Relationship between insomnia with alcohol drinking before sleep (Ne-Zake) or in the morning (Mukae-Zake) among Japanese farmers

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Abstract

Background: Ne-Zake is the drinking of alcohol before sleeping for helping to fall asleep and sleep well, and Mukae-Zake is the drinking of alcohol in the morning for "calming down" or "curing hangovers". **Objective:** We sought to examine the relationship of insomnia with Ne-Zake and Mukae-Zake among healthy middle-aged Japanese farmers. **Methods:** In a cross-sectional study of 746 participants (mean age, 59.5 years; women, 25.9%), Ne-Zake and Mukae-Zake were defined based on a self-administered questionnaire. Insomnia was defined as the Athens Insomnia Scale Japanese version ≥6 or usage of sleeping pills in the previous year. Logistic regression was used to calculate odds ratio (OR) of insomnia related to Ne-Zake and Mukae-Zake adjusting for sex, age, presence of sleep-related disorders, frequency of alcohol consumption, and quantity of alcohol consumed per one occasion. **Results:** We observed insomnia, Ne-Zake, and Mukae-Zake in 174 (23.3%), 140 (18.8%), and 37 (5.0%) participants, respectively. After adjustment for demographic and confounding factors, participants with Ne-Zake had a significantly higher prevalence of insomnia (OR 2.00 [95% confidence interval, 1.273.16]), compared to those without Ne-Zake. Mukae-Zake was also independently associated with a higher prevalence of insomnia among men (OR 3.26 [1.55–6.87]). Participants with both Ne-Zake and Mukae-Zake had a highly significant association with insomnia (OR 4.77 [2.01–11.3]) than those with neither Ne-Zake nor Mukae-Zake. Additionally, for insomnia, the association of Mukae-Zake was more pronounced than that of Ne-Zake (OR 4.09, 95% CI 1.14–14.7, $p = 0.031$; and OR 1.81, 95%

CI 1.08–3.06, $p = 0.026$, respectively). **Conclusion:** Ne-Zake and Mukae-Zake were associated with insomnia independent of the quantity and frequency of alcohol consumption among Japanese farmers. This finding can be used for stratifying individuals with insomnia not only to improve sleep hygiene but also to prevent alcohol dependence by informing the general population that alcohol has a negative effect on sleep, contrary to popular beliefs.

Highlights

- Ne-Zake is the drinking of alcohol before sleep to help falling asleep and sleeping well.
- Mukae-Zake is the drinking of alcohol in the morning to “calm down” or “cure hangovers”.
- Participants with Ne-Zake had a significantly higher prevalence of insomnia.
- Mukae-Zake was also independently associated with a higher prevalence of insomnia.
- Having both Ne-Zake and Mukae-Zake was highly significantly associated with insomnia.

Keywords
alcohol
epidemiology
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Ne-Zake
sleep

Introduction

Sleep is a restorative physiologic phenomenon that is essential for maintaining a healthy physical and mental condition; thus, impaired sleep could have a significant negative impact on health (Allatar, Harrington, Mitchell, & Sloane, 2007). Insomnia is a sleep disorder characterized by a significant distress or impairment in functioning and daytime symptoms, including fatigue, daytime sleepiness, impairment in cognitive performance, and mood disturbance (Levenson, Kay, & Buysse, 2015). Insomnia has been reported to increase the risk of physical diseases, such as cardiovascular diseases (Bollu & Kaur, 2019; Bonnet & Arand, 1998; Javaheri & Redline, 2017), hypertension (Bollu & Kaur, 2019; Vgontzas, Liao, Bixler, Chrousos, & Vela-Bueno, 2009), type 2 diabetes mellitus (Bollu & Kaur, 2019; Kawakami, Takatsuka, & Shimizu, 2004), and self-reported chronic health problems (Daley et al., 2009), as well as of psychiatric disorders, such as depression, anxiety, and substance abuse (Bollu & Kaur, 2019; Daley et al., 2009), leading to subsequent morbidity (Daley et al., 2009) and mortality (Bonnet & Arand, 1998; Kripke, Simons, Garfinkel, & Hammond, 1979) and a decline in the quality of life (Ishak et al., 2012). Hence, insomnia is an important issue not only from a clinical perspective, but also in view of public health. Therefore, it is crucial to improve sleep hygiene.

