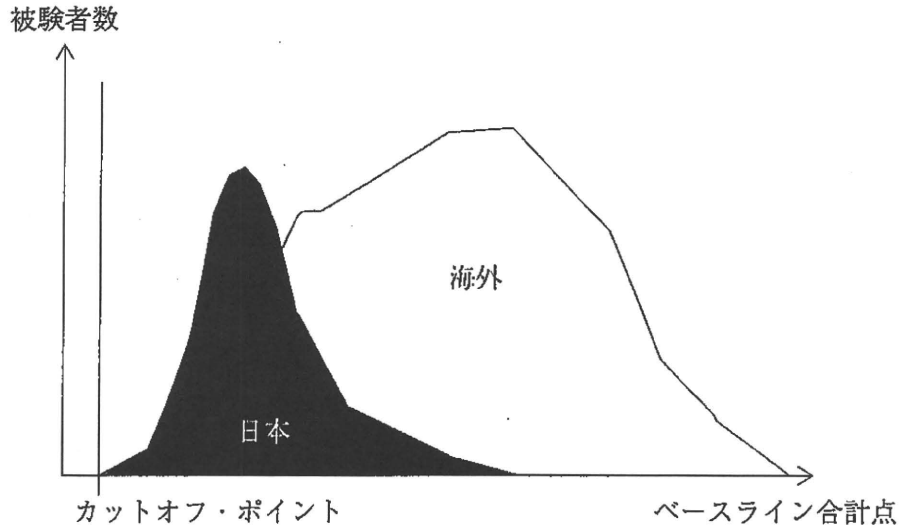

図５　国内外で同一の試験計画で実施した場合の被験者の重症度分布の差異

●被験者のベースライン重症度

前述のとおり、有効性評価は症状評価尺度合計点のベースラインから最終観察時までの変化量が検討されるため、ベースラインでの重症度は有効性評価に影響する（Kirsch, et al（2008）; Fournier, et al (2010)）。つまり、被験者集団のベースライン重症度が低い場合、得られたエフェクトサイズが小さくなり、統計学的な検出力が担保された試験計画でも検証が困難になることがある。現に、欧州医薬品委員会（CPMP: Committee for Proprietary Medical Products）も、抗うつ薬の臨床試験においては、軽度の患者では有効性を検討することが困難であることを指摘（European Medicines Agency（2002））している。また、国内と海外で同一の計画により臨床試験が実施された場合に、被験者の重症度の分布が国内外で異なることが経験される（図5)。これにより、海外試験で有効性が示されても、国内試験でより軽度の患者の組み入れが多くなると、成功確率が低下し有効性が示されないことが起こりうる。前述の通り選択基準と主要評価項目とで異なる評価尺度を使用することは組み入れの際のバイアスを軽減するため

の方策であるが、安全確保策を十分に検討するとともに、薬効評価に適した重症度の被験者を選択していく必要がある。

●併用薬・併用療法の影響

うつ病の臨床においては、抗うつ薬の他にベンゾジアゼピン系薬剤等が併用されることもある。うつ病に対するベンゾジアゼピン系薬剤の長期投与の有効性は明確になっていないが、短期の使用ではその有効性が示されている（Furukawa（2000））。一般に、抗うつ薬の臨床試験の投与期間は6週間もしくは8週間と設定されることが多い（表1）ことから、ベンゾジアゼピン系薬剤をはじめとする併用薬や併用療法は、有効性評価に影響する可能性があることにも留意する必要がある。

●症例の集積性

臨床試験における症例の集積性については2つの問題があり、1つは施設当たりの被験者数であり、2つ目は被験者の組み入れ速度に関するものである。

これまでにも筆者は、本邦の臨床試験は海外と比較して、1施設当たりの被験者数が極端に少なく、参加施設数が多いことを報告（中林ほか（2010））している。これにより、被験者集団や症状評価の方法にもばらつきが大きくなり、有効性評価に影響する可能性がある。ICH E9ガイドライン（厚生省医薬安全局審査管理課長（1998））で指摘されている通り、参加施設の特性や施設ごとの被験者数に大きく差異がないように配慮するなど、実施体制につても検討していく必要がある。

本邦での治験における被験者の組み入れ速度については、初期の組み入れが少なく試験終了に近くなると急激に組み入れが多くなることが経験される（図6）。国際共同治験では、参加国ごとの目標症例数

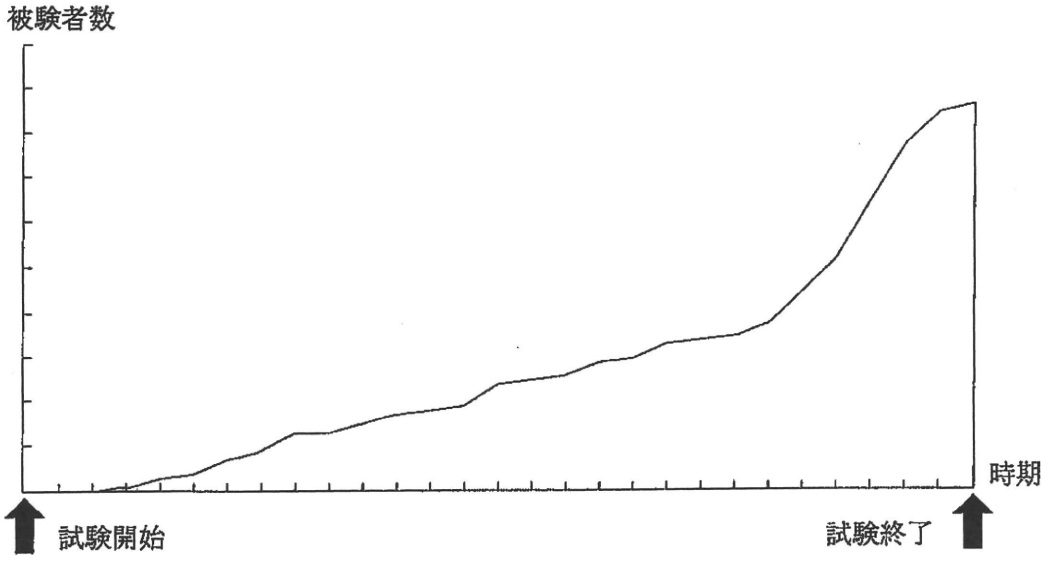

図６　試験開始から累積被験者数の一般的な推移

が設定（厚生労働省医薬食品局審査管理課長（2007））されていても、一般的に競争的に組み入れが行われるため、日本人症例の試験成績を検討するためには計画的な組み入れを行う必要がある。

おわりに

抗うつ薬の臨床試験の特徴を説明するとともに、有効性評価に影響を及ぼす可能性がある問題について説明した。これらは個々が独立した問題ではなく相互に関係することもあるため、試験の実施にあたっては種々の検討が必要となる。治験を行う医師や医療環境に関わる問題も多いため、より適切に試験を実施していくためには、今後も具体的な問題を理解し共有することが重要であると考える。また、欧米のみならずアジア諸国での臨床試験の実施も活発化（中林ほか（2010））しており、リーダーシップを保ち続けていくために、臨床試験のための基盤の整備についても継続的に行っていく必要があると考える。

文献

- European Medicines Agency (2002). Note for Guidance on Clinical Investigation of Medical Products in the Treatment of Depression. Doc.Ref. CPMP/EWP/518/97, Rev. 1. available online at http://www.ema.europa.eu/pdfs/human/ewp/051897en.pdf
- Fava M, Evins AE, Dorer DJ et al (2003). The problem of the placebo response in clinical trials for psychiatric disorders: culprits, possible remedies, and a novel study design approach. *Psychother Psychosom.* 72: 115-127.
- Fournier JC, DeRubeis RJ, Hollon SD, et al (2010). Antidepressant drug effects and depression severity: a patient-level meta-analysis. *JAMA.* 303: 47-53.
- Frank R, Hargreaves R (2003). Clinical biomarkers in drug discovery and development. Nature Rev Drug Discov. 2: 566-580.
- Furukawa TA, Streiner DL, Young LT (2000). Antidepressant and benzodiazepine for major depression. *Cochrane Database Syst Rev.* (4) : CD001026.
- Karlberg JP (2008). Trends in disease focus of drug development. *Nat Rev Drug Discov.* 7: 639-640.
- Khan A, Kolts RL, Rapaport MH, Krishnan KR, et al (2005). Magnitude of placebo response and drug-placebo differences across psychiatric disorders. *Psychol Med.* 35: 743-749.
- Kirsch I, Deacon BJ, Huedo-Medina TB, et al (2008). Initial severity and antidepressant benefits: a meta-analysis of data submitted to the Food and Drug Administration. *PLoS Med.* 5: e45.
- Kola I, Landis J (2004). Can the pharmaceutical industry reduce attrition rates? *Nat Rev Drug Discov.* 3: 711-715.
- 厚生省医薬安全局審査管理課長 (1998).「『臨床試験のための統計的原則』について」医薬審第 1047 号, 平成 10 年 11 月 30 日.
- 厚生省医薬局審査課長 (2001).「『臨床試験における対照群の選択とそれに関連する諸問題』について」医薬審発第 136 号, 平成 13 年 2 月 27 日.
- 厚生労働省医薬食品局審査管理課長 (2007)「国際共同治験に関する基本的考え方について」薬食審査発第 0928010 号, 平成 19 年 9 月 28 日.
- Laughren TP (2001). The scientific and ethical basis for placebo-controlled trials in depression and schizophrenia: an FDA perspective. *Eur Psychiatry.* 16: 418-423.
- Marks DM, Thanaseelan J, Pae CU (2009). Innovations in clinical research design and conduct in psychiatry: shifting to pragmatic approaches. *Psychiatry Investig.* 6: 1-6.
- 中林哲夫, 中村治雅, 岡本長久 (2010).「本邦における国際共同治験の現状と課題――抗うつ薬開発の最近の動向」『臨床精神神経薬理』13 : 255-263.
- Walsh BT, Seidman SN, Sysko R, et al (2002). Placebo response in studies of major depression: variable, substantial, and growing. *JAMA.* 287: 1840-1847.
- World Health Organization (WHO) (2004). The global burden of disease, update 2008.

· World Health Organization (WHO) (2009). Global health risks. Mortality and bu den of disease attributable to selected major risks.

