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Original Article

Relapse insomnia increases greater risk of anxiety and depression: evidence from a population-based 4-year cohort study

Ping-Jen Chen [a, b], Charles Lung-Cheng Huang [c, d], Shih-Feng Weng [e], Ming-Ping Wu [f, g, h], Chung-Han Ho [g, i], Jhi-Joung Wang [g], Wan-Chi Tsai [j], Ya-Wen Hsu [g, i, *]

[a] Department of Geriatrics and Gerontology, Chi-Mei Medical Center, Tainan, Taiwan
[b] Department of Family Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan
[c] Department of Psychiatry, Chi-Mei Medical Center, Tainan, Taiwan
[d] Department of Social Work, Chia Nan University of Pharmacy and Science, Tainan, Taiwan
[e] Department of Healthcare Administration and Medical Informatics, Kaohsiung Medical University, Kaohsiung, Taiwan
[f] Department of Obstetrics and Gynecology, Chi-Mei Medical Center, Tainan, Taiwan
[g] Department of Medical Research, Chi-Mei Medical Center, Tainan, Taiwan
[h] Center of General Education, Chia Nan University of Pharmacy and Science, Tainan, Taiwan
[i] Department of Hospital and Health Care Administration, Chia Nan University of Pharmacy and Science, Tainan, Taiwan
[j] Department of Medical Laboratory Science and Biotechnology, Kaohsiung Medical University, Kaohsiung, Taiwan

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ABSTRACT

Objective: We investigated the longitudinal impacts of insomnia on the subsequent developments of anxiety and depression during a four-year follow-up. We further categorized individuals with insomnia into different insomnia subgroups to examine whether the risk of anxiety and depression varies by subtype.

Methods: Participants were identified from National Health Insurance enrollees in Taiwan during 2002–2009. The study included 19,273 subjects with insomnia and 38,546 matched subjects without insomnia. All subjects did not have previous diagnosis of insomnia, sleep apnea, anxiety, or depression.

Results: Compared with non-insomniacs, insomniacs had a higher risk of developing anxiety only [adjusted hazard ratio (HR) = 8.83, 95% CI = 7.59–10.27], depression only (adjusted HR = 8.48, 95% CI = 6.92–10.39), and both anxiety and depression (adjusted HR = 17.98, 95% CI = 12.65–25.56). When breaking down the insomnia subgroups, individuals with a relapse of insomnia (adjusted HR = 10.42–26.80) had the highest risk of anxiety only, depression only, and both anxiety and depression, followed by persistent insomnia (adjusted HR = 9.82–18.98), then remitted insomnia (adjusted HR = 4.50–8.27). All three insomnia subgroups had a greater four-year cumulative incidence rate than the non-insomnia group for anxiety only, depression only, and both anxiety and depression ($p < 0.0001$).

Conclusion: Our findings reinforce the clinical predictor role of insomnia in the future onset of anxiety or/and depression. Awareness of insomnia and treatment of insomnia should be recommended at clinics, and patterns of insomnia should be monitored to help treatment and control of subsequent psychiatric disorders. Future research with comprehensive data collection is needed to identify factors that contribute to different insomnia subtypes.

1. Introduction

Insomnia, which is defined by the presence of an individual's report of difficulties initiating and/or maintaining sleep and/or early morning awakening [1], is a common condition among adults worldwide with rates ranging from 3.9% to 39.4% [2–6]. In spite of the high prevalence of insomnia and availability of treatments, people often perceive insomnia as trivial or as an associated complaint of poor physical health [7] and do not seek clinical assistance when needed. Underscoring the clinical relevance of the under-treatment of insomnia is the fact that it could worsen the severity of insomnia symptoms and lead to a range of somatic and psychiatric conditions [8–10].

* Corresponding author. Chia Nan University of Pharmacy & Science, Department of Hospital and Health Care Administration, 60 Erh-Jen Road, Sec. 1, Build. Q, Room 413-3, Jen-Te, Tainan 71710, Taiwan. Fax: +886 6 213 3199.
E-mail address: janiceywhsu@gmail.com (Y.-W. Hsu).

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While there are a wealth of theoretical perspectives and cross-sectional studies assessing the link between insomnia and mental illness, there are only a handful of retrospective/prospective longitudinal studies with a longer follow-up duration or a bigger sample size. Prior epidemiologic findings on the longitudinal associations between insomnia, anxiety, and depression have been mixed. One Swiss cohort followed 591 adults for 20 years with six assessment points (ranging from two to five years in between each evaluation) [11], and they found that while insomnia without concurrent depression ('pure' insomnia) was not longitudinally related to depressive disorders/depressive symptoms without concurrent insomnia ('pure' depression), insomnia lasting two weeks or longer was related to future major depressive episodes. Another study found that prior insomnia was associated with the onset of major depression, whereas prior insomnia was not related to the onset of anxiety disorders among American youth [12]. However, close relationships between insomnia, symptoms of anxiety, and symptoms of depression have been reported in varied populations [13–15]. In a cohort of Japanese adults, baseline insomnia was related to depressive symptoms at the two-year follow-up [15]. Using two general health surveys conducted 11 years apart among a population-based cohort, it was concluded that insomnia increased the likelihood of developing anxiety symptoms [13]. More research with the longitudinal design is needed to confirm the causal relationships between insomnia and psychiatric illness.

