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# Clinical application of headache impact test (HIT)-6 and epworth sleepiness scale (ESS) for sleep apnea headache

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## Abstract

**Background** Sleep apnea headache is a major symptom accompanying obstructive sleep apnea (OSA), but relatively little evidence has been reported on the magnitude of its negative effects on patients or the evaluation of therapeutic effects. We quantitatively assessed sleep apnea headache using the Epworth sleepiness scale (ESS) and headache impact test (HIT)-6.

**Methods** The first part of this study enrolled 86 patients (72 male; mean [± standard deviation] age 53.2 ± 13.8 years) who had been diagnosed with OSA by polysomnography in our sleep center and investigated the prevalence and characteristics of sleep apnea headache. The second part enrolled 21 patients (12 male; mean age, 47.5 ± 13.0 years) diagnosed with sleep apnea headache by polysomnography and/or peripheral arterial tonometry and evaluated the effects of OSA therapy on headache. Medical records including ESS, HIT-6, and polysomnographic data were retrospectively analyzed.

**Results** The prevalence of sleep apnea headache among OSA patients was 22.1%, and was higher in female (50.0%) than in male (16.7%). The proportion of N3 and HIT-6 score showed a significant negative correlation (Pearson's R = -0.51, $p < 0.05$). In female, median apnea–hypopnea index (AHI) was significantly lower in patients with headache (26.1 /h [interquartile range 21.4–29.6 /h]) than in patients without (54.2 /h [41.3–73.9 /h], $p < 0.05$, Wilcoxon rank-sum test). HIT-6 and ESS scores improved from 56.4 ± 9.7 to 45.9 ± 8.4 and from 9.0 ± 4.4 to 5.3 ± 4.2 in patients with oral appliance (OA), and from 54.3 ± 10.7 to 44.6 ± 6.1 and from 10.0 ± 4.0 to 4.9 ± 2.9 with continuous positive airway pressure (CPAP). In patients with good CPAP adherence, these scores improved from 58.1 ± 10.8 to 44.0 ± 6.0 and from 9.6 ± 3.8 to 3.6 ± 1.7.

**Conclusion** Among patients with OSA, prevalence of sleep apnea headache was higher in female than in male. In female, headache was associated with relatively mild OSA. OA showed substantial effects on headache in mild to moderate OSA patients. CPAP adherence was important for improving the headache. HIT-6 score appears useful for the diagnosis and management of sleep apnea headache.

**Keywords** Obstructive sleep apnea, Sleep apnea headache, Morning headache, Headache impact test 6, Epworth sleep scale, Polysomnography

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## Introduction

Excessive daytime sleepiness is one of the most common symptoms of obstructive sleep apnea (OSA), which impairs daytime performance and quality of life (QOL). Use of continuous positive airway pressure (CPAP) or an oral appliance (OA) can improve OSA, and subsequently improve OSA-related symptoms and QOL (Patil et al. 2019). Excessive daytime sleepiness can be improved by OSA treatment, and can be evaluated quantitatively using a questionnaire such as the Epworth Sleepiness Scale (ESS) (Johns 1991).

Morning headache is an important but less common OSA-related symptom. A recent cross-sectional survey in Japan revealed that approximately 20% of patients with OSA experienced headache (Suzuki et al. 2015). Morning headache related to OSA was defined as sleep apnea headache in the third edition of the International Classification of Headache Disorders (ICHD-3) (code 10.1.4). Sleep apnea headache is characterized as bilateral pressing pain unaccompanied by nausea, photophobia, or phonophobia, occurring after sleep and resolving within 4 h, and showing a close relationship with temporal development and improvement of sleep apnea. OSA patients with morning headache have shown higher ESS scores than those without such headache (Miyamoto et al. 2003). We therefore hypothesized that sleep apnea headache is closely related to subjective sleepiness and would have further negative effects on QOL in patients with OSA.

The Headache Impact Test (HIT)-6 is a questionnaire used to evaluate the effects of headache on QOL (Kosinski et al. 2003). HIT-6 quantitatively evaluates the impact of headache on QOL using a scale ranging from 36 to 78. To the best of our knowledge, no previous studies have focused on the association between sleep apnea headache and HIT-6. HIT-6 score could provide a novel index to evaluate improvements in sleep apnea, and could provide an opportunity to quantitatively study the relationship between headache and polysomnographic data. The first aim of the study was to explore the relationships among ESS, HIT-6, and polysomnographic parameters. The second aim was to quantitatively evaluate changes in sleep apnea headache with OA or CPAP therapy.

