

Sleep disturbances in tension-type headache and migraine

César Fernández-de-las-Peñas, Juan J. Fernández-Muñoz, María Palacios-Ceña, Paula Parás-Bravo, Margarita Cigarán-Méndez and Esperanza Navarro-Pardo

Ther Adv Neurol Disord

2018, Vol. 11: 1–6

DOI: 10.1177/
1756285617745444

© The Author(s), 2018.
Reprints and permissions:
[http://www.sagepub.co.uk/
journalsPermissions.nav](http://www.sagepub.co.uk/journalsPermissions.nav)

Abstract: Current research into the pathogenesis of tension-type headache (TTH) and migraine is focused on altered nociceptive pain processing. Among the potential factors that influence sensitization mechanisms, emotional stress, depression, or sleep disorders all have an essential role: they increase the excitability of nociceptive firing and trigger hyperalgesic responses. Sleep disturbances and headache disorders share common brain structures and pathogenic mechanisms and TTH, migraine, and sleep disturbances often occur together; for example, 50% of individuals who have either TTH or migraine have insomnia. Moreover, insomnia and poor sleep quality have been associated with a higher frequency and intensity of headache attacks, supporting the notion that severity and prevalence of sleep problems correlate with headache burden. It should be noted that the association between headaches and sleep problems is bidirectional: headache can promote sleep disturbances, and sleep disturbances can also precede or trigger a headache attack. Therefore, a better understanding of the factors that affect sleep quality in TTH and migraine can assist clinicians in determining better and adequate therapeutic programs. In this review, the role of sleep disturbances in headaches, and the association with depression, emotional stress, and pain sensitivity in individuals with TTH or migraine are discussed.

Keywords: headache, insomnia, migraine, sleep, tension-type headache

Received: 3 July 2017; revised manuscript accepted: 31 October 2017.

Introduction

Tension-type headache (TTH) and migraine are the most common headache disorders, and both have an important socio-economic impact and burden for society.¹ For example, the general costs of headache in Europe, mostly attributed to migraine and TTH, were €13.8 billion in 2010.² The global prevalence of TTH has been estimated to be around 42%,³ and that of migraine to be almost 12%.⁴ In the Global Burden of Disease Study, headache was the second most prevalent disorder in the world, leading to a high economic burden, estimated to be around 1.6 billion dollars.⁵ In fact, most of the costs from the Global Burden of Disease Study derived from TTH and migraine headaches.⁵

Current research into the pathogenesis of TTH⁶ and migraine⁷ is focused on altered nociceptive pain processing and its role on chronification. Although both primary headaches can exhibit

similar pathogenic mechanisms, some differences can be observed. In TTH, sensitization of the pain pathways seems to result in facilitation of nociceptive gain due to sensitization of the trigeminocervical nucleus caudalis, leading to typical clinical manifestations of TTH,⁶ whereas in migraine, it has been established that the pain is associated with abnormal neuronal excitability leading to cortical spreading depression and to central sensitization of the trigeminovascular pain pathways.⁷

Several factors, including physical, neurophysiologic, or emotional, can increase the excitability of nociceptive firing to the central nervous system. For example, stress can precipitate a headache attack in patients with TTH by reducing the thresholds to noxious input from pericranial sensitized structures.⁸ In individuals with chronic headaches, defined in the International Classification of

Correspondence to:

César Fernández-de-las-Peñas
Facultad de Ciencias de la Salud, Universidad Rey Juan Carlos, Avenida de Atenas s/n, 28922 Alcorcón, Madrid, Spain
cesar.fernandez@urjc.es

Juan J. Fernández-Muñoz
Department of Psychology, Universidad Rey Juan Carlos, Alcorcón, Spain

María Palacios-Ceña
Department of Physical Therapy, Occupational Therapy, Rehabilitation, and Physical Medicine, University Rey Juan Carlos, Alcorcón, Spain

Paula Parás-Bravo
Department of Nursing, Universidad de Cantabria, Santander, Spain

Margarita Cigarán-Méndez
Department of Psychology, Universidad Rey Juan Carlos, Alcorcón, Spain

Esperanza Navarro-Pardo
Department of Psicología Evolutiva y de la Educación, Universitat Valencia, Spain

d Headache Disorders 3rd edition (beta version) as persistent headache for 15 days or more per month on average for more than 3 months, stress and sleep disturbances are the most common headache triggers⁹ and, when combined, have an additive effect.¹⁰ For example, two consecutive days of decreased sleep have been associated with an increased risk for headache, and in individuals with chronic headaches, shorter sleep duration has been associated with more severe pain.¹⁰ Moreover, 48–74% of patients with migraine and 26–72% of patients with TTH identified “lack of sleep” as a factor triggering a headache attack.^{11,12} Interestingly, although stress is considered to precipitate headaches, its role has been proposed to be less robust than previously suggested, at least in migraine.¹³

In this review, we discuss the role of sleep disturbances in TTH and migraine, as well as potential interactions between emotional and psychological factors with sleep quality. We conducted a search in PubMed for English-language papers published between 1990 and July 2017. The following search terms were used: ‘tension-type headache’, ‘migraine’, ‘sleep disturbances’, ‘sleep deprivation’, ‘sleep quality’, ‘depression’, ‘anxiety’, ‘pressure pain sensitivity’, and ‘insomnia’. Reference lists of included articles were searched for additional articles, and articles introducing general concepts were included. Papers were selected by reading the method section of the full papers. Articles on other headache conditions were excluded.

Sleep disturbances in TTH and migraine

Prevalence and comorbidities

The term ‘sleep disturbances’ includes sleep disorders, such as insomnia or obstructive sleep apnea, as well as other sleep perturbations, such as poor sleep quality.¹⁴ Sleep deprivation has been proposed to have severe effects on human health: it is a risk factor for the presence of neurologic diseases in general, and particularly, headaches.¹⁵ Indeed, headache disorders and sleep disorders have a well-established comorbid association.^{16,17}

In patients with chronic headache, insomnia seems to be the most common sleep disorder. Kelman and Rains found that approximately half of individuals with migraine reported at least occasional symptoms of insomnia, 38% reported sleeping for less than 6 h per night, and 50% reported that sleep disturbances triggered their

migraines.¹⁸ Uhlig and colleagues observed that the prevalence of insomnia was 1.8 times higher in subjects with TTH compared with those without headache.¹⁹ The same study also found migraine to be linked with an increased risk of insomnia (odds ratio [OR] 1.4–2.6).¹⁹ In another study, insomnia was found to be even more common in individuals with TTH than in those with migraine.²⁰ De Luca Canto and colleagues reported that TTH and migraine were also associated with sleep bruxism with respective ORs of 3.12 (95% confidence interval [CI] 1.25–7.7) and 3.8 (95% CI 1.8–7.8).²¹

It is important to note that the sleep problems increase in line with the frequency of headaches; indeed, the majority (68–84%) of individuals with chronic migraine suffer from insomnia on a near-daily basis.²² In fact, insomnia is considered a risk factor for higher headache frequency, particularly in TTH and migraine.²³

Besides loss of sleep, poor sleep quality may also be a risk factor for progression from episodic to chronic TTH.²⁴ Moreover, worse sleep quality has been associated with a higher intensity of headache in patients with TTH.²⁵ Chronic headaches have been linked with daytime sleepiness and snoring.²⁶ Poor sleep quality has several components such as sleep disruption, early morning awakening, and difficulty in falling asleep, which may explain some of the inconsistency in studies evaluating its role in headache. Although Caspersen and colleagues found worse self-perceived sleep quality in patients with TTH, they also reported that the hours of sleep per night were not significantly different between headache patients and healthy controls.²⁷

According to a recent study, subjects with migraine experience more insufficient sleep than those with nonmigraine headache.²⁸ Discrepancies between studies are related to the fact that sleep disturbances can have different manifestations depending on each particular headache. Supporting this hypothesis, Verma and colleagues observed that subjects with chronic TTH showed better slow-wave sleep but significantly increased daytime sleepiness compared with those with chronic migraine.²⁹

Bidirectional relationship

Finally, clinicians should be aware that association between headaches and sleep disorders is

bidirectional: headache promotes sleep disturbances, but sleep disturbances can also precede and trigger headaches. For example, a large population-based cohort study reported a higher risk (adjusted hazard ratio 3.52, 95% CI 3.28–3.79) of developing a subsequent migraine in subjects with non-apnea sleep disorders.³⁰ Further, patients with headaches are at significantly higher risk of developing sleep problems (OR 2.5, 95% CI 2.0–3.1) than headache-free subjects, regardless of specific headache type.³¹ In this study, adults with headache reported more difficulty in initiating sleep (OR 2.0, 95% CI 1.6–2.5), difficulty staying asleep (OR 2.5, 95% CI 2.1–3.0), early morning awakening (OR 2.0, 95% CI 1.7–2.5), and more daytime fatigue (OR 2.6, 95% CI 2.2–3.2).³¹ This bidirectional relationship can be related to the fact that sleep and headaches share common brain structures, such as the thalamus, hypothalamus, and brainstem nuclei, including the locus coeruleus and raphe nuclei.³²

Poor sleep quality is an umbrella term including symptoms that can interact with several other variables. Sleep quality is usually self-defined by the patient on the basis of several characteristics such as total sleep time, sleep onset latency, total wake time, sleep fragmentation, sleep efficiency, and the presence of sleep-disruptive events.³³ An individual will describe their sleep quality based on several aspects, including tiredness on waking and throughout the day, feeling rested and restored on waking, and the number of awakenings that they experienced in the night. A better understanding of the potential relationships between these variables potentially associated with sleep quality in patients with TTH and migraine could assist clinicians in determining better therapeutic programs.

Clinical and emotional variables associated with sleep quality

Sleep and depression

A recent systematic review found moderate evidence indicating that depression, anxiety, poor sleep, medication overuse, stress, and poor self-efficacy for managing headaches were potential factors associated with poor prognosis and unfavorable outcomes from preventive drug treatment in chronic headaches.³⁴ It is possible that these variables interact at the same time, but at different levels, in patients with headache. Among these variables, particular attention has been

given to mood disorders, i.e. depression and anxiety, because they are commonly associated with sleep disturbances.³⁵

In the general population, prevalence of depression is 4.4–5.0%³⁶ and that of anxiety 4.8–11%,³⁷ respectively. TTH is often associated with comorbid anxiety and depression.³⁸ For example, a recent study has reported anxiety to feature in 9.5% of individuals with TTH and depression in 14.2%.³⁹ Individuals with chronic TTH were particularly likely to experience anxiety (21.4%, OR 4.0).³⁹ Another study reported the prevalence of depression to be increased (64%) in patients with chronic headaches.⁴⁰

Sleep, depression, and pain sensitivity

Chronic pain,⁴¹ including headache,⁴² has been reported to be associated with impaired sleep quality and depression, and poor sleep quality has been linked to higher levels of depression and pain.⁴³ Moreover, poor sleep quality is associated with lower daily life activities⁴⁴ in patients with chronic pain, including those with migraine.⁴⁵ This association may be mediated by the capability of depression and sleep disorders to trigger hyperalgesic responses within the central nervous system by increasing excitability of nociceptive firing.⁴⁶ An example of this hyperexcitability, allodynia, is a clinical sign of central sensitization strongly related to sleep quality in individuals with migraine.⁴⁷ Moreover, patients with TTH who exhibit sleep disturbances also show lower pressure pain thresholds.⁴⁸ Bezov and colleagues suggested that unfulfilled need for sleep enhances central sensitization, probably underlying the observed pressure sensitivity to pain in patients with TTH.⁴⁹ Others have reported sleep disturbances and depression to be independently associated with sensitivity to pressure, supporting an independent role for each factor.⁵⁰ Although it is possible that a bilateral relationship exists, it is more likely that depression leads to a lowered pain threshold than *vice versa*, particularly given that the relationship persisted after adjustment for pain group.⁵⁰ These findings have led to the hypothesis that underlying etiology of depression, sleep, and headaches can share common brain mechanisms,²⁴ that is, hypothalamic alterations and serotonin and melatonin dysregulation.⁵¹ Another mechanism may be an emotional modulation of pain by depression *via* supraspinal mechanisms.⁵² It is more plausible that depression and poor sleep quality enhance central

sensitization leading to decreased pain thresholds, rather than the opposite.

