Table 4. Stepwise linear regression for variables contributing to ESS score

	Explanatory variables in model	Coefficient	*t*	*P*	R^2
Total subjects ($n = 230$)	Age	−0.08	−3.77	<0.001	
	AHI	0.03	3.34	0.001	
	Hs	0.07	2.92	0.004	0.14

AHI, apnea–hypopnea index; ESS, Epworth Sleepiness Scale; Hs, hypochondriasis.

remained within normal limits,[20] and there was no significant correlation between the SDS score or D score on MMPI and ESS among the OSAS subjects from the results of multiple regression analysis. Therefore, we speculated that the modest variation in depressive symptoms would not influence subjective daytime sleepiness.

It was noteworthy that Hs score on MMPI appeared as an independent factor influencing subjective daytime sleepiness despite a lack of pathological deviation of all items on this test among the subjects. Considering the strong correlation between Hs and D or Hy or Pd or Pt or Sc, certain personality characteristics relating to these scores could affect the level of subjective daytime sleepiness in patients with OSAS.

The present study had several limitations as follows. First, we did not analyze the relationship between ESS and objective measures of sleepiness including Multiple Sleep Latency Test (MSLT) or Maintenance of Wakefulness Test (MWT). It has been reported that there is a discrepancy between ESS and the results of MSLT or MWT.[6,7] In order to clarify whether subjective sleepiness reflects sleep tendency or perception of sleepiness in OSAS patients, we should compare the finding of ESS with the results of MSLT or MWT. Second, we could not estimate the difference in the ESS findings and its associated factors between male and female OSAS patients. It has been shown that female OSAS patients tend to be more depressive than male patients.[34,35] Future study would be necessary for clarifying the gender difference in daytime sleepiness among OSAS subjects. Third, in the present study we could not compare the findings of psychometric variables between OSAS patients and normal controls. However, it has been reported that OSAS patients had higher scores on some MMPI items compared with normal controls.[36,37] Moreover, Ramos *et al.* indicated that the scores could change after appropriate treatment for OSAS.[38] To clarify the cause and effect relationship between personality characteristics and subjective sleepiness, we should investigate the changes in both the MMPI and ESS after appropriate treatment. Fourth, although it has been reported that educational status may influence subjective sleepiness,[39] we did not investigate the relationship between ESS and this factor. However, the present results suggest that subjective daytime sleepiness in patients with OSAS is significantly influenced not only by the respiratory disorder indices but also by both personality characteristics and age. Taking the present results into consideration, we would like to conduct a systematic investigation on the mechanisms of residual sleepiness in OSAS patients after treatment with nasal continuous positive airway pressure.[40]

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ORIGINAL ARTICLE

Functional contribution of mandibular advancement to awake upper airway patency in obstructive sleep apnea

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Abstract In the narrowed upper airway of patients with obstructive sleep apnea (OSA), a neuromuscular compensatory mechanism augments the activity of the upper airway dilator muscles in defense of upper airway patency, particularly during inspiration. We hypothesized that mechanical enlargement of the upper airway by a mandibular advancement oral appliance would permit a reduction in this neuromuscular compensation during wakefulness. To test this hypothesis, we focused on changes in the cross-sectional (CS) area of the upper airway before and after emplacement of a ventrally titrated oral appliance in 12 awake OSA patients. The CS areas at the end of tidal expiration (CS area-EET) and at the nadir of intraluminal pressure during inspiration (CS area-IN) were obtained using videoendoscopy. The median apnea–hypopnea index decreased with mandibular advancement. Before mandibular advancement, there was no difference between CS area-EET and CS area-IN in the velopharynx, oropharynx, and hypopharynx. This indicates that upper airway dilator muscle activity increased during inspiration to counteract the intraluminal negative pressure of the upper airway. After mandibular advancement, CS area-EET increased in the velopharynx, oropharynx, and hypopharynx, but CS area-IN was unchanged at any level and was less than CS area-EET in the velopharynx and oropharynx. These findings suggest that mandibular advancement enlarges the upper airway and may reduce upper airway dilator muscle activity during inspiration. We conclude that oral appliances act to return the upper airway towards a normal configuration and pattern of muscle function in OSA patients.

Keywords Obstructive sleep apnea · Mandibular advancement · Upper airway · Cross-sectional area · Upper airway muscle activity

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Introduction

Recent practice parameters have clearly summarized the usefulness of oral appliances not only for individuals with mild obstructive sleep apnea (OSA) but also for moderate OSA patients [1]. Anatomically, oral appliances increase the upper airway size at multiple levels by mandibular advancement, and this may be important in producing their clinical effect [2]. However, effects of oral appliances on functional aspects including upper airway dilator muscle activity are still unknown [3].

The compliant human upper airway exhibits unique static and dynamic behavior. The cross-sectional (CS) area of the upper airway is determined by transmural pressure (Ptm), the difference between intraluminal pressure (Plumen) and

oropharyngeal soft tissue pressures (Ptissue) [4, 5]. Thus, airflow during inspiration (IN), which reduces the Plumen, might decrease the Ptm, leading to a decreased upper airway CS area. However, this is not always the case with OSA patients during wakefulness because a neuromuscular compensatory mechanism augments the activity of the upper airway dilator muscles in defense of upper airway patency [6]. This increase in dilator muscle activity acts to stiffen as well as enlarge the upper airway, which would result in reducing the Ptissue [7]. By focusing on the changes in the CS area during wakefulness, we can increase our understanding of the functional effects on the upper airway of mandibular advancement produced by an oral appliance used in the treatment of OSA.

Under static conditions (i.e., end-tidal expiration; EET), mandibular advancement increases the CS area of the upper airway in both control subjects and patients with OSA [2]. However, the influence of mandibular advancement on the CS area during IN, when actual collapse of the upper airway during sleep occurs, is not known. We have previously shown in a subgroup of eight patients with OSA and comparable control subjects in terms of body mass index (BMI) that the CS area of the upper airway did not change significantly between EET and the nadir of Plumen during IN, although the shape of the upper airway changed [8]. We have also demonstrated that oral appliances increase the CS area of the upper airway during wakefulness at EET [9]. Because mandibular advancement increases the CS area and decreases the collapsibility of the passive pharynx [10], oral appliance emplacement would also be expected to alter the dynamic changes in the upper airway during the respiratory cycle while awake and asleep. A larger, less-collapsible upper airway would improve airflow dynamics, which in turn would require less activity of the upper airway dilator muscles to maintain patency.

We hypothesized that the CS area at EET (CS area-EET) would be increased but the CS area at the nadir of Plumen during IN (CS area-IN) would remain unchanged after mandibular advancement by oral appliance emplacement, the resultant tidal difference in the CS area reflecting a lesser degree of Pmuscle. Thus, the purpose of this study was to evaluate changes in the CS area of the upper airway during wakefulness at EET and IN in response to a ventrally titrated oral appliance in patients with OSA. Some of the results of this study have been reported previously [9].

Materials and methods

Subjects

Twelve male OSA patients who elected to pursue oral appliance therapy were recruited for this study. Their median (interquartile range) age was 46 (32–53) years and BMI was 31 (27–34) kg/m^2. Each patient provided written informed consent, and the study protocol was approved by the Clinical Screening Committee for Research and Other Studies Involving Human Subjects at the University of British Columbia (UBC). Details of study aims and methods were introduced to all subjects; however, they were blinded to the possible results of the study.

