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(OSA) in patients with headache
referred to a neurological specialist
examination**

**5.årsoppgave i stadium IV
– medisinstudiet i Tromsø.**

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august 02, Tromsø

**Obstructive sleep apnea syndrome (OSA) in patients
with headache referred to a neurological specialist
examination**

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Word count (exclusive of title, abstract, references and tables):

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Background: Obstructive sleep apnea syndrome (OSA) is a common disorder in the general population. Although the mechanisms remain obscure, an association with headache has been reported. Most studies are cross-sectional in design with a limited number of patients. We aimed to assess the frequency of OSA in a population of patients with difficult headache referred to a neurological specialist consultation.

Methods: We included all patients referred to neurological specialists for headache in Northern Norway during a period of two years. Patients who reported heavy snoring and episodes of breathing pauses at night underwent overnight 18 channels polysomnographic (PSG) examination. We regarded an apnea/hypopnea index of 5 or higher as abnormal.

Results: Of 903 headache patients, 75 reported heavy snoring and episodes of interrupted nocturnal breathing (8%). Among 43 patients examined with PSG, 14 (1.5% of the total study population) had an apnea/hypopnea index of 5 or higher. Eleven of the patients reported morning headache.

Conclusions: The frequency of OSA in a sample of patients referred to specialist for headache problems is not higher than what is reported for the general population. The relatively low rate of OSA in this selected group of patients with headache referred to neurology for second opinion does not support the notion that OSA brings about headache.

The prevalence of obstructive sleep apnea syndrome (OSA) in an adult population is estimated to be 2% in women and 4% in men, applying the minimum diagnostic criteria of nocturnal apnea/hypopnea index > 5 per hour and daytime sleepiness.¹ Sleep-associated disturbances of breathing without daytime sleepiness was even more frequent, demonstrating the importance of applying standardised diagnostic criteria.¹ Headache is a common complaint indeed in Western societies. The prevalence of chronic daily headache is about 4-5%.^{2,3} Due to the extremely high prevalence of troublesome headache, any association with specific disorders, including OSA, and headache, should be viewed with extreme caution.

Several studies have addressed the relationship between OSAS and headache. Paiva et al found that about half of patients with nocturnal or early morning headache suffered from a sleep disorder including OSA.⁴ When the sleep disorder was treated with success, the headache generally disappeared, supporting a causal role of the sleep disorder for headache.⁴ Morning headache seems to be a characteristic feature of a sleep disorder.^{4,5} Furthermore, the prevalence of headache is reported to be higher in patients with OSA than in a control group.⁵ Assuming a cause-relationship between OSA and headache, one would expect an increased frequency of OSA in patients referred to a neurological specialist for second opinion. We aimed to assess the frequency of OSA in a group of headache patients consecutively referred to a neurologist for specialist evaluation.

SUBJECTS AND METHODS

The present study is based on data from the North Norway Headache Study (NNHS). Northern Norway comprises the three counties north to the Arctic circle; Nordland, Troms and Finnmark. Two neurological departments (Tromsø and Bodø) serve a total of 460.000 inhabitants living in this area. In addition, out-patients referred from community physicians are seen by consulting neurologists visiting a third hospital (Vefsn) regularly. We included all patients being referred from general practitioners to these centres during a two-year period. No neurologists worked in private centres during the survey period. Norway has a kind of managed care; i.e. all patients seen by specialists working in public hospitals need a referral from their general practitioner or another specialist. While most private clinics welcome self-referring patients, the lack of private neurological clinics in northern Norway therefore vouch for a representative population of patients in this study.

From hospital databases, we registered 1403 consecutive patients with a major diagnosis of headache examined from July 1st 1996 to June 30th 1998 (two years). We mailed a questionnaire to all these patients, asking whether they had experienced interrupted breathing during sleep and whether they snored heavily. A total of 1052 persons (75%) returned the questionnaire, some after one reminder. Altogether, 903 respondents answered questions concerning history of heavy snoring and episodes of breathing pauses at night. Seventy-five patients reported heavy snoring and breathing pauses at night, and were thus regarded as patients at risk of OSA. All were invited to participate in a second part of the study which included PSG and completing a 30-days diary of headache occurrence and characteristics. Altogether, 42 of 75 patients (56%) volunteered to take part.

Daytime sleepiness was assessed by the Epworth Sleepiness Scale (ESS).⁶ Falling frequently in sleep in one or more different daytime situations (category 2 according to ESS) was applied as a criterion for daytime sleepiness.