52

Sleep Medicine 11 (2010) 452–457

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

Effects of insomnia and sleep medication on health-related quality of life

Taeko Sasai [a,d,*], Yuichi Inoue [a,b], Yoko Komada [b], Takashi Nomura [c], Masato Matsuura [e], Eisuke Matsushima [d]

[a] Japan Somnology Center, Neuropsychiatric Research Institute, Tokyo, Japan
[b] Department of Somnology, Tokyo Medical University, Japan
[c] Department of Neurology, Institute of the Neurological Sciences, Tottori University Faculty of Medicine, Tottori, Japan
[d] Section of Liaison Psychiatry and Palliative Medicine, Graduate School of Tokyo Medical and Dental University, Japan
[e] Department of Life Sciences and Bio-Informatics, Division of Biomedical Laboratory Sciences, Graduate School of Health Sciences, Tokyo Medical and Dental University, Japan

ARTICLE INFO

Article history:
Received 3 July 2009
Received in revised form 6 September 2009
Accepted 11 September 2009

Keywords:
Quality of life
SF-8
Sleep medication
Insomnia
MCS
PCS

ABSTRACT

Objective: This study, using Short-Form 8 (SF-8), was undertaken to assess the effects of insomnia and sleep medication use on quality of life (QOL) in 2822 people (ages 20–97 years) in a rural population. Factors associated with deterioration of the mental component summary (MCS) score and physical component summary (PCS) score were investigated.

Methods: Questionnaires asked participants' basic information and included assessments using SF-8, the Pittsburgh Sleep Quality Index (PSQI), and a 12-item version of the Center for Epidemiological Studies Depression scale. Results of PSQI supported the classification of subjects as good sleepers, good sleepers using sleep medication, insomniacs, and insomniacs using sleep medication.

Results: Insomnia was associated with low scores of MCS and PCS. Nevertheless, sleep medication use was associated with low PCS scores only. Good sleepers using sleep medication had significantly higher MCS scores than either insomniacs or insomniacs using sleep medication, but lower scores than good sleepers. Similarly to insomniacs using sleep medication, good sleepers using sleep medication had significantly lower PCS scores than either good sleepers or insomniacs.

Conclusions: Sleep medication was useful to improve mental QOL. That usage, however, might degrade the physical QOL, possibly because of the medication's adverse effects.

1. Introduction

Insomnia is well known as a common disorder [1–3] with a prevalence of about 20% among the general population [4,5]. Major symptoms of insomnia are poor nocturnal sleep and impaired daytime functioning during wakefulness [6]. In the 2nd edition of International Classification of Sleep Disorders (ICSD-2) [7], daytime impairment as well as nighttime sleep difficulties – difficulty initiating sleep, difficulty maintaining sleep, waking up too early or sleep that is chronically nonrestorative or poor in quality – are emphasized among the diagnostic criteria.

Reports describing clinical populations show that patients with chronic insomnia commonly complain of subjective daytime impairments including mood disturbances, concentration problems, elevated fatigue, and sleepiness [6,8]. Regarding objective daytime impairments, these patients show impairments in tasks evaluating vigilance, working memory, and motor control [9,10]. These various daytime dysfunctions attributable to insomnia are presumed to degrade quality of life (QOL), an evaluation of general daytime functioning [11,12]. Reportedly, degradation of QOL, as evaluated using the standardized 36-item Short Form Health Survey of the Medical Outcomes Study (SF-36), is associated with insomnia's severity [13]. Because QOL is a complex and multidimensional term, it can reflect the lifestyle, health status, and socio-environmental background of subjects. Although such factors should be analysed when evaluating QOL, few reports have described an association between insomnia and QOL in a general population with due consideration of these demographic factors.

Results of previous studies revealed the use of sleep medication for insomnia by approximately 5–8% of the general population [1,14,15]. The relative frequency among the general population of people with at least occasional use of sleep medication is approximately 3–11% [1,16,17]. Several studies conducted in clinical settings have revealed that the use of sleep medication improves not only sleep quality but also daytime ability to function and a sense of physical well being of patients with insomnia [18,19]. In addition, long-term nightly pharmacologic treatment of primary insomnia with any hypnotic has been reported to enhance both

* Corresponding author. Address: Japan Somnology Center, Neuropsychiatric Research Institute, 1-24-10 Yoyogi, Shibuya-ku, Tokyo, Japan. Tel.: +81 3 3374 9112; fax: +81 3 3374 9125.
E-mail address: taeko_ssi@yahoo.co.jp (T. Sasai).

1389-9457/$ - see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.sleep.2009.09.011

mental QOL and physical QOL [20]. Contrary to those reports, others have described sleep medication as having no significant effect on next-day psychomotor performance or QOL [21,22]. Furthermore, differences in the effects of sleep medication between mental and physical QOL among the general population have not been clarified yet.

In the series of Daisen sleep health care studies, we first reported the prevalence of restless legs syndrome (RLS) among residents in rural areas and the negative impact of the disorder on QOL [23]. Secondly, we presented data related to the influence of insomnia and sleep medication use on depressive symptoms [unpublished observations]. For the present study, we used the 8-item Short Form Health Survey of the Medical Outcomes Study (SF-8) – a simpler version of SF-36 that is nevertheless as useful as SF-36 for evaluating QOL [24,25] – to clarify the above-described issue of the association between insomnia, sleep medication use, and QOL. This study was designed to evaluate QOL among the general population in a rural community using SF-8, particularly addressing the impact of insomnia and sleep medication use on the mental component summary (MCS) score and physical component summary (PCS) score.

2. Methods

2.1. Subjects and procedures

The ethics committees of Tottori University approved this study. All subjects gave their informed consent to take part in this investigation.

This survey was conducted as a part of the above-described Daisen sleep health care studies undertaken in a rural community in Tottori prefecture in western Japan [23]. The total population of the town was 6643 in 2004, with 5528 residents aged 20 years or older (2521 men and 3007 women). Major industries in this area are agriculture, farming, and tourism. The questionnaire survey was conducted during November 2005–January 2006. With the cooperation of local public health nurses, questionnaires were delivered to all residents who were 20 years of age or older.

The questionnaires requested information related to family circumstances, existence of family members who need home-based nursing care (home-based nursing care), existence of any currently treated disease, smoking habits, and drinking habits. We used SF-8 for assessing QOL [26], a Japanese version of the Pittsburgh Sleep Quality Index (PSQI) [27,28] for inferring sleep disturbances in the subjects, and a 12-item version of the Center for Epidemiological Studies Depression scale (CES-D) [29] for estimating depressive symptoms. The SF-8, consisting of domains including vitality, social function, mental health, role emotional, general health, physical function, role physical, and bodily pain, were calculated according to standard methods. The MCS scale of the SF-8 was evaluated as an index of mental QOL; the PCS subscale was evaluated as an index of physical QOL. General population averages for these scores were set at 50 points. Consequently, a subject with a score of less than 50 points was inferred to have deteriorated QOL [25,30].

The PSQI included sub-items evaluating sleep quality (C1), sleep latency (C2), sleep duration (C3), habitual sleep efficiency (C4), frequency of sleep disturbance (C5), use of sleep medication (C6), and daytime dysfunction (C7), of which C1–C5 indicate problems with nocturnal sleep [27,28]. After excluding items of C6, we used the total score of the Pittsburgh Sleep Quality Index as the score of insomnia and defined greater than one standard deviation (SD) of the mean sum score (6.4) as designating insomnia, using a similar method to that used in our previous report (in submission). Based on the answers to C6, we defined subjects who used sleep medications less than once a week as "not using sleep medication" and once or more a week as "using sleep medication." According to these PSQI sub-items, subjects were classified into four groups: good sleepers ($n = 2070$), good sleepers using sleep medication ($n = 95$), insomniacs ($n = 264$), and insomniacs using sleep medication ($n = 85$). In addition, the subjects were categorized based on the frequency of sleep medication use obtained from the answer to C6: no use ($n = 2300$), less than once a week ($n = 50$), 1–2 times a week ($n = 43$), and more than three times a week ($n = 137$).

We also used total scores of CES-D as parameters of depressive symptoms. The CES-D had four response options for each question: "never or rarely," "sometimes," "often," and "always," coded as 0–3. We divided responses into two categories: 0–11 as normal and 12–36 as depressive [29].

Of the 5528 eligible subjects, 2937 subjects (53.1%) responded to our questionnaires and 2822 (51.0%) completed the questionnaires (1222 male, 1600 female; ages 20–97 years; mean [SD]: 57.4 [17.7] years).

2.2. Statistical analyses

Student's *t*-test was used to compare the MCS scores and PCS scores between the insomniac group and the group of good sleepers. One-way analysis of variance (ANOVA) was used to compare respective MCS scores and the PCS scores among the four groups described above: good sleepers, good sleepers using sleep medication, insomniacs, and insomniacs using sleep medication. In addition, ANOVA was used to compare these scores among the four groups, categorized based on the frequency of sleep medication use described above: no use, less than once a week, 1–2 times a week, and more than three times a week. When significant differences were found using ANOVA, a Bonferroni's *post hoc* analysis was used. The chi-square test and subsequent residual analysis were used to compare differences in the rates of insomniacs in the four groups categorized based on the frequency of sleep medication use. The factors associated with deterioration of the MCS score and those of the PCS score were examined using a series of logistic regression analyses. All variables were examined initially in univariate models. To control for confounding factors and to determine main correlates, we then performed multivariate logistic regression analyses for all variables that showed a significant correlation in univariate models. Statistical tests of the regression estimates' odds ratios (ORs) were based on Wald statistics. Odds ratios and their 95% confidence intervals (CIs) were presented to show the association. These statistical analyses were conducted using software (Statistical Package for the Social Sciences [SPSS], ver. 11.5J, SPSS Inc., Tokyo, Japan).

3. Results

3.1. Sample characteristics

Demographic characteristics of the sample population are presented in Table 1. The sample comprised 1222 men (43.3%) and 1600 women (56.7%) with mean [SD] age of 57.4 [17.7] years (range 20–97 years). The mean family size in this cohort was 4.6 [1.6]: 120 subjects (4.3%) lived alone and 1210 responders (43.9%) lived with more than five family members.

