

Morning headache in habitual snorers: Frequency, characteristics, predictors and impacts Ping-Kun Chen, Jong-Ling Fuh, Hsien-Yuan Lane, Pai-Yi Chiu, Hui-Chi Tien and Shuu-Jiun Wang *Cephalalgia* 2011 31: 829 DOI: 10.1177/0333102411403635

> The online version of this article can be found at: http://cep.sagepub.com/content/31/7/829

> > Published by: **SAGE** http://www.sagepublications.com On behalf of: International Headache Society

International Headache Society

Additional services and information for Cephalalgia can be found at:

Email Alerts: http://cep.sagepub.com/cgi/alerts

Subscriptions: http://cep.sagepub.com/subscriptions

Reprints: http://www.sagepub.com/journalsReprints.nav

Permissions: http://www.sagepub.com/journalsPermissions.nav



Morning headache in habitual snorers: **Frequency, characteristics, predictors** and impacts

Cebhalalgia 31(7) 829-836 © International Headache Society 2011 Reprints and permissions: sagepub.co.uk/journalsPermissions.nav DOI: 10.1177/0333102411403635 cep.sagepub.com



Ping-Kun Chen^{1,2}, Jong-Ling Fuh^{3,4}, Hsien-Yuan Lane¹, Pai-Yi Chiu², Hui-Chi Tien² and Shuu-Jiun Wang^{3,4}

Abstract

Objectives: Morning headache has been considered as an accompanying symptom of obstructive sleep apnoea syndrome (OSAS). However the frequency, characteristics, predictors and impacts of morning headache in habitual snorers are not well defined.

Methods: We studied consecutive patients with habitual snoring in a sleep laboratory using polysomnography. All patients were interviewed by a physician regarding the presence or absence of morning headache, migraine and insomnia. Each patient completed the Short Form-36 health survey (SF-36) and the Hospital Anxiety and Depression Scale (HADS). Morning headache was defined as headache on awakening ≥ 1 day/week for ≥ 6 months.

Results: Of the 268 participants with habitual snoring, 63 (23.5%) had morning headache and 184 (69%) had OSAS. Patients with morning headache reported lower scores in all eight domains of the SF-36 than those without (difference: 10.6 to 29.7 points, all p < 0.005). The independent predictors of morning headache were migraine (adjusted odds ratio (AOR) 6.3), insomnia (AOR 4.2), psychological distress (HADS \geq 8) (AOR 3.9) and OSAS (AOR 2.6). Morning headache in 12 patients (19%) fulfilled the criteria for migraine attacks.

Conclusions: Morning headache was common in habitual snorers and associated with a pervasive impairment of healthrelated quality of life. Migrainous features were not uncommon. Not only OSAS, but migraine, insomnia and psychological distress were also important predictors for morning headache, even in snoring patients.

Keywords

Insomnia, migraine, morning headache, quality of life, sleep apnoea headache, snoring

Date received: 8 October 2010; revised: 6 January 2011; accepted: 21 February 2011

Introduction

Headache and sleep disorders are common in the general population, and their inter-relationship has been known for more than a century (1). Headache present upon awakening, commonly referred to as morning headache, has been considered as a secondary headache resulting from obstructive sleep apnoea syndrome (OSAS) (2,3).Based on the International Classification of Headache Disorders (ICHD-2), sleep apnoea headache (code 10.1.3) is specified as morning headache with tension-type headache features, of a short duration (<30 minutes) or with frequent attacks (Table 1) (4). However, evidence of the relationship between morning headache and OSAS is conflicting (2,3,5-10). It is estimated that 7.6% of the general population has morning headache (5), and a high frequency

of morning headache has also been reported in patients with depression, migraine, periodic leg movement disorder (PLMD), insomnia or snoring (5,6,9–11). The criteria for morning headache vary among studies, which makes comparisons difficult. The criteria have included: three or more morning headaches in the past year (2), the presence of any morning headache

Corresponding author:

Dr Shuu-Jiun Wang, Neurological Institute, Taipei Veterans General Hospital, Taipei 11217, Taiwan Email: sjwang@vghtpe.gov.tw

¹China Medical University, Taiwan.