It is well known that alcohol affects sleep, daytime alertness, and physiological functioning during sleep, and that alcohol has been associated with sleep disorders (Roehrs & Roth, 2001b). Nonetheless, alcohol is often used as a self-treatment for sleeplessness in the

general population as it is perceived to be a convenient, cost-effective, low-risk hypnotic (Stein & Friedmann, 2005). Previous studies have reported that about 15–30% of the general population used alcohol as a self-treatment for sleeplessness (Johnson, Roehrs, Roth, & Breslau, 1998; Roehrs & Roth, 2001b), and Japan had the highest prevalence of using alcohol as a sleep aid in the world at 30.3% (Soldatos, Allaert, Ohta, & Dikeos, 2005).

In Japan, alcohol is occasionally used before sleeping (Ne-Zake), for helping to fall asleep and sleep well, or in the morning (Mukae-Zake), for "calming down" or "curing hangovers". Although many studies have investigated the association of alcohol consumption with sleep disorders, to the best of our knowledge, there has been no study to evaluate the effect of both Ne-Zake and Mukae-Zake on sleep disorders.

Thus, the purpose of this study was to examine the relationship of insomnia with Ne-Zake and Mukae-Zake among healthy middle-aged farmers in a countryside prefecture in Japan, while adjusting for the influence of the quantity and frequency of alcohol consumption on the relationship.

Materials and methods

Ethical considerations

All the procedures of this study were reviewed and approved by the Institutional Review Board of Shimane University Faculty of Medicine (No. 2711, Approved on June 14, 2017). All participants provided written informed consent.

Study design and sample

This cross-sectional study was conducted by collaboration between the Department of Environmental Medicine and Public Health of the Faculty of Medicine of Shimane University and the Health Promotion and Health Checkup Center, Japan Agriculture (JA) -Shimane. Agriculture workers aged 21 to 87 years who underwent the annual medical checkups and lifestyle questionnaires provided by the Health Promotion and Health Checkup Center, JA-Shimane, in Shimane prefecture, Japan, between June 2017 and March 2018 were invited to participate in the survey. After completing the questionnaire, well-trained public health nurses checked them face-to-face with the participants. Participants who were not engaged in actual agriculture works, who had not completed or had made inappropriate notations in the questionnaires, were excluded.

Assessment of sleep status

Insomnia was evaluated using the Japanese version of the Athens Insomnia Scale (AIS-J) (Okajima, Nakajima, Kobayashi, & Inoue, 2013). The AIS is a globally widely used, authorized, and validated (Chiu, Chang, Hsieh, & Tsai, 2016; Jeong et al., 2015; Soldatos, Dikeos, & Paparrigopoulos, 2000, 2003; Sun, Chiou, & Lin, 2011) questionnaire regarding insomnia and insomnia-related symptoms in the previous month. The AIS-J score is calculated as the sum of the points of eight questions and ranges from 0 (denoting absence of any sleep-related problems) to 24 (representing the most severe degree of insomnia). The questions are grouped in two sections. The first five items detect changes in the quantity and

quality of sleep, and the last three items detect daytime symptoms that often emerge as a consequence of nocturnal sleep disturbance. The cutoff AIS-J score to identity pathological insomnia was set at 6 points (Okajima et al., 2013; Soldatos et al., 2003). A self-administered questionnaire was also used to obtain information about usage of sleeping pills and medical history of sleep-related diseases, such as sleep apnea syndrome and depression. Participants were divided into two groups, non-insomnia (AIS-J score <6 and no history of usage of sleeping pills in the previous year) and insomnia group (AIS-J score ≥6 or history of usage of sleeping pills in the previous year).