Diagnostic polysomnography

All patients were diagnosed with OSA based on full overnight polysomnography performed at the Sleep Disorders Clinic of the UBC Hospital in Vancouver. After the maximal ventral advancement consistent with patient comfort had been attained, a second overnight polysomnogram was performed with the titratable oral appliance in place.

Titration of oral appliance

A two-piece titratable oral appliance (Klearway™; Space Maintainers Laboratories Canada, Vancouver, BC, Canada; Fig. 1) was used to reposition the mandible ventrally [11, 12]. Optimal jaw position was defined as a comfortable forward repositioning of the mandible whereby OSA symptoms were reduced. Details of the oral appliance including adjustment and titration protocol have been reported previously [11, 12].

Videoendoscopy and Image analysis

Videoendoscopic images from all subjects were obtained at the Respiratory Sleep Laboratory of Vancouver Hospital and

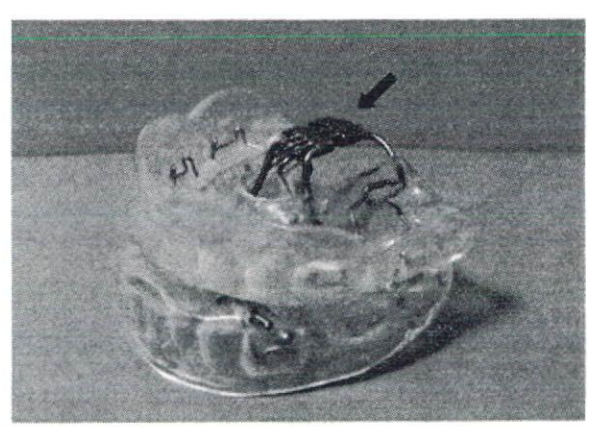

Fig. 1 Klearway™ titratable oral appliance. The adjustable screw mechanism (*arrow*), which is located in the palatal arch, permits 11 mm of mandibular protrusion in 44 increments of 0.25 mm and also allows vertical and horizontal jaw movement

Health Sciences Centre. After applying topical anesthesia (cocaine 4%, less than 1 mL total dose) with cotton swabs to the nasal passages only with the patient seated upright, each patient was studied in the supine position while awake during quiet nasal breathing with the mouth closed. The subject's head position was fixed with the soft tissue Frankfort horizontal plane perpendicular to the floor using tape placed across the forehead. A thin, flexible fiberoptic endoscope (Olympus LF2; Olympus Corporation, Lake Sweeny, NY; outer diameter 3.8 mm) and an esophageal pressure transducer (Model MPC-500; Millar Instruments, Houston, TX; outer diameter 1.7 mm) were passed through the nose into the pharynx and lower esophagus, respectively. The pressure transducer was positioned in the esophagus approximately 10 cm above the diaphragm. The pressure signals were amplified (Millar), displayed on a computer monitor, and stored in a computer (Direct Physiological Recording System; Raytech Instruments, Vancouver, BC, Canada) for later analysis. A medical television camera (Olympus OTV2), attached to the endoscope, generated images of the upper airway lumen, which were recorded continuously and time coded on videotape (Video Cassette Recorder Model VO9850; Sony, Japan) using a time code generator for subsequent analysis. Specific anatomical levels were measured in sequence beginning in the hypopharynx (just distal to the tip of the epiglottis), then the oropharynx (between the uvula and the epiglottis), and the velopharynx (just proximal to the free margin of the soft palate). Images were first obtained without the oral appliance and then with the oral appliance in place.

Image analysis

The analysis of the videoendoscopic images was performed using our previously reported technique by a technician who was blinded to the polysomnographic data [2]. The upper airway CS area was measured from the stored images using a high-resolution frame grabber (Model DT3851; Data Translation, Marlboro, MA) and image-processing software (Global Lab Image; Data Translation). Signals from the time code generator and esophageal pressure transducer were stored online in a computer (80486; ANO Automation, Vancouver, BC, Canada), enabling selection of images based on simultaneous pressure measurements. Measurements were at EET and IN as determined from the simultaneous esophageal pressure recording.

The representative videoendoscopic images and the reproducibility of our image analysis have already been reported in our previous study [2, 9]. Briefly, the airway lumen was traced freehand to generate a region of interest that was quantified based on the number of enclosed pixels. The border between the airway and the soft tissues was determined visually. To ensure the consistency of location of the traced images before and after oral appliance emplacement, unique mucosal landmarks on the posterior pharyngeal wall in each patient were used. All measurements of the CS area were made using the diameter of the intraluminal catheter as a linear calibration. Only images which encompassed the entire upper airway lumen were included in the analysis. Measurements were carried out in duplicate for 15 separate determinations of the CS area, five each in the hypopharynx, oropharynx, and velopharynx. These measurements yielded a coefficient of variation of 3.8%. Accordingly, errors of less than 5% were obtained when measurements using this tracing technique were performed on images of the upper airway CS area ranging between 100 and 400 mm^2 [9].

Statistical analysis

The distribution of the data was checked before statistical analysis. Data were expressed as median (interquartile range), and Wilcoxon signed rank test was used to compare the differences in each variable between EET and IN values and between baseline and after titration values. A p value of less than 0.05 was considered to be statistically significant.

Results

The time from initiation of oral appliance usage to the commencement of titration was 28 (10–35) days. The titration period lasted 98 (82–119) days. The effects of the oral appliance on respiratory and sleep variables are summarized in Table 1. Median apnea index (AI) and apnea–hypopnea index (AHI) decreased with oral appliance therapy after ventral titration of the mandibular position (AI, $p<0.01$; AHI, $p<0.001$). Nine of 12 patients (75%) showed a reduction in AHI to less than 10. In addition, based on a robust definition of AHI cutoff criteria [13], a complete response to the oral appliance (follow-up AHI of <5) was observed in four patients (33%), and a partial response (follow-up AHI of >50% reduction in AHI) was seen in 6 (50%) of the 12 patients (Fig. 2). The minimum arterial oxygen saturation (SaO_2) improved ($p<0.05$). The arousal index decreased ($p<0.001$). There was no significant change in BMI during the study.

Table 2 shows the effects of mandibular advancement by the ventrally titrated oral appliance on the CS area of the upper airway in 12 male OSA patients. Before mandibular advancement, there was no significant difference between CS area-EET and CS area-IN in the velopharynx, oropharynx, or hypopharynx. After mandibular advancement with the oral appliance in place, the CS area-EET of the velopharynx increased by 26% ($p<0.01$), the oropharynx by 10% ($p<0.05$), and the hypopharynx by 15% ($p<0.05$). There were no significant changes in the CS area-IN at any level of the

Table 1 Effects of a mandibular advancement oral appliance on respiratory and sleep variables in 12 male patients with obstructive sleep apnea

	Before insertion	After titration
BMI (kg/m^2)	31 (28–34)	30 (26–32)
AI (events/h)	4 (2–50)	0 (0–1)**
AHI (events/h)	28 (9–32)	8 (2–12)***
Minimum SaO_2 (%)	81 (79–83)	86 (82–92)*
Total sleep time (min)	332 (303–350)	344 (327–359)
Non-REM sleep (%)	83 (81–85)	81 (78–83)
REM sleep (%)	17 (15–18)	19 (17–22)
Arousal Index (/h)	24 (12–26)	14 (5–22)**

Values are expressed as median (interquartile range)
BMI Body mass index, *AI* apnea index, *AHI* apnea–hypopnea index, SaO_2 arterial oxygen saturation, *REM* rapid eye movement
*p<0.05 versus before insertion,
**p<0.01 versus before insertion
***p<0.001 versus before insertion

upper airway after oral appliance emplacement. The median CS area from EET to IN decreased significantly by 28% ($p<0.05$) in the velopharynx and 41% ($p<0.05$) in the oropharynx. This contrasted with increases in the CS area from EET to IN before mandibular advancement of 30% in the velopharynx and 10% in the oropharynx.