²Lin-Shin Hospital, Taiwan.

³Neurological Institute, Taipei Veterans General Hospital, Taiwan. ⁴National Yang-Ming University School of Medicine, Taiwan.

Diagnostic criteria	Morning headache in habitual snorers with OSAS (n = 50)
A. Recurrent headache with at least one of the following characteristics, and fulfilling criteria C and D:	9 (18%)
A1. Occurs on >15 days per month	
A2. Bilateral, pressing quality and not accompanied by nausea, photophobia or phonophobia	20 (40%)
A3. Each headache resolves within 30 minutes	16 (32%)
At least one of the A1–A3 criteria	31 (62%)
B. Sleep apnoea (Respiratory Disturbance Index \geq 5) demonstrated by overnight polysomnography	50 (100%)
C. Headache is present upon awakening	50 (100%)
D. Headache ceases within 72 hours, and does not recur after effective treatment of sleep apnoe	a Not available

Table 1. Diagnostic criteria of sleep apnoea headache proposed by the International Classification of Headache Disorders (ICHD-2, code 10.1.3) and the frequencies of each criterion in our snoring patients with OSAS and morning headache

(3,5), morning headache equal to or more than once every week (8), 'always', 'often' or 'sometimes' having headaches when waking up in the morning (9), and 'often' or 'very often' having headaches when waking up in the morning (7,10).

Habitual snoring is a common health problem (12) and also a sensitive symptom of OSAS (13), but the predictors for morning headache in patients with snoring are not known. In addition, the impact of morning headache on the health-related quality of life (HRQoL) in habitual snorers is not well defined.

This study sought to investigate the frequency of morning headache, its impact on HRQoL and relevant predictors in habitually snoring patients. All these patients underwent a study of overnight polysomnography (PSG).

Subjects and methods

We prospectively enrolled consecutive patients, males and females, >18 years old, who had been referred to our sleep laboratory between 1 January 2009 and 31 March 2010 with the complaint of habitual snoring, i.e. daily or near-daily snoring. Patients were excluded if they (i) had undergone an operation or continuous positive airway pressure (CPAP) treatment for snoring or OSAS; (ii) had persistent headache without remission, because this headache pattern was difficult to differentiate from morning headache; or (iii) had medication overuse headache based on the ICHD-2 criteria (14). This study had no limits regarding body mass index (BMI) levels, and infrequent painkiller usage was allowed. One physician (Chen PK) interviewed all patients to determine whether they had morning headache, migraine or insomnia. Diagnoses of migraine and other headache disorders were based on ICHD-2 (4). Diagnosis of insomnia was based on the International Classification of Sleep Disorders (ICSD-2) (15). Because there were no globally accepted diagnostic criteria for 'morning headache', we defined it in this study as headache on awakening ≥ 1 day/week for ≥ 6 months.

All patients filled out a structured questionnaire designed for morning headache. Information included demographics, BMI, headache frequency, duration, location, quality, intensity, and accompanying symptoms such as nausea, vomiting, photophobia and phonophobia. The study also investigated whether the patient's morning headache fulfilled the criteria for migraine attacks based on ICHD-2 (4), i.e. duration > 4 hours with two or more of the headache symptoms, including pulsatile quality, unilateral location, moderate or severe intensity and exacerbation due to physical activities; and one or more accompanying symptoms, including either 'nausea or vomiting' or 'photophobia and phonophobia'. Each patient also completed the Hospital Anxiety and Depression Scale (HADS) (16), and the Short Form-36 health survey (SF-36) (17). All patients underwent an overnight PSG study after the questionnaire survey. This study protocol was approved by the Institutional Review Board at the Lin-Shin Hospital, Taichung, Taiwan. Patients signed an informed consent form before entering the study.