Sleep and headache frequency

Poor sleep may contribute to this increased pain sensitivity by also increasing the frequency of headache attacks, given the finding that severity and frequency of sleep problems increase in line with the frequency of headaches.¹⁰ In fact, it has been found recently that depression and sleep quality mediated the relationship between headache frequency and the emotional burden of headache and pain experience in a sample of patients with chronic TTH.⁵³ To summarize, a complex interplay of sleep quality, depression, and headache seems to underlie the increased excitability of the central nervous system.

Clinical applications

Despite the uncertainty over the biological mechanisms of the interactions described above, they have several implications for clinical practice. Given that poor sleep quality is a common trigger of TTH and migraine, management of sleep perturbations seems crucial. In this review, we have described factors associated with poor sleep quality, including depression, emotional stress, and pain hypersensitivity. Some of these factors, namely, emotional stress and depression, are also modifiable risk factors of chronic pain.⁵⁴

Pain alleviation *per se* may not be the most effective strategy to improve sleep quality in patients with headache. Rather, sleep quality may be best restored by reducing emotional stress and pain sensitivity, potentially combined with proper management of depressive symptoms. Therefore, current findings suggest that therapeutic management of patients with TTH and migraine should include approaches targeting depression (i.e. psychological approaches), the emotional burden of the headache (i.e. cognitive behavioral techniques), quality of sleep (i.e. coping strategies, a conscious effort from the patient to solve a personal problem), and pain (i.e. pharmacologic drugs and physical interventions). This multimodal therapeutic proposal agrees with current literature showing that longer sleep periods is a common self-management coping strategy used by subjects with TTH⁵⁵ and that cognitive behavioral treatment of insomnia produced large reductions in the frequency of headache.⁵⁶ This multimodal approach, comprising pharmacologic

treatment, education, and lifestyle modification including sleep hygiene, has been also proposed as a therapeutic strategy in children suffering from headaches.⁵⁷

Conclusion

Research findings support an association between TTH, migraine, and sleep disturbances. This association is bidirectional: headache can promote sleep disturbances but sleep problems can also trigger headache. The bidirectional association can be explained by the fact that sleep and headache share common brain structures and pathogenic mechanisms. The interactions between sleep quality, depression, headache, and pain sensitivity provide an opportunity for multimodal therapeutic intervention.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The authors declare no conflicts of interest in preparing this article.

References

1. Dowson A. The burden of headache: global and regional prevalence of headache and its impact. *Int J Clin Pract Suppl* 2015; 182: 3–7.
2. Raggi A and Leonardi M. Burden and cost of neurological diseases: a European North-South comparison. *Acta Neurol Scand* 2015; 132: 16–22.
3. Ferrante T, Manzoni GC, Russo M, *et al.* Prevalence of tension-type headache in adult general population: the PACE study and review of the literature. *Neurol Sci* 2013; 34: S137–S138.
4. Woldeamanuel YW and Cowan RP. Migraine affects 1 in 10 people worldwide featuring recent rise: a systematic review and meta-analysis of community-based studies involving 6 million participants. *J Neurol Sci* 2017; 372: 307–315.
5. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016; 388: 1545–1602.

6. de Tommaso M and Fernández-de-las-Peñas C. Tension type headache. *Curr Rheumatol Rev* 2016; 12: 1–13.
7. de Tommaso M and Sciriuicchio V. Migraine and central sensitization: clinical features, main co-morbidities and therapeutic perspectives. *Curr Rheumatol Rev* 2016; 12: 113–126.
8. Cathcart S, Petkov J, Winefield AH, *et al.* Central mechanisms of stress-induced headache. *Cephalalgia* 2010; 30: 285–295.
9. Wang J, Huang Q, Li N, *et al.* Triggers of migraine and tension-type headache in China: a clinic-based survey. *Eur J Neurol* 2013; 20: 689–696.
10. Houle TT, Butschek RA, Turner DP, *et al.* Stress and sleep duration predict headache severity in chronic headache sufferers. *Pain* 2012; 153: 2432–2440.
11. Barbanti P, Fabbrini G, Aurilia C, *et al.* A case-control study on excessive daytime sleepiness in episodic migraine. *Cephalalgia* 2007; 27: 1115–1119.
12. Boardman HF, Thomas E, Millson DS, *et al.* Psychological, sleep, lifestyle, and comorbid associations with headache. *Headache* 2005; 45: 657–669.
13. Wober C, Brannath W, Schmidt K, *et al.*; the PAMINA Study Group. Prospective analysis of factors related to migraine attacks: the PAMINA study. *Cephalalgia* 2007; 27: 304–314.
14. Diagnostic Classification Steering Committee. *International classification of sleep disorders: diagnostic and coding manual (ICSD)*. Rochester, MN: American Sleep Disorders Association, 1990.
15. Palma JA, Urrestarazu E and Iriarte J. Sleep loss as risk factor for neurologic disorders: a review. *Sleep Med* 2013; 14: 229–236.
16. Freedom T and Evans RW. Headache and sleep. *Headache* 2013; 53: 1358–1366.
17. Almozni G, Benoliel R, Sharav Y, *et al.* Sleep disorders and chronic craniofacial pain: characteristics and management possibilities. *Sleep Med Rev* 2017; 33: 39–50.
18. Kelman L and Rains J. Headache and sleep: examination of sleep patterns and complaints in a large clinical sample of migraineurs. *Headache* 2005; 45: 904–910.
19. Uhlig BL, Engstrøm M, Ødegård SS, *et al.* Headache and insomnia in population-based epidemiological studies. *Cephalalgia* 2014; 34: 745–751.
20. Engstrøm M, Hagen K, Bjørk MH, *et al.* Sleep quality and arousal in migraine and tension-type headache: the headache-sleep study. *Acta Neurol Scand* 2014; 198: S47–S54.
21. De Luca Canto G, Singh V, Bigal ME, *et al.* Association between tension-type headache and migraine with sleep bruxism: a systematic review. *Headache* 2014; 54: 1460–1469.
22. Calhoun AH, Ford S, Finkel AG, *et al.* The prevalence and spectrum of sleep problems in women with transformed migraine. *Headache* 2006; 46: 604–610.
23. Tran DP and Spierings E. Headache and insomnia: their relation reviewed. *Cranio* 2013; 31: 165–170.
24. Rains JC, Davis RE and Smitherman TA. Tension-type headache and sleep. *Curr Neurol Neurosci Rep* 2015; 15: 520.
25. Kikuchi H, Yoshiuchi K, Yamamoto Y, *et al.* Does sleep aggravate tension-type headache? An investigation using computerized ecological momentary assessment and actigraphy. *Biopsychosoc Med* 2011; 5: 10.
26. Sancisi E, Cevoli S, Vignatelli L, *et al.* Increased prevalence of sleep disorders in chronic headache: a case-control study. *Headache* 2010; 50: 1464–1472.
27. Caspersen N, Hirsvang JR, Kroell L, *et al.* Is there a relation between tension-type headache, temporomandibular disorders and sleep? *Pain Res Treat* 2013; 2013: 845684.
28. Kim J, Cho SJ, Kim WJ, *et al.* Insufficient sleep is prevalent among migraineurs: a population-based study. *J Headache Pain* 2017; 18: 50.
29. Verma R, Nagar KK, Garg RK, *et al.* Study of sleep disorders and polysomnographic evaluation among primary chronic daily headache patients. *J Neurosci Rural Pract* 2016; 7: S72–S75.
30. Harnod T, Wang YC and Kao CH. Higher risk of developing a subsequent migraine in adults with non-apnea sleep disorders: a nationwide population-based cohort study. *Eur J Intern Med* 2015; 26: 232–236.
31. Lateef T, Swanson S, Cui L, *et al.* Headaches and sleep problems among adults in the United States: findings from the National Comorbidity Survey-Replication study. *Cephalalgia* 2011; 31: 648–653.
32. Lovati C, D'Amico D, Raimondi E, *et al.* Sleep and headache: a bidirectional relationship. *Expert Rev Neurother* 2010; 10: 105–117.
33. Krystal AD and Edinger JD. Measuring sleep quality. *Sleep Med* 2008; 9: S10–S17.

34. Probyn K, Bowers H, Caldwell F, *et al.*; CHESSTeam. Prognostic factors for chronic headache: a systematic review. *Neurology* 2017; 89: 291–301.
35. Spiegelhalder K, Regen W, Nanovska S, *et al.* Comorbid sleep disorders in neuropsychiatric disorders across the life cycle. *Curr Psychiatry Rep* 2013; 15: 364.
36. Ferrari AJ, Somerville AJ, Baxter AJ, *et al.* Global variation in the prevalence and incidence of major depressive disorder: a systematic review of the epidemiological literature. *Psychol Med* 2013; 43: 471–481.
37. Baxter AJ, Scott KM, Vos T, *et al.* Global prevalence of anxiety disorders: a systematic review and meta-regression. *Psychol Med* 2013; 43: 897–910.
38. Beghi E, Bussone G, D'Amico D, *et al.* Headache, anxiety and depressive disorders: the HADAS study. *J Headache Pain* 2010; 11: 141–150.
39. Song TJ, Cho SJ, Kim WJ, *et al.* Anxiety and depression in tension-type headache: a population-based study. *PLoS One* 2016; 11: e0165316.
40. Zebenholzer K, Lechner A, Broessner G, *et al.* Impact of depression and anxiety on burden and management of episodic and chronic headaches – a cross-sectional multicentre study in eight Austrian headache centres. *J Headache Pain* 2016; 17: 15.
41. George SZ, Coronado RA, Beneciuk JM, *et al.* Depressive symptoms, anatomical region, and clinical outcomes for patients seeking outpatient physical therapy for musculoskeletal pain. *Phys Ther* 2011; 91: 358–372.
42. Zwart JA, Dyb G, Hagen K, *et al.* Depression and anxiety disorder associated with headache frequency: The Nord-Trøndelag Health Study. *Eur J Neurol* 2003; 10: 147–152.
43. Naughton F, Ashworth P and Skevington SM. Does sleep quality predict pain-related disability in chronic pain patients? The mediating roles of depression and pain severity. *Pain* 2007; 127: 243–252.
44. Baldwin CM, Ervin AM, Mays MZ, *et al.* Sleep disturbances, quality of life, and ethnicity: the Sleep Heart Health Study. *J Clin Sleep Med* 2010; 6: 176–183.
45. Zhu Z, Fan X, Li X, *et al.* Prevalence and predictive factors for poor sleep quality among migraineurs in a tertiary hospital headache clinic. *Acta Neurol Belg* 2013; 113: 229–235.
46. de Tommaso M, Delussi M, Vecchio E, *et al.* Sleep features and central sensitization symptoms in primary headache patients. *J Headache Pain* 2014; 15: 64.
47. Lovati C, D'Amico D, Bertora P, *et al.* Correlation between presence of allodynia and sleep quality in migraineurs. *Neurol Sci* 2010; 31: S155–S158.
48. Engstrøm M, Hagen K, Bjørk M, *et al.* Sleep quality, arousal and pain thresholds in tension-type headache: a blinded controlled polysomnographic study. *Cephalalgia* 2014; 34: 455–463.
49. Bezov D, Ashina S, Jensen R, *et al.* Pain perception studies in tension-type headache. *Headache* 2011; 51: 262–271.
50. Chiu YH, Silman AJ, Macfarlane GJ, *et al.* Poor sleep and depression are independently associated with a reduced pain threshold: results of a population based study. *Pain* 2005; 115: 316–321.
51. Dodick DW, Eross EJ, Parish JM, *et al.* Clinical, anatomical, and physiologic relationship between sleep and headache. *Headache* 2003; 43: 282–292.
52. Terry EL, DelVentura JL, Bartley EJ, *et al.* Emotional modulation of pain and spinal nociception in persons with major depressive disorder (MDD). *Pain* 2013; 154: 2759–2768.
53. Palacios-Ceña M, Fernández-Muñoz JJ, Castaldo M, *et al.* The association of headache frequency with pain interference and the burden of disease is mediated by depression and sleep quality, but not anxiety, in chronic tension type headache. *J Headache Pain* 2017; 18: 19.
54. Rains JC. Chronic headache and potentially modifiable risk factors: screening and behavioral management of sleep disorders. *Headache* 2008; 48: 32–39.
55. Ong JC, Stepanski EJ and Gramling S. Pain coping strategies for tension-type headache: possible implications for insomnia? *J Clin Sleep Med* 2009; 5: 52–56.
56. Smitherman TA, Walters AB, Davis RE, *et al.* Randomized controlled pilot trial of behavioral insomnia treatment for chronic migraine with comorbid insomnia. *Headache* 2016; 56: 276–291.
57. Guidetti V, Dosi C and Bruni O. The relationship between sleep and headache in children: implications for treatment. *Cephalalgia* 2014; 34: 767–776.