## Materials and methods

### Study protocol

We undertook a retrospective observational study as part of a study protocol on the impact of sleep apnea headache on patient QOL. The study protocol was approved by the ethics committee at Osaka Kaisei Hospital. The need to obtain written informed consent was waived based on the retrospective, noninvasive, and anonymous nature of the study design. This study was conducted in accordance with the Declaration of Helsinki.

### Patients

We retrospectively screened the medical charts of the first author's patients who had visited the sleep center in Osaka Kaisei Hospital between April 2018 and January 2020. Among these, we enrolled all patients diagnosed with OSA based on overnight attended polysomnography for the first part of the study. The sleep apnea headache was diagnosed based on ICHD 3 code 10. 1. 4. For the second part, we enrolled all patients who fulfilled the following criteria: 1) diagnosis of OSA by peripheral arterial tonometry (PAT) (Pillar et al. 2003; Schnall et al. 1999) and/or overnight attended polysomnography; 2) initiation of treatment with OA or CPAP; 3) diagnosis of sleep apnea headache based on ICHD 3 code 10.1.4; and 4) ability to complete the HIT-6 and ESS questionnaires by themselves. Patients were excluded if they: 1) were lost to follow-up within 1 month; or 2) dropped out of OA or CPAP therapy.

### Sleep duration and coffee consumption

We collected information of lifestyle habits such as sleep duration on weekdays and weekends and coffee consumption. For coffee consumption, we adopted the mean daily intake in cups; for example, if 2 or 3 cups of coffee were recorded at the same frequency, a value of 2.5 cups would be recorded. For patients who answered that they usually consumed canned coffee, we estimated one canned of coffee to be 190 ml and converted the mean based on a value of 150 ml for one cup of coffee (Buhler et al. 2013).

### Questionnaires

Patients answered the HIT-6 and ESS by filling out the questionnaires independently. A HIT-6 score of 36–49 indicates that headache has no impact on QOL, 50–55 indicates moderate impact, 56–59 indicates substantial impact, and $\geq 60$ indicates severe impact (Kosinski et al. 2003). ESS score ranges from 0 to 24, with higher scores indicating more severe daytime sleepiness (Johns 1991).

### Diagnosis for OSA

In our sleep center, PAT and/or overnight attended polysomnography (level 1 PSG) were performed to diagnose OSA. PAT was evaluated using Watch-PAT (WP200; Itamar Medical, Caesarea, Israel), a portable device for measuring respiratory events based on PAT signals (Schnall et al. 1999). We used Watch-PAT as a home screening test for OSA, whereas all polysomnographic recording was performed in-hospital (overnight and attended). Polysomnography was scored by one or two board-certified expert human scorers based on the American Academy of Sleep Medicine (AASM) scoring manual version 2.4.

### Therapy for OSA

Patients with OSA were treated with OA or CPAP. The type of treatment device was selected based on the apnea hypopnea index (AHI), using CPAP for patients with an AHI ≥ 30 /h, and custom made OA for patients with AHI < 20 /h, and according to the preference of the patient for AHI of 20–29 /h. Good therapeutic adherence to CPAP was defined as nightly use > 4 h in ≥ 70% of days in a month according to a CPAP compliance report.

### Statistics

Data were assessed for normality using the Shapiro–Wilk test. Mean and standard deviation (SD) are shown for data with a normal distribution, and median and interquartile range (IQR) for data violating the normality assumption. We adopted non-parametric statistical methods if any set of data did not follow the normality assumption. Differences among obtained means and medians for unpaired samples were analyzed using Student's t-test and the Wilcoxon rank sum test, respectively. For non-parametric paired samples, Wilcoxon signed-rank test was used. Comparisons among three groups were performed using Kruskal–Wallis analysis of variance and Tukey–Kramer post hoc test. Pearson's correlation coefficient (Pearson's R) was used to assess linear regression. Categorical variables were analyzed using the chi-squared test. All statistical tests were performed using RStudio version 1.2.1335 (R Core Team (2019). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.). Values of $p < 0.05$ were considered statistically significant. The effect size was calculated by Cramer's V for chi-squared test, by Cohen's d for Student's t-test, and by $Z/\sqrt{n}$ for Wilcoxon signed-rank test.

## Results

### Analyses of ESS, HIT-6, and polysomnographic parameters

Eighty-six patients (72 male; mean age ± SD, 53.2 ± 13.8 years) participated in the first part of the study. Table 1 shows the characteristics of sleep apnea patients with and without headache. Of the 86 patients who underwent polysomnography, 19 patients (22.1%) were diagnosed with sleep apnea headache. Mean HIT-6 score in patients with headache was 55.0, suggesting that sleep apnea headache had a moderate impact on QOL. A significantly higher frequency of female was seen among patients with headache than among patients without headache ($p = 0.016$, Cramer's V = 0.297). Sleep duration on both weekdays and weekends tended to be longer and ESS score tended to higher in patients with headache than in patients without headache, although the differences were not significant.