Study assessment

Hospital Anxiety and Depression Scale (HADS). The HADS is a self-administered instrument designed to detect states of depression and anxiety in the setting of a hospital outpatient clinic (16,18). It does not

consider the somatic symptoms of anxiety and depression, and thereby excludes the influence of the confounding factors of physical symptoms and signs. The questionnaire includes 14 questions: seven for depression and seven for anxiety. Each question is rated with a score of 0 to 3, depending on the severity of the problem, with a total score ranging from 0 to 42. Psychological distress was defined as a total score ≥ 8 in this study (19).

Short Form-36 health survey (SF-36). The SF-36 is a self-administered 36-item scale widely used for the measure of generic HRQoL (17,20). It evaluates eight domains of health, including physical functioning (PF), role limitations due to physical problems (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE), and mental health (MH) during the preceding 4 weeks. All items were scored on a scale from 0 to 100. Higher scores indicated better health. A difference of >5 points in each domain was considered clinically significant (17,20).

Polysomnography (PSG). The PSG was performed on Embla S4500 (Flaga, Reykjavik, Iceland) and Alice 4 (Healthdyne, Atlanta, GA, USA) sleep systems. The EEG (C3/A2-C4/A1, and O1/A2 according to the 10-20 international electrode placement system), the two-channel electro-oculogram, chin electromyogram and electrocardiogram were recorded with surface electrodes. Airflow was detected by two channels through a thermal sensor (one channel) and nasal pressure transducer (one channel), and respiratory movements with thoracic and abdominal inductive plethysmography. Oxygen saturation during sleep was measured continuously using pulse oximetry with a finger probe. Snoring was evaluated with a neck microphone. Leg movements were recorded by bilateral tibial electromyograms. Apnoea, hypopnea and periodic leg movements in sleep (PLMS) were defined based on The AASM Manual for the Scoring of Sleep and Associated Events (21). The approved is a period of breathing cessation. The hypopnea is defined as $a \ge 30\%$ reduction in breathing with a > 4% oxygen desaturation or arousal. The minimum duration of an event was 10 seconds. The apnoea-hypopnea index (AHI) was calculated as the number of approved and hypopneas per hour of total sleep time. PLMS was scored if there were at least four consecutive leg movements of 0.5-10 seconds' duration, and between 5 and 90 seconds apart. The minimum amplitude of a leg movement event was an 8 µV increase in EMG. The PLMS index was calculated as the number of PLMS per hour. OSAS was defined as $5 \le AHI < 15$ if patients had at least one of the following complaints: loud snoring, daytime sleepiness,

fatigue, and breathing interruptions during sleep or $AHI \ge 15$ regardless of any additional complaints (15). PLMD was defined as a periodic leg movement index of >15 per hour of sleep with disturbed sleep or daytime fatigue (15).

Statistical analyses. Descriptive data were presented as mean \pm standard deviation (SD) or percentages. For categorical data, a chi-square test or Fisher's exact test was used to test the difference between groups. The Student's t-test was used to compare the means of continuous variables. The potential predicting variables for the presence of morning headache included age, gender, smoking habits, migraine, HADS score (>8 or <8), insomnia, OSAS and PLMD. The predictors for morning headache were presented as odds ratios (ORs) with 95% confidence intervals (CIs). Logistic regression was used to calculate adjusted ORs (AORs) after controlling for potential confounders. An estimated difference of each domain of the SF-36 due to morning headache was calculated after controlling for potential confounders by general linear models. All calculated *p*-values were two-tailed and statistical significance was defined as a *p*-value of < 0.05.

Results

During the study period, 284 patients with habitual snoring who were referred to our sleep laboratory were recruited. After excluding two patients because of refusal, seven with persistent headache and five with medication overuse headache, 270 patients signed informed consent forms to enter the study. Two patients were excluded due to incomplete data. A total of 268 patients (178M/90F, mean age 44.4 ± 12.2 , range 18–76 years) completed the study. Of them, 184 (68.7%) (135M/49F) were diagnosed with OSAS and 33 (12.3%) (21M/12F) were diagnosed with PLMD, according to both the PSG results and relevant clinical symptoms. Based on the physician interview, 116 patients (43.3%) (73M/43F) had insomnia and 58 (21.6%) (35M/23F) had migraine, including eight with and without aura and 50 without aura. Based on the HADS, 193 (72.0%) (123M/70F) had psychological distress (HADS > 8 points).