RESEARCH ARTICLE

Open Access

Tension-type headache associated with obstructive sleep apnea: a nationwide population-based study

Yu-Chwen Chiu¹, Hsiao-Yun Hu^{2,3}, Fei-Peng Lee^{4,5} and Hung-Meng Huang^{1,4*}

Abstract

Background: There is still controversy regarding the association between primary headaches and obstructive sleep apnea. We explored the relationship between tension-type headache (TTH) and obstructive sleep apnea (OSA) using a large nationwide population-based data set in Taiwan.

Methods: We identified 4759 patients diagnosed with OSA from the Taiwan Longitudinal Health Insurance Database, based on polysomnography, as the OSA group. We then randomly selected 19036 subjects without OSA, matched by sex and age, to serve as the non-OSA group. The multivariate Cox proportional hazards model with matching for age and sex was used to assess the possible associations between TTH and OSA among the patients.

Results: The prevalence of TTH was 10.2% among OSA patients and 7.7% among non-OSA patients ($p < 0.001$). The multivariate Cox proportional hazards model revealed patients with OSA were more likely to have TTH (hazard ratio, 1.18; 95% CI, 1.06–1.31) ($p = 0.003$) than patients in the non-OSA group.

Conclusion: Patients with OSA had a higher likelihood of developing TTH than patients in the non-OSA group. Further studies of physiological patterns between OSA and TTH are needed to confirm the study findings.

Keywords: Polysomnography; Sleep study; Health insurance database; Taiwan; Sleep disturbance; Headache; Hypopnea

Background

Obstructive sleep apnea (OSA) is by far the most common sleep disturbance, affecting some 24% of men and 9% of women by the time they reach middle age [1]. Repeated episodes of apnea or hypopnea caused by upper airway blockage during sleep characterize OSA. A typical measurement of sleep apnea is the apnea-hypopnea index. This is an average that represents the combined number of episodes of apnea and hypopnea that occur per hour of sleep, which is calculated from the results of overnight polysomnography. The definitive diagnostic test for OSA is polysomnography. Obstructive sleep apnea is receiving increased attention as an important cause of medical morbidity, including excessive daytime

sleepiness, metabolic derangement, and cardiovascular disease.

People in the general population frequently experience headache pain, placing a burden on health care and other economic expenditures. Headaches may be intrinsically related to sleep, may cause sleep disturbances, or manifestations of sleep apnea. The International Classification of Headache Disorders (ICHD II) [2] includes two specific diagnoses for sleep-related headaches, “sleep apnea headache” and “hypnic headache”. Sleep apnea headaches present upon awakening with an apnea-hypopnea index ≥ 5 , as demonstrated by overnight PSG. Hypnic headaches develop only during sleep and always awaken patients. Nevertheless, sleep disorders may still be associated with other primary headaches, especially tension-type headaches (TTH).

Several studies [3–6] have illustrated positive correlations between TTH and sleep disturbances including sleep apnea. Nevertheless, several studies [7–9] have shown no

* Correspondence: hmengh@yahoo.com.tw

¹Department of Otolaryngology, Taipei City Hospital, Taipei, Taiwan

⁴Department of Otolaryngology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan

Full list of author information is available at the end of the article

correlation. In a recent cross-sectional population-based study, Kristiansen et al. [8,9] showed that sleep apnea had little if any influence on the development of TTH. Therefore, the goal of this research was to explore the possible association between TTH and OSA within a nationwide, population-based data set in Taiwan.

Methods

Data sources

Taiwan's National Health Insurance (NHI) program, which started March 1, 1995, provides comprehensive coverage for medical care of people living in Taiwan. This program was built on the concept of mutual assistance, and it depends on the insured paying their premiums according to regulations. At the end of 2012, there were 23 million people (approximately 99% of Taiwan's population) enrolled in the program. The Bureau of NHI collects data from the NHI program and sends it to the National Health Research Institutes (NHRI) to form the original files of National Health Insurance Research Database (NHIRD). The study used data from the Longitudinal Health Insurance Database 2000 (LHID2000), which was created by the NHRI and contained all the original claims data for one million individuals (approximately 5% of Taiwan's population) randomly sampled from the 2000 Registry of Beneficiaries of the NHIRD. The NHRI confirmed that there was no significant difference in gender distribution between the patients in the LHID2000 and the original NHIRD.

All information allowing a specific patient to be identified was encrypted. The encryption procedure was consistent between datasets; thus, all claims belonging to each patient were linked. The confidentiality of the data abides by the data regulations of the Bureau of National Health Insurance. The Institutional Review Board of Taipei City Hospital approved this study (IRB no.: TCHIRB-1020715-W).

Study sample

We first identified all patients with a new diagnosis of OSA (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes 327.23, 780.51, 780.53, or 780.57) based on polysomnography (AHI ≥ 5) between January 1, 2004 and December 31, 2010 ($n = 5023$). We excluded patients younger than 18 years from the analysis ($n = 264$). For each case, the date of the first diagnosis was assigned as the index date. Finally, the OSA group included 4759 patients.

We selected 19,036 patients without OSA (four for each OSA case) from the remaining subjects of the LHID2000 as the non-OSA group. The patients in the non-OSA group were matched with the case subjects in OSA group by sex, age group (<30, 30–39, 40–49, 50–59, ≥ 60), and year of the index date. None of the selected non-OSA

patients had been diagnosed with OSA after 1995, the initiation year of the NHI program.

We also investigated the pre-existing comorbidities of hypertension (ICD-9-CM 401), epilepsy (ICD-9-CM 345), major depression disorders (ICD-9-CM 296.2 and 296.3), and anxiety disorders (ICD-9-CM 300.00, 300.01, 300.02 and 300.09). We selected these comorbidities due to their possible associations with OSA and TTH as documented in earlier studies [10–14].

Cases of TTH were identified based on their corresponding ICD-9-CM codes. We used ICD-9-CM codes 307.81 and 339.1 for TTH. Neurologists diagnosed all headaches. We included patients in this group only when TTH was diagnosed after the OSA index date.

Statistical analysis

SAS version 9.3 (SAS Institute Inc., Cary, NC, USA) was used to link the data in the LHID2000; Stata 13 (Stata Corporation, College Station, TX, USA) was used to perform the statistical analyses. Demographic information of patients with or without OSA were compared using a χ^2 test for categorical variables. The threshold for statistical significance was set at two-tailed P value < 0.05 . The risk of TTH among OSA patients and OSA-free group between January 1, 2004 and December 31, 2010 was analyzed. The log-log survival curve was used to test the proportional assumption. The log-log plots indicated that the data might be suitable for the Weibull distribution parameters estimation. A sensitivity test of the Weibull model was performed. Cox proportional hazards regression model was used to estimate the adjusted hazard ratio (HR) and 95% confidence intervals (CI) for developing TTH. The analysis included potential correlation factors of TTH such as hypertension, epilepsy, major depression disorder, and anxiety disorder. Finally, HRs were calculated for specific subgroups with adequately adjusted regression models.

Results

After matching for sex and age, we found that patients with OSA had higher proportions of certain comorbidities than the non-OSA group did (Table 1), including hypertension (38.3% vs. 30.2%, $p < 0.001$), epilepsy (2.5% vs. 1.6%, $p < 0.001$), major depression disorder (5.5% vs. 2.7%, $p < 0.001$), and anxiety disorder (26.7% vs. 15.3%, $p < 0.001$). Table 1 shows the relationships between sociodemographic characteristics and OSA. Patients with OSA were more likely to have monthly incomes of NT\$ 40,000 or higher ($p < 0.001$) and live in northern and central Taiwan ($p < 0.001$).

The prevalence of TTH was 10.2% among OSA patients, and was higher than in non-OSA patients (7.7%, $p < 0.001$).

Table 2 shows the incidence rates (IR) in each group over the 6-year follow-up period. The incidence rate of

Table 1 Demographic characteristics of patients with obstructive sleep apnea (OSA) and non-OSA-diagnosis patients from 2004 to 2010

Variable	Matched controls		Patients with OSA		p-value
	(N = 19036)	%	(N = 4759)	%	
Sex					1.000
Female	5,524	29.0	1,381	29.0	
Male	13,512	71.0	3,378	71.0	
Age					1.000
<30	1,956	10.3	489	10.3	
30-39	3,780	19.9	945	19.9	
40-49	4,720	24.8	1,180	24.8	
50-59	4,768	25.0	1,192	25.0	
≥60	3,812	20.0	953	20.0	
Monthly Income, NT\$					<0.001
<20,000	2,285	12.0	515	10.8	
20,000-39,999	6,599	34.7	1,461	30.7	
≥40,000	4,447	23.4	1,588	33.4	
Union/association member	2,647	13.9	455	9.6	
Local government enrollee	3,058	16.1	740	15.5	
Region					<0.001
Northern	8,529	44.8	2,476	52.0	
Central	4,131	21.7	1,434	30.1	
Southern	5,943	31.2	811	17.0	
Eastern	433	2.3	38	0.8	
Comorbidity					
Hypertension	5,755	30.2	1,823	38.3	<0.001
Epilepsy	297	1.6	121	2.5	<0.001
Major depression disorder	520	2.7	264	5.5	<0.001
Anxiety disorder	2,911	15.3	1,270	26.7	<0.001
Tension type headache					<0.001
No	17,567	92.3	4,275	89.8	
Yes	1,469	7.7	484	10.2	
Total	19,036		4,759		

TTH was higher in OSA patients (37 per 1000 person-years) than in non-OSA patients (28 per 1000 person-years).

We used multivariate Cox proportional hazards regression model for predicting the chances of developing TTH (Table 3). After adjustment for sex, age, sociodemographic factors, and comorbidities, patients with OSA were more likely to have TTH (HR = 1.18, 95% CI 1.06–1.31, $p = 0.003$) than patients in the non-OSA group. Patients with hypertension tended to have TTH (HR = 1.28, 95% CI 1.16–1.42, $p < 0.001$).

Among affective disorders, patients with major depression disorder were more likely to have TTH (HR = 1.73, 95% CI 1.47–2.03, $p < 0.001$). Patients with anxiety

disorder also had greater chances of developing TTH (HR = 2.30, 95% CI 2.09–2.54, $p < 0.001$).

We found that men had a lower chance of having TTH (HR = 0.61, 95% CI 0.56–0.67, $p < 0.001$) than did women. TTH occurred more often among older age adults (age 50–59 years, HR = 1.76, 95% CI 1.42–2.18, $p < 0.001$).