Discussion

There are two main findings in this study. First, before mandibular advancement, the CS area at each level of the upper airway remained essentially unchanged throughout the respiratory cycle. This suggests that upper airway dilator muscle activity probably increased during IN to counteract the negative Plumen in the upper airway. Second, although mandibular advancement increased the CS area at EET in the velopharynx, oropharynx, and hypopharynx, the CS area during IN remained unchanged. Simultaneously, the CS area from EET to IN decreased in the velopharynx and oropharynx. To explain these findings, we speculate that a reduction in upper airway collapsibility produced by mandibular advancement lessens the requirement for an increase in upper airway dilator muscle activity during IN in defense of upper airway patency in OSA patients.

Although our data suggest that mandibular advancement affects the dynamic behavior of the awake upper airway during the respiratory cycle, our technique and measurements have significant limitations. First, results obtained from an awake study should be interpreted with caution regarding inferences about upper airway occlusion that occurs during sleep. It is not possible to directly translate physiological responses of the upper airway observed during wakefulness to those occurring during sleep. We did not record upper airway dilator muscle (e.g., genioglossus [GG]) activity during our study, as it is difficult to obtain consistent signals with an oral appliance in place. Thus, our conclusions about upper airway muscle activity are inferential. Second, insertion of an endoscope and catheter into the upper airway might have had a significant effect on the airflow and pharyngeal resistance. However, the CS area of the instruments was small in relation to the upper airway CS area, and furthermore, cocaine acts as a nasal decongestant, thereby increasing the CS area of the nasal passages. Still, topical anesthesia applied to the nasal passages could affect reflex activities in the upper airway. Third, we selected only male subjects, and the influence of gender on the CS area changes was not addressed in this study. Women are reported to have a different upper airway configuration than men [14], and female OSA patients have a less compromised upper airway than male patients with OSA from an anatomical [15] and functional [16] perspective. These differences may yield different effects of mandibular advancement on the CS area of the upper airway in women. Fourth, our study is limited to an assessment of the CS area. In other words, it does not include other dimensions such as airway length. One of the factors in the male predisposition to upper airway collapse is an increased upper airway length [15]. Finally, selection bias because of the small study population needs to be emphasized. For example, we could not standardize the craniofacial features and baseline AHI, which might be factors determining the response to the oral appliance. In addition, the fact that the hypopharynx showed somewhat different behavior compared to the velopharynx and the oropharynx merits further study in a larger sample size.

The CS area of the upper airway is an exponential function of Ptm across the upper airway wall [4, 5]. As described earlier, Ptm of the upper airway is defined as Plumen minus surrounding tissue pressure, Ptissue. An increase in Ptm, caused either by a more positive Plumen or more negative Ptissue, increases the CS area of the upper airway. Conversely, a decrease in Ptm, caused either by a

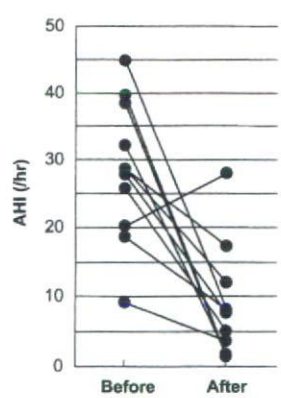

Fig. 2 Apnea–hypopnea index (*AHI*) before and after mandibular advancement

Table 2 Effects of mandibular advancement on the cross-sectional area of the upper airway in 12 male patients with obstructive sleep apnea

	EET	IN	r(EET→IN) (%)
Velopharynx			
Before (mm^2)	82 (60–144)	97 (65–161)	30 (−43–247)
After (mm^2)	124 (113–156)****	102 (87–169)	−28 (−60–63)*
r (Before→After) (%)	26 (5–80)	10 (−18–56)	
Oropharynx			
Before (mm^2)	100 (89–148)	115 (107–183)	10 (−26–93)
After (mm^2)	119 (90–175)***	101 (72–113)	−41 (−46–25)*
r(Before→After) (%)	10 (−6–47)	−17 (−35–10)**	
Hypopharynx			
Before (mm^2)	63 (41–79)	46 (26–115)	−12 (−27–62)
After (mm^2)	57 (44–90)***	105 (24–127)	−34 (−47–112)
r (Before→After) (%)	15 (−5–51)	10 (−12–50)	

Note that the cross-sectional area of the hypopharynx at end-tidal expiration decreased from 63°mm^2 before mandibular advancement to 57°mm^2 after protrusion; however, ρ(Before→After) (%) in 12 patients are statistically significant. This is because data are not normally distributed and statistics were calculated nonparametrically. Values are expressed as median (interquartile range).

EET Cross-sectional area at end-tidal expiration, *IN* cross-sectional area at the nadir of intraluminal pressure during inspiration, *Before* cross-sectional area before mandibular advancement, *After* cross-sectional area after mandibular advancement, *ρ(EET→IN) (%)* difference in cross-sectional area between end-tidal expiration and inspiration, *ρ(Before→After) (%)* difference in cross-sectional area between before and after mandibular advancement

*p<0.05 versus before insertion

**p<0.05 versus EET

***p<0.05 versus before insertion

****p<0.01 versus before insertion

more negative Plumen or more positive Ptissue, decreases the CS area of the upper airway. At a constant Plumen, Ptissue is determined by the balance between the amount of soft tissue inside the bony enclosure of the upper airway (i.e., positions of the maxilla and the mandible) and the size and position of the bony enclosure [5]. Mandibular advancement by an oral appliance in the present study had no effect on the volume of the upper airway soft tissues. Thus, quite apart from modulation of upper airway dilator muscle activity, we speculate that protrusion of the mandible itself acts to change the position and size of the bony enclosure, thereby reducing Ptissue in awake OSA patients as reported by Isono et al. [17] when they succeeded in decreasing Ptissue in the passive pharynx in patients with OSA. This speculation is also supported by a recent animal study in which mandibular advancement reduced the anterior and lateral soft tissue pressure in anesthetized rabbits [18].