Assessment of alcohol consumption

Information on alcohol consumption was acquired using a self-reporting questionnaire. Alcohol consumption was evaluated by two categories, which were quantity and frequency of alcohol consumption. Among seven alcohol-related questions in the questionnaire provided in the Japanese specific health check-up (Ministry of Health, Labor, and Welfare, Japan, 2018), two questions were used to detect the quantity and frequency of alcohol consumption. Although this questionnaire has not been fully validated, it is used in the specific health check-ups applicable for all Japanese. It is supplied by the Ministry of Health, Labor, and Welfare, Japan. This questionnaire was created referring to the Industrial Safety and Health Act and the National Health and Nutrition Survey conducted by the National Institute of Health and Nutrition (National Institute of Health and Nutrition, Japan,

2020). It is widely used in many studies conducted in Japan and the methods are almost all the same (Karaswa, Yamada, Sakurai, & Kurita, 2019). The quantity of alcohol consumed per one occasion was classified into four categories according to the Japanese sake units (<1, 1–2, 2–3, and >3 units of the Japanese sake unit). One unit of the Japanese sake scale is 180 mL, which equals 22 g of ethanol. Five hundred mL of beer, 110 mL of Shochu (another type of Japanese sake,, 60 mL of doubled whiskey, and 240 mL of wine were calculated as one Japanese sake unit. The frequency of alcohol consumption was classified into three categories (none or almost none, sometimes, and every day). Ne-Zake is defined as alcohol consumption before sleep for helping to fall asleep and sleep well, not including drinking alcohol with dinner. Ne-Zake was detected by a dichotomous question, “Have you had alcohol as a sleep aid in the previous year?”, which was quoted from the nationwide survey on smoking behavior and exposure to passive smoking among Japanese adults (Osaki, 2010). This questionnaire also has not been validated; however, it was conducted by the Ministry of Health, Labor, and Welfare, Japan. Mukae-Zake is defined as alcohol consumption in the morning for “calming down” or “curing hangovers”. Drinking alcohol in the morning after returning home for nightshift workers is not classified as Mukae-Zake, as the main purpose is not for calming down or curing hangovers. Mukae-Zake was also detected by a dichotomous question, “Have you had a morning eye-opener to get rid of a hangover in the previous year?”, which was quoted from the CAGE questionnaire (Bernadt, Mumford, Taylor, Smith,

& Murray, 1982; Ewing, 1984; Mayfield, McLeod, & Hall, 1974; Williams, 2014), which was validated by Bernadt and co-workers (Bernadt et al., 1982). The CAGE questionnaire had a sensitivity of 91% and a specificity of 77% in the identification of alcoholism.

Statistical analysis

The participants' characteristics were examined according to the presence of insomnia using the chi-square test and unpaired *t* test. Multivariable logistic regression models were prepared to calculate the odds ratios (ORs) and 95% confidence intervals (95% CIs) of insomnia associated with Ne-Zake and Mukae-Zake. The multivariable logistic regression model for Ne-Zake was adjusted for age, sex, presence of sleep-related diseases, frequency of alcohol consumption, and quantity of alcohol consumed per one occasion. These covariates were selected *a priori* because they have known correlations with insomnia and are risk factors for insomnia (Baekeland, Lundwall, Shanahan, & Kissin, 1974; Brower, 2015; Brower, Krentzman, & Robinson, 2011; Ishigooka et al., 1999; Shinba, Murashima, & Yamamoto, 1994; Zhabenko, Wojnar, & Brower, 2012). There was no multicollinearity between the independent variables that were used in the multiple logistic regression analysis, as all the absolute values of the correlation coefficients between independent variables were less than 0.7. The Hosmer-Lemeshow statistics indicated that both of the significance values of Ne-Zake and Mukae-Zake were not less than 0.05, which meant the model adequately fit the data for the logistic regression. As there was only one female participant who did Mukae-

Zake, the analyses on Mukae-Zake were conducted only among male participants. The multivariable logistic regression model for Mukae-Zake was adjusted for age, presence of sleep-related diseases, frequency of alcohol consumption, and quantity of alcohol consumed per one occasion. Multivariable logistic regression models were constructed to calculate the ORs and 95% CIs of insomnia according to four groups: those who did neither Ne-Zake nor Mukae-Zake (none), those who did only Ne-Zake (only Ne-Zake), those who did only Mukae-Zake (only Mukae-Zake), and those who did both Ne-Zake and Mukae-Zake (both). Finally, we assessed the association of Ne-Zake with insomnia stratified by men and women and further tested a multiplicative interaction.