Regarding economic condition and geographic location, we found that the chances of developing TTH increased when monthly income was less than NT\$ 20,000 and patients resided outside of northern Taiwan.

Table 4 shows the subgroup analysis of the variables. Regardless of gender, patients with OSA were more likely to have TTH than were non-OSA patients. Patients with

Table 2 The incidences of tension-type headache in each group from 2004 to 2010

Variables	Tension-type headache		
	Person-Years	TTH (N)	IR (%/yr)
Total	64,864	1,953	30
Sex			
Female	18,102	810	45
Male	46,762	1,143	24
Age			
<30	6,938	104	15
30-39	13,122	316	24
40-49	16,460	464	28
50-59	15,996	579	36
≥60	12,348	490	40
Monthly Income			
<20,000	9,122	217	24
20,000-39,999	20,610	628	30
≥40,000	16,365	384	23
Union/association member	8,564	363	42
Local government enrollee	10,202	361	35
Region			
Northern	30,023	749	25
Central	14,865	448	30
Southern	18,709	719	38
Eastern	1,266	37	29
Comorbidity			
Hypertension	21,434	882	41
Epilepsy	1,153	34	29
Major depression disorder	2,226	177	80
Anxiety disorder	11,579	769	66
Obstructive sleep apnea			
No	51,824	1,469	28
Yes	13,040	484	37

p-value < 0.001 in all results.

IR: incidence rate.

OSA 50–59 years of age with monthly income of NT\$ 40,000 or more had a statistically significant association with TTH. All OSA patients, even those without the selected comorbidities, showed a statistically significant association with TTH compared to non-OSA patients.

Discussion

According to our results, obstructive sleep apnea is associated with gender, age, sociodemographic characteristics, metabolic consequences, and affective disorders (Table 1). TTH is the most common primary headache. Nonetheless, there has been much less study of TTH compared with migraine. It is likely that patients suffer

Table 3 Multivariate Cox regression model for predictor of tension-type headache development

Variable	Tension-type headache		
	HR	95% CI	<i>p</i> -value
Sex			
Female	1.00		
Male	0.61	0.56-0.67	<0.001
Age			
<30	1.00		
30-39	1.56	1.25-1.94	<0.001
40-49	1.58	1.27-1.96	<0.001
50-59	1.76	1.42-2.18	<0.001
≥60	1.65	1.31-2.06	<0.001
Monthly Income			
<20,000	1.00		
20,000-39,999	1.34	1.14-1.56	<0.001
≥40,000	1.09	0.92-1.30	0.298
Union/association member	1.51	1.27-1.80	<0.001
Local government enrollee	1.35	1.14-1.60	<0.001
Region			
Northern	1.00		
Central	1.09	0.96-1.23	0.173
Southern	1.50	1.35-1.67	<0.001
Eastern	1.06	0.76-1.48	0.720
Comorbidity			
Hypertension	1.28	1.16-1.42	<0.001
Epilepsy	0.79	0.56-1.11	0.170
Major depression disorder	1.73	1.47-2.03	<0.001
Anxiety disorder	2.30	2.09-2.54	<0.001
Obstructive sleep apnea			
No	1.00		
Yes	1.18	1.06-1.31	0.003

less with TTH than other chronic headaches. A recent study showed that headache patients who do not seek medical assistance are more likely to have TTH [15]. TTH is associated with certain mental illnesses, especially anxiety and major depression disorder [16]. We extracted possible overlapping variables from the database to make clear their direct or indirect effects on migraine and TTH.

In accordance with our findings, one cross-sectional population based study with 297 participants enrolled from Norway used a modified short form of the Karolinska Sleep Questionnaire and Epworth Sleepiness Scale. They found severe sleep disturbance was three times more likely for individuals with TTH [6]. Authors of another retrospective analysis reported that among 82 chronic headache patients with migraine or TTH or both, 52

Table 4 Risk comparison of tension-type headache between OSA and non-OSA participants

Variable	N	Tension-type headache	
		HR	95% CI
Sex			
Female	6,905	1.17	1.00-1.39
Male	16,890	1.17	1.02-1.35
Age			
<30	2,445	1.27	0.80-2.00
30-39	4,725	1.03	0.78-1.35
40-49	5,900	1.40	1.13-1.73
50-59	5,960	1.29	1.06-1.56
≥60	4,765	0.93	0.74-1.17
Monthly Income			
<20,000	2,800	1.05	0.75-1.47
20,000-39,999	8,060	1.16	0.96-1.41
≥40,000	6,035	1.37	1.11-1.70
Union/association member	3,102	0.88	0.65-1.18
Local government enrollee	3,798	1.22	0.96-1.54
Region			
Northern	11,005	1.22	1.04-1.43
Central	5,565	1.25	1.02-1.53
Southern	6,754	0.99	0.80-1.23
Eastern	471	2.47	0.90-6.81
Comorbidity			
Hypertension			
No	16,217	1.22	1.06-1.42
Yes	7,578	1.08	0.92-1.26
Epilepsy			
No	23,377	1.19	1.07-1.32
Yes	418	0.75	0.31-1.82
Major depression disorder			
No	23,011	1.18	1.06-1.32
Yes	784	1.18	0.86-1.61
Anxiety disorder			
No	19,614	1.25	1.08-1.45
Yes	4,181	1.10	0.94-1.28

Each factor was adjusted for all other factors.

patients (63%) also had OSA. The headache improvement rate was up to 49% after receiving either standard medical therapy or continuous positive airway pressure therapy [17].

The main finding of our study showed a positive relationship between OSA and TTH. Regardless of gender, patients with OSA were more likely to have TTH after adjustment for age, residential region, monthly income, and possible comorbidities. In Table 4, patients with OSA

showed stronger positive associations with TTH in most comorbidity-free groups than in comorbidity groups. We assumed patients with the selected comorbidities had poorer health-related quality of life and did not undergo OSA testing, which is not considered an emergency, but needs to be confirmed by a time-consuming polysomnography study.

Lack of sleep itself is related to headaches. Common sleep disorders include OSA, central sleep apnea, insomnia, periodic limb movement disorder [18], and bruxism [19]. The mechanisms by which headaches are associated with specific sleep disturbances are complex and manifold. In cluster headaches, oxygen desaturation below 89% during sleep preceded 8 out of 14 attacks of cluster headache among 10 patients [20], giving positive support for the relationship of cluster headache and OSA.

Serotonin and several other neurotransmitters influence TTH. Pain thresholds elicited in patients with chronic, painful pathologies are linked to serum serotonin levels [21]. Additionally, many TTH patients show changes in serotonin levels [22-26]. Interestingly, serotonin dysfunction may also play a role in OSA [27,28]. Serotonin delivery is reduced to upper airway dilator motor neurons during sleep, and this contributes to sleep-related reductions in dilator muscle activity and thus, upper airway obstruction [27]. Fluctuation of serotonin concentrations could be a primary or secondary factor common to different mechanisms. Such a hypothesis provides a possible explanation for the manifestation of OSA and TTH. Furthermore, a growing number of studies show that sleep disturbance increases pain sensitivity and exacerbates chronic pain, including fibromyalgia, rheumatoid arthritis, and headache [29-31]. Smith et al. [32] suggested that sleep fragmentation impairs endogenous pain inhibitory function and increases spontaneous pain in middle-aged healthy women. Lentz et al. [33] found that slow wave sleep disruption without reducing total sleep was also associated with decreased pain thresholds in middle-aged women. Khalid et al. [34] demonstrated that patients with severe OSA were hyperalgesic, and their pain sensitivity improved with continuous positive airway pressure treatment, and the improvement disappeared immediately with discontinuation of continuous positive airway pressure therapy. We suggest patients with refractory TTH undergo evaluation for OSA. Treating OSA might not only improve headaches, but also decrease the risk of related comorbidities.

Clinical importance and limitations

In this study, we utilized a nationwide population database to investigate the epidemiologic associations between OSA and TTH. One of the key strengths of the study, in addition to a large sample size, was selecting patients with an OSA diagnosis confirmed by polysomnography. We

believe this selection criterion is more precise and strict than patient recall in response to a questionnaire. Nonetheless, this could also lead to underestimation of the enrolled OSA patients in the total population. The National Health Insurance Administration in Taiwan samples the medical charts routinely and makes detailed assessments for accuracy of medical coding. The reliability and validity of the NHI research database for epidemiologic investigation has been reported [35].

A key limitation of the study is the relatively low prevalence of OSA and headache. The prevalence of TTH in the general population varies from 30% to 78% (2) because of differences in research study design. A diagnosis of TTH may be overlooked or delayed because symptoms can be mild or infrequent. In addition, some symptoms can mimic TTH of other conditions, such as acute or chronic paranasal sinusitis, transient ischemic attack, meningitis, chronic subdural hemorrhage, and brain tumor. TTH diagnoses of patients enrolled in our study were made by neurologists, which means we may have reliable accuracy of the clinical diagnoses in our study. Similarly, according to epidemiological studies, the prevalence rates of OSA in the general population vary from 3% to 7% [36]. It was about 0.48% (4759/1000000) in our study due to the strict selection of polysomnography-confirmed cases only. A disadvantage of our study is that we could not have face-to-face interviews with patients. Thus, we can only set higher limitations on case selection to lower inaccuracy from such a large study sample. Even if the prevalence were underestimated, we still would have convincing findings.

Another limitation of the study is that the degree of OSA and the pattern of headache attack could not be determined from the database. Thus, we could not determine whether the severity of OSA influenced TTH frequency, duration, and pain characteristics. We could not differentiate TTH from episodic and chronic type headaches. Additionally, some possibly relevant confounding factors, such as body mass index, smoking, and alcohol consumption were not included in the data set. Therefore, they were not analyzed.

In our findings, the incidence rates (Table 2) over the 6-year follow-up period (from 2004 to 2010, 30 to 78 per 1,000 person-years) were higher than some earlier studies (13). Not being able to completely exclude recurrences should be taken into account, especially in older age group. The substantially increasing trend in the incidence of frequent headache in past 10 years was also found in other studies [37]. Additional researches on the occurrence and causes of increasing headache incidences are needed.

Conclusions

Our results support the notion that patients with OSA are more likely to develop TTH. The mechanism underlying

this association is not clear but includes changes in serotonin levels. Further studies of physiological patterns of OSA and TTH are needed to confirm the study findings and to enrich our understanding of their interactions.

Abbreviations

TTH: Tension-type headache; OSA: Obstructive sleep apnea; NHRI: National health research institutes; NHIRD: National health insurance research database; LHID2000: Longitudinal health insurance database 2000; ICD-9-CM: International classification of diseases, ninth revision, clinical modification; HR: Hazard ratio; CI: Confidence interval.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Chiu YC and Huang HM prepared the study design and initial draft. Hu HY performed the statistical analysis. Lee FP had the original idea of the study. All authors have contributed to the practical plans for the study, revised and approved the final manuscript.

Acknowledgements

This work was supported by a grant from Taipei City Hospital (grant no.: TPECH-103-06).

Author details

¹Department of Otolaryngology, Taipei City Hospital, Taipei, Taiwan.

²Department of Education and Research, Taipei City Hospital, Taipei, Taiwan.

³Department of Public Health, Institute of Public Health, National Yang Ming University, Taipei, Taiwan. ⁴Department of Otolaryngology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan.

⁵Department of Otolaryngology, Wan Fang Hospital, Taipei Medical University, Taipei, Taiwan.