Before describing the possible effects of a ventrally titrated mandibular position on the maintenance of velopharyngeal and oropharyngeal airway patency, the authors feel that the factors controlling the GG muscle activity should be summarized here. White [19] reported that there are three primary neural inputs controlling GG muscle activity. First, negative pressure in the upper airway reflexively activates mechanoreceptors in the upper airway that ultimately leads to an increased hypoglossal output to the GG muscle. Second, motor nuclei-controlling GG muscle receives input from central pattern-generating neurons located in the ventral medulla. Third, neurons modulating arousal have a tonic excitatory influence on the GG muscle through hypoglossal motoneurons. All of these three inputs would mainly form the inspiratory-phasic and tonic activity of the GG muscle. Activation of the GG muscle is clinically appealing in that it would reduce Ptissue and increase Ptm by stiffening the upper airway, although it is currently unknown whether mandibular advancement could either decrease or increase GG muscle activity in patients with OSA. However, both the phasic and tonic activity of GG should be differentiated when it comes to discussing the influence on these activities by external stimuli. In a subsequent discussion, we define tonic GG muscle activity as the baseline activity of the GG and phasic GG muscle activity as the difference between peak inspiratory-phasic and tonic GG muscle activity.

Before mandibular advancement, despite a more negative Plumen and, therefore, a decreased Ptm during IN, there was no significant difference between the CS area-EET and CS area-IN (Fig. 3a–b). We speculate that the CS area is maintained during IN mainly by augmented input from the mechanoreceptor in the upper airway, which could increase phasic GG muscle activity as an effort to defend upper airway patency. This result is similar to a report from Schwab et al. [20]. They reported in a computed tomographic study of OSA patients that CS area-IN was greater than CS area-EET and concluded that augmentation of

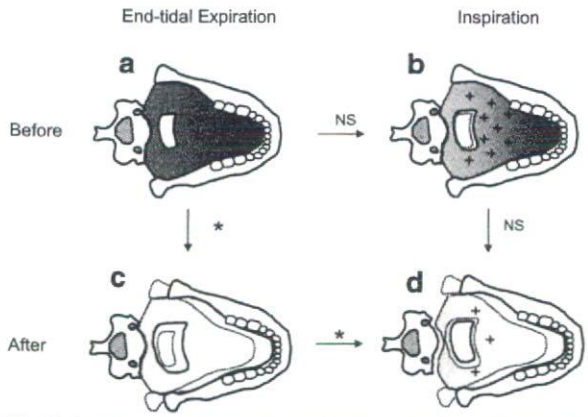

Fig. 3 Schematic illustration to show the possible effects of mandibular advancement on the maintenance of velopharyngeal and oropharyngeal patency. The fewer the number of *plus symbols*, the less the upper airway muscle activity. *Increased shading density* indicates increased tissue pressure (Ptissue). *Asterisk*, $p<0.05$; *NS* not significant. **a, b** Before mandibular advancement. **c, d** After advancement of the mandible

upper airway dilator muscle activity during IN might be a factor. Increased phasic GG muscle activity could also act to stiffen the upper airway and thereby decrease Ptissue [7].

After advancement of the mandible, the CS area-EET increased significantly (Fig. 3a–c). This increase is probably due to a reduction in Ptissue and a configurational change in the upper airway caused by ventral traction on the tongue and passive stretching of the upper airway soft tissues including the muscles, although it is unknown whether mandibular advancement could reduce or augment tonic activity of the GG muscle. Currently, effects of mandibular advancement on tonic GG activity remain to be investigated. However, tonic GG muscle activity is augmented in OSA patients compared to controls as a defensive mechanism to maintain the compromised upper airway throughout respiration, although the underlying mechanism is also unclear [6, 21]. Anatomically, we speculate that a few peripheral factors could contribute to increasing the tonic activity of the GG muscle by mandibular advancement because protrusion of the mandible also changes the configuration of the GG muscle. Tsuiki et al. [22] demonstrated that mandibular advancement augmented tonic GG muscle activity in awake control subjects. Takahashi et al. [23] also succeeded in confirming an increase in the tonic GG muscle activity with mandibular advancement in healthy controls during wakefulness. To support these findings, there are some plausible explanations. The hyoid bone as well as the tongue moves forward in association with the mandibular protrusion because some fibers of the inferior portion of the GG muscle run from the mental spine to the hyoid bone [24], similar to the geniohyoid muscle. However, the degree of forward movement of the hyoid bone is less than that of the mandible [25] because the pharyngeal muscles that attach to the hyoid bone antagonistically restrict the ventral repositioning of the hyoid bone. Accordingly, it appears that mandibular advancement lengthens and tenses the GG muscle, leading to augmentation of the input from the proprioceptors in the GG muscle. In addition, some electromyographic studies have revealed that GG muscle activity was reflexively increased by receiving outputs from the proprioceptors in the temporal muscle (the jaw–tongue reflex) both in cats [26] and humans [27] when mandibular position changed. This would provide additional tonic excitatory effects on the GG muscle throughout the respiratory phase, regardless of whether it was on control subjects or OSA patients. However, it is possible that the augmented tonic GG muscle activity itself in OSA decreases remarkably without much influence by additional inputs to the GG muscle when patency of the upper airway is successfully improved by mandibular advancement. Contrary to OSA patients, the tonic excitatory influences on the GG muscle because of mandibular advancement is consequently predominant in control subjects whose tonic GG muscle activity is originally much smaller than that of OSA patients. Thus, we reason that mandibular advancement provides different effects on OSA and healthy subjects during wakefulness. Our speculation should be tested further because the tonic GG muscle activity could not respond quickly to changes in pharyngeal pressure or airflow in OSA patients [21], whereas the activity easily responded to a body position change in both controls [22, 28] and patients with OSA [28].

Of particular interest, after oral appliance emplacement, CS area-IN was significantly smaller than CS area-EET (Fig. 3c–d). We speculate that this resulted from a relative reduction in the change of phasic GG muscle activity at IN versus EET compared with before oral appliance insertion. Considering that protrusion of the mandible reduced the propensity of upper airway collapse, it would in turn decrease the input from the upper airway mechanoreceptors during IN, leading to decreased phasic GG activity (Fig. 3b–d). In other words, the activity of the phasic GG muscle increased to a lesser extent during IN with the oral appliance in place, resulting in a reduction in the CS area at the velopharynx and the oropharynx. The fact that there was no difference in CS area during IN with or without the oral appliance suggests that phasic GG muscle activity was titrated precisely to maintain a target level of the CS area and patency of the upper airway (Fig. 3b–d). The difference between this speculation of a decrease in phasic GG muscle activity with mandibular protrusion in OSA patients and previous results from control subjects that showed an increase in phasic GG muscle activity [22] may be partly related to the definition of the activity as well as the small number of subjects. However, Tsuiki et al. [22] inferred that

input from the upper airway mechanoreceptor might also decrease in healthy volunteers as is the case with OSA patients. The results of the current study help to increase our understanding of the functional contribution of mandibular advancement in oral appliance therapy for OSA patients. It should again be stressed that our study contains no electromyographic data on the GG muscle.

In conclusion, mandibular advancement reduces the severity of OSA and changes both the size and dynamic behavior of the upper airway. These changes in the upper airway structure and function after mandibular advancement during wakefulness suggest that oral appliance emplacement reduces the increased upper airway muscle activity in patients with OSA. However, the effects of mandibular advancement on upper airway muscle activity during sleep remains to be reported in a future study.

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Is Passive Smoking Associated With Sleep Disturbance Among Pregnant Women?

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Study Objective: Pregnant women suffer from sleep disturbance, which may be aggravated by passive smoking. In this study we investigated the effects of passive smoking on sleep disturbance during pregnancy.