**Table 1** Characteristics of sleep apnea patients with and without morning headache

| | With headache | Without headache | *p* |
|---|---|---|---|
| Case | 19 | 67 | |
| Age, years | 48.4 ± 12.7 | 54.5 ± 13.9 | 0.079 |
| Sex, male/female | 12/7 | 60/7 | 0.016* |
| BMI, kg/m$^2$ | 27.4 ± 5.9 | 27.0 ± 4.3 | 0.76 |
| Sleep duration (weekend), h | 7.0 ± 1.4 | 6.7 ± 1.3 | 0.43 |
| Sleep duration (weekday), h | 7.9 ± 1.4 | 7.5 ± 1.5 | 0.32 |
| Coffee, cups/day | 1.5 (1.0–3.0) | 2.0 (1.0–3.0) | 0.42 |
| ESS | 9.0 (6.5–12.5) | 7.0 (5.0–10.0) | 0.18 |
| HIT-6 | 55.0 ± 9.8 | | |

*BMI* Body mass index. Values represent mean ± SD or median (IQR) for parametric and non-parametric data, respectively

**Table 2** Polysomnography parameters in sleep apnea patients

| | With headache | Without headache | *p* |
|---|---|---|---|
| SE, % | 83.4 (74.8–89.7) | 83.1 (71.9–89.4) | 0.81 |
| SL, min | 10.0 (6.5–14.8) | 4.5 (2.5–10.8) | 0.04 |
| Stage REM, % | 12.7 (3.4–21.5) | 14.5 (8.3–19.6) | 0.53 |
| Stage N1, % | 22.2 (17.5–40.1) | 29.4 (21.8–46.4) | 0.16 |
| Stage N2, % | 47.8 (43.0–56.3) | 48.5 (32.5–58.5) | 0.53 |
| Stage N3, % | 3.2 (0.0–14.9) | 1.2 (0.0–5.3) | 0.15 |
| AHI, events/h | 32.5 (23.0–71.7) | 45.3 (32.3–67.0) | 0.43 |
| AROI, events/h | 32.5 (21.5–57.3) | 38.9 (26.3–51.6) | 0.44 |
| PLMI, events/h | 0.0 (0.0–1.5) | 0.0 (0.0–4.3) | 0.28 |
| Lowest $SpO_2$, % | 81.0 (70.0–87.0) | 78.0 (70.0–84.0) | 0.40 |

*SE* Sleep effect, *SL* Sleep latency, *AHI* Apnea–hypopnea index, *AROI* Arousal index, *PLMI* Periodic limb movement index. Values represent median and IQR of each polysomnography parameter

Table 2 shows the results of polysomnography. No significant differences in these parameters were evident between patients with and without headache. We then investigated the correlations between polysomnographic parameters and HIT-6 and ESS scores (Table 3). The proportion of stage N3 sleep showed a significant negative correlation with HIT-6 score ($R = -0.514$, $p = 0.02$). The relationship was shown in Fig. 1, suggesting that the larger the effect of headache on QOL, the lower the proportion of slow-wave sleep. The median proportion of slow-wave sleep was 12.1% (IQR, 2.4–18.7%) in patients with relatively

**Table 3** Relationship between polysomnography parameters and questionnaire scores

| | With headache | | | | | Without headache | | |
|---|---|---|---|---|---|---|---|---|
| | | HIT-6 | | ESS | | ESS | | |
| | **Median** | **R** | ***p*** | **R** | ***p*** | **Median** | **R** | ***p*** |
| SE, % | 83.4 | -0.314 | 0.19 | 0.191 | 0.43 | 83.1 | 0.169 | 0.17 |
| SL, min | 10.0 | 0.229 | 0.35 | -0.190 | 0.44 | 4.5 | -0.079 | 0.52 |
| Stage REM, % | 12.7 | 0 | 1 | 0.109 | 0.66 | 14.5 | 0.010 | 0.94 |
| Stage N1, % | 22.2 | 0.163 | 0.50 | 0.036 | 0.89 | 29.4 | -0.078 | 0.53 |
| Stage N2, % | 47.8 | 0.725 | 0.48 | 0.002 | 0.99 | 48.5 | 0.219 | 0.08 |
| Stage N3, % | 3.2 | **-0.514** | **0.02** | -0.035 | 0.89 | 1.2 | -0.170 | 0.17 |
| AHI, events/h | 32.5 | 0.100 | 0.68 | 0.124 | 0.61 | 45.3 | -0.03 | 0.98 |
| AROI, events/h | 32.5 | -0.086 | 0.73 | -0.061 | 0.80 | 38.9 | -0.075 | 0.55 |
| PLMI, events/h | 0 | -0.041 | 0.87 | 0.013 | 0.96 | 0 | -0.108 | 0.386 |
| Lowest $SpO_2$, % | 81.0 | -0.228 | 0.35 | -0.339 | 0.16 | 78.0 | -0.220 | 0.074 |