Statistical analyses were performed using STATA version 16.0 (StataCorp LP; College Station, Texas, United States). Two-tailed *p* values less than 0.05 were considered statistically significant.

Results

Among 1,072 agriculture workers who underwent the annual medical checkups between June 2017 and March 2018, 986 agreed to participate in the survey (participation rate, 92.0%). After the exclusion of those who were not engaged in actual agriculture work (n = 70), and those with incomplete or inappropriately filled questionnaires (n = 170), a total of 746 participants were included in the analysis (mean age, 59.5 ± 14.4 years; women, 25.9%).

Among 746 participants, we observed insomnia, Ne-Zake, and Mukae-Zake in 174

(23.3%), 140 (18.8%), and 37 (5.0%) participants, respectively. The demographic characteristics of the participants according to the presence of insomnia are shown in Table 1. Compared with those without insomnia, participants with insomnia had a higher prevalence of sleeping-related disorders; whereas there were no significant differences in the frequency of alcohol consumption and quantity of alcohol consumed per one occasion between those with and without insomnia.

Compared to those without Ne-Zake, participants with Ne-Zake had a significantly higher prevalence of insomnia (OR 2.00, 95% CI 1.27–3.16, $p < 0.001$) after adjustment for sex, age, presence of sleep-related disorders, frequency of alcohol consumption, and quantity of alcohol consumed per one occasion. Mukae-Zake also had a significantly higher prevalence of insomnia (OR 3.26, 95% CI 1.55–6.87, $p < 0.001$) among male participants, compared to those without Mukae-Zake, adjusting for demographic and confounding factors (Table 2).

In the stratified analysis on Ne-Zake by sex, women had a trend to have more insomnia among those who did Ne-Zake; the OR for insomnia was greater among women (OR 4.26, 95% CI 1.07–16.8) than men (OR 1.88, 95% CI 1.14–3.09) (Supplementary Table 2). Although the OR for insomnia was greater among women than men, there was no sex difference for insomnia among those who did Ne-Zake, as the interaction p value for Ne-Zake and sex was not statistically significant (p for interaction = 0.09).

Among 746 participants, 114 did only Ne-Zake (15.3%), 11 did only Mukae-Zake (1.5%), and 26 did both Ne-Zake and Mukae-Zake (3.5%). The characteristics of participants according to their alcohol consumption status are shown in Supplementary Table 1. The multivariable logistic regression models revealed that, compared with those with neither Ne-Zake nor Mukae-Zake, participants with both of them had a highly significant association with insomnia (OR 4.77, 95% CI 2.01–11.3, $p = 0.001$). Additionally, for insomnia, the association of Mukae-Zake was more pronounced than that of Ne-Zake (OR 4.09, 95% CI 1.14–14.7, $p = 0.031$; and OR 1.81, 95% CI 1.08–3.06, $p = 0.026$, respectively) (Table 3).

Discussion

In the present study, Ne-Zake and Mukae-Zake were associated with insomnia independent of the quantity and frequency of alcohol consumption among apparently healthy middle-aged farmers in a countryside prefecture in Japan. Mukae-Zake was more strongly associated with insomnia than Ne-Zake. The association of Mukae-Zake with insomnia was observed in men. Although women had a trend to have more insomnia among those who did Ne-Zake compared with men, there was no sex difference for insomnia among those who did Ne-Zake, as there was no significant interaction for insomnia in the stratified analysis on Ne-Zake by sex.