Design: Two cross-sectional questionnaire surveys conducted in 2002 and 2006.

Setting: Clinical institutions specializing in obstetrics and gynecology that participated in the nationwide surveys: 260 in the 2002 survey and 344 in the 2006 survey.

Participants: 16,396 and 19,386 pregnant women in Japan surveyed in 2002 and 2006, respectively.

Intervention: N/A.

Measurements and Results: Pregnant women exposed to passive smoking were likely to have sleep disturbances, such as subjective insufficient sleep, difficulty in initiating sleep, short sleep duration, and snoring loudly/breathing uncomfortably. Smoking pregnant women had the same sleep disturbances and also experienced excessive daytime sleepiness and early morning awakening. The prevalence of 5 types of sleep disturbance (insufficient sleep, difficulty in initiating sleep, short sleep duration, excessive daytime sleepiness, and snoring loudly/breathing uncomfortably) among nonsmokers with environmental tobacco smoke showed a mean value intermediate between that of active smokers and that of nonsmokers without environmental tobacco smoke.

Conclusion: Passive smoking is independently associated with increased sleep disturbance during pregnancy.

Keywords: Sleep disturbance, passive smoking, pregnant women, Japan, epidemiology

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INTRODUCTION

MANY PREVIOUS STUDIES HAVE REPORTED THAT PREGNANT WOMEN OFTEN SUFFER FROM SLEEP DISTURBANCE, AND THAT CHANGES IN SLEEP PATTERNS begin to occur during pregnancy.[1-11] Many epidemiological studies have examined the relationship between sleep disturbance and social factors, such as socioeconomic group and lifestyle.[12-15] Among lifestyle factors, an association has been observed between sleep disturbance and smoking.[16-22] With regard to smoking, it is reported that the pharmacological effects of nicotine exacerbate sleep problems.[19] Therefore, it is inferred that tobacco is detrimental to healthy sleep.

A previous study reported that pregnant women were more likely to have sleep disturbance than non-pregnant women of the same age group in the general population, and if they smoked, then the possibility of their suffering from sleep disturbance increased. According to the report, active smoking of pregnant women is most likely to induce excessive daytime sleepiness, among other sleep disturbances.[1,8]

Although associations between active smoking and sleep disturbance have been reported in many previous studies, to our knowledge few studies have reported associations between passive smoking and sleep disturbance. So far, only 3 studies have reported associations between passive smoking and sleep apnea, and passive smoking and snoring.[23-25] In these 3 studies, however, apnea and snoring were the only types of sleep disturbance investigated. Therefore, associations between passive smoking and sleep related issues such as difficulty in initiating sleep, difficulty maintaining sleep, early morning awakening, and sleep duration, have not been examined.

The aim of the present study was to clarify the association between passive smoking and sleep disturbance by analyzing the results of 2 epidemiological studies conducted on 16,396 and 19,386 pregnant women in Japan in 2002 and 2006, respectively.[1,8,26]

METHODS

The surveys were conducted in 2002 and 2006. The details of the procedure of the 2002 survey have been described elsewhere.[8,26]

Subjects and Procedure

Our 2 studies were part of a nationwide survey on smoking, alcohol consumption and sleep among Japanese pregnant women. The study subjects were women with a confirmed pregnancy who had attended for a second or subsequent consultation at one of

Disclosure Statement

This was not an industry supported study. Drs. Ohida, Kaneita, Osaki, Harano, Tanihata, Takemura, Wada, Kanda, Hayashi, and Uchiyama have indicated no financial conflicts of interest.

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Table 1—Sociodemographic Status of a Sample of Pregnant Women Living in Japan (2002 and 2006 Surveys)

	2002 Survey		2006 Survey	
Items	**N**	**%**	**N**	**%**
Age (y)				
19 ≤	230	1.4	279	1.4
20-29	8401	51.2	8340	43.0
30-39	7509	45.8	10392	53.6
40 ≥	250	1.5	375	1.9
Unknown	6	0.0	0	-
Schooling completed				
Junior college ≥	13787	84.1	15682	80.9
College ≤	2538	15.5	3610	18.6
Unknown	71	0.4	94	0.5
Employment				
Employed	4285	26.1	5279	27.2
Unemployed	11978	73.1	13961	72.0
Unknown	133	0.8	146	0.8
Pregnancy trimester				
1st	1145	7.0	1244	6.4
2nd	5709	35.1	6793	35.0
3rd	9068	55.8	10991	56.8
Unknown	474	2.1	350	1.8
Number of pregnancies				
1st	8180	49.9	9316	48.1
2nd or subsequent	8174	49.8	10032	51.7
Unknown	42	0.3	38	0.2

these institutions during the period 1–14 February 2002 and 6–18 February 2006.

Each subject was asked to complete a self-administered questionnaire during the time that she was waiting for a consultation. The subject was then asked to seal the completed questionnaire in an envelope, which was then collected. In each of the institutions, all of the pregnant women who met the inclusion criteria were selected as subjects, and there was no sampling of this group. The questionnaires included a statement that the staff of the institution had not seen the completed questionnaires, and the questionnaires were collected in sealed envelopes. This was done in order to protect the privacy of the subjects and to obtain responses that were as candid as possible.

The 2002 and 2006 surveys differed in the number of obstetrics and gynecology clinics that participated: 260 for the 2002 survey and 344 for the 2006 survey. In the 2002 survey, 16,528 questionnaires were collected. After exclusion of 132 subjects who did not answer the questions relating to active and passive smoking, the data for the remaining 16,396 subjects were analyzed. In the 2006 survey, 19,650 questionnaires were collected, and after exclusion of 264 subjects, the data for the remaining 19,386 subjects were analyzed. The differences of the 2002 and 2006 surveys are as follows.

2002 Survey

A random sample of 500 clinical institutions with maternity patients was selected. These institutions had been stratified according to the type of institution (clinic, public hospital, or private hospital) and the area bloc, based upon 1,000 all survey points that had been fixed by the Japan Association of Obstetricians and Gynecologists (JAOG). A letter was sent to each of these 500 randomly selected institutions inviting them to participate in our survey. A total of 390 institutions replied, of which 110 rejected the request and were excluded from the study. Study questionnaires were sent to the 280 institutions that had agreed to take part in the study, and questionnaires were returned by 260 of these institutions. The estimated response rate was 95.7%. During 2002, JAOG had a membership of approximately 13,000.

2006 Survey

The 2006 survey differed from the 2002 survey in that all of the fixed survey points in existence at the time, 940 were sent letters of invitation to participate in the survey, as opposed to selecting a random sample as was done for the 2002 survey. A total of 508 institutions responded to our request, with 360 expressing their willingness to participate (344 actually eventually participated) and 208 declining to participate. The estimated response rate was 86.6%, which was about 10 percentage points lower than that for the 2002 survey. The reason for this may be that we did not strongly enough request return of unused questionnaires from the participating institutions.

