

This is a wakeup call: Alarm clock headache

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Abstract

Hypnic headache, also known as alarm clock headache is one of the rare subtypes of primary headaches described in literature. It is a typical nocturnal headache which only occurs in sleep and generally affects elderly population. It needs to be differentiated from the other common primary headaches as the therapeutic options for it are very different from the other common headaches. The description is only through case reports and small case series. A review of this less known entity is discussed here.

Abbreviations: HH: Hypnic Headache; ICHD: International Classification of Headache Disorders

Introduction

Hypnic headache [HH] is one of the primary headache disorders first described by Raskin in 1988 [1] and subsequently included in the International Classification of Headache Disorders (ICHD-II) [2]. It occurs exclusively during sleep and affects population generally over 50 years of age. It is still poorly understood and rarely diagnosed. It is known as alarm clock headache or clockwise headache [3] as it always occurs over same time of night (generally 2-4 AM) and wakes up the patient from sleep. The pattern of headache needs to be differentiated from other common primary headaches like migraine and cluster headache before start of therapy.

Clinical presentation

International Classification of headache disorders has revised the diagnostic criteria for HH in their 3rd version in 2018 [Table 1] [4]. The headache is described as mild to moderate and localized, mainly bilateral but sometimes unilateral with dull character in majority of cases but can also be throbbing or stabbing type. The typical duration of an attack is at least 15 min and averages about 80 min but can last up to 6 h. The frequency per night is average 1 to 2 attacks, with a mean frequency per month of about 20-25. Most patients display motor behaviour when awakening with headache at night, such as reading, eating, drinking, watching TV, listening to radio, walking around, taking a hot shower, or cooling the head, but these symptoms never reach the level of agitation or restlessness that can be observed in cluster headache attacks [5]. The natural course of the disorder is unknown. Some authors have classified HH into two different forms, chronic and

episodic form. The episodic form is further subdivided into two types, episodic with no recurrence, and relapsing and remitting variety [6].

Pathophysiology

The pathophysiology of HH is still unclear. It was previously suggested that HH attacks might be associated with REM sleep, based on polysomnographic reports [7]. But recent studies have contradicted this assumption.

A different hypothesis suggested a crucial role of obstructive sleep apnea in the underlying pathophysiology of HH. Although all sleep studies in HH showed an increased apnea/hypopnea-index, the onset of the recorded HH attacks was not temporally correlated with the observed drop of oxygen saturation [8]. Presumably, the increased prevalence of obstructive sleep apnea is related to the age of the population rather than to the disease itself [9].

The clinical features of HH, with its chronobiological presentation, lead to the hypothesis of a hypothalamic alteration in HH. The hypothalamus is involved in regulation of the sleep-wake cycle as well as in central pain processing [10]. Structural imaging of 14 HH patients using voxel-based morphometry (VBM) showed a decrease of gray matter within the posterior hypothalamus [11]. Changes of trigeminal pain processing in terms of central facilitation and alteration of habituation, which were commonly observed in other primary headache disorders such as migraine, were not detected in HH [12]. Further investigation of HH pathophysiology may offer a better understanding of the disease and may provide new treatment approaches in the future.

Diagnosis

HH can be diagnosed only when other primary headache disorders that may also present with sleep related headache attacks are ruled out.

Table 1. International Headache Society diagnostic criteria for hypnic headache

A	Recurrent headache attacks fulfilling criteria B-E
B	Developing only during sleep, and causing wakening
C	Occurring on 10 days/month for >3 months
D	Lasting from 15 minutes up to four hours after waking
E	No cranial autonomic symptoms or restlessness
F	Not better accounted for by another ICHD-3 diagnosis

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The International Classification of Sleep Disorders classifies besides HH a few other primary headaches as so-called sleep-related headaches, which are cluster headache, chronic paroxysmal hemicrania and migraine [13]. Sleep independent headache attacks also occur in most cluster headache patients, which helps to differentiate cluster headache from HH. Other clinical features for differentiation are distinct trigemino-autonomic features and headache-accompanied restlessness that can be observed only in cluster headache. In Chronic paroxysmal hemicranias, along with ipsilateral trigemino-autonomic symptoms in regard to the headache side, duration of headache is usually shorter than in HH attacks (i.e. 2-30 minutes). Headache frequencies above five per day are typically seen in chronic paroxysmal hemicrania. In migraine, on waking up, patient generally tries to keep immobile in contrast to the physical activity seen in HH. Also, the headache does not strictly occur only at the time as seen in HH. It is a common clinical observation that migraine attacks often occur during night sleep and upon awakening. If a patient has headache attacks fulfilling ICHD criteria for other primary headaches such as those mentioned above, these headache entities should be considered first before diagnosing a patient with HH, because these headache disorders are much more common than HH.