Received: 8 March 2015 Accepted: 11 April 2015

Published online: 21 April 2015

References

- Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S (1993) The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med* 328:1230–5
- Headache Classification Subcommittee of the International Headache Society (2004) The international classification of headache disorders, 2nd Edition. *Cephalalgia* 24:1–160
- Mitsikostas DD, Vekelis M, Viskos A (2008) Refractory chronic headache associated with obstructive sleep apnoea syndrome. *Cephalalgia* 28(2):139–43
- Karthik N, Sinha S, Taly AB, Kulkarni GB, Ramachandiraiah CT, Rao S (2013) Alternation in polysomnographic profile in 'migraine without aura' compared to healthy controls. *Sleep Med* 14(2):211–4
- Yeung WF, Chung KF, Wong CY (2010) Relationship between insomnia and headache in community-based middle-aged Hong Kong Chinese women. *J Headache Pain* 11(3):187–95
- Odegard SS, Engstrom M, Sand T, Stovner LJ, Zwart JA, Hagen K (2010) Associations between sleep disturbance and primary headaches: the third Nord-Trøndelag Health Study. *J Headache Pain* 11(3):197–206
- Jensen R, Olsborg C, Salvesen R, Torberqsen T, Bekkelund SI (2004) Is obstructive sleep apnea syndrome associated with headache? *Acta Neurol Scand* 109(3):180–4
- Kristiansen HA, Kværner KJ, Akre H, Overland B, Russell MB (2011) Tension-type headache and sleep apnea in the general population. *J Headache Pain* 12(1):63–9
- Kristiansen HA, Kværner KJ, Akre H, Overland B, Russell MB (2011) Migraine and sleep apnea in the general population. *J Headache Pain* 12(1):55–61
- Huang QR, Qin Z, Zhang S, Chow CM (2008) Clinical patterns of obstructive sleep apnea and its comorbid conditions: a data mining approach. *J Clin Sleep Med* 4(6):543–50
- Drager LF, Togeiro SM, Polotsky VY, Lorenzi-Filho G (2013) Obstructive sleep apnea: a cardiometabolic risk in obesity and the metabolic syndrome. *J Am Coll Cardiol* 62(7):569–76

12. Babson KA, Del Re AC, Bonn-Miller MO, Woodward SH (2013) The comorbidity of sleep apnea and mood, anxiety, and substance use disorders among obese military veterans within the Veterans Health Administration. *J Clin Sleep Med* 9(12):1253–8
13. Jensen R, Stovner LJ (2008) Epidemiology and comorbidity of headache. *Lancet Neurol* 7(4):354–61
14. Scher AI, Bigal ME, Lipton RB (2005) Comorbidity of migraine. *Curr Opin Neurol* 18(3):305–10
15. Oliveira DR, Leite AA, Rocha-Filho PA (2011) Which patients with headache do not seek medical attention. *Headache* 51(8):1279–84
16. Juang KD, Wang SJ, Fuh JL, Lu SR, Su TP (2000) Comorbidity of depressive and anxiety disorders in chronic daily headache and its subtypes. *Headache* 40(10):818–23
17. Johnson KG, Ziemba AM, Garb JL (2013) Improvement in headaches with continuous positive airway pressure for obstructive sleep apnea: a retrospective analysis. *Headache* 53(2):333–43
18. Esposito M, Parisi P, Miano S, Carotenuto M (2013) Migraine and periodic limb movement disorders in sleep in children: a preliminary case-control study. *J Headache Pain* 14:57
19. Bailey DR (1990) Tension headache and bruxism in the sleep disordered patient. *J Craniomandib Pract* 8:174–82
20. Kudrow L, MacGinty DJ, Phillips ER, Stevenson M (1984) Sleep apnea in cluster headache. *Cephalalgia* 4(1):33–8
21. Jung AC, Staiger T, Sullivan M (1997) The efficacy of selective serotonin reuptake inhibitors for the management of chronic pain. *J Gen Intern Med* 12:384–9
22. Scuteri F (1972) Headache as possible expression of deficiency of brain 5-hydroxytryptamine (central denervation supersensitivity). *Headache* 12:69–72
23. Ferrari MD, Odink J, Tapparelli C, Van Kempen GM, Pennings EJ, Bruyn GW (1989) Serotonin metabolism in migraine. *Neurology* 39(9):1239–42
24. Lothe A, Merlet I, Demarquay G, Costes N, Ryvlin P, Mauguère F (2008) Interictal brain 5-HT_{1A} receptors binding in migraine without aura: an 18 F-MPPF-PET study. *Cephalalgia* 28(12):1282–91
25. Aylin A, Cenqiz T, Emin E, Neriman A, Sacide P (2008) Serotonin transporter gene polymorphisms in patients with chronic tension-type headache: a preliminary study. *Neurol India* 56(2):156–60
26. Bendtsen L (2000) Central sensitization in tension-type headache—possible pathophysiological mechanisms. *Cephalalgia* 20:486–508
27. Veasey SC (2003) Serotonin agonists and antagonists in obstructive sleep apnea: therapeutic potential. *Am J Respir Med* 2:21–9
28. McCann UD, Sgambati FP, Schwartz AR, Ricaurte GA (2009) Sleep apnea in young abstinent recreational MDMA (“ecstasy”) consumers. *Neurology* 73(23):2011–7
29. Lautenbacher S, Rollman GB (1997) Possible deficiencies of pain modulation in fibromyalgia. *Clin J Pain* 13:189–96
30. Pielsticker A, Haag G, Zaudig M, Lautenbacher S (2005) Impairment of pain inhibition in chronic tension-type headache. *Pain* 118(1–2):215–23
31. Leffler AS, Kosek E, Lerndal T, Nordmark B, Hansson P (2002) Somatosensory perception and function of diffuse noxious inhibitory controls (DNIC) in patients suffering from rheumatoid arthritis. *Eur J Pain* 6(2):161–76
32. Smith M, Edwards R, McCann U, Haythornthwaite JA (2007) The effects of sleep deprivation on pain inhibition and spontaneous pain in women. *SLEEP* 30(4):494–505
33. Lentz MJ, Landis CA, Rothermel J, Shaver JL (1999) Effects of selective slow wave sleep disruption on musculoskeletal pain and fatigue in middle aged women. *J Rheumatol* 26(7):1586–92
34. Khalid I, Roehrs TA, Hudgel DW, Roth T (2011) Continuous positive airway pressure in severe obstructive sleep apnea reduces pain sensitivity. *SLEEP* 34(12):1687–91
35. Cheng CL, Kao YH, Lin SJ, Lee CH, Lai ML (2011) Validation of the national health insurance research database with ischemic stroke cases in Taiwan. *Pharmacoepidemiol Drug Saf* 20(3):236–42
36. Punjabi NM (2008) The epidemiology of adult obstructive sleep apnea. *Proc Am Thorac Soc* 5:136–43
37. Anttila P, Metsähonkala L, Sillanpää M (2006) Long-term trends in the incidence of headache in Finnish schoolchildren. *Pediatrics* 117:1197–201

Submit your manuscript to a SpringerOpen[®] journal and benefit from:

- Convenient online submission
- Rigorous peer review
- Immediate publication on acceptance
- Open access: articles freely available online
- High visibility within the field
- Retaining the copyright to your article

Submit your next manuscript at ► springeropen.com



Excessive Daytime Sleepiness in Tension-Type Headache: A Population Study

Kyung Min Kim¹, Jiyoung Kim², Soo-Jin Cho³, Won-Joo Kim⁴, Kwang Ik Yang⁵, Chang-Ho Yun⁶ and Min Kyung Chu^{1*}

¹ Department of Neurology, Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea, ² Department of Neurology, Bio Medical Research Institute, Pusan National University Hospital, Pusan National University School of Medicine, Busan, South Korea, ³ Department of Neurology, Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong, South Korea, ⁴ Department of Neurology, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea, ⁵ Sleep Disorders Center, Department of Neurology, Soonchunhyang University College of Medicine, Cheonan Hospital, Cheonan, South Korea, ⁶ Department of Neurology, Bundang Clinical Neuroscience Institute, Seoul National University Bundang Hospital, Seongnam, South Korea

OPEN ACCESS

Edited by:

Vincenzo Guidetti,
Sapienza University of Rome, Italy

Reviewed by:

Rosalía Cesarea Silvestri,
University of Messina, Italy
Marcelo M. Valença,
Federal University of
Pernambuco, Brazil

*Correspondence:

Min Kyung Chu
chumk@yonsei.ac.kr

Specialty section:

This article was submitted to
Headache Medicine and Facial Pain,
a section of the journal
Frontiers in Neurology

Received: 11 June 2019

Accepted: 19 November 2019

Published: 03 December 2019

Citation:

Kim KM, Kim J, Cho S-J, Kim W-J,
Yang KI, Yun C-H and Chu MK (2019)
Excessive Daytime Sleepiness in
Tension-Type Headache: A Population
Study. *Front. Neurol.* 10:1282.
doi: 10.3389/fneur.2019.01282

Excessive daytime sleepiness (EDS) is a prevalent sleep-related complaint across the general population and has been reported to be associated with headache. Tension-type headache (TTH) is the most commonly encountered headache and accounts for a significant amount of disease burden. However, the association between EDS and TTH is currently scarce. In the present study, we investigated the impact of EDS on the prevalence and clinical presentation of TTH. We utilized data from the Korean Headache-Sleep Study, a national survey that sought to identify headache and sleep characteristics in Korean adults. Participants with an Epworth sleepiness scale score greater or equal to 11 were considered as having EDS. Of the 2,695 participants enrolled, 570 (21.2%) and 313 (11.6%) had TTH and EDS, respectively. EDS was highly prevalent in individuals with chronic tension-type headache (CTTH) than in those without headache (35.7 vs. 9.4%, $p < 0.001$). The prevalence of EDS in episodic tension-type headache (ETTH) individuals with a headache frequency <1 per month (8.3%, $p = 0.511$) and ETTH individuals with a headache frequency of 1–14 per month (13.5%, $p = 0.054$) was not significantly different from that in individuals without headache (9.4%). TTH participants with EDS had a higher headache frequency per month (4.3 ± 8.1 vs. 1.7 ± 4.2 , $p = 0.013$), more severe headache intensity (Visual Analog Scale, $5.0 [3.0–6.0]$ vs. $4.0 [3.0–6.0]$, $p = 0.008$), a higher impact of headache (Headache Impact Test-6 score, 47.1 ± 7.3 vs. 43.5 ± 7.6 , $p < 0.001$), and a higher prevalence of depression (12.7 vs. 3.2%, $p < 0.001$) than TTH participants without EDS. Consequently, CTTH is associated with higher EDS prevalence compared to ETTH and without headache. Moreover, TTH with EDS had more severe TTH symptoms compared to TTH without EDS.

Keywords: excessive daytime sleepiness, tension-type headache, headache, sleep, epidemiology

INTRODUCTION

Excessive daytime sleepiness (EDS) is a well-known complaint encountered in sleep clinics and can occur in up to 12% of the general population (1, 2). EDS can result in reduced quality of life, accidents, reduced performance, and cognitive and mood impairment (3–5). Various neurological and psychological conditions have been reported to contribute to EDS. Patients with common

neurological disorders such as parkinsonism, multiple sclerosis, stroke, and epilepsy often present with EDS. Moreover, a previous study showed that individuals with depression, anxiety, and schizophrenia often reported EDS (5).

Tension-type headache (TTH) is the most prevalent type among primary headaches and individuals with TTH usually have mild or no disability. However, some individuals with TTH experience disabling symptoms that result in a significant amount of disability and reduced quality of life (6). Because of its high prevalence, the disease burden of TTH is estimated to be greater than that of migraine (7).

Previous studies have reported a significant association between EDS and headache. It has been reported that migraineurs experience more EDS than non-migraineurs, with EDS being associated with the exacerbation of migraine symptoms (8, 9). Frequency of EDS was shown to be higher among individuals with episodic and chronic migraine than among individuals without headache (10, 11). However, there is currently limited information on the prevalence of EDS in TTH individuals and the impact of EDS on TTH. Therefore, we conducted a study with a population-based sample to investigate the following: (1) the prevalence of EDS in TTH individuals; (2) the clinical presentations of TTH associated with EDS; (3) The factors contributing EDS occurrence in TTH individuals.