Measures

The major items included in the questionnaires used for the 2002 and 2006 surveys were: (1) active smoking status; (2) passive smoking status (whether or not a subject was exposed to environmental tobacco smoke [ETS]); (3) sleep status; and (4) personal data. The 2002 survey included 6 sleep-related items, and the 2006 survey had 7, with the addition of the question "Do you wake up during nocturnal sleep because of snoring loudly or breathing uncomfortably?" (hereafter, SB stands for snoring loudly/breathing uncomfortably). Questions on 7 items

Table 2—Prevalence of Sleep Disturbances According to Self-Reported Smoking Status

	2002 Survey					2006 Survey				
	Nonsmoker without ETS	Nonsmoker with ETS	Active smoker	Total	Sig.	Nonsmoker without ETS	Nonsmoker with ETS	Active smoker	Total	Sig.
SIS	15.0%	19.1%	25.0%	18.1%	*	13.4%	16.9%	23.5%	15.8%	*
(N)	(6050)	(8606)	(1621)	(16277)		(9037)	(8,837)	(1474)	(19348)	
DIS	16.6%	18.0%	27.9%	18.5%	*	13.2%	15.1%	23.2%	14.9%	*
(N)	(6049)	(8604)	(1621)	(16274)		(9037)	(8837)	(1474)	(19348)	
DMS	43.3%	42.5%	45.6%	43.1%	ns	37.6%	39.4%	40.5%	38.7%	**
(N)	(6048)	(8594)	(1623)	(16265)		(9035)	(8836)	(1474)	(19345)	
EMA	9.5%	9.2%	12.5%	9.6%	*	8.5%	8.8%	11.7%	8.9%	*
(N)	(6045)	(8598)	(1622)	(16265)		(9037)	(8837)	(1474)	(19348)	
SSD	20.2%	25.2%	31.6%	24.0%	*	21.4%	26.5%	32.1%	24.5%	*
(N)	(6036)	(8569)	(1612)	(16217)		(9005)	(8789)	(1460)	(19254)	
EDS	24.2%	25.1%	32.6%	25.5%	*	23.1%	24.3%	32.7%	24.4%	*
(N)	(6033)	(8582)	(1614)	(16229)		(9020)	(8791)	(1463)	(19274)	
SB						2.3%	2.9%	3.3%	2.6%	*
(N)						(9023)	(8803)	(1466)	(19292)	

Note: SIS; subjective insufficient sleep, DIS; difficulty in initiating sleep, DMS; difficulty maintaining sleep, EMS; early-morning awakening, SSD; short sleep duration (<7 h), EDS; excessive daytime sleepiness, SB; snoring loudly/breathing uncomfortably, ETS; environmental tobacco smoke
χ^2-test: *P<0.01, **P<0.05, ns: not significant.
Sig.: Significance.

related to sleep status during the previous month were included in the questionnaire: (1) subjective insufficient sleep (SIS); (2) difficulty in initiating sleep (DIS); (3) difficulty maintaining sleep (DMS); (4) early morning awakening (EMA); (5) short sleep duration (SSD); (6) excessive daytime sleepiness (EDS); and (7) snoring loudly or breathing uncomfortably (SB). The definitions of sleep disorders in the present study were as follows: SSD was defined as getting <7 h sleep per night. SIS was ascribed to subjects who answered "insufficient" or "very insufficient" for the corresponding question. The remaining 5 items (DIS, DMS, EMA, EDS, and SB) were ascribed to subjects who answered "often" or "always" for the corresponding questions.

The questionnaire also included items on active and passive smoking at the time of the survey, when pregnancy had been confirmed. A question on who had exposed the pregnant women to ETS ([1] family, [2] friends or coworkers, and [3] others) was also included.

The demographic variables were age (younger than 20 years, 20-29 years, 30-39 years, or 40 years or older), schooling completed (junior college or lower, college or higher), employment status (employed, unemployed), and alcohol consumption (yes, no). There were also questions on pregnancy status, including the number of pregnancies (1st, 2nd, or subsequent) and pregnancy trimester (1st, 2nd, 3rd). These 5 items of personal data, including missing data on the subjects, are shown in Table 1. Details of the sleep questions used in the 2002 survey have been described elsewhere.[1,8,26]

Analysis

We divided the sample into 3 groups according to smoking status: (1) nonsmokers without ETS: Nonsmoking; (2) nonsmokers with ETS: Passive smoking; and (3) active smokers: Smoking at the time of the survey, when pregnancy had been confirmed. We then calculated the prevalence of each of the 7 sleep-related items.

In Table 3, excluding active smokers, only nonsmokers with and without ETS are divided into 5 groups in a similar manner to Table 2, with the calculated prevalence of each sleep related item. The subjects in the 5 groups were all nonsmokers, with those in Group 1 not exposed to ETS; those in Group 2 exposed to ETS from family, friends, and coworkers; those in Group 3 exposed to ETS from family, but not from friends or coworkers; those in Group 4 exposed to ETS from friends or coworkers, but not from family; and those in Group 5 exposed to ETS from sources other than family, friends, and coworkers.

Logistic regression analyses was used to compare the odds of suffering from 7 types of sleep disturbances (SIS, DIS, DMS, EMA, SSD, EDS, and SB) by smoking status, while controlling for age, highest educational level, employment status, alcohol consumption, pregnancy trimester, and number of pregnancies. Logistic regression was also used to compare the odds of suffering these same sleep disturbances by the source of the passive smoke exposure (family & friend smoker, family smoker & friend nonsmoker, family nonsmoker & friend smoker, other smoker). Subjects who failed to answer any one of the questions pertaining to the covariates were excluded from the analyses. SPSS for Windows, Version 11.0 was used for all statistical analyses.

Table 3—Sleep Disturbances Among Only Nonsmokers With and Without ETS

	2002 Survey							2006 Survey						
	Nonsmoker with ETS							Nonsmoker with ETS						
	Group 1 Nonsmoker without ETS	Group 2 Family & Friends smoker	Group 3 Family smoker & friend nonsmoker	Group4 Family nonsmoker & friend smoker	Group 5 Other Smoker	Total	Sig.	Group 1 Nonsmoker without ETS	Group 2 Family & friend smoker nonsmoker	Group 3 Family smoker & friend smoker	Group4 Family nonsmoker & friend	Group 5 Other smoker	Total	Sig.
Prevalence of SIS	15.0%	22.4%	17.5%	24.4%	14.9%	17.4%	*	13.4%	19.2%	15.7%	21.9%	16.2%	15.1%	*
(N)	(6050)	(1827)	(5667)	(832)	(363)	(14739)		(9037)	(1648)	(6011)	(745)	(433)	(17874)	
Prevalence of DIS	16.6%	18.5%	18.6%	14.3%	14.9%	17.5%	*	13.2%	16.5%	14.7%	14.4%	17.4%	14.2%	*
(N)	(6049)	(1826)	(5668)	(830)	(363)	(14736)		(9037)	(1647)	(6013)	(745)	(432)	(17874)	
Prevalence of DMS	43.3%	42.7%	43.2%	38.7%	40.4%	42.9%	ns	37.6%	39.6%	39.9%	35.4%	38.6%	38.5%	**
(N)	(6048)	(1862)	(5660)	(830)	(361)	(14725)		(9035)	(1648)	(6012)	(743)	(433)	(17871)	
Prevalence of EMA	9.5%	10.0%	9.0%	8.4%	9.6%	9.3%	ns	8.5%	10.0%	8.7%	7.0%	8.5%	8.6%	ns
(N)	(6045)	(1822)	(5666)	(830)	(363)	(14726)		(9037)	(1648)	(6011)	(745)	(433)	(17874)	
Prevalence of SSD	20.2%	27.8%	23.3%	34.9%	20.1%	23.1%	*	21.4%	30.0%	25.0%	32.9%	21.7%	23.9%	*
(N)	(6036)	(1817)	(5645)	(827)	(363)	(14688)		(9005)	(1640)	(5979)	(742)	(428)	(17794)	
Prevalence of EDS	24.2%	26.9%	25.3%	21.9%	21.9%	24.8%	**	23.1%	26.5%	24.3%	19.9%	25.0%	23.7%	*
(N)	(6033)	(1818)	(5660)	(826)	(361)	(14698)		(9020)	(1637)	(5980)	(742)	(432)	(17811)	
Prevalence of SB								2.3%	3.5%	2.6%	3.0%	3.5%	2.6%	**
(N)								(9023)	(1638)	(5992)	(741)	(432)	(17826)	