It is important to differentiate HH from two other confusing conditions:

a) The exploding head syndrome [14] is the sensation for few seconds that an explosive noise has occurred in the head, which awakens the patient from sleep. These also occur in patients more than 50 years of age but the occurrence of this in all sleep stages and the hearing of waking sound rather than headache differentiates it from HH.

b) Turtle headache [15] occurs in morning after awakening and going back to sleep. The headache is bilateral and only occurs if the patient pulls the bed covers over his or her head, or retracts his or her head under the blankets, like a turtle retreating under its carapace. It has been suggested that hypoxia is the underlying cause and so this should be regarded as a symptomatic headache.

Investigatory modalities include brain imaging to rule out secondary causes of headache such as brain tumours. 24-hour blood pressure monitoring should be done ideally in all such cases to rule out nocturnal arterial hypertension. Polysomnographic study may be done to look for sleep apnoea.

Treatment

As data regarding HH is scarce, no controlled trials for the treatment of HH are found. Acute therapy for HH is generally ineffective. Oxygen therapy and drugs such as sumatriptan which forms the mainstay of treatment in cluster headache are not effective in HH while other drugs like acetylsalicylic acid and acetaminophen have got a very limited action in cessation of acute headache.

As regards to preventive therapy, lithium is found to be most effective as the first line therapy [1]. It interacts with the pain modulating system possibly involved in HH and seems to increase indirectly nocturnal production of melatonin. Moreover, lithium may exert an enhancing effect on cerebral serotonin functions. Lithium carbonate can be initiated at 300 mg at night and increased to 600 mg after 1 or 2 weeks if necessary [1]. Poor tolerability to lithium is not rare, mainly in elderly patients. Renal and thyroid function should be assessed before initiating therapy, and periodically during treatment. Serum lithium concentrations should be monitored as well to avoid toxicity. Side effects include tremor, diarrhoea, increased thirst and

polyuria. Many other agents that have been reported to effectively treat HH include bedtime doses of caffeine (40–60 mg tablet, or as a cup of coffee), indomethacin, flunarizine, tricyclic antidepressants, verapamil, prednisone, topiramate, gabapentin, melatonin, benzodiazepines, pregabalin and acetazolamide.

Indomethacin, which is the mainstay of treatment in chronic paroxysmal hemicranias, may be helpful in those patients whose HH attacks are unilateral [16]. It was shown to be effective in extremely variable doses, ranging from 25 mg to 150 mg/day. Some patients who responded to indomethacin before bedtime developed daytime headaches, which resolved after indomethacin was discontinued. This phenomenon was termed as “the paradox of indomethacin”, whose most prominent side effect and reason for discontinuation (headache) is the very symptom for which it provides a remarkable therapeutic efficacy [16]. Hence, a practical approach can be a course of 300–600 mg lithium to be tried first, on some instances in association with caffeine and/or melatonin, followed, 3–4 months later, by tapering. If headache recurs during tapering, a longer duration of therapy may be needed. The treatment with caffeine and in particular with melatonin alone did not yield robust evidence to recommend their use as single preventive agents. Their association with the recommended medications (i.e. lithium and indomethacin) seems to produce an additional overall therapeutic efficacy. If lithium treatment does not provide a significant response, as second line approach indomethacin can be commenced, at a dose ranging from 25 to 75 mg at bedtime; caffeine can also be tried, alone or in combination with indomethacin. If these treatments prove to be ineffective, other medications, such as verapamil, flunarizine or topiramate, can be administered. These drugs are also recommended when lithium and indomethacin are contraindicated or are related to significant side effects.

Conclusion

Hypnic headache is one of the rare primary headache disorders. It should be suspected in elderly patients presenting with headaches awakening them from sleep on most days of a month. It should be differentiated from the more common primary headaches and secondary causes of headaches such as intracranial space occupying lesions by means of meticulous history, examination and investigations. Once labelled as hypnic headache, therapy should be started with a keen eye on the response. Due to scarcity of literature on this entity, further trials are needed to come up with more therapeutic options in future.

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