3.2. Differences in scores of MCS and PCS between the insomniac group and good sleepers group

Supplementary Fig. 1 (in online supplementary material) portrays comparisons between the MCS score and the PCS scores of the insomniac group's insomniacs and those using sleep medica-

Table 1
Demographic characteristics of the sample.

	n	%
Sex		
Male	1222	43.3
Female	1600	56.7
Age group		
20s	242	9.5
30s	266	10.4
40s	339	13.3
50s	574	22.5
60s	461	18.0
70s	444	17.4
80s	204	8.0
90s	25	1.0
Number of family members		
Alone	120	4.3
2 (with partner)	351	12.6
3 person	752	27.0
4 person	504	18.1
⩾5	1210	43.6
Habitual alcohol consumption		
Yes	1083	39.0
No	1697	61.0
Smoking habit		
Yes	609	21.9
No	2174	78.1

tion ($n = 365$) and comparisons of the good sleepers groups' good sleepers and those using sleep medication ($n = 2165$). Regarding these two values, significant differences were found between these two groups [MCS score, $t_{(2498)} = 14.5$, $p < 0.01$; PCS score, $t_{(2498)} = 9.9$, $p < 0.01$]. The insomniac group showed a significantly lower MCS score than the good sleepers group (45.3 ± 8.0 vs. 50.5 ± 5.9, $p < 0.01$). The insomniac group also showed significantly lower PCS scores than the good sleepers group (44.3 ± 8.6 vs. 48.3 ± 6.9, $p < 0.01$).

3.3. Factors associated with MCS score deterioration

The mean [SD] score of the MCS was 49.7 [6.6] in the total sample. We designated subjects whose scores were below those of the population average (50 points) as poor MCS. Results show that the mean [SD] score was 44.0 [5.3] in the group with poor MCS; the value was 54.4 [2.8] in the group with good MCS.

Univariate logistic regression analyses were performed for 10 independent variables: sex, age, smoking habit, habitual alcohol ingestion, living alone, home-based nursing care, existence of disease currently treated, depression, insomnia, and use of sleep medication (C6). Among these variables, five items (sex, age, home-based nursing care, depression, and insomnia) were significantly associated with MCS score deterioration in the univariate model. Multivariate logistic regression analysis revealed that MCS score deterioration was significantly associated with being female (OR = 1.52, 95%CI: 1.23–1.89), younger than the median age (<58 years, OR = 0.75, 95%CI: 0.61–0.92), having a family member requiring home-based nursing care (OR = 1.67, 95%CI: 1.31–2.12), depression (OR = 5.83, 95%CI: 4.60–7.38), and insomnia (OR = 2.29, 95%CI: 1.71–3.05) (Supplementary Table 2 in online supplementary material).

3.4. Factors associated with PCS score deterioration

The mean [SD] score of the PCS was 47.5 [7.4] in the total sample. We determined the subjects whose scores were below the general population averages (50 points) as poor PCS. The mean [SD] score of this value was 42.5 [6.3] in the group with poor PCS, although the value was 53.7 [2.2] in the group with good PCS.

Univariate logistic regression analyses were performed for the same 10 independent variables used for analysis of associated factors for MCS score deterioration. Among these variables, seven items (age, smoking habit, habitual alcohol ingestion, existence of disease currently treated, depression, insomnia, and use of sleep medication) showed significant correlations with deterioration of the PCS score. Multivariate logistic regression analysis revealed that PCS score deterioration was significantly associated with being older than the median age (⩾58 years, OR = 2.68, 95%CI: 2.21–3.25), existence of a disease currently treated (OR = 1.95, 95%CI: 1.59–2.39), depression (OR = 1.64, 95%CI: 1.31–2.05), insomnia (OR = 1.69, 95%CI: 1.27–2.24), and use of sleep medication (OR = 1.36, 95%CI: 1.16–1.61) (Supplementary Table 3 in online supplementary material).

3.5. Differences in MCS scores among the four groups categorized by both insomnia symptoms and sleep medication use

Fig. 1 presents a comparison of the MCS scores among the four groups: good sleepers, good sleepers using sleep medication, insomniacs, and insomniacs using sleep medication. Among the four groups, this value was significantly different ($F_{(3, 2496)} = 79.2$, $p < 0.01$), showing the following order: good sleepers (50.7 ± 5.8) > good sleepers using sleep medication (48.1 ± 7.7) > insomniacs (45.9 ± 7.8) > insomniacs using sleep medication (43.6 ± 8.7). Results of *post hoc* analyses show that the insomniacs using sleep medication had significantly lower MCS scores than those of the good sleepers ($p < 0.01$), the insomniacs ($p < 0.01$), or the good sleepers using sleep medication ($p < 0.01$). The insomniacs also had significantly lower scores than the good sleepers ($p < 0.01$). The good sleepers using sleep medication had significantly lower scores than the good sleepers ($p < 0.01$) but had significantly higher scores than those of the insomniacs ($p < 0.01$).

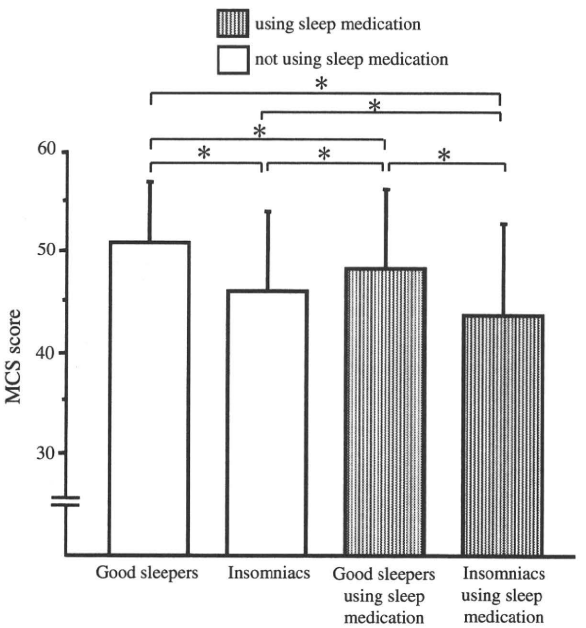

Fig. 1. Differences in MCS scores among four groups categorized by both insomnia symptoms and sleep medication use. MCS, mental component summary; good sleepers ($n = 2070$); insomniacs ($n = 280$); good sleepers using sleep medication ($n = 95$); insomniacs using sleep medication ($n = 85$); * $p < 0.01$, one-way ANOVA.

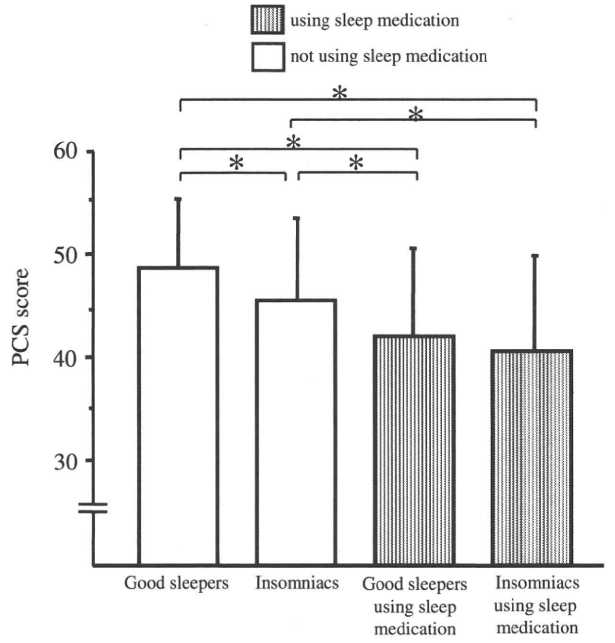

Fig. 2. Differences in PCS scores among four groups categorized by both insomnia symptoms and sleep medication use. PCS, physical component summary; good sleepers ($n = 2070$); insomniacs ($n = 280$); good sleepers using sleep medication ($n = 95$); insomniacs using sleep medication ($n = 85$); $p < 0.01$, one-way ANOVA.

3.6. Differences in PCS scores among the four groups categorized by both insomnia symptoms and sleep medication use

Fig. 2 presents a comparison of PCS scores among the four groups. A significant difference in this value was found among the four groups ($F_{(3, 2496)} = 72.7$, $p < 0.01$). The scores showed the following order: good sleepers (48.6 ± 6.6) > insomniacs (45.4 ± 8.0) > good sleepers using sleep medication (41.9 ± 8.5) > insomniacs using sleep medication (40.5 ± 9.2). *Post hoc* analyses revealed that the insomniacs using sleep medication had a significantly lower value than that of either the good sleepers or the insomniacs using sleep medication ($p < 0.01$, respectively). The insomniacs also had a significantly lower value than the good sleepers ($p < 0.01$). The good sleepers using sleep medication showed a significantly lower value than the good sleepers or the insomniacs ($p < 0.01$). No significant difference was found between the good sleepers using sleep medication and the insomniacs using sleep medication.

3.7. Differences in MCS and PCS scores among the four groups categorized by frequency of sleep medication use

Table 2 presents a comparison of the MCS and PCS scores among four groups categorized according to frequency of sleep medication use. Among the four groups, the MCS scores were significantly different ($F_{(3, 2496)} = 24.5$, $p < 0.01$). *Post hoc* analyses revealed that the group using sleep medication 1–2 times a week and that with sleep medication more than three times a week had significantly lower values than that with no sleep medication use ($p < 0.01$, respectively). For the PCS score, the value was significantly different among the four groups ($F_{(3, 2496)} = 64.5$, $p < 0.01$). *Post hoc* analyses revealed that the group using sleep medication 1–2 times a week and the group using sleep medication more than three times a week had significantly lower MCS scores than the group using no sleep medication ($p < 0.01$, respectively). The PCS scores were significantly different among the four groups ($F_{(3, 2496)} = 64.5$, $p < 0.01$). *Post hoc* analyses revealed that all three groups using sleep medication had significantly lower scores than the group of subjects using no sleep medication ($p < 0.01$, respectively). The group using sleep medication more than three times a week had a lower value than that using sleep medication less than once a week and 1–2 times a week ($p < 0.01$, respectively). The group using sleep medication 1–2 times a week had a significantly lower value than that using sleep medication less than once a week ($p < 0.01$). For respective groups, the numbers and rates of insomniacs were as follows: no use ($n = 264$, 11.5%), less than once a week ($n = 50$, 32.0%), 1–2 times a week ($n = 43$, 55.8%), and more than three times a week ($n = 137$, 44.5%). As Table 2 shows, significant differences were found in the rates of insomniacs among the four patient groups ($\chi^2_{(3)} = 188.9$, $p < 0.01$). The rest error test revealed that the two groups using sleep medication more than once a week showed higher rates of insomniacs than either the group with no medication use or the group using sleep medication once a week.

