 5 to 1, and even 9 to 1 men to female. In more recent works the authors describe a decline in this male to female preponderance, with ratios of 2.4:1 and 3.2:1 male to female in chronic CH in episodic forms and chronic CH in unremitting forms, respectively.

Regarding to treatment, it is also necessary to fractionate into abortive and prophylactic treatment. In acute situations the abortive methods encompass the oxygen inhalation at 100%, the use of subcutaneous sumatriptan, dihydroergotamine in injectable and intranasal forms, intranasal lydocaine, and as a resource for oral treatment it has been mentioned the zolmitriptan. The prophylaxis commonly involves verapamil as the main alternative, and other drugs as lithium carbonate, methysergide, valproic acid, topiramate, melatonin, capsaicin, indometacin, prednisone, gabapentin and some antipsychotic drugs, namely olanzapine and clozapromazin. Other studies, small and open-labeled ones, mention methylphenidatem tizanidine, histamine, somatostatin and pizotifen.

It is worth to point out, related to therapeutics, a case of a 32 years old pregnant woman, who suffered from CH, and whose response to oxygen treatment was none, who had a relief with intranasal lydocaine. As lydocaine has minimal risk for the pregnant woman and fetus, due to its low toxicity, it may be useful as a primary step in acute treatment for CH pregnant patients. And there is also a case report describing remission of refractory chronic CH after warfarin administration.

**RELATIONS AMONG ALLODYNA AND CLUSTER HEADACHE**

Regarding to the number of patients involved in each of the main studies, accessing the association between allodynia and CH, it is remarkable that there is no study with a great number of patients. It is understandable when one considers the low prevalence of cluster headache in general population, affecting 0.01% to 0.9% of general population, and representing 8% to 10% of headache patients. The number of patients with CH tested for allodynia in all studies analyzed vary from as few as two to as much as 41.

Considering the method of allodynia detection, one study used a pin prick testing in two patients. Another study by Ashkenazi et al. used a test for brush allodynia (BA) in ten male patients, which was performed using a 4 x 4 - inch gauze pad, applied repetitively at a rate of two per second, to six skin areas bilaterally in trigeminal and cervical distributions [frontal (V1), maxillary (V2), mandibular (V3), posterior neck (C2,C3), shoulder (C5), and inner forearm (C8)]. Ladda et al. used a quantitative sensory test performed in 16 CH patients and ten healthy ones. This method aimed to determine the subjects perception and pain thresholds for thermal (use of thermode) and mechanical (vibrations, pressure pain thresholds, pin prick, von Frey hairs) stimuli. Marmura et al. also used the same test for BA described above.

The skin areas put to test by Ladda et al. were the right and left cheeks and the back of right and left hands. Marmura et al., nevertheless, tested the forehead (V1), posterior neck (C2/C3) and inner forearm (C8) on
both sides.\textsuperscript{3} Ashkenazi et al. approached six skin areas bilaterally in trigeminal and cervical distributions (frontal (V1), maxillary (V2), mandibular (V3), posterior neck (C2,C3), shoulder (C5), and inner forearm (C8)).\textsuperscript{13} In one study, a series of cases, Riederer et al. did not mention the skin areas put to test.\textsuperscript{12}

When an analysis approaches the gender distribution through the studies, the males are the majority. Marmura et al. encompass 22 males and 19 females in the study.\textsuperscript{3} Ashkenazi et al. interestingly includes 10 males and no females.\textsuperscript{13} In the study by Riederer et al. males and females comprise equal parts, but this particular study presents only one man and one woman, making any assumptions regarding gender unreliable.\textsuperscript{12}

Taking into account the types of CH, whether episodic or chronic, the literature includes a short series of cases with two episodic cluster headache (ECH) patients.\textsuperscript{14} Another study made by Ashkenazi et al. included seven ECH and three chronic cluster headache (CCH) patients.\textsuperscript{13} And Marmura et al. describes 22 CCH and 19 ECH patients.\textsuperscript{3} The study made by Ladda et al. comprises 8 CCH and 8 ECH patients.\textsuperscript{14}

Moving towards the mean duration of disease, Marmura et al. described a 14.1 years duration (12.3 for CCH group and 15.7 for ECH group), Ashkenazi et al. reports a duration from 18 months to 38 years.\textsuperscript{3,13} Riederer et al. in his series contemplates one patient with a 13 year history of ECH and another patient with a 20 years history also of ECH.\textsuperscript{12}

As a final regard, the prevalence of allodynia in CH patients according to Marmura et al. was 49%; and 40% (28.6% for ECH patients, and 66.7% for CCH patients) according to Ashkenazi et al.\textsuperscript{3,13} Although reporting allodynia during the attacks, both patients included by Riederer et al. tested negative for allodynia.\textsuperscript{13} Ladda et al. found no allodynia in three patients examined during the attacks, but a significant difference in pain thresholds.\textsuperscript{14}

**CONCLUSION**

Cluster Headache patients do not represent an insignificant part of all headache patients, and thus this clinical entity cannot go on being considered as a worthless rare headache. The few authors devoted to this relevant matter are mentioned repeatedly, making it evident the need for more research and interest. The prevalence of allodynia in CH is a theme which was neglected until recent times, and the small number of studies demands more attention, and finally more prevalence studies.

**REFERENCES**


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