Insomnia has been suggested to be a chronic condition and it may be a dynamic process in which the status of insomnia is changing over time [16–18]. Nevertheless, there has not been a study that assessed how the course of insomnia (eg, remission, relapse, and persistence) affects the future onsets of psychiatric disorders. If the magnitude of risks for psychiatric disorders occurring differs by insomnia subtype, identifying people who hold the subtype with the highest risks is crucial for the prevention of anxiety and depression. Understanding the role that the natural history of insomnia plays in the development of psychiatric evaluation has the potential to guide intervention strategies particularly in clinical settings, where psychiatric illnesses are most commonly examined.

Therefore, the aims of this study were to investigate the impacts of predisposed insomnia and the clinical course of insomnia on subsequent risks for anxiety and depression in a large general sample using a longitudinal design. Insomnia was defined as encompassing a broad range of insomnia symptoms and disorders, and insomnia was further categorized into persistent, relapse, and remission subtypes based on the incidence of insomnia episodes, and the risks of developing anxiety and/or depression was assessed for each subtype. We hypothesized that (1) insomnia would lead to higher risks of developing subsequent anxiety and depression and (2) the risks of anxiety and depression would vary by insomnia subtype. Due to the lack of literature on the role insomnia subtype plays in the relationship with psychiatric illness, it was difficult to hypothesize a priori what results would be found in the comparisons of these groups. Investigating both anxiety and depression allows us to assess the degree to which insomnia's relationship with each type of disorder may be different [16]. By excluding individuals who had been previously diagnosed with insomnia, anxiety, and depression, we avoided the confounding effects caused by insomnia as a residual symptom or a comorbid feature of anxiety and depression.

2. Methods

2.1. Database

The National Health Insurance (NHI) program, which provides a universal health insurance, was implemented in Taiwan in March 1995 for all citizens. The NHI is a mandatory system, and all outpatient and inpatient medical benefit claims are included in the NHI Research Database (NHIRD). Data used in this study came from the Longitudinal Health Insurance Database 2000 (LHID2000), which contains all claims data (from 1996 to 2009) for 1 million beneficiaries who were randomly selected from the NHIRD in 2000. The LHID2000 provides encrypted patient identification numbers, gender, date of birth, dates of admission and discharge, the International Classification of Diseases – Ninth Revision – Clinical Modification (ICD-9-CM) diagnosis and procedure codes, detailed prescriptions, and expenditure amounts. To protect patient privacy, a unique patient identifier and medical institutes were cryptographically scrambled to ensure anonymity. Confidentiality assurances were addressed by abiding by data regulations of the Bureau of NHI (BNHI), and a formal written waiver for ethical approval was obtained from the Chi-Mei Medical Center Institutional Review Board.

2.2. Study population

A population-based retrospective cohort study, which included a case cohort and a comparison cohort and was based on outpatient and inpatient claims in the LHID2000, was conducted. From 1 January 1 2002 to 31 December 2007, individuals $\geq$18 years of age with newly diagnosed insomnia were selected for the study cohort using the following criteria: (1) at least one single hospitalization with a diagnosis code of insomnia, or (2) at least three outpatient visits with a diagnosis code of insomnia within the same year. The latest insomnia diagnosis (eg, the third outpatient visit or the first hospitalization with a diagnosis code for insomnia) for each study subject was designated as the index date of enrollment. To avoid potential confounding effects, subjects with sleep apnea (ICD-9-CM codes: 327.2 organic sleep apnea, 780.51 insomnia with sleep apnea, unspecified, 780.53 hypersomnia with sleep apnea, and 780.57 unspecified sleep apnea), and those with previous diagnosis of insomnia, anxiety, or depression before the index enrollment date were excluded. Within the subjects without insomnia, sleep apnea, anxiety, or depression in the LHID2000, a comparison group was assembled by matching an insomniac with two non-insomnia individuals on index enrollment date, sex, and age. Subjects in the study and comparison cohorts were tracked for four years from their index enrollment date until death or until the end of 31 December 2011, which allowed us to examine the risk of developing anxiety and/or depression during the follow-up period.

2.3. Definition of insomnia

For cases in this study, we attempted to include individuals who met general criteria for insomnia (insomnia symptoms and insomnia disorder) and we thus defined insomnia using the following insomnia-related ICD-9-CM codes: 780.52 (insomnia, unspecified), 307.41 (transient disorder of initiating or maintaining sleep), and 307.42 (persistent disorder of initiating or maintaining sleep) [9,19,20]. As the code 307.42 may include psychophysiological insomnia, from those meeting the initial inclusion criteria, we additionally excluded individuals who presented both insomnia and anxiety or depression at the same index entry date to reduce selection bias. Then, we further categorized individuals with insomnia into one of the three insomnia subtypes based on their incidence of insomnia episodes during the four-year follow-up period since the index date of enrollment. A relapse of insomnia was defined as a return of insomnia after being diagnosed free of the disease for more than 180 days at any assessment time point (eg, after having a diagnosis of insomnia, the duration between the next insomnia diagnosis and the previous one was longer than 180