Note: friend; friends and coworkers
χ^2-test: **P<0.01, *P<0.05, ns: not significant.
Sig.: Significance.
SIS; subjective insufficient sleep, DIS; difficulty in initiating sleep, DMS; difficulty maintaining sleep, EMS; early-morning awakening, SSD; short sleep duration (<7 h), EDS; excessive daytime sleepiness, SB; snoring loudly/breathing uncomfortably, ETS; environmental tobacco smoke

RESULTS

The prevalence of smoking among Japanese pregnant women was 9.9% in 2002 and 7.8% in 2006. The percentages of pregnant women exposed to ETS were 62.1% in 2002 and 52.7% in 2006. In both studies, the spouse was the source of the environmental tobacco smoke for 80% or more of pregnant women who responded that they had been exposed to ETS.

As shown in Table 2, active smokers showed the highest prevalence of all 6 items related to sleep disturbance in 2002 and all 7 in 2006. In the meantime, the prevalence of each sleep related item among nonsmokers with ETS (Passive smoking) showed a mean value intermediate between that among active smokers (Smoking) and that among nonsmokers without ETS (Nonsmoking).

Among nonsmoking women, the prevalence of all sleep disturbance items was higher in those exposed to ETS than those not exposed to ETS (Table 3). After further dividing the nonsmokers with ETS into 4 groups based upon the source of the smoke exposure and comparing among these groups, no trend could be distinguished. However, when the 6 sleep related items included in the 2002 survey and the 7 included in the 2006 survey were compared among the 4 groups, the prevalence of sleep disturbance was found to be comparatively higher among nonsmokers whose family and friends smoked.

Tables 4 and 5 show the results of multiple logistic regression analyses to estimate the association between sleep disorders and smoking status after adjusting for covariates. Nonsmoking pregnant women who were exposed to ETS were significantly more likely than those not exposed to ETS to suffer from SIS (subjective insufficient sleep), DIS (difficulty in initiating sleep), and SSD (short sleep duration) in the 2002 survey and significantly more likely to suffer from SIS, DIS, EMA (early morning awakening), SSD, and SB (snoring loudly or breathing uncomfortably) in 2006 survey (Table 4). As shown in Table 5, nonsmokers with family and friends who smoked were significantly more likely to suffer from SIS, DIS, EMA, SSD, EDS (excessive daytime sleepiness) than nonsmokers without ETS in both the 2002 and 2006 surveys.

DISCUSSION

We found statistically significant associations in the 2 nationwide surveys conducted in 2002 and 2006 between passive smoking and sleep disturbances among pregnant women. Previous studies have explored associations between active smoking among pregnant women and sleep disturbances,[1,8,26] but to our knowledge, the present study is the first to report an association between passive smoking exposure among pregnant women and sleep disturbances.

In the surveys, the spouse was the source of the environmental tobacco smoke for 80% or more of pregnant women. The prevalence of smoking among Japanese men was 53%, which is higher than that among men in the United States (26%) or in the United Kingdom (27%).[27] With this in mind, it is important to study the issue of passive smoking among Japanese pregnant women and their health.

It is known that pregnant women tend to suffer from sleep disturbance caused by diverse factors, such as nocturia, difficulty assuming the habitual sleep posture owing to enlargement of the abdomen, fetal movements, lower back pain during pregnancy,

Table 4—Multiple Logistic Regression Results for Prediction of Sleep Disturbance Items Among Japanese Pregnant Women

	SIS OR	DIS OR	DMS OR	EMA OR	SSD OR	EDS OR	SB OR
2002 Survey							
Nonsmokers without ETS	1.00	1.00	1.00	1.00	1.00	1.00	
Nonsmokers with ETS	1.38 (1.12-1.44)	1.11 (1.01-1.21)	0.99 (0.93-1.07)	1.03 (0.91-1.15)	1.51 (1.29-1.76)	1.04 (0.96-1.13)	
Active smokers	1.74 (1.51-2.01)	1.87 (1.63-2.15)	1.06 (0.94-1.19)	1.32 (1.10-1.59)	2.75 (2.23-3.38)	1.53 (1.34-1.73)	
2006 Survey							
Nonsmokers without ETS	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Nonsmokers with ETS	1.31 (1.20-1.43)	1.15 (1.05-1.26)	1.11 (1.04-1.18)	1.07 (0.96-1.19)	1.30 (1.20-1.39)	1.07 (0.99-1.15)	1.25 (1.03-1.52)
Active smokers	1.87 (1.62-2.16)	1.93 (1.67-2.23)	1.08 (0.96-1.21)	1.45 (1.20-1.74)	1.74 (1.52-1.97)	1.61 (1.42-1.83)	2.23 (1.50-3.32)

Note: ( ); 95% confidence interval, OR; odds ratio.
Adjusted for sociodemographic (age, final academic background, employment status and drinking status) and pregnancy-status (number of pregnancies and pregnancy trimester) factors in multiple logistic regression
SIS; subjective insufficient sleep, DIS; difficulty in initiating sleep, DMS; difficulty maintaining sleep, EMS; early-morning awakening, SSD; short sleep duration (<7 h), EDS; excessive daytime sleepiness, SB; snoring loudly/breathing uncomfortably, ETS; environmental tobacco smoke

Table 5—Multiple Logistic Regression Results for Prediction of Sleep Disturbance Items Among Japanese Pregnant Women