Headache profile of morning headache

Overall, 63 patients (23.5%) (37M/26F) had morning headache based on the physician interview. The characteristics of morning headache are shown in Table 2. The locations of the morning headache were not specific, and a side-locked unilateral location was unusual (4.8%). Dull pain was more common (n = 33, 52.4%)

	All patients (n=63)	In relation to OSAS			In relation to migraine		
		OSAS (n = 50)	No OSAS $(n = 13)$	P-value	Migraine (n = 35)	No migraine (n = 28)	P-value
Locations							
Frontal	12 (19.0%)	9 (18.0%)	3 (23.1%)	0.70	7 (20.0%)	5 (17.9%)	0.83
Occipital	18 (28.6%)	14 (28.0%)	4 (30.8%)	1.0	12 (34.3%)	6 (21.4%)	0.26
Temporal	25 (39.7%)	18 (36.0%)	7 (53.8%)	0.24	13 (37.1%)	12 (42.9%)	0.65
Vertex	(7.5%)	8 (16.0%)	3 (23.1%)	0.55	6 (17.1%)	5 (17.9%)	0.94
Side-locked	3 (4.8%)	2 (4.0%)	I (7.7%)	0.58	2 (5.7%)	l (3.6%)	0.69
Characteristics							
Pulsatile	29 (46.0%)	23 (46.0%)	6 (46.2%)	0.99	22 (62.9%)	7 (25.0%)	0.003
Dull	33 (52.4%)	26 (52.0%)	7 (53.8%)	0.91	12 (34.3%)	21 (75.0%)	0.001
Intensity							
Mild	17 (27.0%)	14 (28.0%)	5 (38.5%)		5 (14.3%)	14 (50.0%)	
Moderate	29 (46.0%)	25 (50.0%)	7 (53.8%)		20 (57.1%)	12 (42.9%)	
Severe	17 (27.0%)	11 (22.0%)	I (7.7%)	0.47	10 (28.6%)	2 (7.1%)	0.004
Frequency (days/m)	11.7 ± 6.2	11.7 ± 6.3	11.8 ± 6.3	0.93	11.3 ± 4.8	12.3 ± 7.7	0.52
Duration							0.03
<0.5 hour	21 (33.3%)	16 (32.0%)	5 (38.5%)		9 (25.7%)	12 (42.9%)	
0.5–4 hours	25 (39.7%)	20 (40.0%)	5 (38.5%)		12 (34.3%)	13 (46.4%)	
\geq 4 hours	17 (27.0%)	14 (28.0%)	3 (23.1%)	0.89	14 (40.0%)	3 (10.7%)	
Accompanying symptoms							
Nausea	20 (31.7%)	18 (36.0%)	2 (15.4%)	0.14	15 (42.9%)	5 (17.9%)	0.03
Vomiting	4 (6.3%)	4 (8.0%)	0	0.39	4 (11.4%)	0	0.09
Photophobia	4 (6.3%)	4 (8.0%)	0	0.39	3 (8.6%)	l (3.6%)	0.40
Phonophobia	(7.5%)	9 (18.0%)	2 (15.4%)	0.60	9 (25.7%)	2 (7.1%)	0.05
Physical activity exacerbations	23 (36.5%)	17 (34%)	6 (46.2%)	0.42	18 (51.4%)	5 (17.9%)	0.006
Fulfilling migraine attack criteria	12 (19%)	10 (20%)	2 (15.4%)	0.71	(31.4%)	5 (17.9%)	0.005

Table 2. Clinical profiles of morning headaches (n = 63) in habitual snorers and comparisons in relation to obstructive sleep apnoea syndrome (OSAS) and migraine

than pulsatile headache (n = 29, 46.0%). The headache intensity was most commonly moderate (n = 29, 46.0%). The headache profile did not differ between morning headache patients with and without OSAS. In contrast, compared with those without migraine (n = 28), the headache profile of morning headache patients with migraine (n = 35) was more likely to be pulsatile, of severe intensity and longer duration, and associated with nausea. The morning headache profile fulfilled the criteria of ICHD-2 migraine attacks in 19% (12/63) of all morning headache patients, especially in those with migraine, compared with those without (31.4% (11/35) vs. 3.6% (1/28), p = 0.005).