Furthermore, we asked for headache characteristics including the presence of accompanying symptoms to be able to identify patients with migraine and tension-type headache (TTH) according to the IHS criteria.⁷ Migraine was diagnosed when patients reported at least four main migraine features (unilateral location, pulsating quality of pain, aggravation by walking stairs or similar physical activity, nausea and/or vomiting, photophobia and phonophobia) and not more than one feature of TTH (pressing/tightening quality, bilateral location, no aggravation by walking stairs or similar routine physical activity, no nausea). Patients with three migraine symptoms and maximum one TTH characteristic were categorised as migrainous headache. Patients with mixed migraine and TTH had at least two main symptoms from either group according to the IHS criteria.⁷ In order to minimise recall-bias, we defined patients who reported troublesome headache three or more days per week as suffering from chronic daily headache. According to IHS, chronic daily headache is usually defined as occurrence of headache >15 days per months.⁷

All patients who underwent PSG examination, completed a headache diary for 30 days prior to examination, including severity assessment (mild, moderate or severe) and the occurrence of wake-up headache. In addition to age, sex, duration of headache and level of education (number of years at school), we assessed headache symptom score by using a visual analogue scale ranging from 1 (almost no headache) to 10 (worst possible headache).

POLYSOMNOGRAPH RECORDINGS

The polysomnographic examination (PSG) consisted of continuous polygraphic recordings of electroculography (EOG), electroencephalography (EEG), single-leaded electrocardiography (ECG), electromyography (EMG), thoracic, nasal airflow (end-tidal carbon dioxide concentration) and abdominal respiratory effort and oxhemoglobin saturation (finger-pulse oximeter, Oxypal model OLV-1200K; Nihon Kohden). We used a polygraph model Medilog SAC; Oxford Instruments, Oxon, England, program version 9.3, 1994). The data were continuously obtained during the registration by using a connected computer. Respiration was evaluate for apnea (cessation of airflow for 10 secs or more) and hypopnea (reduction in respiratory effort accompanied by a 4% drop in oxyhemoglobin saturation). Apnea-hypopnea index (AHI) was defined as the number of apneas plus hypopneas per hour of total sleep time. We regarded a sleeping time at night of 240 min sleep (observed by the technicians; RJ) and at least one REM period as a minimum to be accepted for the study.

STATISTICAL ANALYSIS

Results are calculated using Stat View Graphics (Macintosh) and presented as the mean \pm standard deviation (SD) and median (range). We used a non-parametric statistical test (Mann Whitney) to compare continuous variables and Chi square test for categorical data between subgroups of patients, regarding $p < 0.05$ as the level of statistical significance.

RESULTS

Social and clinical characteristics of headache patients are listed in table 1. Out of all 903 patients with difficult headache referred to a specialist neurological evaluation, fourteen patients (1.5%) (seven male and seven females) fulfilled the minimal criteria of OSA. All of them reported frequent daytime sleepiness in at least one category using ESS.⁶ Table 2 displays PSG characteristics in the 14 patients with an apnea-hypopnea index >5 per hour. The most commonly reported feature of headache in these patients was presence of headache in the morning. Altogether 11/14 patients reported morning headache as obtained from the 30-days prospective headache diary (table 3).

Table 4 demonstrates the frequency of self-reported headache during a prospective diary registration period of 30 days. Headache occurred more frequently in OSA patients compared with patients with heavy snoring but with a normal apnea index, although the difference did not reach statistical significance ($p=0.11$). Due to the small sample size of patients fulfilling the criteria of OSA, statistical comparison with other headache patients may not be performed. Chronic daily headache, however, defined as headache three or more days per week, seems to be more frequent in patients with co-existing OSA (table 3).

DISCUSSION

We identified a subgroup of 1.5% patients consecutively referred to a neurological specialist examination for headache who fulfilled the criteria of OSA. Since the prevalence of OSA in the general population probably is 2-4%, this finding weighs against the hypothesis of an association between OSA and frequent headache.¹ Our patient sample probably was biased in favour of more severe headache, and consequently the prevalence of OSA would be expected to be even higher. Since we included all patients with headache referred to a neurologist within a defined geographical area (North Norway), we probably have avoided exclusion of selected groups of patients, making the sample representative. Despite the lack of a control group, our findings may suggest that OSA occurs less frequently in patients with difficult headache, thus arguing against the assumption that headache represents a very common clinical feature of OSA.