MATERIALS AND METHODS

Study Protocol

We conducted a cross-sectional study to analyze data from the Korean Headache-Sleep Study (KHSS), which is a national population study for headache and sleep. Detailed methods of this survey were previously described (12). Briefly, two-stage random cluster sampling was used to reflect the regional distribution in Korea except for Jeju-do. Well-trained interviewers performed this survey by door-to-door visiting using a structured questionnaire. The questionnaire was composed of questions asking yes-no answers or Likert scales. Each participant provided informed consent before the survey and the study protocol was reviewed and approved by the Institutional Review Board and Ethics Committee of Hallym University Sacred Heart Hospital (Approval No. 2011-1077).

Headache Assessment

Participants that experienced more than 1 min of headache during the previous year, they were classified as having headache. If participants did not experience a headache lasting more than 1 min during the previous year, they were classified as participants without headache.

TTH Assessment

For TTH diagnosis, we used diagnostic criteria B to D for infrequent episodic TTH (code 2.1) in the third edition, beta version of the International Classification of Headache Disorders (ICHD-3 beta) (B: lasting from 30 min to 7 days; C: at least two of the following four characteristics [i.e., bilateral location, pressing or tightening (non-pulsating) quality, mild or moderate intensity, and not aggravated by routine physical activity such as walking or

climbing stairs]; D: attacks associated with both of the following: no nausea or vomiting and no more than one of photophobia or phonophobia). Participants who fulfilled these criteria were classified as having TTH. Diagnostic criterion A (at least 10 episodes of headache) was not applied in TTH diagnosis. Thus, TTH individuals included in this study had infrequent TTH (code 2.1), frequent TTH (code 2.2), and chronic TTH (code 2.3). If a participant classified as having headache and fulfilling B to D criteria for infrequent episodic TTH, she/he was classified as having TTH. Based on ICHD-3 beta, participants that fulfilled with both diagnostic criteria for probable migraine (PM) and TTH were considered as having TTH.

EDS Assessment

The Epworth Sleepiness Scale (ESS) was used for EDS assessment. The total ESS score ranges from 0 to 24 points. Participants with a score equal to or >11 were considered as having EDS. We used a previously verified Korean version of ESS (13).

Short Sleep Duration and Poor Sleep Quality Assessment

Short sleep duration was defined as an average sleep duration of 6 h or less. The average sleep duration was calculated using the following formula; $[(\text{workday sleep duration} \times 5) + (\text{free day sleep duration} \times 2)]/7$; the sleep durations on the weekdays and free days were independently measured using the survey data on sleep onset and wakeup time.

The Pittsburgh Sleep Quality Index (PSQI) was adopted to assess sleep quality. The PSQI consists of 19 questions on various aspects of perceived sleep status. The total PSQI score ranges from 0 to 21 points. Poor sleep quality was defined as a PSQI score of 6 or more (14).

Anxiety and Depression Assessment

Anxiety was assessed using the Goldberg Anxiety Scale (GAS), which is composed of a total of nine items, four screening items, and five supplementary items (15). Participants who had five or more positive answers for all the items, with two or more being for the screening items, were considered as having anxiety. The Korean version GAS has a sensitivity of 82.0% and a specificity of 94.4% for diagnosing anxiety (16). This study evaluated depression using the Patient Health Questionnaire-9 (PHQ-9) (17). The PHQ-9 was developed based on the DSM-IV criteria for major depression and has been widely used in epidemiological studies (18–20). Response options were rated on a four-point scale from 0 to 3, regarding the past 2 weeks experienced. Participants with a PHQ-9 score of 10 or more were classified as having depression. The sensitivity and specificity of the Korean version of PHQ-9 were previously validated as 81.1 and 89.9%, respectively (21).

Statistical Analysis

Normality of distribution was evaluated using Kolmogorov-Smirnov test. After normality of distribution was confirmed, Student's *t*-test was used to compare two groups. If the normality of distribution was not confirmed, Mann-Whitney *U*-test was used to compare two groups. Chi-square test was used to

compare the prevalence rates. Univariable and multivariable analyses were performed to determine factors contributing to EDS among TTH individuals. For univariable analyses, factors with significant differences between TTH individuals with EDS and those without EDS were considered. For multivariable analyses, three models were developed to examine the association between EDS and TTH. In Model 1, sociodemographic factors (sex, age, size of residential area, and level of education) were adjusted. In Model 2, sociodemographic factors and sleep-related parameters (short sleep duration and poor sleep quality) were adjusted. In Model 3, sociodemographic factors and psychiatric comorbidity (anxiety and depression) were adjusted. In the final model (Model 4), sociodemographic factors, sleep-related parameters, and psychiatric comorbidity were adjusted. Statistical Package for Social Sciences version 22.0 (SPSS 22.0; IBM, Armonk, NY, USA) was used for all statistical analysis. Statistical significance was defined as a two-tailed $p < 0.05$.

Several variables had missing data because of non-response. Available data were used for the final analysis. There was no missing data for all 2,695 participants except for educational level, which had 26 non-respondents.

RESULTS

Survey

We approached 7,430 subjects and 3,114 (41.9%) subjects agreed to respond to the survey. Finally, 2,695 (36.3%) participants

completed the survey (**Figure 1**). Collected data on demographic factors (age, sex, size of residential area, and level of education) revealed no significant difference from that of the Korean general population (**Table 1**).

Prevalence of TTH, Non-headache, and EDS

Of the 2,695 participants, 570 (21.2%) had TTH while 1,422 (52.8%) did not have a headache during the previous year. Among TTH individuals, 113 (19.8%) also had PM. Three-hundred and thirteen (11.6%) participants were classified as having EDS (**Table 1**).

Prevalence of Anxiety, Depression, Short Sleep Duration, and Poor Sleep Quality

A total of 268 (9.9%) participants had anxiety while 116 (4.3%) had depression. The prevalence rates of anxiety (9.5 vs. 5.3%, $p = 0.001$) and depression (4.2 vs. 1.8%, $p = 0.001$) were significantly higher among TTH individuals than among individuals without headache. A total of 469 (17.4%) participants reported having an average sleep duration of <6 h, and were classified as having short sleep duration. A total of 715 (26.5%) participants were classified as having poor sleep quality.

EDS Prevalence in Individuals With TTH

Among the 570 participants with TTH, 63 (11.1%) reported experiencing EDS. The EDS prevalence in individuals with TTH

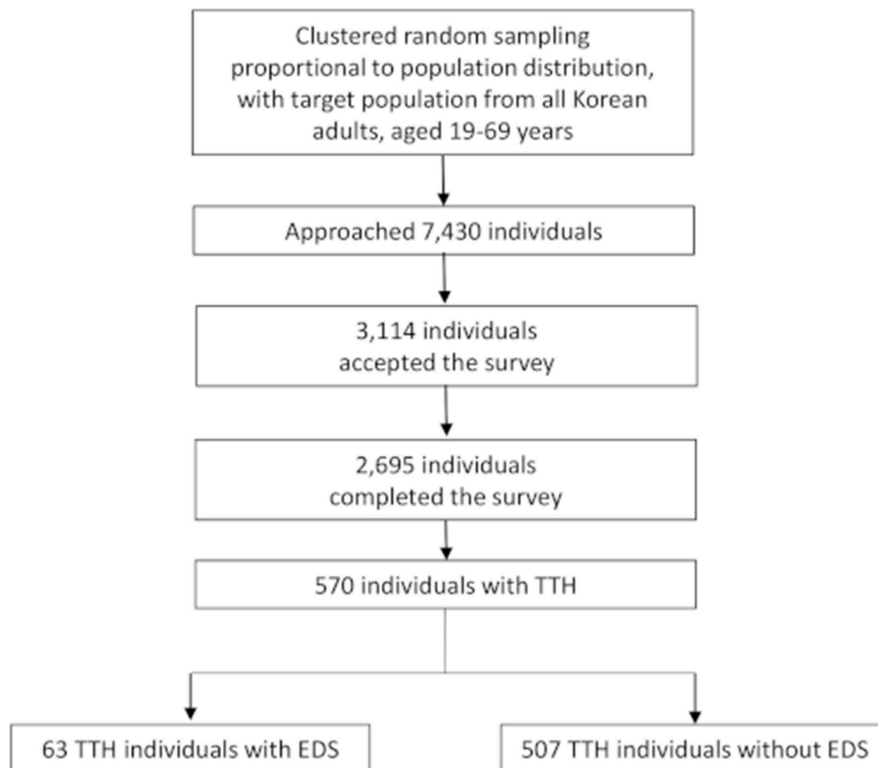


FIGURE 1 | Flow chart depicting the participation of subjects in the Korean Headache-Sleep Study.

TABLE 1 | Demographic characteristics of the survey participants; total population; and participants with tension-type headache (TTH) and excessive daytime sleepiness (EDS).

	Survey participants, N (%)	Total population, N (%)	P	TTH, N, % (95% CI)	EDS, N, % (95% CI)
Sex					
Men	1,345 (49.3)	17,584,365 (50.6)	0.854*	268, 19.9 (17.8–22.0)	161, 12.0 (10.2–13.7)
Women	1,350 (50.7)	17,198,350 (49.4)		302, 22.3 (20.1–24.6)	152, 11.3 (9.6–12.9)
Age					
19–29	542 (20.5)	7,717,947 (22.2)	0.917*	119, 22.0 (18.5–25.5)	52, 9.6 (7.1–12.1)
30–39	604 (21.9)	8,349,487 (24.0)		127, 21.0(17.8–24.3)	71, 11.8 (9.2–14.3)
40–49	611 (23.1)	8,613,110 (24.8)		131, 21.4 (18.2–24.7)	62, 10.1 (7.7–12.5)
50–59	529 (18.9)	6,167,505 (17.7)		107, 20.2 (16.8–23.7)	66, 12.5 (9.7–15.3)
60–69	409 (15.6)	3,934,666 (11.3)		86, 21.0 (17.1–25.0)	62, 15.2 (11.7–18.6)
Size of residential area					
Large city	1,248 (46.3)	16,776,771 (48.2)	0.921*	251, 20.1 (17.9–22.4)	150, 12.0 (10.2–13.8)
Medium-to-small city	1,186 (44.0)	15,164,345 (43.6)		243, 20.5 (18.2–22.8)	134, 11.3 (9.5–13.1)
Rural area	261 (9.7)	2,841,599 (8.2)		76, 29.1 (23.6–34.7)	29, 11.1 (7.3–14.9)
Education level					
Middle school or less	393 (14.9)	6,608,716 (19.0)	0.752*	96, 24.5 (20.1–28.7)	58, 14.8 (11.2–18.3)
High school	1,208 (44.6)	15,234,829 (43.8)		247, 20.5 (18.2–22.7)	135, 11.2 (9.4–13.0)
College or more	1,068 (39.6)	12,939,170 (37.2)		223, 20.9 (18.4–23.3)	119, 11.1 (9.3–13.0)
Not responded				4, 15.4 (0.5–30.2)	1, 3.8 (0.0–11.8)
Total	2,695 (100.0)	34,782,715 (100.0)		570, 21.2 (19.6–22.7)	313, 11.6 (10.4–12.8)

*Comparison of sex, age group, size of residential area, and educational level distributions between the sample in the present study and the total population of Korea.

TTH, tension-type headache; EDS, excessive daytime sleepiness; N, number; CI, confidence interval.

was not significantly different from that in individuals without headache (11.1 vs. 9.4%, $p = 0.271$). The prevalence of EDS was not significantly different between TTH participants fulfilling PM criteria and TTH participants not-fulfilling PM (11.6 vs. 8.8%, $p = 0.404$).