4. Discussion

Leger et al. reported that chronic insomniacs showed lower scores of SF-36 than good sleepers in all eight domains. The more severe the insomnia symptoms were, the worse the QOL [13]. Compatible with their results, our results showed that both the MCS scores and the PCS scores were significantly lower for insomniacs than for good sleepers in the study area population.

Results of multiple logistic analysis show that depression and age are associated with the deterioration of physical QOL and mental QOL. Younger age (<58 year) was associated with lower MCS scores, and older age (⩾58 year) was associated with lower PCS scores, as previous studies have also shown [31,32]. Being a woman and the presence of a family member needing home-based nursing care were also associated with lower mental QOL; the existence of currently treated diseases was associated with lower physical QOL. These results were compatible with those of previous reports [33–37]. In addition to these factors, insomnia was found to be a significant factor associated with deterioration of both the mental QOL and the physical QOL. Results of earlier reports have described that sleep loss deteriorates physical function such as postural sway [38], blood pressure elevation [39], glucose

Table 2
Differences in scores of MCS and PCS among four groups categorized by frequency of sleep medication use.

Frequency of sleep medication use (/week)	No use ($n = 2300$)	<1 ($n = 50$)	1⩽, 2⩽ ($n = 43$)	⩾3 ($n = 137$)
MCS	50.1 ± 6.2	48.2 ± 7.2	46.4 ± 7.4*	45.8 ± 8.8*
PCS	48.3 ± 6.8	46.8 ± 8.3*	44.0 ± 6.7*,a	40.4 ± 9.3*, a,b
Number of insomniacs (%)c	264 (11.5)	16(32.0)	24 (55.8)	61 (44.5)

MCS, mental component summary; PCS, physical component summary.
[a] $p < 0.01$ compared to the value in the group using sleep medication less than once a week.
[b] $p < 0.01$ compared to the value in the group using sleep medication 1–2 times a week.
[c] $\chi^2 = 188.9$ (df = 3), chi-square test.
* $p < 0.01$ compared to the value in the no use group.

intolerance [40], and immunological dysfunction [41]. Regarding mental function, insomnia has been identified as a risk factor for developing depression or anxiety disorder [42]. Furthermore, insomniacs undergo psychomotor performance degradation, including impairment of both cognitive function and short-term memory [9,43]. These physiological and/or psychological dysfunctions brought about by sleep loss and/or subjective insomnia might contribute to deterioration of mental QOL and physical QOL.

The most remarkable finding of this study was the different influences of sleep medication use on mental QOL and physical QOL: multiple logistic analyses revealed that sleep medication use is a significant factor associated with deterioration of physical QOL, but not mental QOL. To our knowledge, few reports in the relevant literature have described evaluation of the association between sleep medication use and physical QOL, especially in a large general population. Zammit et al., however, reported that no differences in SF-36 domains were observed between insomniac subjects receiving treatment for the disorder versus those who were untreated in a general population [12]. Inconsistent with their result, the present study showed that insomniacs using sleep medication have lower physical QOL than those not using sleep medication. More strikingly, good sleepers using sleep medication showed significantly lower PCS scores than insomniacs not using sleep medication, and the scores in this group were almost equal to that of insomniacs using sleep medication. Consequently, sleep medication use was thought to affect physical QOL negatively, irrespective of the improvement of insomnia symptoms. Benzodiazepine/non-benzodiazepine hypnotics are known to be effective for treatment of chronic non-organic insomnia. Nevertheless, many reports have described adverse effects of such medications on physical function, e.g., myorelaxant effects, amnesia, or next-day hangover effects [44–46]. It is possible, therefore, that the adverse effects of sleep medication contribute to deterioration of physical QOL in the subject population. Adverse effects would interfere with physical QOL improvement after the dissolution of insomnia if this were the case.

In contrast, sleep medication use was proven not to be a significant factor for deterioration of mental QOL. This fact might be reflected in the results showing that good sleepers using sleep medication showed a significantly higher MCS value than insomniacs who did not use sleep medication. As described above, several clinical studies have revealed that sleep medication has positive effects not only on sleep parameters, but also on daytime consequences of insomnia [20,47]. Given this fact, our results suggest that dissolution of insomnia symptoms with sleep medication can improve mental QOL, even in the general population.

Regarding the impact of the frequency of sleep medication use on QOL, for the MCS scores, the group using sleep medication 1–2 times a week and that using medication more than three times a week had significantly lower scores than that using no sleep medication use. For the PCS score, all groups with sleep medication had significantly lower scores than the group with no sleep medication use. These findings imply that the frequency of sleep medication use adversely affects both physical QOL and mental QOL. But the rate of incidence of insomniacs in each of the two groups using sleep medication more than once a week was higher than in either the group using sleep medication less than once a week or the group using no sleep medication. Therefore, the lack of a significant association between sleep medication use and the deterioration of mental QOL in our logistic regression analysis results was explainable by the greater negative impact of insomnia on mental QOL than that of frequency of sleep medication use.

This study has several limitations. First, it was impossible to obtain detailed information about medication usage, e.g., the kind and dosage of medication or the duration of usage. Future examination of the information described above related to sleep medication usage would clarify the influence of its adverse effects on QOL. Secondly, the differences in PCS scores among the four groups might reflect other causes which might bias the findings, i.e., individuals with insomnia or medical disease are more likely to have lower PCS scores because of disease processes and are more likely to take sleep medication because they are receiving medical attention. Our results, however, showed that the use of sleep medication use appeared as a significant factor for the deterioration of PCS independent of the existence of insomnia or any currently treated disease. Thirdly, we used six items of the PSQI after excluding items related to sleep medication use (C6). Therefore, different from standard scoring, the cut-off value of insomnia was set at 1 SD of the mean sum score (6.4). Doi et al. developed a Japanese version of PSQI and showed a mean score of each component for both their control and primary insomnia groups [28]. In their report, the mean sum score [SD] of the PSQI (C1 – C5 + C7) in the control group was 3.78 [1.78]; it was 7.86 [2.77] in the group with primary insomnia. The mean sum scores obtained in this study were, respectively, 3.95 [2.40] in the group without insomnia and 8.33 [2.19] in the insomniac group. Therefore, the cut-off value used for this study was considered reasonable. In addition, the results in this rural cohort study might differ from those for urban areas in Japan: they might not be representative of the Japanese general population.

Conclusively, results of this study demonstrate that insomnia is closely associated with deterioration of both mental QOL and physical QOL in this rural cohort. Sleep medication might be associated with improvement of mental QOL. Nevertheless, such medication might adversely affect physical QOL through disadvantageous effects. This finding underscores the importance of appropriate use of sleep medication for patients with insomnia.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.sleep.2009.09.011.

References

[1] Ohayon M. Epidemiological study on insomnia in the general population. Sleep 1996;19(Suppl. 3):S7–S15.
[2] Walsh JK, Ustun TB. Prevalence and health consequences of insomnia. Sleep 1999;22:S427–36.
[3] Weyerer S, Dilling H. Prevalence and treatment of insomnia in the community: results from the Upper Bavarian Field Study. Sleep 1991;14:392–8.
[4] Liu X, Uchiyama M, Kim K, Okawa M, Shibui K, Kudo Y, et al. Sleep loss and daytime sleepiness in the general adult population of Japan. Psychiatry Res 2000;93:1–11.
[5] Ohayon MM. Prevalence of DSM-IV diagnostic criteria of insomnia: distinguishing insomnia related to mental disorders from sleep disorders. J Psychiatr Res 1997;31:333–46.
[6] Moul DE, Nofzinger EA, Pilkonis PA, Houck PR, Miewald JM, Buysse DJ. Symptom reports in severe chronic insomnia. Sleep 2002;25:553–63.
[7] American Academy of Sleep Medicine. International classification of sleep disorders. Diagnostic and coding manual. 2nd ed. Westchester: American Academy of Sleep Medicine; 2005.
[8] Varkevisser M, Van Dongen HP, Van Amsterdam JG, Kerkhof GA. Chronic insomnia and daytime functioning: an ambulatory assessment. Behav Sleep Med 2007;5:279–96.
[9] Edinger JD, Means MK, Carney CE, Krystal AD. Psychomotor performance deficits and their relation to prior nights' sleep among individuals with primary insomnia. Sleep 2008;31:599–607.
[10] Varkevisser M, Kerkhof GA. Chronic insomnia and performance in a 24-h constant routine study. J Sleep Res 2005;14:49–59.
[11] Leger D, Scheuermaier K, Raffray T, Metlaine A, Choudat D, Guilleminault C. HD-16: a new quality of life instrument specifically designed for insomnia. Sleep Med 2005;6:191–8.
[12] Zammit GK, Weiner J, Damato N, Sillup GP, McMillan CA. Quality of life in people with insomnia. Sleep 1999;22(Suppl. 2):S379–85.
[13] Leger D, Scheuermaier K, Philip P, Paillard M, Guilleminault C. SF-36: evaluation of quality of life in severe and mild insomniacs compared with good sleepers. Psychosom Med 2001;63:49–55.