*SE* Sleep effect, *SL* Sleep latency, *AHI* Apnea–hypopnea index, *AROI* Arousal index, *PLMI* Periodic limb movement index, *R* Pearson's correlation coefficient

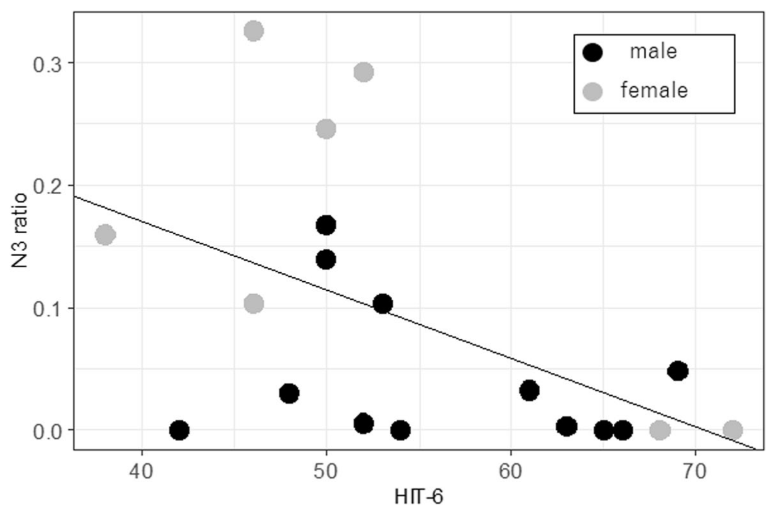


**Fig. 1** Relationship between HIT-6 score and ratio of sleep stage N3. Black and grey circles correspond to data for male and female, respectively. In the simple regression analysis, the slope and intercept were -0.00056 ± 0.0023 and 0.39 ± 0.13 (mean ± S.E., $p = 0.024$).

mild headache (HIT-6 ≤ 55) and 0% (IQR, 0–1.8%) in patients with severe headache (HIT-6 > 55). Conversely, the median proportion of slow-wave sleep was only 1.2% (IQR, 0–5.3%) in patients without headache. Taken together, the proportion of slow-wave sleep was significantly larger in the group with relatively mild headache than in other groups (Fig. 2A). Median ESS score was 7.0 (IQR, 5.0–10.0) in patients without headache, 7.0 (IQR, 4.8–9.3) in patients with relatively mild headache, and 11.0 (IQR, 10.0–14.0) in patients with relatively severe headache, showing a significant difference between patients with no and relatively severe headache (Fig. 2B). These results suggest that severity of headache was associated with daytime sleepiness, and that the degree of daytime sleepiness was similar in patients with no or only mild headache. AHI did not differ significantly among groups (Fig. 2C). Interestingly, the negative correlation between HIT-6 and N3 ratio was more marked in female than in male (Fig. 1, black v.s. grey circles).

We then studied sex differences in polysomnographic parameters. AHI and arousal index (AROI) in female are depicted in Fig. 3A. Median AHI was significantly lower in female patients with headache (26.1 /h [IQR, 21.4–29.6 /h]) than in those without headache (54.2 /h [IQR, 41.3–73.9 /h], $p < 0.05$]. No such tendency was observed in male patients (Fig. 3B). These results suggests that in female, sleep apnea headache could