	SIS OR	DIS OR	DMS OR	EMA OR	SSD OR	EDS OR	SB OR
2002 Survey							
Nonsmoker without ETS	1.00	1.00	1.00	1.00	1.00	1.00	
Nonsmokers with ETS							
Family & friend smoker	1.52 (1.32-1.76)	1.24 (1.07-1.44)	1.08 (0.97-1.21)	1.24 (1.03-1.51)	1.94 (1.56-2.42)	1.16 (1.02-1.32)	
Family smoker & friend nonsmoker	1.23 (1.11-1.37)	1.07 (0.97-1.19)	0.97 (0.90-1.05)	0.95 (0.84-1.09)	1.38 (1.17-1.64)	1.04 (0.95-1.13)	
Family nonsmoker & friend smoker	1.55 (1.29-1.88)	1.27 (1.01-1.59)	1.09 (0.92-1.28)	1.22 (0.92-1.62)	1.76 (1.30-2.37)	0.93 (0.77-1.13)	
Other smoker	1.01 (0.74-1.38)	0.88 (0.65-1.19)	0.90 (0.71-1.21)	1.06 (0.73-1.52)	0.99 (0.58-1.69)	0.89 (0.68-1.15)	
2006 Survey							
Nonsmoker without ETS	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Nonsmokers with ETS							
Family & friend smoker	1.51 (1.30-1.74)	1.40 (1.20-163)	1.25 (1.11-1.40)	1.31 (1.09-1.59)	1.42 (1.25-1.61)	1.24 (1.10-1.41)	1.64 (1.19-2.25)
Family smoker & friend nonsmoker	1.22 (1.10-1.34)	1.06 (0.96-1.17)	1.07 (0.99-1.15)	1.01 (0.90-1.14)	1.26 (1.16-1.37)	1.05 (0.97-1.14)	1.10 (0.88-1.36)
Family nonsmoker & friend smoker	1.63 (1.31-1.98)	1.51 (1.20-1.90)	1.16 (0.98-1.37)	1.01 (0.74-1.37)	1.40 (1.18-1.67)	0.90 (0.74-1.10)	1.64 (1.03-2.60)
Other smoker	1.39 (1.06-1.82)	1.31 (1.01-1.70)	1.09 (0.89-1.34)	1.05 (0.73-1.48)	1.07 (0.84-1.36)	1.08 (0.86-1.36)	1.48 (0.86-2.54)

Note: ( ); 95% confidence interval, OR; odds ratio.
Adjusted for sociodemographic (age, final academic background, employment status and drinking status) and pregnancy-status (number of pregnancies and pregnancy trimester) factors in multiple logistic regression
SIS; subjective insufficient sleep, DIS; difficulty in initiating sleep, DMS; difficulty maintaining sleep, EMS; early-morning awakening, SSD; short sleep duration (<7 h), EDS; excessive daytime sleepiness, SB; snoring loudly/breathing uncomfortably, ETS; environmental tobacco smoke.

and hormonal effects.[1-6] Sleep disturbance is more commonly reported among pregnant women than among the general female population.[1] Therefore, pregnant women are considered to be a group prone to sleep disturbance.

As mentioned above, many epidemiological studies have already suggested associations between active smoking and sleep disturbance.[1,16-26,29] Wetter et al, in an epidemiological study, reported that active smoking was associated with difficulty initiating sleep (DIS), excessive daytime sleepiness (EDS), nonrestorative sleep, and difficulty waking up.[28] In addition, both polysomnography and questionnaire studies have revealed increased sleep latency, increased arousal, and difficulty staying asleep at night among active smokers, compared with nonsmokers. In the present study, we also observed an association between active smoking and sleep disturbances (SIS: subjective insufficient sleep, DIS: difficulty in initiating sleep, EMA: early morning awakening, SSD: short sleep duration, EDS: excessive daytime sleepiness, and SB: snoring loudly or breathing uncomfortably) suggesting that active smoking contributes to sleep disturbances.

As to the association of passive smoking with sleep disturbance among the general population, to our knowledge, only an association with snoring[23-25] has been reported, but no epidemiological study among pregnant women has reported an association with snoring. Therefore, this study is significant in that it focused on the association between passive smoking and SB (snoring loudly or breathing uncomfortably) specifically in pregnant women, who are prone to suffer from sleep disturbance.

Our findings suggest that exposure to ETS might increase nocturnal awakening in nonsmoking pregnant women by contributing toward snoring or sleep disordered breathing. As shown in Table 4, the odds ration (OR) for loud snoring or uncomfortable breathing (SB) among nonsmokers with ETS was 1.25 (95% CI: 1.03-1.52) after adjusting for the 6 covariates. Nonsmokers who were exposed to ETS were significantly more likely to suffer from SB than nonsmokers who were not exposed ETS and active smokers were over twice as likely (OR=2.23, 95%CI: 1.50-3.32) to suffer from loud snoring or uncomfortable breathing (SB) than nonsmokers who were not exposed to ETS. Moreover, we found a significant association between exposure to ETS from family and friends and loud snoring or uncomfortable breathing (SB). Franklin et al,[23] on the basis of a large population-based sample, reported that snoring was more prevalent among people who had never smoked but who were exposed to passive smoking than among nonsmokers without such exposure. However, as a limitation to their study, they pointed out that no question on alcohol consumption had been posed. Previous studies reported that pregnant women tend to snore more often than before they became pregnant.[9-11] From the present study, it is inferred that pregnant women who have been exposed to tobacco smoke tend to snore even more often. In the present study, the ORs were also calculated after adjusting for alcohol consumption as a potential confounding factor.

Our results suggest that pregnant women who are exposed to passive smoking are prone to sleep disturbance. It has been reported that nicotine stimulates the central nervous system and promotes wakefulness, resulting in an increase of sleep latency and a reduction of both total sleep time and REM sleep.[19] However, as the amount of nicotine absorbed by passive smoking is smaller than that absorbed by active smoking,[30] there is doubt as to whether the amount absorbed by passive smoking is large enough to cause sleep disturbance. In addition, as shown in Table 5, the ORs for SIS (subjective insufficient sleep), and DIS (difficulty in initiating sleep) among nonsmokers who were exposed to tobacco smoke from family and friends were lower than those among nonsmokers who were exposed to tobacco smoke from friends but not from family. This indicates that the dose-response relationship has not yet been clarified. Associations between active smoking and sleep disturbance have been sufficiently shown in previous studies.[8] Family or friends who suffer from sleep disturbance because of smoking may also directly affect the sleep of nonsmoking pregnant women. Replication studies are needed to help clarify the association that we found between passive smoke exposure and sleep disturbance.

The present study, which is the first epidemiological study to investigate the association between passive smoking and sleep disturbance among pregnant women in Japan, had some limitations. First, since this was a cross-sectional survey, a causal relationship could not be determined. Second, the data on sleep, smoking, and alcohol consumption were all self-reported. However, several studies have indicated that self-reported data on sleep status show at least moderate agreement with data from laboratory studies.[31] Third, as this was a cross-sectional study conducted on women whose pregnancy had been confirmed, the reliability of data on smoking status before pregnancy collected via questionnaires needs to be studied further. As most pregnant women probably knew that smoking had an adverse effect on their health, some may not have answered the questions truthfully. Fourth, the questionnaire used in the present study did not include items on unhealthy lifestyles, poor general health, stress, and worries.[13,16,30-32] Furthermore, there was no question on caffeine intake in the questionnaire, which is a limitation of the present study. Previous studies indicated that regular caffeinated beverage drinkers had difficulty in initiating sleep (DIS), short sleep duration (SSD), and sleep deprivation, and that the combination of alcohol and caffeine could synergistically induce insomnia.[33-35] In this study, it is possible that that caffeine might have contributed to sleep disturbance, especially to difficulty initiating sleep and short sleep duration. Therefore, epidemiological studies using questionnaires that include these 2 items should be conducted in the future.

In conclusion, this study found a positive relationship between exposure to environmental tobacco smoke and sleep disruption in pregnant women. The relationship between passive smoking exposure and some negative health outcomes in pregnant women could therefore be mediated by the ability of passing smoke to disrupt sleep. Educational programs that point out the adverse effects of passive smoking during pregnancy could help improve sleep hygiene in this group of individuals and help prevent other negative health outcomes associated with disrupted sleep.

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