To the best of our knowledge, this is the first report that indicates the association of insomnia with both Ne-Zake and Mukae-Zake. It is well known that alcohol has extensive

effects on sleep, daytime alertness and sleepiness, and sleep disorders, such as insomnia (Roehrs & Roth, 2001b). Our results are in agreement with those from previous studies that determined an association of insomnia with alcohol consumption (Roehrs & Roth, 2001a, 2001b; Stein & Friedmann, 2005). Ne-Zake is an action of consuming alcohol for helping to fall asleep and sleep well, and it appears to be common worldwide (Ancoli-Israel & Roth, 1999; Johnson et al., 1998; Kaneita et al., 2007; Soldatos et al., 2005; Roehrs, Hollebeek, Drake, & Roth, 2002). Some previous studies investigated the prevalence of Ne-Zake (Ishigooka et al., 1999; Kaneita et al., 2007; Roehrs et al., 2002), and others revealed that Ne-Zake is associated with difficulty maintaining sleep (Kaneita et al., 2007) or daytime sleepiness (Roehrs et al., 2002). Mukae-Zake is an action of consuming alcohol for the purpose of "calming down" or "curing hangovers" (Williams, 2014); however, there seems to be no previous study that investigated its association with insomnia.

There are several previous studies on frequencies of Ne-Zake. Our results showed that the prevalence of Ne-Zake among Japanese middle-aged farmers was 18.8%. This finding is consistent with that from a previous report in 10 countries (19.4% of participants from Austria, Belgium, Brazil, China, Germany, Japan, Portugal, Slovakia, South Africa, and Spain) (Soldatos et al., 2005), but larger than several previous reports from the United States, in which the prevalence of Ne-Zake was 10 to 13% (Ancoli-Israel & Roth, 1999; Johnson et al., 1998; Roehrs et al., 2002). Hypnotic medicines are not as popular in Japan as in the

United States, and more people generally tend to believe that alcohol is effective as a sleep aid (Kaneita et al., 2007; Roehrs et al., 2002; Soldatos et al., 2005). In Japan, the prevalence of alcohol use as a sleep aid in the present study was lower than that of a previous study, in which the prevalence was 48.3% among men and 5.9% among women from the general population (Kaneita et al, 2007). The reason for the smaller prevalence of Ne-Zake in the present study is thought to be that farmers generally tend to start working earlier in the morning than office workers, so that they might not have Ne-Zake as frequently as the general population. The prevalence of Mukae-Zake was 5.0% and, to our knowledge, this is the first report of the prevalence of Mukae-Zake.

We found the association of Mukae-Zake with insomnia was stronger than that of Ne-Zake. The exact mechanism of the association between Mukae-Zake and insomnia remains unclear, but several speculations can be made. People who do Mukae-Zake are considered to have a high likelihood of developing alcohol dependence, and individuals with alcohol dependence more commonly experience sleep problems than those without alcohol dependence (Aldrich, 1998; Brower, 2001). Sleep problems, such as poor efficiency, prolonged latency (longer time to fall asleep), short overall sleep time, and fragmented and light sleep, are often observed among individuals with alcohol dependence and are the result of reduced non-REM (NREM) sleep, in particular, stage 2, stage 4, and total delta (stage 3 and 4) sleep (Gillin, Smith, Irwin, Kripke, & Schuckit, 1990). Moreover, such individuals

consume alcohol at any time, leading to 24-hour sleep problems (Mello & Mendelson, 1970; Roehrs & Roth, 2001b). Further studies are needed to elucidate the exact mechanism linking Mukae-Zake and insomnia.

The mechanisms of the association of Ne-Zake with insomnia have also been discussed in previous studies (Aldrich, 1998; Conroy & Arnedt, 2014; Kaneita et al., 2007; Roehrs and Roth, 2001b; Stein & Freedman, 2005). Alcohol can have both a stimulatory effect by increasing the sleep onset latency (the time to fall asleep) and a sedative effect by inducing sleep, depending on the dose and the plasma concentration phase, which is determined by a number of factors, including the interval from alcohol consumption to bedtime, blood alcohol levels at sleep onset, the time taken to metabolize alcohol and eliminate it and its major metabolites, age, sex, and body fat percentage (Koob & Colrain, 2020; Stein & Friedmann, 2005). Most studies have reported that alcohol consumption before bedtime reduced the sleep onset latency (Conroy & Arnedt, 2014; Roehrs & Roth, 2001b), which makes it easier to fall asleep, and this effect is thought to be similar to that which Zolpidem, the current gold standard pharmacological treatment of insomnia, has when administered to healthy controls (Koob & Colrain, 2020). Lower doses of alcohol induce nocturnal awakeningin the second half of the night due to increases of REM sleep. Middle to higher doses of alcohol induce shallow sleep throughout the night due to the increased REM sleep for the whole night (Koob & Colrain, 2020; Stein & Friedmann, 2005). Higher doses,

especially intoxicating doses of alcohol, have effects on NREM sleep leading to deep sleep early in the night and shallow sleep later in the night (Koob & Colrain, 2020; Stein & Friedmann, 2005). In addition, gastric irritation, headache, and a full bladder may disturb sleep (Kaneita et al., 2007).