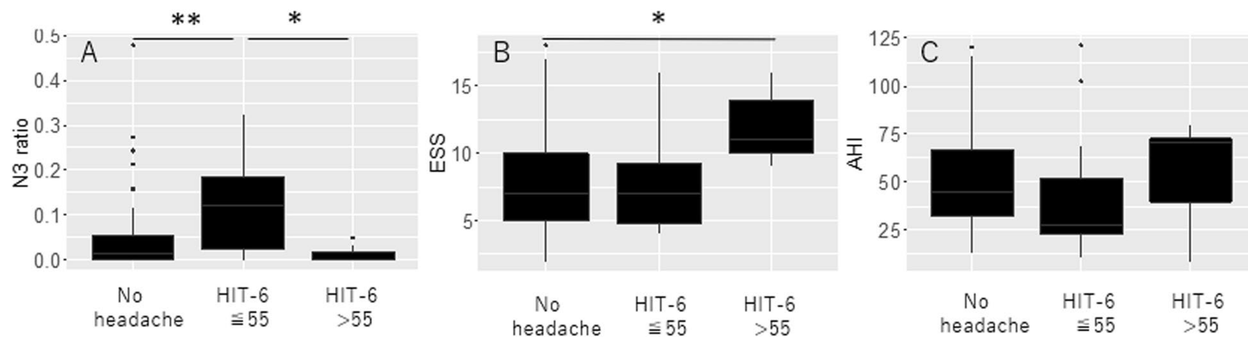


**Fig. 2** N3 ratio (A), ESS (B), and AHI (C) among patients with no headache, relatively mild headache (HIT-6 ≤ 55), and relatively severe headache (HIT-6 > 55). Kruskal-Wallis analysis of variance and Tukey-Kramer post hoc test were performed to compare each group.( $*p < 0.05$ and $**p < 0.01$). The results of Kruskal-Wallis test were shown as follows; chi-square = 9.41, df = 2, p = 0.009 for N3 ratio (A), chi-square = 8.53, df = 2, p = 0.014 for ESS (B), and chi-square = 2.38, df = 2, p = 0.30 for AHI (C).

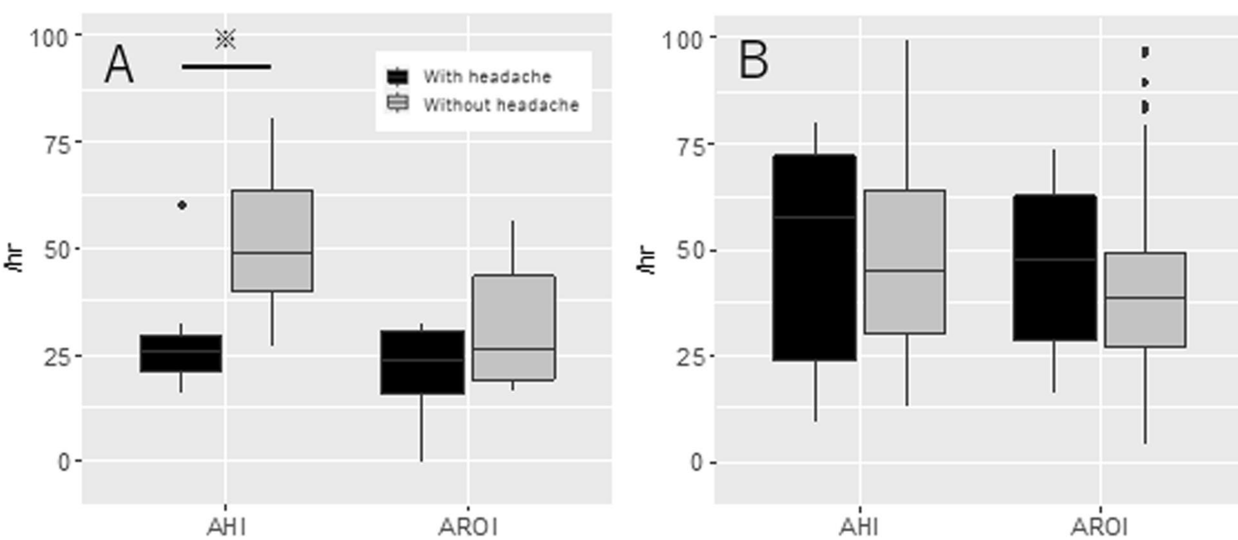


**Fig. 3** AHI and AROI in patients with and without sleep apnea headache. Results for female are shown in A, and results for male in B. $*p < 0.05$ based on the Wilcoxon rank-sum test.

accompany relatively mild OSA. The proportions of different sleep stage did not show any significant differences between patients with and without headache.

Other sex differences parameters were shown summarized in Table 4. Among male patients, patients with headache was significantly younger than those without headache (t-test, $p < 0.01$, Cohen's d = 0.819). Among patients with headache, females tended to be elder than males.

### Quantitative evaluation of sleep apnea headache following OA or CPAP therapy

The second part of this study investigated therapeutic effects on sleep apnea headache using ESS and HIT-6. Twenty-one patients with sleep apnea headache (19 patients who underwent polysomnography and 2 patients who underwent Watch-PAT) were analyzed. One of the 21 patients was diagnosed with mild OSA (AHI = 13.5 /h, HIT-6 = 68, ESS = 15) based on the Watch-PAT study, but was later diagnosed with idiopathic hypersomnia based on polysomnography and the multiple sleep latency test during OA treatment.

