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Chronic headaches: from research to clinical practice

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Abstract Chronic daily headache (CDH) is a heterogeneous group of headaches that includes primary and secondary varieties. Primary CDH is a frequent entity that probably affects 4–5% of the population. It can be subdivided into headaches of short duration (<4 h/attack) like chronic cluster headache, and disorders of long duration (>4 h/attack). Primary CDH of long duration includes transformed migraine, chronic tension-type headache, and new daily

persistent headache and hemicrania continua. Analgesics, ergots and triptan overuse are frequent in all types of CDH. We revise recent insights into the epidemiology, pathophysiology, clinical characteristics and prognosis of CDH.

Key words Chronic migraine • Chronic tension-type headache • New persistent daily headache • Pathophysiology • Epidemiology

Introduction

When we consider chronic daily headache (CDH), we refer to a heterogeneous group of headaches whose common characteristic is its chronicity. There is consensus to use the term “chronic daily headache” to refer to headaches occurring 15 or more days per month, including those associated with medication overuse.

Epidemiology

The first population-based studies on CDH have been published in recent years [1, 2]. In these population-based

surveys, primary CDH occurs in approximately 4%–5% of the general population (Spain 4.7%, US 4.1% and China (elderly) 3.9%). In population samples, chronic tension-type headache (CTTH) is the leading cause of primary CDH with a one-year period estimated prevalence of 2.2% in Spain and in the United States, and 2.7% in China [1]. Epidemiological data are different when analysing the distribution of CDH patients that account for consultation in headache clinics. In subspecialty practices, CDH evolves from an episodic headache disorder in over 92% of cases, usually migraine (72% of cases), and from episodic tension-type headache (ETTH) in only 20% of the patients. CDH appears without history of previous headache and is unremitting from onset in about 8% of cases (NDPH). In headache clinic groups, the proportion of women is even higher with a female-male ratio of 4.6:1 [3].

Pathophysiology

Different mechanisms are involved in the development of CDH. In these patients there is an altered central sensitisation which is manifested by increased spontaneous impulse discharges, increased responsiveness to noxious and non-noxious peripheral stimuli, and expanded receptive fields of nociceptive neurons. Migraine patients evolve a sensitisation of the trigeminal nucleus caudalis neurons caused by frequent vascular input due to frequent attacks, which may explain the development of CDH [4]. The enhanced neuronal responses represent a state of central sensitisation and, in addition, the cardiovascular response threshold to facial and intracranial stimuli is reduced, representing a state of intracranial hypersensitivity and cutaneous allodynia [5]. Migraine patients who had allodynia ipsilateral to the headache were significantly older than those who did not, hinting at a possible correlation between age and sensitisation. These findings provide a neural basis for the pathophysiology of migraine pain and suggest a basis for continued head pain.

In CTTH a central sensitisation appears, generated by prolonged nociceptive input from the periphery, particularly from myofascial tissues. Nitric oxide (NO) is involved in the development of this central sensitisation and it has been recently demonstrated that NO synthase inhibition has an analgesic effect in CTTH patients; this effect could be related to reduction in muscle hardness that could cause succeeding reduction of central sensitisation [6].

A down-regulation or suppression of an already partly suppressed or abnormal antinociceptive system also appears, particularly in individuals with analgesic overuse. The “rebound headache” does not appear in non-headache sufferers who use daily analgesics for another ailment such as arthritis pain, expressing an inherent vulnerability in the primary headache population that predisposes them to drug-induced headache.

Genetic factors should be considered in CDH. The genetic vulnerability of primary headaches is well known and has been demonstrated in a number of CDH patients [7].

Imaging

One very interesting paper has shown, using a special MRI sequence, that iron homeostasis in the periaqueductal grey matter (PAG) was progressively impaired in patients with chronic or frequent migraine and possibly caused by repeated migraine attacks. These results emphasise the possible role of changes in the central pain structures as a possible cause of pain chronification [8].