Sleep apnoea headache

Habitual snorers with OSAS were more likely to have morning headache than those without (27.2% (50/184))

vs. 15.5% (13/84), p < 0.001). The frequencies of the three proposed headache symptoms (A1 to A3) of ICHD-2 sleep apnoea syndrome in our morning headache patients are shown in Table 1. Forty percent of patients with morning headache could fulfil the criteria for sleep apnoea headache symptoms (A2), 32% experienced a short duration of <30 minutes (A3) and 18% had morning headache more than 15 days per month (A1). Overall, 62% (n=31) of OSAS patients fulfilled criterion A, i.e. at least one of three proposed headache symptoms. In this study, we did not test criterion D, i.e. disappearance of morning headache after treatment of OSAS.

The impact of morning headache on the SF-36

Patients with morning headache had significantly lower scores in all eight domains of the SF-36 (Figure 1).

832



Figure 1. The SF-36 domain scores between snoring patients with and without morning headache. PF = physical functioning;RP = role limitations due to physical problems; BP = bodily pain; VT = vitality; GH = general health; SF = social functioning; RE = role limitations due to emotional problems; MH = mental health. *p < 0.005, **p < 0.001.

The general linear model showed that the presence of morning headache independently accounted for more than 5 points of estimated difference in the domains of RP (-19.1 points, p=0.006), BP (-11.5 points, p=0.002), SF (-8.4 points, p=0.02) and RE (-22.5 points, p=0.02), after controlling for age, gender, BMI, smoking, insomnia, OSAS, migraine, psychological distress (HADS ≥ 8) and PLMD.

Predictors for morning headache in habitual snorers

The frequencies of morning headache were higher in subjects with migraine, insomnia, $HADS \ge 8$, and OSAS than those without (Table 3). In contrast, the frequencies were not associated with gender, smoking habits, $BMI \ge 27$ or PLMD. Except for the frequency of OSAS (AHI > 5), the other sleep parameters of the PSG, including percentages of stage 1, stage 2, stage 3 and 4, and REM sleep, mean AHI, mean SaO₂, lowest SaO₂, desaturation index, snoring index and arousal index, did not differ between habitual snorers with and without morning headache (data not shown). The logistic regression model showed the presence of migraine, insomnia, HADS > 8, and OSAS were independent predictors for morning headache in habitual snorers after adjustment of age, gender, smoking habits and BMI (Table 3). Because of the high correlation between medications and relevant disorders, such as sedatives or hypnotics for insomnia, anti-depressants for psychological distress and painkillers for migraine, these medications were not further controlled during the analyses. Migraine had the highest AOR (6.3), whereas OSAS had the lowest (2.6).

Discussion

The study found that 23.5% of habitual snorers had morning headache, with those with OSAS having a higher frequency than those without (27.2% vs. 15.5%). These findings were similar to those of prior studies, in which 7.4% to 33.6% of OSAS subjects (2,3,5-10) and 16.2% of snorers without OSAS had morning headache (9), even though different diagnostic criteria for morning headache were used. Of 63 habitual snorers with morning headache, 12 (19%) suffered from morning headaches with characteristics fulfilling the criteria of migraine attacks. Eleven of them had a history of migraine, accounting for 31.4% (11/35) of migraine patients with morning headache. Based on the ICHD-2 criteria for sleep appoea headache, 62% of the morning headaches in our OSAS patients had at least one of three proposed headache symptoms (A1 to A3, Table 1). This is because only 40% of the patients with morning headaches had tension-type features (A2), and only one-third had a short duration (A3). We do not know if comorbidity with migraine in our snoring patients complicated the headache pattern, or the subjects fulfilling these ICHD-2 criteria were more compatible with OSAS-induced headache, because our study did not test these criteria by treating these morning headache patients with OSAS.