Of the 21 patients with OSA and sleep apnea headache, 7 received OA treatment (AHI = 17.2 ± 6.3, mean ± SD) and 14 received CPAP treatment (AHI = 58.2 ± 31.4, mean ± SD). Changes in HIT-6 and ESS over time are shown in Fig. 4. Both OA and CPAP treatments were associated with significant improvements in both HIT-6 and ESS.

To evaluate the effects of CPAP adherence on improvements in ESS and HIT-6, subgroups showing good or poor adherence to CPAP treatment were compared. Scores in the good-adherence subgroup improved more than those in the poor-adherence

**Table 4** Sex differences in parameters

| | Female | | | Male | | |
|---|---|---|---|---|---|---|
| | With headache | Without headache | *p* | With headache | Without headache | *p* |
| Case | 7 | 7 | | 12 | 60 | |
| HIT-6 | 53.1 ± 12.4 | | | 56.1 ± 8.4 | | |
| Age, years | 58.5 ± 7.0 | 59.4 ± 4.6 | 0.79 | 42.4 ± 11.6 | 53.9 ± 14.5 | < 0.001 |
| BMI, kg/m$^2$ | 26.2 ± 5.5 | 28.1 ± 3.5 | 0.45 | 28.2 ± 6.2 | 26.9 ± 4.4 | 0.49 |
| Sleep duration (weekend), h | 7.2 ± 1.8 | 6.7 ± 0.9 | 0.53 | 6.8 ± 1.2 | 6.7 ± 1.3 | 0.67 |
| Sleep duration (weekday), h | 7.9 ± 2.0 | 7.1 ± 1.2 | 0.37 | 6.5 (6.0–7.1) | 6.7 (6.0–7.5) | 0.99 |
| Coffee, cups/day | 1.3 ± 0.6 | 2.6 ± 1.9 | 0.11 | 2.0 (1.0–4.0) | 2.0 (1.0–3.0) | 0.89 |
| ESS | 9.0 (8.0–10.0) | 8.0 (6.5–8.5) | 0.10 | 9.0 (4.8–14.0) | 7.0 (5.0–10.0) | 0.55 |
| PSG full study/split night | 3/4 | 4/3 | 1 | 5/7 | 30/30 | 0.83 |

PSG full study means full-night polysomnography to diagnose OSA. Split night means both diagnostic and therapeutic studies performed in one study, where the first half is used for OSA diagnosis and the second half for CPAP titration. Values represent mean ± SD and median (IQR) for parametric and non-parametric data, respectively