To the best of our knowledge, no previous epidemiological study has estimated the prevalence of OSA in groups of headache patients. In a large study from Copenhagen, headache was associated with self-reported snoring, but not with cognitive dysfunction.⁸ Ulfberg et al found that morning headache was about three times more common in heavy snorers and those with OSA than in the general population.⁵ Some patients with OSA may develop morning headache that responds to specific treatment of the sleep disorder although the mechanism remains unknown.⁹ Along this line, a majority of our patients reported headache in the morning, consistent with other reports.^{4,5,9} No other distinguishing headache characteristic was obtained from this small material. In a previous study in 304 patients with OSA by Aldrich,

18% of patients with sleep apnea reported frequent morning headache compared with 6% in the controls.¹⁰ Frequent headache was not statistically more prevalent in the OSA patients compared with other sleep disorders such as narcolepsy and nocturnal myoclonus. The authors concluded that frequent morning headache was a nonspecific symptom in patient with a variety of sleep disorders and was not a consistent or reliable symptom of sleep apnea syndrome.¹⁰ Obviously, a larger sample size comparing the results with control groups is desirable to assess in detail the prevalence and features of sleep disturbances in headache patients.

Another drawback of our study is the relatively large number of drop-outs from the group of patients who reported heavy snoring along with nocturnal breathing disturbances, but not wanting to undergo a PSG examination. A long waiting time for routine PSG examination in our area, due to low priority of sleeping disorders, may motivate symptomatic patients to participate in the study. The drop-outs may therefore represent persons without OSA. The possible over-estimation of OSA by using a questionnaire as a screening method is a matter of speculation, however. We selected snoring as a disease marker because it has been reported as a strong predictor of OSA.¹¹ However, even if the drop-outs should represent patients with true OSA, our main conclusion that OSA is not overrepresented in a headache population will probably remain unchanged.

In conclusion, we demonstrate that OSA is rather uncommon in patients with difficult headache. Some patients may suffer from morning headache, but this symptom is probably less specific than other symptoms such as heavy snoring and excessive daytime sleepiness.

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Table 1. Demographic characteristics in patients with headache referred to a neurological clinic. Values are mean values (\pm SD)

	Men n=292	Women n=611	Total n=903
Age in years	42.0 (14.4)	40.1 (14.1)	40.8 (14.3)
BMI (kg/m ²)*	25.4 (3.9)	24.3 (4.2)	24.6 (4.1)
Education (years)	11.3 (3.7)	11.7 (3.3)	11.6 (3.4)
Duration of headache (years)	11.2 (11.2)	13.4 (11.5)	12.7 (11.5)

Body mass index (BMI) is a measure of weight in kilograms divided by the square of the height in meters

Table 2. Polysomnographic characteristics of headache patients with OSA (n=14)

	Mean (SD)	Median (range)
Age (years)	49.6 (16.0)	57.0 (11.0-66.0)
BMI (kg/m ²)	26.3 (4.6)	24.8 (20.8-35.0)
Epsworth sleeping scale (ESS)	4.6 (3.2)	4.0 (0-11.0)
Apopnea/hypopnea index	14.6 (11.6)	11.4 (5.2-48.8)
Respiratory disturbance index (RDI)	41.4 (63.3)	26 (0-351)
Lowest oxygen saturation (%)	81.3 (6.2)	82.0 (71.0-92.0)
Length of PSG (min)	475.7 (21.8)	475.0 (442.0-513.0)
Time to sleep onset (min)	45.6 (25.9)	42.0 (9.0-91.0)
Numbers of arousal's	31.8 (31.8)	25.5 (1.0-125.0)
Deep sleep (stage 3 or 4) (min)	51.6 (36.2)	52.0 (0-119.0)
REM sleep (min)	58.8 (18.3)	60.3 (22.0-86.5)

Table 3. Headache features in patients with OSA compared to non-OSA patients referred to neurologist for headache. Number of patients (% in parentheses)

	OSA (n=14)	Others (n=889)
Migraine	4 (29)	354 (40)
Tension type headache (TTH)	1 (7)	78 (9)
Mixed TTH and migraine	4 (29)	127 (14)
Morning headache	11 (79)	566 (64)
Headache >3 days/week	6 (43)	293 (33)

Table 4. Severity and frequency of headache in subgroups of patients with OSAS and patients with only heavy snoring

Headache characteristics*	OSA (n=14)		Snorers (n=29)	
	Mean (SD)	Median (range)	Mean (SD)	Median (range)
Mild (no. of days)	7.8 (4.2)	8.5 (0-15)	6.8 (5.7)	6 (0-25)
Moderate (no. of days)	10.9 (5.4)	10.5 (3-20)	5.7 (3.8)	5.0 (0-15)
Severe (no. of days)	3.3 (2.6)	2.5 (0-8)	3.6 (4.7)	2.0 (4-15)
No. of days with headache	22.0 (7.9)	24 (10-30)	16.6 (8.1)	13 (3-30)

*Patient's assessment of headache during 30 days