Hypnic headache – a rare primary headache disorder with very good response to indomethacin

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Abstract

Hypnic headache (HH) is considered as a disorder of the circadian rhythm, mostly affecting the elderly and generally considered a benign disorder, but the pathophysiology of hypnic hedache remains unclear. Various treatments have been suggested for hypnic headache, especially lithium and indomethacin. We report the case of HH fulfilling The International Classification Headache Disorders, 2nd edition criteria (ICHD-II). A 64-year-old woman, who suffered from dull headaches strictly during the night for a period of 5 months. Attacks of headache lasted from 30 to 150 minutes, with a frequency usually 4 times per week. The patient was started on indomethacin 50 mg twice a day (BID). From day 25 on she was free of hypnic headache. On day 31 we tapered the daily dose of indomethacin to 50mg at bedtime, the patient was still without headache. On day 60 the treatment was stopped. 30 months after day 60, the patient was still headache free. We reported the first Czech patient with HH with very good therapeutic response to indomethacin. The effect of therapy with indomethacin 50mg BID was very fast and stable.

Abbrevitions:

BID	- twice a day
CT	- computed tomography
ECG	- electrocardiogram
EEG	- electroencephalogram
ICHD-II	- The International Classification Headache Disorders, 2nd edition
HH	- hypnic headache
MRI	- magnetic resonance imaging
REM	- rapid eye movement

INTRODUCTION

Hypnic headache (HH) or "alarm clock headache" is a rare primary headache disorder, first described by Raskin (1988) and characterized by frequent nocturnal attacks of a generalized headache. Attacks of dull headache usually last from 15 to 180 minutes and always awaken the patient from sleep. The pain of HH is usually mild to moderate, severe pain is reported by approximately 20% of patients, but never have been reported the picture of thunderclap headache (Doležil *et al.* 2010). Pain is bilateral in about 60–70% of cases. First attack of HH occurred after age of 50 years. Distinction from one of the trigeminal autonomic headaches (as a cluster headache) is necessary for effective

CASE REPORT

treatment. ICHD-II (2004) has well established diagnostic criteria for HH (Doležil 2009).

CASE REPORT

A 64-year-old woman suffering from dull headaches strictly during the night for a period of 5 months. The patient had a history of hypertension for last 4 years and had been successfully treated with Perindoprilum. Other relevant history, including primary headaches was negative. The headache began between 120 and 240 minutes after she fell asleep, usually between 00:30 h and 03:30 h, waking the patient from sleep. Attacks of headache lasted from 30 to150 minutes with a frequency usually 4times per week. Nausea, vomiting, photophobia, phonophobia, osmophobia, dysautonomic features and focal neurological deficits had never been associated with her headaches. For correct diagnosis of HH she provided 4 weeks patient diary. Time of sleep, time of onset of headache, duration, location and intensity of pain, nausea, vomiting, changes in sensitivity to sound or light, osmophobia and autonomic symptoms were monitored. No general medical or neurological abnormalities were evident on examination. Standard blood chemistries, complete blood count and erythrocyte sedimentation rate were normal. ECG and EEG were performed, as well as CT and MRI of the head was done with negative result.

Based on the above mentioned information, a final diagnosis was established during the 4 week follow-up visit (Table 1, Table 2). After this follow-up visit, the patient was started on indomethacin 50 mg BID (day 1). This treatment reduced the headache frequency and also reduced pain intensity. From day 25 she was free of HH. On day 31 we tapered the daily dose of indomethacin to 50mg at bedtime, the patient was still without headache. On day 60 the treatment was stopped. 30 months after day 60, the patient was still headache free (Table 2).

Tab. 1. Hypnic headache ICHD-II criteria.

Diagnostic criteria ICHD-II	Fulfilment ICHD-II criteria by patient
A. Dull headache fulfilling criteria B–D	Yes
B. Develops only during sleep, and awakens patient	Yes
C. At least two of the following characteristics:	
1. occurs >15 times per month	Yes
2. lasts ≥15 minutes after waking	Yes
3. first occurs after age of 50 years	Yes
D. No autonomic symptoms and no more than one of nausea, photophobia or phonophobia	Yes
E. Not attributed to another disorder	Yes

DISCUSSION

We reported the first Czech patient with HH fully satisfying ICHD-II criteria with good therapeutic response to indomethacin and with duration of a pain free period 30 months after the discontinuation of treatment.