In the present study, consistent with the findings of previous studies (Ishigooka et al., 1999; Kaneita et al., 2007; Roehrs et al., 2002), the prevalence of Ne-Zake was greater among men than among women. Although women had a trend to have insomnia associated with Ne-Zake compared with men, there was statistically no sex difference in the association between Ne-Zake and insomnia. There are several previous reports concerning the sex differences in alcohol effects. There is a report that pointed out the sex differences among insomnia related to alcohol with the statement “the high dose of alcohol would worsen sleep more in women than men” (Arnedt et al., 2011). On the other hand, there is a report which indicated no sex differences with the statement “No main effects of interactions for sex were observed in any analysis of alcohol levels, drinking history, or sleep quality or architecture measures” (Chan, Trinder, Andrewes, Colrain, & Nicholas, 2013). Although this study supported the latter perspective, this issue needs further investigations and discussion.

There are several limitations to our study. First, it was a cross-sectional study; thus, it cannot prove a causal relationship. Second, participants were limited to those who were engaged in agriculture and may not have been representative of the general population.

Therefore, the results cannot be generalized to populations with different backgrounds. Additionally, individuals who gave incomplete or inappropriate answers were older than those who gave complete answers (65.7 ± 10.6 and 59.5 ± 14.4 years old, respectively; $p < 0.001$), whereas there were no significant differences in other characteristics, including alcohol consumption, between those with complete and with incomplete/inappropriate answers for questionnaires. Third, insomnia was assessed by the AIS-J score, which was based on a self-reporting questionnaire, rather than an objective marker, such as the length of sleeping time or polysomnography, which could have led to underestimation of the true associations. Furthermore, our alcohol consumption data were generated from self-reported measures that typically underestimate the actual consumption (Stockwell et al., 2004). Adding to this, the questionnaire for the alcohol consumption has not been fully validated. However, it is provided by the Japanese government and is widely used for not only many studies but also many policymakings in Japan. Fourth, our findings may partly be explained by differences in unknown confounders. For example, it remains unclear that Mukae-Zake is one of the symptoms of alcoholism; sleep disorders are also one of the symptoms of alcoholism and they are likely to coexist. Finally, the present study was limited to a relatively small sample size and was underpowered to detect true associations, particularly in the stratified analyses by sex.

In conclusion, Ne-Zake and Mukae-Zake were associated with insomnia independent

of the quantity and frequency of alcohol consumption among apparently healthy middle-aged farmers living in a countryside prefecture in Japan. This finding indicates that Ne-Zake, which is alcohol consumption before going to bed for helping to fall asleep and sleep well, or Mukae-Zake, which is alcohol consumption in the morning for "calming down" or "curing hangovers", can be used for stratification of individuals with insomnia. Among Japanese adults, alcohol is used more commonly than hypnotic medications as it is considered a facile sleep aid, which can cause serious problems in sleep hygiene in Japan. People with insomnia are more likely to use alcohol as a sleep aid; however, as their sleep continuity gets worse over time, they might eventually develop severe alcohol dependence and mental diseases such as depression, which possibly make their insomnia much worse. Informing the Japanese general population that alcohol has a negative effect on sleep, contrary to the popular belief, is essential not only for improving sleep hygiene, but also for the prevention of alcohol dependence. There might be a possibility to improve sleep disorder by stopping Ne-Zake and Mukae-Zake, but further prospective observational and investigational studies will deepen our understanding of the link between Ne-Zake, Mukae-Zake, and insomnia.

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Declarations of interest

None.

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