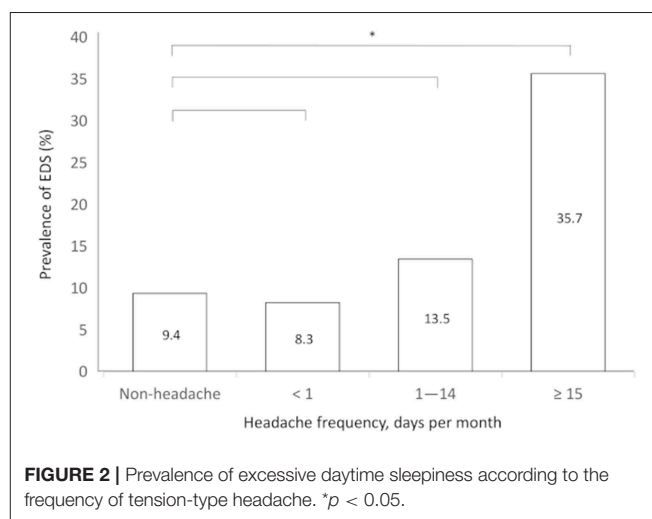
EDS prevalence was analyzed with regard to headache frequency. Individuals with 15 or more TTH attacks per month had a significantly higher EDS prevalence compared to those without headache (35.7 vs. 9.4%, $p < 0.001$). Individuals with 1–14 TTH attacks per month (13.5 vs. 9.4%, $p = 0.054$) and with <1 attack per month (8.3 vs. 9.4%, $p = 0.511$) did not have a significantly different EDS prevalence compared to those without headache (Figure 2).

Clinical Presentation of TTH According to the Presence of EDS

Osmophobia and depression were more prevalent among TTH participants with EDS compared to those without. TTH participants with EDS showed significantly higher headache frequency, visual analog scale (VAS) scores for headache intensity, and Headache Impact Test-6 scores compared to those without EDS (Table 2).

Univariable and Multivariable Analysis for Contributing Factors to EDS Among TTH Individuals

Univariable analysis showed that depression (odds ratio [OR] = 4.5, 95% confidence interval [CI] = 1.8–10.9) and poor sleep



quality (OR = 5.0, 95% CI = 2.9–8.7) were associated with an increased risk of EDS in TTH individuals. Multivariable analysis of sociodemographic factors revealed no statistically significant association with EDS (Model 1). In Model 2, which included sociodemographic factors, depression, and anxiety, depression (OR = 4.5, 95% CI = 1.7–11.7) showed increased ORs for EDS. In Model 3, which included sociodemographic factors, short sleep time, and poor sleep quality, poor sleep quality (OR = 6.6, 95% CI = 3.6–12.1) showed increased ORs for EDS; however, high school

TABLE 2 | Demographics and clinical presentation of individuals with tension-type headache (TTH) according to the presence of excessive daytime sleepiness (EDS).

	TTH with EDS (N = 63)	TTH without EDS (N = 507)	P
Demographics			
Mean age $\pm$ SD (years)	45.4 $\pm$ 13.5	42.4 $\pm$ 13.7	0.092
Women, N (%)	31 (49.2)	271 (53.5)	0.524
Headache characteristics			
Bilateral pain, N (%)	36 (57.1)	338 (66.7)	0.133
Non-pulsating quality, N (%)	24 (38.1)	203 (40.0)	0.766
Mild-to-moderate severity, N (%)	62 (98.4)	498 (98.2)	0.915
Non-aggravation by movement, N (%)	51 (81.0)	400 (78.9)	0.705
Associated symptoms			
Photophobia, N (%)	6 (9.5)	40 (7.9)	0.653
Phonophobia, N (%)	22 (34.9)	159 (31.4)	0.567
Osmophobia, N (%)	17 (27.0)	78 (15.4)	0.020
Headache frequency per month, mean $\pm$ SD	4.3 $\pm$ 8.1	1.7 $\pm$ 4.2	0.013
VAS score, mean $\pm$ SD	4.9 $\pm$ 1.6	4.3 $\pm$ 1.9	0.007
HIT-6 score, mean $\pm$ SD	47.1 $\pm$ 7.3	43.5 $\pm$ 7.6	<0.001
Anxiety	9 (14.3)	45 (8.9)	0.167
Depression	8 (12.7)	16 (3.2)	<0.001

TTH, tension-type headache; EDS, excessive daytime sleepiness; N, number; SD, standard deviation; VAS, visual analog scale; HIT-6, headache impact test-6.

graduates (OR = 0.4, 95% CI = 0.1–0.9) showed decreased ORs for EDS. In Model 4, which included sociodemographic factors, anxiety, depression, short sleep time, and poor sleep quality, poor sleep quality (OR = 6.0, 95% CI = 3.2–11.2) showed increased ORs for EDS while high school graduates (OR = 0.4, 95% CI = 0.1–0.9) showed decreased ORs for EDS (Table 3).

DISCUSSION

The key findings of this study include: (1) The overall prevalence of EDS in TTH participants was similar to that in participants without headache; (2) The prevalence of EDS among individuals with chronic tension-type headache (CTTH) was higher than that in individuals with episodic tension-type headache (ETTH) and without headache; and (3) TTH participants with EDS had a higher headache frequency, severe headache intensity, increased impact of headache, and a higher prevalence of depression compared to TTH participants without EDS.

There have been limited reports on the prevalence and impact of EDS in TTH. The prevalence of EDS in CTTH participants was found to be similar to that in participants with chronic migraine (CM). It has also been reported that individuals with a headache frequency ≥ 80 per 3 months experience EDS more frequently compared to those with a headache frequency < 80 per 3 months (22). Moreover, a previous study reported that EDS prevalence in TTH individuals did not significantly differ from that in individuals without headache (9). However, the

prevalence of EDS among individuals with CTTH in comparison with those with ETTH and without headache has not yet been reported in a population-based setting. The present study is the first to report a significantly higher prevalence of EDS among individuals with CTTH compared to that in individuals with ETTH and individuals without headache.

Epidemiological studies have reported the prevalence of EDS to range from 8 to 30%. A Singaporean study reported an EDS prevalence of 9.0% (23). A Korean population-based study using data from the Korean Genome Epidemiology Study found an EDS prevalence of 12.2% (24). An Australian study reported an EDS prevalence of 15.3% (25). The similarity in EDS prevalence between this study and previous studies suggests that the assessment of EDS in this study is reliable.

The present study found that the overall prevalence of EDS in TTH individuals was similar to that in individuals without headache; however, the EDS prevalence in CTTH individuals was higher than in ETTH and individuals without headache. These findings are similar to those of a Norwegian study that reported that the overall EDS prevalence in TTH individuals was similar to that in non-headache individuals (9). In this previous study, the prevalence of EDS in CTTH, which was reported to be higher in individuals without headache (8, 9), was similar to that in individuals with CM. The prevalence of EDS in CTTH individuals (35.7%) in the present study was somewhat higher than that in the Norwegian study (20.8%). One possible explanation for this discrepancy is the difference in ethnicity and sociodemographic distribution between the two studies. A possible reason for sociodemographic distribution difference could be that while our study used data from the KHSS, which sampled participants proportionally to the regional distribution in Korea, the Norwegian study used a community-based sample aged 30–44 from Akershus County, Norway. Therefore, this difference in sociodemographic distribution may account for the discrepancy in the prevalence of EDS in CTTH individuals between the two studies. Moreover, the cultural difference in ways of reporting sleepiness could be another source of discrepancy. A previous study reported large variations in the EDS prevalence across the world (26), with the difference in survey methods being another possible explanation for the discrepancy.

EDS is defined as the inability to stay awake and alert during major working episodes of the day, resulting in periods of irrepressible need for sleep or unintended lapses into drowsiness or sleep, based on the third edition of International Classification of Sleep Disorders (27). EDS is one of the most disabling conditions caused by poor nocturnal sleep and can lead to poorer occupational and social functioning, and is strongly related to an increased risk of vehicular and occupational accidents (28, 29). The present study found that a significant proportion of individuals with TTH had EDS. Considering the effect of EDS and daytime dysfunction, some of burden by TTH could be attributed to EDS. Therefore, proper diagnosis and treatment of EDS in TTH could be a useful way to reduce burden of TTH.

Univariable analysis in the present study showed that depression and poor sleep quality among TTH individuals were significant factors for EDS. After adjusting for potential covariates, multivariable analyses only showed high school

TABLE 3 | Logistic regression for the contributing factors of excessive daytime sleepiness (EDS) among individuals with tension-type headache (TTH).

	Univariable analysis OR, 95% CI	Multivariable analysis OR, 95% CI (Model 1)	Multivariable analysis OR, 95% CI (Model 2)	Multivariable analysis OR, 95% CI (Model 3)	Multivariable analysis OR, 95% CI (Model 4)
Sex	1.2 (0.7–2.0)	1.2 (0.7–2.1)	1.2 (0.7–2.1)	1.2 (0.7–2.2)	1.2 (0.7–2.2)
Age					
19–29	Reference	Reference	Reference	Reference	Reference
30–39	1.5 (0.6–3.6)	1.6 (0.7–4.0)	1.5 (0.6–3.8)	1.4 (0.6–3.6)	1.4 (0.6–3.5)
40–49	1.7 (0.7–4.0)	1.9 (0.8–4.6)	1.9 (0.8–4.6)	2.0 (0.8–5.0)	2.0 (0.8–5.0)
50–59	1.4 (0.6–3.5)	1.2 (0.4–3.5)	1.3 (0.4–3.6)	1.0 (0.3–2.9)	1.0 (0.3–3.1)
60–69	2.2 (0.9–5.4)	1.7 (0.6–5.3)	1.8 (0.6–5.4)	1.5 (0.5–4.6)	1.5 (0.5–4.7)
Size of residential area					
Large city	Reference	Reference	Reference	Reference	Reference
Medium-to-small city	1.2 (0.7–2.0)	1.2 (0.7–2.0)	0.5 (0.2–1.2)	1.2 (0.7–2.1)	1.1 (0.6–2.0)
Rural area	0.4 (0.2–1.3)	0.4 (0.7–2.1)	0.6 (0.2–1.6)	0.4 (0.1–1.2)	0.4 (0.1–1.2)
Educational level					
Middle school or less	Reference	Reference	Reference	Reference	Reference
High school	0.6 (0.3–1.2)	0.5 (0.2–1.2)	0.5 (0.2–1.2)	0.4 (0.1–0.9)	0.4 (0.1–0.9)
College or more	0.7 (0.3–1.3)	0.6 (0.2–1.6)	0.6 (0.2–1.6)	0.4 (0.2–1.2)	0.4 (0.2–1.3)
Anxiety	1.7 (0.8–3.7)		1.2 (0.5–2.8)		1.1 (0.5–2.7)
Depression	4.5 (1.8–10.9)		4.5 (1.7–11.7)		1.8 (0.7–5.3)
Short sleep duration (≤ 6 h)	1.2 (0.6–2.2)			0.5 (0.3–1.1)	0.5 (0.3–1.1)
Poor sleep quality (PSQI > 5)	5.0 (2.9–8.7)			6.6 (3.6–12.1)	6.0 (3.2–11.2)

Model 1, adjusted for sociodemographic factors (age, sex, size of residential area, educational level); Model 2, adjusted for sociodemographic factors, anxiety, and depression; Model 3, adjusted for sociodemographic factors, short sleep duration, and poor sleep quality; Model 4, adjusted for sociodemographic factors, anxiety, depression, short sleep duration, and poor sleep quality. OR, odds ratio; CI, confidence interval; PSQI, pittsburgh sleep quality index.

educational level and poor sleep quality as significant factors for EDS. These findings are similar to those of other studies on the association between EDS and migraine. A Norwegian study revealed that a high headache frequency and depression were significant factors for EDS in migraineurs and TTH individuals (9). Our previous study also found that depression and poor sleep quality were significant factors for EDS in migraineurs (8). These findings suggest that EDS in CM and CTTH may be improved by improving depression and poor sleep quality. Depression has been shown to be successfully treated by pharmacological and non-pharmacological treatment (30). A previous study reported that poor sleep quality was closely associated with insomnia and that insomnia could be successfully managed by improving sleep hygiene, behavioral cognitive therapy, pharmacological treatment, etc. (31). Considering that EDS is associated with an exacerbation of TTH symptoms, improving EDS may be helpful in improving TTH symptoms.