HH is considered as a disorder of the circadian rhythm, mostly affecting the elderly and generally considered a benign disorder, but the pathophysiol-

Tab. 2. Headache characteristic before and after treatment with indomethacin.

Headache characteristic	Before a treatment	After start of the treatment		
	1 month before start of a treatment	1st month (Indomethacin 50mg BID)	2nd month (Indomethacin 50mg at bedtime)	3-30 months (Without a treatment)
Frequency of attacks (days/month)	18	8	0	0
Frequency of attacks per night*	1	1		
Average time of initiation of headache after fell asleep (min)	165	160		
Average of duration of attacks (min)	91	54		
Average of headache intensity (0–10 pain scale)	4.6	3.6		
Localization of headache	Bilateral frontal and temporal	Bilateral frontal and temporal		
Associated symptom**	No	No		
Autonomic sing***	No	No		

*in the event of attack
** nausea, vomiting, photophobia, phonophobia, osmophobia
***conjuctival injection, tearing, rhinorhhoea, nasal congestion, forehead and facial sweating and/or erythema

ogy of HH remains unclear (Evers & Goadsby 2003). Similar circadian rhythmicity has been indentified also in cluster headache and migraine (Alstadhaug *et al.* 2007). HH has been reported to be related to REM (rapid eye movement) sleep (Dodick 2000), but a few of case reports showed association with Non-REM sleep (Doleso 2006). Anecdotal reports also suggested an association between HH and obstructive sleep apnea or REM-related oxygen desaturation. HH is typical in the elderly and melatonin secretion declines significantly with ageing, one may speculate that melatonin deficiency is another possible cause of HH (Evers & Goadsby 2003). Since Raskin´s initial description, there have been more than 100 cases reported in the literature. Donnet and Lantéri-Minet (2009) reported the biggest series of 22 consecutive cases of HH patients in France, Liang *et al.* (2008) reported17 consecutive Taiwanese patients with HH. Meta-analysis of data pooled from 71 cases of HH showed that the average duration of headache was 67±44 minutes, the frequency of attacks was 1.2±0.9 per night, onset of HH was between 120 and 480 minutes in 77% of patients after asleep and a mean onset of age of 63±11 years (range 38–83 years) (Evers & Goadsby 2003). In our patient (64-year-old woman) the average duration of attacks was 91 minutes, the frequency of attacks was 1 per night and the average time of initiation of headache after falling asleep was 165 min, before treatment with indomethacin. Soon after the treatment with indomethacin 50mg BID was initiated the headache frequency and pain intensity was reduced. During the 1st month she had only 8 attacks of HH with reduction of both, average headache intensity (from 4,6 to 3,6) and average duration of attacks (from 91 to 54 min).

Various treatments have been suggested for HH, especially lithium and indomethacin (Liang *et al.* 2008). Other treatments with reported benefit in HH include flunarizin, triptans, atenolol, prednisone, nimesulide, oxetorone and caffeine (Donnet & Lantéri-Minet 2009, Evers & Goadsby 2003, Relja 2002). There are also few cases reported to respond to pregabalin (Ulrich *et al.* 2006) or topiramate (Guido & Specchio 2006). Indomethacin was introduced in the clinical medicine in 1963 (Hart &Boardman 1963) and its use for treatment of headache disorders was first demonstrate in 1965 in patients with migraine (Sicuteri *et al.* 1965). Since the time, many others headache disorders, such as hypnic headache, were shown to have a response to indomethacin (Buzzi *et al.* 2005, Dodick *et al.* 2000, Ivañez *et al.* 1998, Peters *et al.* 2006, Seidel *et al.* 2008). We started treatment with indomethacin, because of our lack of experience with lithium, which is recommended as first choice for HH (the preferable dosage of lithium in terms of preventive is 300 to 600 mg once a day, it seems to be the most effective, but its frequent side-effects often limit its use in the elderly). Surprisingly, the effect of therapy with indomethacin 50mg BID was very fast and stable.

CONCLUSION

Our patient responded very well to treatment with indomethacin, which is both effective in the treatment of HH as well as a safe alternative to Lithium. The patient didn't have any adverse event during treatment period and after day 25 she was headache free. She was still headache free after 30 months without indomethacin.

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