[14] Kaneita Y, Uchiyama M, Takemura S, Yokoyama E, Miyake T, Harano S, et al. Use of alcohol and hypnotic medication as aids to sleep among the Japanese general population. Sleep Med 2007;8:723–32.
[15] Ohayon MM, Caulet M. Insomnia and psychotropic drug consumption. Prog Neuropsychopharmacol Biol Psychiatry 1995;19:421–31.
[16] Englert S, Linden M. Differences in self-reported sleep complaints in elderly persons living in the community who do or do not take sleep medication. J Clin Psychiatry 1998;59:137–44.
[17] Mellinger GD, Balter MB, Uhlenhuth EH. Insomnia and its treatment. Prevalence and correlates. Arch Gen Psychiatry 1985;42:225–32.
[18] Asnis GM, Chakraburtty A, DuBoff EA, Krystal A, Londborg PD, Rosenberg R, et al. Zolpidem for persistent insomnia in SSRI-treated depressed patients. J Clin Psychiatry 1999;60:668–76.
[19] Krystal AD, Walsh JK, Laska E, Caron J, Amato DA, Wessel TC, et al. Sustained efficacy of eszopiclone over 6 months of nightly treatment: results of a randomized, double-blind, placebo-controlled study in adults with chronic insomnia. Sleep 2003;26:793–9.
[20] Walsh JK, Krystal AD, Amato DA, Rubens R, Caron J, Wessel TC, et al. Nightly treatment of primary insomnia with eszopiclone for six months: effect on sleep, quality of life, and work limitations. Sleep 2007;30:959–68.
[21] Walsh JK, Roth T, Randazzo A, Erman M, Jamieson A, Scharf M, et al. Eight weeks of non-nightly use of zolpidem for primary insomnia. Sleep 2000;23:1087–96.
[22] Zammit GK, McNabb LJ, Caron J, Amato DA, Roth T. Efficacy and safety of eszopiclone across 6-weeks of treatment for primary insomnia. Curr Med Res Opin 2004;20:1979–91.
[23] Nomura T, Inoue Y, Kusumi M, Uemura Y, Nakashima K. Prevalence of restless legs syndrome in a rural community in Japan. Mov Disord 2008;23:2363–9.
[24] Lefante Jr JJ, Harmon GN, Ashby KM, Barnard D, Webber LS. Use of the SF-8 to assess health-related quality of life for a chronically ill, low-income population participating in the Central Louisiana Medication Access Program (CMAP). Qual Life Res 2005;14:665–73.
[25] Ware JE, Kosinski M. Interpreting SF-36 summary health measures: a response. Qual Life Res 2001;10:405–13.
[26] Tokuda Y, Okubo T, Ohde S, Jacobs J, Takahashi O, Omata F, et al. Assessing items on the SF-8 Japanese version for health-related quality of life: a psychometric analysis based on the nominal categories model of item response theory. Value Health 2009;12:568–73.
[27] Buysse DJ, Reynolds 3rd CF, 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.
[28] Doi Y, Minowa M, Uchiyama M, Okawa M, Kim K, Shibui K, et al. Psychometric assessment of subjective sleep quality using the Japanese version of the Pittsburgh Sleep Quality Index (PSQI-J) in psychiatric disordered and control subjects. Psychiatry Res 2000;97:165–72.
[29] Honaga K, Yamada S, Liu M. Use of the SF-8 to assess health-related quality of life (HRQOL) in elderly patients with SMON (Subacute Myelo-Optico-Neuropathy). Jpn J Rehabil Med 2006;43:762–6.
[30] Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Measur 1977;1:385–401.
[31] Tokuda Y, Ohde S, Takahashi O, Shakudo M, Yanai H, Shimbo T, et al. Relationships between working status and health or health-care utilization among Japanese elderly. Geriatr Gerontol Int 2008;8:32–40.
[32] Takata Y, Ansai T, Soh I, Awano S, Yoshitake Y, Kimura Y, et al. Quality of life and physical fitness in an 85-year-old population. Arch Gerontol Geriatr, in press.
[33] Kennedy SH, Eisfeld BS, Cooke RG. Quality of life: an important dimension in assessing the treatment of depression? J Psychiatry Neurosci 2001;26(Suppl):S23–8.
[34] Linzer M, Spitzer R, Kroenke K, Williams JB, Hahn S, Brody D, et al. Gender, quality of life, and mental disorders in primary care: results from the PRIME-MD 1000 study. Am J Med 1996;101:526–33.
[35] Michalak EE, Tam EM, Manjunath CV, Solomons K, Levitt AJ, Levitan R, et al. Generic and health-related quality of life in patients with seasonal and nonseasonal depression. Psychiatry Res 2004;128:245–51.
[36] McCall WV, Dunn AG. Cognitive deficits are associated with functional impairment in severely depressed patients. Psychiatry Res 2003;121:179–84.
[37] Schulz R, Beach SR. Caregiving as a risk factor for mortality: the Caregiver Health Effects Study. JAMA 1999;282:2215–9.
[38] Nakano T, Araki K, Michimori A, Inbe H, Hagiwara H, Koyama E. Nineteen-hour variation of postural sway, alertness and rectal temperature during sleep deprivation. Psychiatry Clin Neurosci 2001;55:277–8.
[39] Suka M, Yoshida K, Sugimori H. Persistent insomnia is a predictor of hypertension in Japanese male workers. J Occup Health 2003;45:344–50.
[40] Gottlieb DJ, Punjabi NM, Newman AB, Resnick HE, Redline S, Baldwin CM, et al. Association of sleep time with diabetes mellitus and impaired glucose tolerance. Arch Intern Med 2005;165:863–7.
[41] Palma BD, Tiba PA, Machado RB, Tufik S, Suchecki D. Immune outcomes of sleep disorders: the hypothalamic–pituitary–adrenal axis as a modulatory factor. Rev Bras Psiquiatr 2007;29(Suppl 1):S33–38.
[42] Neckelmann D, Mykletun A, Dahl AA. Chronic insomnia as a risk factor for developing anxiety and depression. Sleep 2007;30:873–80.
[43] Fulda S, Schulz H. Cognitive dysfunction in sleep disorders. Sleep Med Rev 2001;5:423–45.
[44] Glass J, Lanctot KL, Herrmann N, Sproule BA, Busto UE. Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits. BMJ 2005;331:1169.
[45] Najib J. Eszopiclone, a nonbenzodiazepine sedative-hypnotic agent for the treatment of transient and chronic insomnia. Clin Ther 2006;28:491–516.
[46] Tagaya H. Pharmacotherapy of insomnia in clinical medicine. Nippon Yakurigaku Zasshi 2007;129:42–6.
[47] Hajak G, Clarenbach P, Fischer W, Haase W, Ruther E. Zopiclone improves sleep quality and daytime well-being in insomniac patients: comparison with triazolam, flunitrazepam and placebo. Int Clin Psychopharmacol 1994;9:251–61.

SLEEP AND BIOLOGICAL RHYTHMS

Sleep and Biological Rhythms 2011; **9**: 35–45 doi:10.1111/j.1479-8425.2010.00483.x

ORIGINAL ARTICLE

Stress coping behaviors and sleep hygiene practices in a sample of Japanese adults with insomnia

Yuichiro ABE, Kazuo MISHIMA, Yoshitaka KANEITA, Lan LI, Takashi OHIDA, Toru NISHIKAWA and Makoto UCHIYAMA

Department of Psychophysiology, National Institute of Mental Health, National Center of Neurology and Psychiatry, Tokyo, Japan

Abstract

This study examined the characteristics of behaviours for coping with stress and sleep hygiene practices utilized by adult people with insomnia. Self-administered questionnaire data from a representative sample of 24 551 adults (completed in 2000) were analyzed. Participants reported insomnia symptoms present during the last 1-month period, answering 11 items on physical and psychological conditions, 7 items on problem-solving and emotion-focused coping behaviors in response to stress (SCBs), 5 items on measures taken to ensure adequate sleep (SHPs), and the Center for Epidemiologic Studies Depression Scale (CES-D). Those presenting with insomnia symptoms accompanied by daytime complaints were defined as having insomnia. Multivariable logistic regressions were performed with sex, age, and the presence of stress as covariants to determine which SCBs and SHPs are factors associated with insomnia. Prevalence of insomnia was 43.4% (n = 10 653) and comorbidity of depression (CES-D > 26) occurred in 12.7% of participants (n = 1357, 5.5% of total sample). Logistic regression analysis controlling for other adjustment factors revealed that insomnia was positively associated with 4 emotion-focused SCBs ("Bearing", "Smoking", "Eating" and "TV/Radio"), negatively associated with "Problem-solving," and positively associated with 3 SHPs ("Alcohol", "Books/Music" and "Bath"). Insomnia comorbid with depression had a strong positive association with Bearing (OR = 3.44), but a strong negative association with Problem-solving (OR = 0.50). Japanese adults with insomnia might engage in various maladaptive SCBs and SHPs. The negative correlate of Problem-solving supports the importance of promoting self-help sleep practices in public health.

Key words: depression, insomnia, Japanese adult population, sleep hygiene practices (SHPs), stress coping behaviors (SCBs).

Correspondence: Dr Yuichiro Abe, Department of Psychophysiology, National Institute of Mental Health, National Center of Neurology and Psychiatry, 4-1-1 Ogawa-Higashi, Kodaira, Tokyo 187-8553, Japan. Email: yuichiro1208@gmail.com

Acronyms used: ICSD-2 = International Classification of Sleep Disorders, 2nd Edition; DSM-IV-TR = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision; SCBs = stress coping behaviors; SHPs = sleep hygiene practices; CES-D = Center for Epidemiologic Studies Depression Scale; OR = odds ratio.

Accepted 8 November 2010.

INTRODUCTION

Insomnia is a common sleep disorder. The reported prevalence of insomnia in the general population varies widely, ranging between 4.4% and 48%, depending on sample characteristics and the definition of insomnia.[1–4] Chronic insomnia not only reduces the quality of sleep during the night, but also causes a variety of impairments in mental and physical functioning during the daytime.[5–10] Chronic insomnia is associated with both human and socioeconomic costs, such as increased long-term absenteeism at work, reduced performance and productivity, and increased industrial accidents and health-care costs.[11–16] Moreover, alongside insomnia being the most common symptom of depression,[17–21] persistent insomnia is a risk or exacerbating factor of depressive disorders.[22–27]

Factors leading to the onset and worsening of insomnia are multidimensional in nature,[28] and many life events and life stresses can result in acute insomnia.[28–30] Based on the 3P model proposed by Spielman that is widely used to explain the onset mechanism of insomnia,[31] three factors (predisposing, precipitating, and perpetuating) are closely linked to insomnia development. With underlying predisposing factors (including age, sex, genetic disposition, and lifestyle), insomnia emerges as precipitating factors (stressful life events such as divorce, pain, and psychological and physical problems) are superimposed, and the insomnia becomes chronic and difficult to treat because of perpetuating factors (maladaptive sleep hygiene practices, dysfunctional cognition about sleep loss and its impact on life).[23,31–34]

Inadequate stress coping behavior also precipitates insomnia, and heightens uneasiness and tension around being unable to sleep, thereby perpetuating the sleeplessness.[7,8,35] Further, insomniacs may often engage in poor sleep hygiene, such as having an inadequate sleep environment, lack of daytime activities, and excessive afternoon napping.[7,8,30–35] It is reported that the majority of people with insomnia attempt to cope with sleep problems in various ways,[36] have fewer adaptive coping skills, rely more on emotion-focused coping strategies than on problem-solving strategies,[37] and report lower feelings of mastery.[24,38–40] Although reduced quality of life associated with insomnia has been reported in a general population sample,[9,10,32] few studies have examined specific daily behaviors and practices of people with insomnia.