Our study found morning headache had a pervasive impact on all domains of the HRQoL as assessed by the SF-36. The differences in scores ranged from 10.6 to 29.7 points, much higher than the suggested scores of clinical significance (>5 points). Moreover, morning headache independently accounted for role limitation due to physical and emotional status, impairment of social functioning, and pain. This suggested that

	Morning headache, n (%)	OR (95% CI)	AOR (95% CI)	
Migraine				
Yes $(n = 58)$	35 (60.3%)	9.9 (5.1–19.1)**	6.5 (3.1–13.7)**	
No (n=210)	28 (13.3%)			
Insomnia				
Yes $(n = 116)$	47 (40.5%)	5.8 (3.I-I0.9)**	4.2 (2.0-8.7)**	
No (n = 152)	16 (10.5%)			
Psychological distress (HAD	DS ≥ 8)			
Yes (n = 193)	58 (30.1%)	6.0 (2.3–15.7)**	3.9 (1.5–10.1)*	
No (n = 75)	5 (6.7%)			
Obstructive sleep apnoea s	yndrome			
Yes (n = 184)	50 (27.2%)	2.0 (1.0-4.0)*	2.6 (1.0–6.7)*	
No (n=84)	13 (15.5%)			
Periodic leg movement disc	orders			
Yes (n = 33)	7 (21.1%)	0.9 (0.4–2.1)	0.7 (0.2–2.0)	
No (n = 235)	56 (23.8%)			
Gender				
Male (<i>n</i> = 178)	37 (20.8%)	0.6 (0.4–1.2)	0.6 (0.3–1.2)	
Female (<i>n</i> = 90)	26 (28.9%)			
Smoking habit				
Yes (n = 82)	22 (26.8%)	1.3 (0.7–2.4)	1.6 (0.5–5.2)	
No (n = 186)	41 (22.0%)			
Body mass index \geq 27 kg/m ²	2			
Yes (n = 88)	27 (30.7%)	1.77 (0.9–3.2)	1.6 (0.8–3.5)	
No (n = 180)	36 (20.0%)			

Table 3. The frequencies, odds ratios (OR) and adjusted odds ratios (AORs) of predictors for morning headache in habitual snorers

HADS = Hospital Anxiety and Depression Scale; OR = odds ratios by univariate analysis; AOR = adjusted OR by multivariate logistic regression after controlling for the other variables.

**p < 0.001, *p < 0.05.

snoring patients comorbid with morning headache were more disabled in their daily activities. In fact, these involved domains and the magnitude of difference were consistent with previous studies of migraine patients (22–24).

Snoring is a sensitive symptom for OSAS (13), and was previously considered an important predictor for morning headache. In contrast to our prior belief, migraine was the most important predictor for morning headache in snoring patients, whereas OSAS was the least. The reasons for the differential impact of these factors were not clear. It is reported that more than 71% of migraine patients had experienced headache on awakening (25). Insomnia and psychological distress are well-known triggers or comorbidities of migraine (26,27), and insomnia-related migraine attacks were more predominant in the morning (28). In contrast, the frequencies of morning headache were similar among patients with different sleep disorders, not only for OSAS (5,6). In our study, more than half of habitual snorers with migraine had morning headache, and 31.4% of their morning headaches fulfilled the criteria for migraine features. The high frequency of OSAS in snorers both with and without morning headache (79.4% vs. 65.4%) downplayed the relationship between OSAS and morning headache. Because we did not have a control group of non-snorers, we do not know if there is a discrepancy in the degree of association between migraine and morning headache in non-snorers.

The pathophysiology of morning headache is still unknown. Hypoxia, hypercapnia (29) and the transient increase of intracranial pressure (30) in OSAS patients were suspected causes. Our study results showed that except for OSAS, the other PSG sleep parameters were not associated with morning headache. Therefore, morning headache in habitual snorers can be, in part, considered as morning attacks of their prior headaches. In addition, we postulated that the four predictors relative to morning headache raised the possibility of hypothalamic involvement. Migraine was related to hypothalamic activation in both neuroimaging and hormonal studies (31,32). The hypothalamus also accounts for sleep regulation and depression (33,34). Recently, abnormal hypothalamic activation was also noted in OSAS patients (35). Further studies are suggested to investigate the role of the hypothalamus in the morning headache of habitual snorers.