This study has several limitations. First, this study assessed EDS using the ESS rather than objective measurement. ESS is a simple self-administered questionnaire, and is the most widely used tool for assessing subjective sleepiness. The ESS score is highly correlated with partners' independent reports of the subjects' report (32). There is evidence on the validity of ESS and its usefulness in assessing EDS and its changes after treatment (33–35). We used the Korean version of the ESS, which was validated in Korean patients. This ensured that we had successfully evaluated EDS in the participants from the Korean general population. Nevertheless, objective

measurement may provide more information regarding total sleep time, sleep architecture, sleep efficacy, and other sleep derivatives. Second, we did not investigate medication use in the present study. Various medications, including anticonvulsants, antidepressants, antiemetics, antihistamines, antihypertensives, hypnotics, and muscle relaxants, may affect sleepiness (3). Third, the response rate in this study, which was 36.3%, was not high. However, we used two-stage random clustered sampling to reflect the population distribution in Korea. Moreover, there was no significant difference in the sociodemographic factors between participants in the present study and the Korean general population. Further, the prevalence of TTH and EDS was similar to that reported in previous studies. Lastly, we used 1-year time interval for the assessment of headache, TTH and without headache. Consequently, participants with TTH experienced TTH attack less than one attack per year, they were classified as participants without headache. We did not investigate participants' life-time headache or TTH and could not assess the difference in EDS prevalence between participants without TTH during their lifetimes and TTH participants experiencing less than one attack per year.

This study has several strengths. First, this study adopted the Korean version of the used questionnaires, which were previously validated for evaluating TTH, EDS, anxiety, depression, and poor sleep quality. Second, this study used a sample that reflected the Korean general population distribution, which allowed us to accurately investigate the prevalence of TTH, EDS,

anxiety, depression, and poor sleep quality with a low sampling error. Third, we investigated potential covariates, including sociodemographic factors, anxiety, depression, and poor sleep quality for EDS, and analyzed the contributing factors to EDS in TTH.

CONCLUSION

Although the overall prevalence of EDS in TTH individuals was not significantly different from that in individuals without headache, CTTH individuals had a higher prevalence of EDS compared to ETTH and individuals without headache. Furthermore, TTH participants with EDS experienced more severe symptoms of TTH compared to those without EDS. Therefore, EDS should be carefully investigated during the management of TTH.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

REFERENCES

1. Klink M, Quan SF. Prevalence of reported sleep disturbances in a general adult population and their relationship to obstructive airways diseases. *Chest*. (1987) 91:540–6. doi: 10.1378/chest.91.4.540
2. Roehrs T, Carskadon M, Dement W, Roth T. Daytime sleepiness and alertness. In: M Kryger, T Roth, W Dement, editors. *Principles and Practice of Sleep Medicine*. Philadelphia, PA: Saunders (2000). p. 43–52.
3. Howard ME, Desai AV, Grunstein RR, Hukins C, Armstrong JG, Joffe D, et al. Sleepiness, sleep-disordered breathing, and accident risk factors in commercial vehicle drivers. *Am J Respir Crit Care Med*. (2004) 170:1014–21. doi: 10.1164/rccm.200312-1782OC
4. Roth T, Roehrs TA. Etiologies and sequelae of excessive daytime sleepiness. *Clin Ther*. (1996) 18:562–76; discussion: 1. doi: 10.1016/S0149-2918(96)80207-4
5. Boullos MI, Murray BJ. Current evaluation and management of excessive daytime sleepiness. *Can J Neurol Sci*. (2010) 37:167–76. doi: 10.1017/S0317167100009896
6. Loder E, Rizzoli P. Tension-type headache. *BMJ*. (2008) 336:88–92. doi: 10.1136/bmj.39412.705868.AD
7. Stovner L, Hagen K, Jensen R, Katsarava Z, Lipton R, Scher A, et al. The global burden of headache: a documentation of headache prevalence and disability worldwide. *Cephalalgia*. (2007) 27:193–210. doi: 10.1111/j.1468-2982.2007.01288.x
8. Kim J, Cho SJ, Kim WJ, Yang KI, Yun CH, Chu MK. Excessive daytime sleepiness is associated with an exacerbation of migraine: a population-based study. *J Headache Pain*. (2016) 17:62. doi: 10.1186/s10194-016-0655-4
9. Stavem K, Kristiansen HA, Kristoffersen ES, Kvaerner KJ, Russell MB. Association of excessive daytime sleepiness with migraine and headache frequency in the general population. *J Headache Pain*. (2017) 18:35. doi: 10.1186/s10194-017-0743-0
10. Barbanti P, Fabbri G, Aurilia C, Vanacore N, Cruccu G. A case-control study on excessive daytime sleepiness in episodic migraine. *Cephalalgia*. (2007) 27:1115–9. doi: 10.1111/j.1468-2982.2007.01399.x
11. Barbanti P, Aurilia C, Egeo G, Fofi L, Vanacore N. A case-control study on excessive daytime sleepiness in chronic migraine. *Sleep Med*. (2013) 14:278–81. doi: 10.1016/j.sleep.2012.10.022

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Institutional Review Board and Ethics Committee of Hallym University Sacred Heart Hospital. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

KK: data analysis and interpretation and manuscript writing. JK and S-JC: data analysis and interpretation. W-JK, KY, and C-HY: collection and assembly of data. MC: conception and design, data analysis and interpretation, manuscript writing and critical revision.

FUNDING

This study was supported by a new faculty research seed money grant of Yonsei University College of Medicine for 2018 (2018-32-0037).

12. Cho SJ, Chung YK, Kim JM, Chu MK. Migraine and restless legs syndrome are associated in adults under age fifty but not in adults over fifty: a population-based study. *J Headache Pain*. (2015) 16:554. doi: 10.1186/s10194-015-0554-0
13. Cho YW, Lee JH, Son HK, Lee SH, Shin C, Johns MW. The reliability and validity of the Korean version of the Epworth sleepiness scale. *Sleep Breath*. (2011) 15:377–84. doi: 10.1007/s11325-010-0343-6
14. Buysse DJ, Reynolds CF III, Monk TH, Berman SR, Kupfer DJ. The pittsburgh sleep quality index: a new instrument for psychiatric practice and research. *Psychiatry Res*. (1989) 28:193–213. doi: 10.1016/0165-1781(89)90047-4
15. Goldberg D, Bridges K, Duncan-Jones P, Grayson D. Detecting anxiety and depression in general medical settings. *BMJ*. (1988) 297:897–9. doi: 10.1136/bmj.297.6653.897
16. Lim JY, Lee SH, Cha YS, Park HS, Sunwoo S. Reliability and validity of anxiety screening scale. *J Korean Acad Fam Med*. (2001) 22:1224–32.
17. Pignone MP, Gaynes BN, Rushton JL, Burchell CM, Orleans CT, Mulrow CD, et al. Screening for depression in adults: a summary of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med*. (2002) 136:765–76. doi: 10.7326/0003-4819-136-10-200205210-00013
18. Han C, Jo SA, Kwak JH, Pae CU, Steffens D, Jo I, et al. Validation of the patient health questionnaire-9 Korean version in the elderly population: the Ansan Geriatric study. *Compr Psychiatry*. (2008) 49:218–23. doi: 10.1016/j.comppsy.2007.08.006
19. Smarr KL, Keefer AL. Measures of depression and depressive symptoms: Beck Depression Inventory-II (BDI-II), Center for Epidemiologic Studies Depression Scale (CES-D), Geriatric Depression Scale (GDS), Hospital Anxiety and Depression Scale (HADS), and Patient Health Questionnaire-9 (PHQ-9). *Arthritis Care Res*. (2011) 63(Suppl. 11):S454–66. doi: 10.1002/acr.20556
20. Ell K, Unützer J, Aranda M, Sanchez K, Lee P-J. Routine PHQ-9 depression screening in home health care: depression, prevalence, clinical and treatment characteristics and screening implementation. *Home Health Care Serv Q*. (2005) 24:1–19. doi: 10.1300/J027v24n04_01
21. Choi HS, Choi JH, Park KH, Joo KJ, Ga H, Ko HJ, et al. Standardization of the Korean version of patient health questionnaire-9 as a screening instrument for major depressive disorder. *J Korean Acad Fam Med*. (2007) 28:114–9.

22. Kristoffersen ES, Stavem K, Lundqvist C, Russell MB. Excessive daytime sleepiness in chronic migraine and chronic tension-type headache from the general population. *Cephalalgia*. (2018) 38:993–7. doi: 10.1177/0333102417721133
23. Ng TP, Tan WC. Prevalence and determinants of excessive daytime sleepiness in an Asian multi-ethnic population. *Sleep Med*. (2005) 6:523–9. doi: 10.1016/j.sleep.2005.01.007
24. Joo S, Baik I, Yi H, Jung K, Kim J, Shin C. Prevalence of excessive daytime sleepiness and associated factors in the adult population of Korea. *Sleep Med*. (2009) 10:182–8. doi: 10.1016/j.sleep.2008.03.017
25. Vashum KP, McEvoy MA, Hancock SJ, Islam MR, Peel R, Attia JR, et al. Prevalence of and associations with excessive daytime sleepiness in an Australian older population. *Asia Pac J Public Health*. (2015) 27:Np2275–84. doi: 10.1177/1010539513497783
26. Soldatos CR, Allaert FA, Ohta T, Dikeos DG. How do individuals sleep around the world? Results from a single-day survey in ten countries. *Sleep Med*. (2005) 6:5–13. doi: 10.1016/j.sleep.2004.10.006
27. American Academy of Sleep Medicine. *The International Classification of Sleep Disorders : Diagnostic & Coding Manual*. Westchester, IL: American Academy of Sleep Medicine (2005).
28. Bittencourt LR, Silva RS, Santos RF, Pires ML, Mello MT. [Excessive daytime sleepiness]. *Braz J Psychiatry*. (2005) 27(Suppl. 1):16–21. doi: 10.1590/S1516-44462005000500004
29. Horne JA, Reyner LA. Sleep related vehicle accidents. *BMJ*. (1995) 310:565–7. doi: 10.1136/bmj.310.6979.565
30. Gartlehner G, Wagner G, Matyas N, Titscher V, Greimel J, Lux L, et al. Pharmacological and non-pharmacological treatments for major depressive disorder: review of systematic reviews. *BMJ Open*. (2017) 7:e014912. doi: 10.1136/bmjopen-2016-014912
31. Schutte-Rodin S, Broch L, Buysse D, Dorsey C, Sateia M. Clinical guideline for the evaluation and management of chronic insomnia in adults. *J Clin Sleep Med*. (2008) 4:487–504.
32. Johns MW. Sleepiness in different situations measured by the Epworth Sleepiness Scale. *Sleep*. (1994) 17:703–10. doi: 10.1093/sleep/17.8.703
33. Engleman HM, Asgari-Jirhandeh N, McLeod AL, Ramsay CF, Deary IJ, Douglas NJ. Self-reported use of CPAP and benefits of CPAP therapy: a patient survey. *Chest*. (1996) 109:1470–6. doi: 10.1378/chest.109.6.1470
34. Parkes D. Introduction to the mechanism of action of different treatments of narcolepsy. *Sleep*. (1994) 17:S93–6. doi: 10.1093/sleep/17.suppl_8.S93
35. Pagel JF. Excessive daytime sleepiness. *Am Fam Phys*. (2009) 79:391–6.

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Copyright © 2019 Kim, Kim, Cho, Kim, Yang, Yun and Chu. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.