The aims of this study are: (i) to investigate the prevalence of insomnia during the past one month associated with daytime impairments among Japanese adults; and (ii) to examine how insomnia and comorbid depression are associated with stress coping behaviors (SCBs) and sleep hygiene practices (SHPs), using data of a representative sample from a large-scale epidemiological study on sleep habits and their correlates.

MATERIALS AND METHODS

Data source

The present study was conducted using partial data from the Active Survey of Health and Welfare performed in June 2000 by the Ministry of Health, Labour and Welfare. The purpose of the survey was to collect basic data on health and welfare, including sleep habits, from the general public of Japan. To provide a representative sample of the general population, the survey was conducted through public health centers in 300 target areas randomly selected from the 881 851 national census areas nationwide. Participants were household members aged ≥12 years, all Japanese. Survey officials for home visits were employed part-time and trained as research associates by public health centers across Japan during this time. For data collection, these research associates visited each participating household to distribute self-administered questionnaires and collect them a few days later.

All survey respondents provided verbal informed consent to participate. Their privacy was protected in accordance with the Declaration of Helsinki guidelines.

Measures

The self-administered questionnaire for the present study was developed by two of the authors (MU and TO.) and an appropriate official from the Ministry of Health, Labour, and Welfare. The self-administered questionnaire consisted of 44 items covering: (ii) sociodemographic characteristics including age and sex; (ii) general health status; (iii) physical and psychological complaints; (iv) information on mental stress; (v) sleep habits and problems; and (vi) Center for Epidemiologic Studies Depression Scale (CES-D) Japanese version.[41]

To examine factors associated with 1-month insomnia and determine whether stress was present, one item ("Have you experienced stress in your daily life during the last one month period?") was extracted from the 44 items on the self-administered questionnaire. Seven items related to mental stress were extracted from the question "What do you do to deal with insomnia, worries, difficulties, and/or stress?" Five items related to sleep habits and problems were extracted from the

question "Have you tried to do any of the following during the last one month period to get enough sleep?" The CES-D is a self-report scale designed specifically to measure depressive symptomatology in the general population during the previous week-long period[42] and has appropriate levels of reliability and validity for use with a general population. Each item is rated on a scale of 1 to 3 points, and the result is evaluated based on the total score for all 20 items (range 0 to 60 points). Higher scores indicate increased severity of depression. This scale is designed to screen, not to diagnose, major depression. The reliability and validity of the CES-D Japanese version has been reported in Japan.[41]

Case definition of insomnia

Based on an algorithm that combined the general criteria of insomnia in ICSD-2[43] and the diagnostic criteria of primary insomnia in DSM-IV,[44] we first selected cases reporting the presence of both insomnia symptoms and physical/psychological complaints during the past one month, identified based on the responses to the survey questionnaire about sleep problems and daytime functioning during the past one month. Then we excluded cases reporting a common comorbid sleep disorder (sleep-disordered breathing and restless leg syndrome). Therefore, people with insomnia were defined here as individuals who reported all of the following.

A) *Sleep problems*. We determined a respondent had insomnia symptoms when reporting any of the following items occurring or persisting during the past one month: "difficulty falling asleep," "waking up frequently during the night," "waking up early in the morning," and "getting up in the morning feeling unrefreshed or not restored (nonrestorative sleep)."
B) *Daytime impairments*. We determined that a respondent had daytime impairments when reporting any of 6 physical complaints (head-heaviness/headache, gastric discomfort, diarrhea/constipation, shoulder/neck stiffness, fatigability, and residual fatigue) or 5 psychological complaints (depression, irritability, anxiety, hypochondria, and daytime sleepiness), which are common symptoms of insomnia,[43] occurring or persisting during the past one month.[44]
C) *No comorbid sleep disorder*. We excluded cases with comorbid sleep-disordered breathing or restless legs syndrome, which are also common in the general population. We excluded respondents reporting either "waking up during the night due to loud snoring and breathing difficulty" or "feeling a crawling sensation deep inside my legs" occurring or persisting during the past one month.

Case definition of insomnia comorbid with depression

We defined the presence of depression as a score of ≥26 (range 0–60) on the 20-item CES-D Japanese version. Studies in West European countries indicate that a score of ≥16 is indicative of probable clinical depression,[42] but we set the cutoff score for depression at 26 according to the criterion used by national census studies conducted in Korea[45] and Japan.[46] Among the respondents of the Active Survey of Health and Welfare, 8.1% scored ≥26 on the CES-D, which was close to the 12-month prevalence of mood disorders based on the DSM criteria (6.8%) obtained in a community survey conducted between 2002 and 2003 in Japan.[47] We defined "people with insomnia comorbid with depression" as those who had 1-month insomnia and scored ≥26 points on the CES-D Japanese version.

Stress coping behaviors (SCBs)

Respondents were asked to answer the following questions: "Do you use the following coping behaviors when you feel dissatisfied or distressed, or experience problems or stress?" (yes = 1, no = 0). They indicated if each of the following 7 items describing everyday stress coping behaviors applied to them: (i) "Making an effort to solve the problems actively [Problem-solving];" (ii) "Making plans to take time off [Time off];" (iii) "Eating something [Eating]," (iv) "Watching TV/ Listening to the radio [TV/Radio];" (v) "Taking it easy [Ease];" (vi) "Smoking [Smoking];" and (vii) "Bearing the stress without taking any action [Bearing]."

Sleep hygiene practices (SHPs)

Respondents were asked to answer the following questions: "Did you engage in any of the following practices in the past one month in order to sleep well?" (yes = 1, no = 0, except for the first item). They indicated whether each of the following 5 items describing everyday sleep hygiene practices applied to them: (i) "Drinking alcohol [Alcohol];" (ii) "Taking light exercise [Exercise];" (iii) "Taking a bath [Bath];" (iv) "Reading books/Listening to music [Books/Music];" and (v) "Trying to have regular daily habits [Regularity]."

Table 1 Demographic characteristics of analyzed subjects in a sample of the Japanese adult general population (n = 24 551)†

	Study subjects			Census 2000 (n = 100 733 618)	
Age class (years)	Subtotal % (n)	Male % (n)	Female % (n)	Male %	Female %
20–29	18.2 (4468)	18.4 (2145)	18.0 (2323)	19.1	17.2
30–39	18.4 (4508)	18.4 (2152)	18.3 (2356)	17.5	16.1
40–49	18.8 (4606)	19.2 (2249)	18.3 (2357)	17.2	16.0
50–59	20.5 (5036)	21.0 (2453)	20.0 (2583)	19.5	18.6
60–69	14.0 (3436)	14.5 (1691)	13.6 (1745)	14.6	14.9
≤70	10.2 (2497)	8.5 (999)	11.6 (1498)	12.1	17.4
Total	100 (24551)	100 (11689)	100 (12862)	100	100

†Data for both the present study and the overall census were obtained in 2000.

Respondents rated the item [Alcohol] on a 4-point scale: "None," "1–2 times per month," "1–2 times per week," and "more than 3 times per week." On this item, we coded "1–2 times per week" and "more than 3 times per week" as "yes."

Presence of stress

Respondents were asked to answer the following question: "Did you feel dissatisfied or distressed, or experience any difficulties or stress during the past one month?" They answered this question on a 4-point scale: "much," "some," "little", and "none." In our study, "much" was coded as "yes" and the other response choices were coded as "no" (yes = 1, no = 0).

Statistical analysis

The prevalence of insomnia and prevalence of insomnia comorbid with depression were compared by sex and age group, using chi-square tests. Associations between individual SCB and SHP factors and insomnia (or comorbid with depression) were examined. Logistic regression analyses were performed to identify associations between each factor and 1-month insomnia.

Sex, age group – younger (20–39), middle-aged (40–59), and old-aged (≥60) – and presence of stress were entered into the regression models to adjust for the confounding effects of sociodemographic and other factors. Odd ratios (ORs) were calculated from both the univariate analyses and the multivariate logistic regression analysis with 95% confidence intervals. Statistical significance was set at $P < 0.01$. All analyses were performed using SPSS 11.5 for Windows (SPSS Inc, Chicago, IL, USA).

RESULTS

Sample characteristics

A total of 32 729 people completed the survey questionnaire. We limited the sample to adults aged ≥20 years and further excluded those with any missing data for the variables included in our analysis. Before conducting analyses, data from 707 participants were excluded for submitting blank survey sheets. Minors aged <20 years (n = 3284) were excluded because this study focused on adults. Additionally, data from respondents who did not answer questions regarding sex and age (n = 208) and data from those who did not answer >6 items on the CES-D were excluded (n = 3979). Thus, the final sample for analysis comprised 24 551 adults: 11 689 (47.7%) men and 12 862 (52.3%) women, with a mean age of 47.1 years (range 20–100 years). Demographic data of the study sample are shown in Table 1.

Compared with the national census data collected around the same time, our study sample included a smaller proportion of adults aged ≥70, but the rates for the other age groups were similar. The national census data were based on all residents of Japan on October 1, 2000, and Table 1 indicates that our study sample was a representative sample of the general population of Japan. Because the total number of residents recruited in each target area was not made public by the Ministry of Health, Labour and Welfare, we were unable to compute the response rate. The Active Surveys of Health and Welfare conducted 3, 4, and 6 years prior to 2000 had response rates of 87.1%, 89.6%, and 87.3%, respectively. Since the methodology of the survey has remained the same over the years, we postulated that the response rate for our study sample was similar to those from previous surveys.[46]

Table 2 Presence of insomnia and insomnia comorbid with depression, by age group and sex

	Insomnia			Insomnia comorbid with depression		
Age class (years)	Subtotal % (*n*)	Male % (*n*)	Female % (*n*)	Subtotal % (*n*)	Male % (*n*)	Female % (*n*)
20–29	37.1 (1661)	33.4 (716)	40.7 (945)	5.6 (252)	4.9 (106)	6.3 (146)
30–39	41.7 (1881)	38.8 (834)	44.4 (1047)	4.4 (198)	3.3 (72)	5.3 (126)
40–49	41.5 (1911)	42.3 (953)	40.6 (958)	5.1 (236)	4.5 (102)	5.7 (134)
50–59	45.5 (2290)	45.1 (1107)	45.8 (1183)	5.0 (253)	4.6 (112)	5.5 (141)
60–69	48.1 (1653)	46.1 (780)	50.0 (873)	4.5 (155)	4.6 (78)	4.4 (77)
≤70	50.3 (1257)	48.8 (488)	51.3 (769)	10.5 (263)	9.0 (90)	9.8 (173)
Total	43.4 (10653)	41.7 (4878)	44.9 (5775)†	5.5 (1357)	4.8 (560)	6.2 (797)†

†Significant difference between men and women ($P < 0.001$, chi-square test).