Our study has clinical implications. The presence of morning headache can be used as an indicator for poor quality of life and possible associations with migraine, insomnia and psychological distress in habitual snorers. Management of migraine, insomnia or psychological distress might be more helpful for morning headache than management of OSAS. The disruptive effect of CPAP on sleep should be taken into consideration in the treatment of morning headache in snorers, because the potential adverse event of sleep disturbance (36,37) may in turn worsen morning headache.

The strengths of this study are the detailed data collection of headache profiles, HRQoL and the PSG study for each participant. However, some limitations need to be addressed. First, all our patients were referred for PSG under a possible diagnosis of OSAS; therefore, one should be cautious in extrapolating to other patient populations. Second, the difference in the definitions of morning headache between our study and prior studies may produce different results. Third, morning headache was diagnosed according to self-reported headache profiles in the past 6 months, and no headache diary was collected in this study. Recall bias should be considered.

Funding

This study was supported in part by grants from the National Science Council of Taiwan (97-2628-B-010-007-MY3), Taipei Veterans General Hospital (V98C1-143), Ministry of Education (Aim for the Top University Plan), and Taiwan Department of Health Clinical Trial and Research Center of Excellence (DOH100-TD-B-111-004).

References

- Jennum P and Jensen R. Sleep and headache. Sleep Med Rev 2002; 6: 471–479.
- Loh NK, Dinner DS, Foldvary N, et al. Do patients with obstructive sleep apnea wake up with headaches? *Arch Intern Med* 1999; 159: 1765–1768.
- Goksan B, Gunduz A, Karadeniz D, et al. Morning headache in sleep apnoea: clinical and polysomnographic evaluation and response to nasal continuous positive airway pressure. *Cephalalgia* 2009; 29: 635–641.
- Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders. *Cephalalgia* 2004; 24(Suppl 1): 1–160.

- 5. Ohayon MM. Prevalence and risk factors of morning headaches in the general population. *Arch Intern Med* 2004; 164: 97–102.
- Göder R, Friege L, Fritzer G, et al. Morning headaches in patients with sleep disorders: a systematic polysomnographic study. *Sleep Med* 2003; 4: 385–391.
- Aldrich MS and Chauncey JB. Are morning headaches part of obstructive sleep apnea syndrome? *Arch Intern Med* 1990; 150: 1265–1267.
- Lucchesi LM, Speciali JG, Santos-Silva R, et al. Nocturnal awakening with headache and its relationship with sleep disorders in a population-based sample of adult inhabitants of São Paulo City, Brazil. *Cephalalgia* 2010; 30: 1477–1485.
- 9. Neau JP, Paquereau J, Bailbe M, et al. Relationship between sleep apnoea syndrome, snoring and headaches. *Cephalalgia* 2002; 22: 333–339.
- Ulfberg J, Carter N, Talbäck M, et al. Headache, snoring and sleep apnoea. J Neurol 1996; 243: 621–625.
- 11. Thoman EB. Snoring, nightmares, and morning headaches in elderly women: a preliminary study. *Biol Psychol* 1997; 46: 275–284.
- Young T, Palta M, Dempsey J, et al. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993; 328: 1230–1235.
- Young T, Shahar E, Nieto FJ, et al. Predictors of sleepdisordered breathing in community-dwelling adults: the Sleep Heart Health Study. *Arch Intern Med* 2002; 162: 893–900.
- Headache Classification Committee. New appendix criteria open for a broader concept of chronic migraine. *Cephalalgia* 2006; 26: 742–746.
- 15. American Academy of Sleep Medicine. Diagnostic and coding manual. *International Classification of Sleep Disorders*, 2nd edn. Westchester, IL: American Academy of Sleep Medicine, 2005.
- Zigmond AS and Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; 67: 361–370.
- Ware JE, Snow KK, Kosinski M, et al. SF-36 Health Survey Manual and Interpretation Guide. Boston, MA: New England Medical Center, The Health Institute, 1993.
- Leung CM, Wing YK, Kwong PK, et al. Validation of the Chinese-Cantonese version of the hospital anxiety and depression scale and comparison with the Hamilton Rating Scale of Depression. *Acta Psychiatr Scand* 1999; 100: 456–461.
- Wilkinson MJ and Barczak P. Psychiatric screening in general practice: comparison of the general health questionnaire and the hospital anxiety depression scale. *J R Coll Gen Pract* 1988; 38: 311–313.
- Fuh JL, Wang SJ, Lu SR, et al. Psychometric evaluation of a Chinese (Taiwanese) version of the SF-36 health survey amongst middle-aged women from a rural community. *Qual Life Res* 2000; 9: 675–683.
- Iber C, Ancoli-Israel S, Chesson A, et al. *The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications*, 1st edn. Westchester, IL: American Academy of Sleep Medicine, 2007.