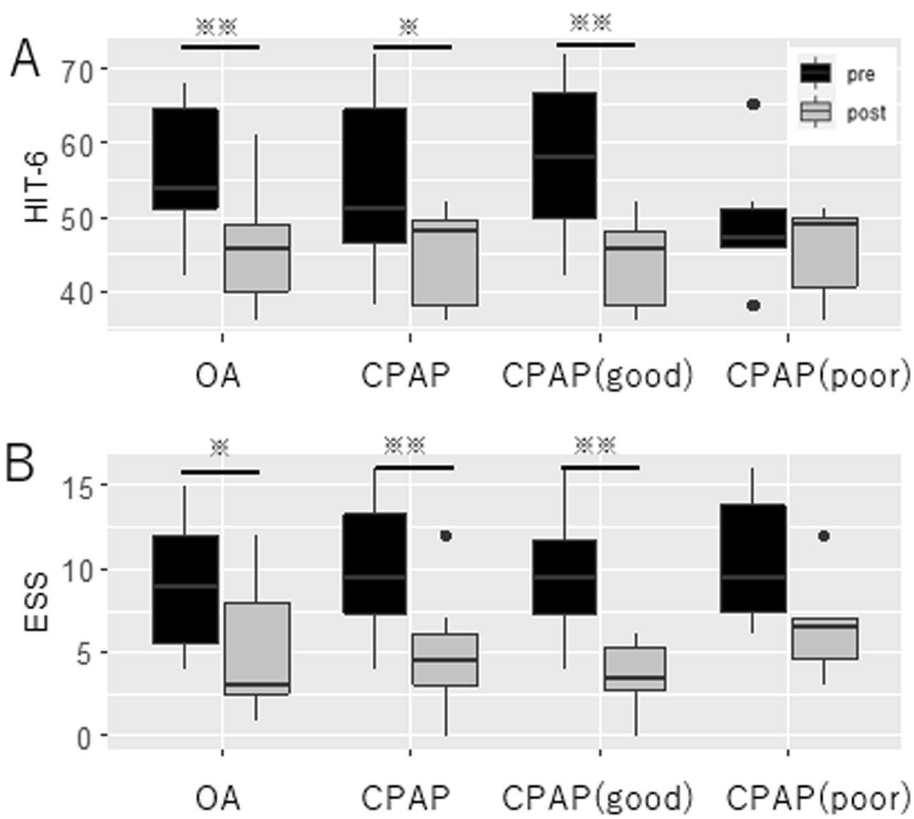


**Fig. 4** HIT-6 (A) and ESS (B) scores before and after treatment. CPAP (good) shows results in the good-adherence subgroup. CPAP (poor) shows results in poor-adherence subgroup. *$p < 0.05$ and **$p < 0.01$ based on the Wilcoxon signed-rank test. The effect size of the results with $p < 0.01$ was at least 0.55, indicating large effect size.

subgroup. In the 8 patients with good CPAP adherence, ESS and HIT-6 scores were significantly improved (Fig. 4). Conversely, no significant improvement was noted in the 6 patients with poor CPAP-adherence (Fig. 4). No significant differences in age, sex ratio, duration of follow-up, or BMI were noted between subgroups before treatment (data not shown). CPAP adherence thus seemed to play an essential role in improving sleep apnea headache. Interestingly, all patients in the poor-adherence subgroup stated that morning headache was better in the morning after using CPAP, but still did not use CPAP consistently.

## Discussion

The present study utilized HIT-6 and ESS to study sleep apnea headache. This appears to be the first report on evaluating sleep apnea headache using HIT-6. Our main results can be summarized as follows. First, the prevalence of sleep apnea headache was higher among women than among men. Second, sleep apnea headache could develop in female patients with relatively mild OSA. Third, in male, headache was accompanied in relatively younger patient. Fourth, the patient with larger effect of headache on QOL tended to show lower proportion of slow-wave sleep in polysomnography study. Finally, HIT-6 could offer a useful outcome measure for evaluating therapeutic efficacy for treatment of sleep apnea headache.

### Comparison of HIT-6 scores in sleep apnea headache and migraine

Mean HIT-6 score in patients with sleep apnea headache was 55.0, which was categorized as moderate impact (HIT-6 score: 50–55). Several studies have investigated migraine using HIT-6. For example, mean HIT-6 scores in episodic and chronic migraine have been reported as $62.5 \pm 7.8$ and $60.2 \pm 6.8$, respectively (Yang et al. 2011). A recent randomized controlled trial of erenumab showed baseline HIT-6 scores of 57.4–58.9 among Japanese patients with episodic migraine (Sakai et al. 2019), and scores of 62.7–63.3 for chronic migraine (Lipton et al. 2019). In refractory chronic migraine, HIT-6 was 67.6 (Lambru et al. 2020). HIT-6 scores in sleep apnea headache were thus generally lower than those seen in migraine.

We also found that HIT-6 scores in patients with sleep apnea headache could be improved by OA or CPAP therapy for OSA. The mean change in score was 10.0, reaching 14.1 in the good adherence group for CPAP. This reduction in the negative impact on patients QOL is not negligible, and these therapies should therefore be applied not only for the improvements in sleep breathing, but also to reduce the negative effects of morning headache on QOL.

The present study of sleep apnea headache patients did not include any with migraine. As sleep apnea could represent an aggravating factor for migraine, clarification of the relationship between sleep apnea and migraine using HIT-6 could be an avenue of future research.

### Correlation between HIT-6 and N3 ratio in sleep apnea headache patients

A significant negative correlation between HIT-6 and N3 ratio was identified in patients with sleep apnea headache. The N3 ratio was higher in patients with relatively mild headache than in patients with either relatively severe headache or no headache at all, whereas ESS scores were similar in patients without headache and patients with relatively mild headache. An increase in slow-wave sleep and relatively mild daytime sleepiness might be characteristic of patients with mild headache. We speculate that the increase in slow-wave sleep may contribute to reducing the severity of headache and sleepiness. However, our results have at least two limitations. First, this study investigated a small cohort, and second, polysomnography was only performed for a single overnight stay. Further accumulation of cases is necessary to confirm the relationship between HIT-6 and slow-wave sleep. Consistent with a previous study (Miyamoto et al. 2003), ESS scores were high in our patients with relatively severe headache, suggesting that sleep apnea headache is closely related to daytime sleepiness.