Prevalence of insomnia

Prevalence of insomnia in the study sample by sex and age group is summarized in Table 2. In the entire sample, the prevalence was 43.4% (n = 10 653). The rate was significantly higher in women than in men: 44.9% (5775/12 862) versus 41.7% (4878/11 689), $\chi^2 = 25.02$, $P < 0.001$. The prevalence comorbid with depression (i.e. people with insomnia who scored ≥26 on the CES-D Japanese version) was 5.5% (n = 1357) of the entire sample and 12.7% of the sample of people with 1-month insomnia. The prevalence was significantly higher in women than in men: 6.2% (797/12 862) versus 4.8% (560/11 689), $\chi^2 = 23.17$; $P < 0.001$.

Percentage of SCBs and SHPs

The frequencies of each SCB and SHP item among people with insomnia and insomnia comorbid with depression are shown in Table 3.

SCB factors associated with insomnia

Table 3 shows the SCB factors associated with insomnia and their ORs. In multivariable logistic regression, incidence was significantly positively associated with four SCB factors: Bearing (OR = 1.69), Smoking (OR = 1.26), Eating (OR = 1.22), and TV/Radio (OR = 1.18), all $P <$ 0.01. Conversely, Problem-solving was the only SCB with a significantly negative correlation (OR = 0.87). Time off and Ease showed no significant association.

SHP factors associated with insomnia

Table 3 also shows the SHP factors associated with insomnia and their ORs. In multivariable logistic regression, insomnia was significantly positively associated with three of the SHP factors: Alcohol (OR = 1.27), Books/Music (OR = 1.24), and Bath (OR = 1.09), all $P < 0.01$. Regularity and Exercise were not significantly correlated. None of the SHPs was negatively correlated.

SCB factors associated with insomnia comorbid with depression

Table 3 shows the SCB factors associated with insomnia comorbid with depression and their odds ratios. Multivariate logistic analysis showed the following four SCB factors had significant positive relations with insomnia comorbid with depression in descending order: Bearing (OR = 3.44), Smoking (OR = 1.73), TV/Radio (OR = 1.52), and Eating (OR = 1.51). Conversely, SCB factors with significant negative relations with insomnia comorbid with depression included Problem-solving (OR = 0.50) and Ease (OR = 0.74). Time off was not significantly related to insomnia comorbid with depression.

SHP factors associated with insomnia comorbid with depression

The SHPs associated with insomnia comorbid with depression and their odds ratios are also shown in Table 3. Multivariate logistic analysis showed insomnia comorbid with depression was significantly and positively related only to Books/Music (OR = 1.36). Conversely, the only factor with a significant negative relationship with insomnia comorbid with depression was Regularity. The individual factors of Alcohol, Bath, and Exercise showed no significant relationship with incidence comorbid with depression.

Table 3 Association between insomnia or insomnia comorbid with depression and each factor of stress coping behaviors and sleep hygiene practices

	Insomnia (n = 10653)					Insomnia comorbid with depression (n = 1357)				
		Crude		Adjusted†			Crude		Adjusted†	
	N	OR	95%CI	OR	95%CI	N	OR	95%CI	OR	95%CI
Stress coping behaviors (SCB)										
Bearing the stress without taking any action (Bearing)	1576	1.97	1.78–2.18	1.69	1.52–1.88	378	3.49	2.96–4.10	3.44	2.92–4.05
Smoking (Smoking)	1954	1.22	1.12–1.33	1.26	1.15–1.38	317	1.48	1.24–1.76	1.73	1.44–2.08
Eating something (Eating)	1663	1.27	1.16–1.39	1.22	1.11–1.34	273	1.58	1.33–1.88	1.51	1.26–1.81
Watching TV/Listening to radio (TV/ Radio)	3650	1.26	1.17–1.35	1.18	1.10–1.27	537	1.57	1.35–1.83	1.52	1.30–1.78
Making an effort to solve problems actively (Problem solving)	1609	0.88	0.80–0.96	0.87	0.80–0.95	121	0.50	0.39–0.64	0.50	0.39–0.65
Taking it easy (Ease)	3630	*n.s.*	–	*n.s.*	–	354	0.72	0.61–0.85	0.74	0.63–0.87
Making plans to take time off (Time off)	734	*n.s.*	–	*n.s.*	–	65	*n.s.*	–	*n.s.*	–
Sleep hygiene practices (SHP)										
Drinking alcohol (Alcohol)	2961	1.24	1.15–1.34	1.27	1.18–1.38	349	*n.s.*	–	*n.s.*	–
Reading books/Listening to music (Books/ Music)	3747	1.20	1.12–1.29	1.24	1.15–1.33	460	1.36	1.16–1.59	1.39	1.19–1.63
Taking a bath (Bath)	4983	1.13	1.05–1.21	1.09	1.01–1.17	587	*n.s.*	–	*n.s.*	–
Trying to have regular daily habits (Regularity)	4114	*n.s.*	–	*n.s.*	–	420	0.69	0.59–0.80	0.64	0.55–0.75
Taking light exercise (Exercise)	2174	*n.s.*	–	*n.s.*	–	239	*n.s.*	–	*n.s.*	–

†Adjusted for sex, age, and presence of stress by multiple logistic regression analyses. CI, confidence interval; Crude, non-adjustment; OR, odds ratio ($P < 0.01$).

DISCUSSION

We found a fairly high prevalence of insomnia (43.4%) as defined in this study in the general Japanese population. Although previous studies have pointed out that Japanese people tend to underreport their sleep problems because of cultural reticence compared with those in Western cultures,[3] our results did not necessarily align with these studies. One previous study based on a sample of 3030 Japanese reported that 21.4% of the general population suffered "always" or "often" from insomnia.[48] Stewart *et al.* have shown the prevalence of insomnia symptoms/syndromes differs dramatically when different definitions of insomnia are applied.[49] More than 50 large-scale surveys have examined the prevalence of insomnia, but variations in the rates are attributable to differences in methodology and confusion over the standardized definitions of insomnia used.[1–5,49]

Possible reasons for the higher prevalence of insomnia obtained in our study include the following. First, following the ICSD-2 criteria, an item on nonrestorative sleep was added to our definition of insomnia. Secondly, our sample may have included cases with short-term insomnia occurring in less than the past one month (e.g. adjustment insomnia) in the absence of specifications on

the duration and frequency of insomnia symptoms. The case definition of insomnia based partially on the ICSD-2 and DSM-IV was more liberal than the original definitions of the disorder. Lastly, the greatest factor responsible for our higher prevalence rate was the inadequate assessment of daytime impairments associated with insomnia. It is possible that the complaints from participants were related to physical or psychological problems, which are separate issues from insomnia. However, as some studies have indicated,[9,10] and to the extent of our knowledge, there is no validated self-reporting tool about which researchers are in consensus for accurately measuring daytime impairments due to insomnia.

The presence of insomnia comorbid with depression was 5.5% (n = 1357), with a rate of 12.7% among the sample of people with insomnia. Ford *et al.* reported 14.0% as a prevalence of insomnia co-occurring with depression in a study based on 7954 American households.[22] Vollarath *et al.* state that insomnia constitutes an independent syndrome,[24] and Buysse *et al.* suggest that insomnia and depression are commonly comorbid, and insomnia comorbid with depression is an important intermediate phenotype.[25] Our study is the first to find that the frequency of insomnia comorbid with depression observed in Western countries is stable in Japanese adults as well (approximately one seventh of the population).

SCBs among people with insomnia

As far as we know, this is the first report that investigates stress-coping behaviors among people with insomnia in the general adult population. According to Lazarus and Folkman,[50] coping behavior refers to cognitive and behavioral efforts to manage external and internal demands. There are two types of coping behaviors: problem-focused and emotion-focused behaviors.[51] With regards to the coping behaviors among people with insomnia, Morin *et al.*[37] indicate that, compared with good sleepers, people with insomnia are apt to perceive their lifestyle as more stressful and choose more emotion-focused coping behaviors. This does not contradict reports indicating that people with insomnia tend to internalize stress, affecting emotions.[8,35–39] Similar trends were observed in the sample of people with insomnia in the present study. Our multivariable logistic regression analysis revealed that, among the seven SCBs, insomnia was positively related to the emotion-focused coping behaviors of bearing, smoking, eating, and TV/radio. Bearing had the strongest positive correlation with insomnia (OR = 1.69), and an even stronger correlation with insomnia comorbid with depression (OR = 3.44). Therefore, our study indicates that problem-focused behaviors represented by Problem-solving could be helpful in overcoming insomnia.

While Ease was not significantly related to insomnia, it had a significant relation with insomnia comorbid with depression (OR = 0.74). This indicates that people with insomnia may not necessarily engage in the same stress-coping behavior as insomniacs comorbid with depression. The present findings indicate that novel therapeutic strategies need to be developed, taking into account both characteristics of insomnia and depression.

This study further revealed a strong positive association between Smoking and insomnia (OR = 1.26). Previous research in Europe and in the United States indicates a relationship between nicotine consumption through smoking and poor sleep quality.[34,52–54] Furthermore, the strong association between Smoking and insomnia comorbid with depression (OR = 1.73) indicates that individuals with insomnia comorbid with depression tend to rely on more unhealthy coping strategies in their daily life. Our results might highlight the importance of strongly urging people complaining of insomnia to quit smoking.[24,33,34]

Eating was significantly related to insomnia. A previous epidemiological study reported that irregular eating habits and subjective sleep insufficiency were closely associated.[55] TV/Radio is also significantly related to insomnia. Morin *et al.* indicated that many individuals initiate a variety of self-help strategies to alleviate insomnia, including listening to music and relaxation.[2] In fact, these individuals may experiment with a variety of these passive emotional focused self-help remedies for a considerable period of time before seeking professional help.