- Wang SJ, Fuh JL, Lu SR, et al. Quality of life differs among headache diagnoses: analysis of SF-36 survey in 901 headache patients. *Pain* 2001; 89: 285–292.
- Aaronson NK, Muller M, Cohen PD, et al. Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations. *J Clin Epidemiol* 1998; 51: 1055–1068.
- Monzón MJ and Láinez MJ. Quality of life in migraine and chronic daily headache patients. *Cephalalgia* 1998; 18: 638–643.
- Kelman L and Rains JC. Headache and sleep: examination of sleep patterns and complaints in a large clinical sample of migraineurs. *Headache* 2005; 45: 904–910.
- Chen PK, Fuh JL, Chen SP, et al. Association between restless legs syndrome and migraine. J Neurol Neurosurg Psychiatry 2010; 81: 524–528.
- 27. Wang SJ, Chen PK and Fuh JL. Comorbidities of migraine. *Front Neurol* 2010; 1: 16.
- Alstadhaug K, Salvesen R and Bekkelund S. Insomnia and circadian variation of attacks in episodic migraine. *Headache* 2007; 47: 1184–1188.
- Olson LG, King MT, Hensley MJ, et al. A community study of snoring and sleep-disordered breathing. Symptoms. *Am J Respir Crit Care Med* 1995; 152: 707–710.

- Sugita Y, Iijima S, Teshima Y, et al. Marked episodic elevation of cerebrospinal fluid pressure during nocturnal sleep in patients with sleep apnea hypersomnia syndrome. *Electroencephalogr Clin Neurophysiol* 1985; 60: 214–219.
- Denuelle M, Fabre N, Payoux P, et al. Hypothalamic activation in spontaneous migraine attacks. *Headache* 2007; 47: 1418–1426.
- Peres MF, Stiles MA, Siow HC, et al. Excessive daytime sleepiness in migraine patients. J Neurol Neurosurg Psychiatry 2005; 76: 1467–1468.
- Mignot E, Taheri S and Nishino S. Sleeping with the hypothalamus: emerging therapeutic targets for sleep disorders. *Nat Neurosci* 2002; 5(Suppl): 1071–1075.
- Bao AM, Meynen G and Swaab DF. The stress system in depression and neurodegeneration: focus on the human hypothalamus. *Brain Res Rev* 2008; 57: 531–553.
- 35. Tasali E and Ip MS. Obstructive sleep apnea and metabolic syndrome: alterations in glucose metabolism and inflammation. *Proc Am Thorac Soc* 2008; 5: 207–217.
- Haynes PL. The role of behavioral sleep medicine in the assessment and treatment of sleep disordered breathing. *Clin Psychol Rev* 2005; 25: 673–705.
- Engleman HM, Asgari-Jirhandeh N, McLeod AL, et al. Self-reported use of CPAP and benefits of CPAP therapy: a patient survey. *Chest* 1996; 109: 1470–1476.