Comorbidity

Anxiety, depression, sleep disturbances and medication abuse are frequent in patients with CDH. In headache sufferers there is a correlation between high headache attack frequency, a long history of headaches and female sex, and rating elevation for both anxiety and depression. Patients with CDH show increased anxiety levels in all, and hysteric traits in some. With time, they may develop a depressive disorder.

Drug overuse

Drug abuse is frequent in CDH patients. Different mechanisms probably contribute to its development. Psychological factors include the reinforcing properties of pain relief by drug consumption, a very powerful component of positive conditioning. Withdrawal headache is an additional problem, because whenever the patient tries to stop or reduce the medication, he experiences a worsening of the headache. Analgesic drugs also have psychotropic side effects such as sedation or euphoria that may stimulate drug dependency [9].

The actual dose limits and time needed to develop rebound headaches have not been defined in rigorous studies, but there is a consensus of the approximate doses [10].

Patients can overuse analgesics, ergots and opioids. In recent years, triptans have shown they could lead to drug-induced headache in patients with or without a previous history of analgesic overuse. The weekly dosages and the time of onset necessary to initiate triptan misuse-induced headache may be lower with the newer centrally penetrant triptans than with ergots or sumatriptan. The alarm sign of overuse is the progressive increase of attack frequency.

Clinical presentation

CDH comprises a heterogeneous group of headaches whose common characteristic is their chronicity. The term “chronic daily headache” only refers to the frequency of headache that appears 15 or more days per month, including those associated with medication overuse.

Chronic migraine

Following the last IHS classification, chronic migraine is a migraine headache occurring on 15 or more days per

month for more than 3 months in the absence of medication overuse [10]. This a very restricted definition and the number of the patients fulfilling this criteria is low. The majority of patients suffering frequent migraines are patients that usually have a past history of episodic migraine of more than 15–20 years of evolution, that typically began in their teens or 20s. As the headaches increase in frequency over months or years, the associated symptoms of nausea, photophobia and phonophobia become less severe and less frequent. Headache may have clinical characteristics of migraine or of tension-type headache (TTH). When the migraine attack appears, it has less associated symptoms. Other migraine features may persist. Familial history of migraine is often present. Patients often continue to have typical migraine attacks, but in some cases their migraine headaches disappear completely. Usually it develops in the setting of analgesic overuse, but in 20%–30% of cases it may occur without it. Patients with medication overuse have a constant low-grade headache, which is aggravated hours after the use of the substance, and only partially alleviated with the consumption of repeated doses of medication. These CDH patients have a significant impairment of their health-related quality of life [11].

Chronic tension-type headache

CDH may also develop in patients who have a history of ETTH. Headache is more often diffuse or bilateral, frequently involving the posterior aspect of the head and neck. These patients do not have migraine features or previous or coexistent episodic migraine. Some mild associated symptoms, such as mild nausea, photophobia or phonophobia may be compatible with the diagnosis of

CTTH. It may also appear associated with or without medication overuse.

In population-based studies, CTTH appears to be the most frequent type of daily headache, even though little is known about its nature and what the syndrome actually represents. Some recent studies support that, at least in some part, CTTH is a disorder of the central nervous system with probable sensitisation of second-order trigeminal neurons and some peripheral component [12]. It has also been suggested that genetic factors influence the risk of CTTH [8]. But other causes of non-genetic familial aggregation or gene-environmental interactions may influence these findings.

New daily persistent headache

Patients with NDPH develop it in the absence of a previous history of episodic migraine or ETTH [10]. It is a rare type of CDH in which the onset of headache is usually abrupt, occurring in a few days. Some patients remember the exact day the headache started. These patients are generally younger than those with other types of CDH, so the proportion of patients diagnosed with NDPH is much higher in children and adolescent CDH series than in adults [13].

Commonly headache is similar to TTH, but there is no progressive evolution from a previous headache. NDPH is likely to be a very heterogeneous disorder. It has been related to a post-viral syndrome or to an unknown chronic infection [13]. In our personal experience, even when some patients referred an infection previous to the development of the headache, we could not serologically demonstrate it.

NDPH has been included in the new classification under the chapter of Other primary headaches.

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