SHPs among people with insomnia

There have been several studies that have shown that individuals with insomnia often engage in some inappropriate sleep practices. In a population-based sample of 258 insomniacs, Jefferson *et al.*[34] reported that, compared with healthy people, insomniacs more habitually drank alcohol before going to bed. Our study also demonstrated that alcohol consumption before going to bed is positively related to insomnia. Research in the United States suggests that drinking alcohol is an important risk factor for sleep problems.[56] In their comparison of sleep habits among people in ten different countries, Soldatos *et al.* found that Japan ranked the highest in terms of the prevalence of alcohol use as a sleep aid (30.3%).[57] Thus,

it is critical to provide sleep hygiene education about minimizing alcohol consumption before bedtime to people with insomnia.

Our analysis further found that Books/Music was also positively related to insomnia. Some previous studies have reported that reading behavior is significantly more frequent among groups with insomnia than control groups.[2,35,58] Morin *et al.* found in their epidemiological survey of a general population in Canada that insomnia syndrome sufferers use music (OR = 2.6) and reading (OR = 1.8) as self-help strategies to facilitate sleeping.[2] In our study, combining Books and Music into one item in the questionnaire may have comparatively reduced the odds ratio.

One epidemiological study among Japanese indicates that poor exercise habits are associated with insomnia.[48] Based on this finding, we hypothesized that physical activity would be an inhibiting factor for insomnia symptoms; however, there was no significant relationship between Exercise and insomnia. Previous research suggests that daytime physical activity improves sleep.[58,59] The inconsistency in the findings might be attributable to the lack of information available regarding the type (level), duration, and frequency of physical activity in our study.

While Bath was slightly related to insomnia, it had no significant association with insomnia comorbid with depression. Subjective sleep sufficiency is better for individuals when they take a bath before going to bed rather than when they do not.[60] Taken together, these observations may indicate that taking a bath improves the subjective quality of comorbid depression.

By contrast with previous studies,[61,62] our analysis found no significant association between Regularity and insomnia. This may be attributable to the fact that we did not define the behaviors belonging to this SHP in a concrete manner. Regular exposure to photic and nonphotic time cues (Zeitgebers) for the circadian clock system supposedly stabilizes the acrophases of the sleep–wake rhythm as well as the physiological rhythm, allowing one to fall asleep and maintain sleep more easily. The strong negative association between Regularity and insomnia comorbid with depression (OR = 0.64) found in the present study supports a treatment emphasis on regularity for mood disorders including bipolar disorder.[63]

Study limitations

We recognize several limitations of this research. Firstly, due to the cross-sectional survey design, the study is unable to establish a direct causal relationship between insomnia and SCBs and SHPs. This study also lacked analysis on the socioeconomic background of participants. This is an essential defect of the study because sleep behaviors are markedly affected by this component. However, the main purpose of this study was not to conclude that SCBs and SHPs in daily life cause or are caused by insomnia, not to investigate socioeconomic background, but rather to examine the psychobehavioral characteristics of people with insomnia based on a large representative sample of the general population, and this purpose was achieved. Secondly, people with insomnia in the present study were identified only by a subjective assessment via a self-administered questionnaire; they were not diagnosed by objective measures such as polysomnography and actigraphy. Since it was a large-scale survey of the general population, subjective responses were not obtained via a rigorous methodology (e.g. a structured interview). For this reason, the definition of insomnia in the study might include other sleep disorders that occur less frequently than insomnia but are observed across a wide range of ages, such as parasomnia and circadian rhythm sleep disorder. Indeed, many physical and other psychiatric problems (schizophrenia, affective disorder and chronic pain, etc.) still included in the study may cause insomnia. Identifying cases with insomnia meeting the general criteria of the ICSD-2 or DSM-IV in a finer-grained manner to claim a prevalence figure not only requires a self-report survey, but also a structured interview and polysomnography. Thus, the prevalence figure in this study is of very limited value, since the case definition of insomnia does not fulfill the frequency, severity and duration criteria. Such data collection for more rigorous epidemiological study would incur an enormous cost. Lastly, as our previous reports have also suggested,[46,55] the stress coping behaviors and sleep hygiene practices defined in this study were not clearly distinguished and selected properties. As a result, it is unknown whether the characteristics of the Japanese population-based sample of people with insomnia will generalize to those of clinically referred people with insomnia.

To date, individuals still underreport possible sleep problems and are unlikely to be receiving proper treatment.[2,3,32,36,64] Many of the participants with insomnia as described in this study are likely those who are in the "preinsomnia" moment,[28] and do not consider themselves insomniacs. They may be characterized by vulnerabilities in how they perceive and experience stressful life events negatively.[28,29,37] Most are not seeking help,[2,6,64] and possibly they will continue to engage in

self-help maladaptive practices, such as substance abuse, until they are finally diagnosed with chronic insomnia or depression.[2,24,35,39] This study mainly targeted adults, but future research needs to examine SCBs and SHPs among minors,[65] as well as study the onset of insomnia and its temporal development into chronic insomnia.[25,28–30,66]

CONCLUSION

We found that the presence of insomnia among Japanese was as high as 43.4% and that insomnia comorbid with depression occurred at a fixed frequency of 12.7% (approximately one seventh) of this general sample. Among the SCBs that people with insomnia use in daily life, emotion-focused coping behaviors such as bearing and smoking may act as precipitating or perpetuating factors for insomnia. With regard to SHPs, we found several distinguishing self-help behaviors among the participants. These findings may offer critical insights for developing effective sleep educational preventative programs.

ACKNOWLEDGEMENTS

This study was supported by a Health Science Research Grant from the Ministry of Health, Labour and Welfare. The authors report no other financial affiliation or relationship relevant to the subject of this article.

REFERENCES

1 Ohayon MM. Epidemiology of insomnia: what we know and what we still need to learn. *Sleep Med. Rev.* 2002; **6**: 97–111.
2 Morin CM, Leblanc M, Daley M, Gregoire JP, Merette C. Epidemiology of insomnia: prevalence, self-help treatments, consultations, and determinants of help-seeking behaviors. *Sleep Med.* 2006; **7**: 123–30.
3 Leger D, Poursain B, Neubauer D, Uchiyama M. An international survey of sleeping problems in the general population. *Curr. Med. Res. Opin.* 2008; **24**: 307–17.
4 Leger D, Gilleminault C, Dreyfus JP, Delahaye C, Pallard M. Prevalence of insomnia in a survey of 12 778 adults in France. *J. Sleep Res.* 2000; **9**: 35–42.
5 National Institutes of Health. National Institutes of Health state of the science conference statement on manifestations and management of chronic insomnia in adults, June 13–15, 2005. *Sleep* 2005; **28**: 1049–57.
6 Buysse DJ. Chronic insomnia. *Am. J. Psychiatry* 2008; **165**: 678–86.
7 Bonnet MH, Arand DL. 24-Hour metabolic rate in insomniacs and matched normal sleepers. *Sleep* 1995; **18**: 581–8.
8 Basta M, Chrousos GP, Vela-Bueno A, Vgontzas AN. Chronic insomnia and stress system. *Sleep Med. Clin.* 2007; **2**: 279–91.
9 Leger D, Scheuermaier K, Philip P, Paillard M, Guilleminault C. SF-36: evaluation of quality of life in severe and mild insomniacs compared with good sleepers. *Psychosom. Med.* 2001; **3**: 49–55.
10 Ohayon MM, Lemoine P. Daytime consequences of insomnia complaints in the French general population. L'Encéphale 2004; 222–7.
11 Leger D, Guilleminault C, Bader G, Levy E, Paillard M. Medical and socio-professional impact of insomnia. *Sleep* 2002; **5**: 625–9.
12 Daley M, Morin CM, LeBlanc M, Grégoire JP, Savard J. The economic burden of insomnia: direct and indirect costs for individuals with insomnia syndrome, insomnia symptoms, and good sleepers. *Sleep* 2009; **32**: 55–64.
13 Sivertsen B, Overland S, Neckelmann D *et al.* The long-term effect of insomnia on work disability: the HUNT-2 historical cohort study. *Am. J. Epidemiol.* 2006; **163**: 1018–24.
14 Ozminkowski RJ, Shaohung SW, Walsh JK. The direct and indirect costs of untreated insomnia in adults in the United States. *Sleep* 2007; **30**: 263–73.
15 Simon GE, VonKorff M. Prevalence, burden, and treatment of insomnia in primary care. *Am. J. Psychiatry* 1997; **154**: 1417–23.
16 Ohayon MM, Smirne S. Prevalence and consequences of insomnia disorders in the general population of Italy. *Sleep Med.* 2002; **3**: 115–20.
17 Mellinger GD, Balter MB, Uhlenhuth EH. Insomnia and its treatment. Prevalence and correlates. *Arch. Gen. Psychiatry* 1985; **42**: 225–32.
18 Soldatos CR. Insomnia in relation to depression and anxiety: epidemiologic considerations. *J. Psychosom. Res.* 1994; **38** (Suppl 1): 3–8.
19 Taylor DJ, Lichstein KL, Durrence HH, Reidel BW, Bush AJ. Epidemiology of insomnia, depression, and anxiety. *Sleep* 2005; **28**: 1457–64.
20 Tsuno N, Besset A, Ritchie K. Sleep and depression. *Clin. Psychiatry* 2005; **66**: 1254–69.
21 Jindal RD, Buysse DJ, Thase ME. Maintenance treatment of insomnia: what can we learn from the depression literature? *Am. J. Psychiatry* 2004; **161**: 19–24.
22 Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders: an opportunity for prevention? *JAMA* 1989; **262**: 1479–84.
23 Foley DJ, Monjan AA, Izmirlian G, Hays JC, Blazer DG. Incidence and remission of insomnia among elderly adults in a biracial cohort. *Sleep* 1999; **22**: S373–78.
24 Vollath M, Wicki W, Angst J. The Zurich Study VIII. Insomnia: association with depression, anxiety, somatic