## Sex differences in sleep apnea headache

The current study showed a sex difference in the characteristics of sleep apnea headache. The prevalence of sleep apnea with morning headache was higher in women than in men. Female patients with sleep apnea headache showed a lower AHI than female patients without headache, suggesting that severity of sleep apnea was not important for the complication of sleep apnea headache. Such tendencies were not observed in male patients. Among male, patients with sleep apnea headache were relatively young. One might concern about small number of female patients, therefore, larger study is necessary to validate our results, especially in sex differences. Recently, the evidence of sex differences in sleep apnea has been growing (Costa et al. 2019). Differences in hormones, structure and physiological behavior of the upper airway, craniofacial morphology, and patterns of fat deposition and respiratory stability may contribute to sex differences in sleep apnea (Manber et al. 2003; Pillar et al. 2000). The present study suggests that the headache induced by sleep apnea represents another important aspect of sex differences in sleep apnea.

### ESS and HIT-6 as outcome measures to evaluate sleep apnea therapy

We studied sleep apnea headache using the ESS and HIT-6 questionnaires as quantitative evaluation scales. Both OA and CPAP treatment improved scores, and patients with good adherence to CPAP showed better improvements than those with poor adherence. Total ESS score changed from 9.0 to 5.3 with OA treatment, and from 9.6 to 3.6 with good adherence to CPAP. HIT-6 score changed from 56.4 to 45.9 in the OA treatment group, and from 58.1 to 44.0 with good adherence to CPAP. These results suggest that, in terms of improving sleep apnea headache, OA provides sufficient efficacy for mild to moderate OSA, while CPAP is effective for severe OSA as long as satisfactory adherence is achieved.

We also found that CPAP adherence was important for improving HIT-6 score. Several studies have examined the importance of CPAP use for ≥ 4 h/night in patients with hypertension (Bratton et al. 2014; Barbé et al. 2012), cardiovascular disease (Peker et al. 2016; Abuzaid et al. 2017), and heart failure (Kasai et al. 2008). The present study provided evidence that, concordant with circulatory disorders, 4 h/night is the target duration for CPAP use among patients with sleep apnea headache.

Thus, CPAP is a highly effective therapy to improve sleep apnea headache, but it strongly depends on the adherence. The previous study of big data on US citizen the 90-days adherence rate (> 4 h usage of CPAP for more than 70% of the night) was 75% (Cistulli et al. 2019). Therefore, in some patients, non-CPAP therapy could be a better sustainable effective therapy (Arachchige and Stieier 2022). In consistent with previous study evaluated by using VAS (Park et al. 2021), our results indicated that OA provided enough effect to improve headache. OA should be considered as a strong candidate of treatment to improve headache for patient with mild to moderate OSA.

### Clinical importance and limitation

To our knowledge, this is the first study to utilize HIT-6 to evaluate the sleep apnea headache defined by ICHD3. Although the OSA could influence on other primary headaches (Johnson et al. 2012; Chiu et al. 2015), we strictly focused on the sleep apnea headache. In addition, level 1 PSG was performed to strict diagnose of OSA in most cases of the study. Nevertheless these some key strengths, the number of the subjects was small, and not enough to get large effect size in some statistical tests (e.g., Cramer's V was 0.297). To generalize the present results, further accumulation of cases is necessary.

## Conclusion

This is a pilot study on evaluating sleep apnea headache using HIT-6. Prevalence of sleep apnea headache was higher among female than among male. The characteristics of patients with sleep apnea headache showed some sex differences; the prevalence of sleep apnea headache was higher among female, in female patients headache was associated with relatively mild OSA and was accompanied in relatively elder patients, and in male patients headache tended to be accompanied in relatively younger patient. HIT-6 score appears useful for the diagnosis and evaluation of sleep apnea headache. OA showed substantial efficacy against mild to moderate OSA and adherence was important for patients treated using CPAP. Due to the small number of subjects, further accumulation of cases is necessary to generalize the results.

### Abbreviations

| | |
|---|---|
| OSA | Obstructive sleep apnea |
| ESS | Epworth sleepiness scale |
| HIT-6 | Headache impact test 6 |
| AHI | Apnea–hypopnea index |
| CPAP | Continuous positive airway pressure |
| ICHD | International classification of headache disorders |


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### Authors' contributions

HT participated in the collection of data, analysis, and prepared the manuscript for publication. MK checked the validity of data analysis. MK, MT, and MO participated in supervising and writing manuscript. All authors read and approved the final manuscript.


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### Availability of data and materials

All data used to support the findings of this study and included within the manuscript and supporting information.

## Declarations

### Ethics approval and consent to participate

The study protocol was approved by the ethics committee at Osaka Kaisei Hospital. The need to obtain written informed consent was waived based on the retrospective, noninvasive, and anonymous nature of the study design. For the purpose of anonymity, the participant's name was not used at the time of data collection, and all other personnel information was kept entirely anonymously and confidentiality was assured throughout the study period.

### Consent for publication

Not applicable.

### Competing interests

The author declares no competing interests.


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