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Meta-Analysis: Stress-Induced Insomnia and its Effect on Blood Pressure

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Abstract

Stress-induced insomnia and hypertension often coexist and are very common. There is adequate evidence to show that the increased prevalence of hypertension over the past few years could be linked to the increased prevalence of insomnia and the reduction of sleep time resulting from a contemporary lifestyle. This paper will decipher clinical evidence of the relationship existing between stress-induced insomnia and hypertension a side by side comparison of the impacts of stress-induced insomnia on a hypertensive and a non-hypertensive patient. The paper will also describe the biological plausibility of stress-induced insomnia and its pathological and physiological mechanisms. Through the use of a systematic search of various medical journals and online searches, the study selected articles that reported the relationship between high blood pressure and stress-related sleep deprivation in participants aged above 19 years. This meta-analysis describes the relationship between experimental stress-related insomnia and hypertension when other known risk factors are controlled. The physiological and pathological mechanisms underlying this relationship could be associated with an arousal that is inappropriate resulting from increased activation of the stress system functions. According to the hypothesis, stress-related insomnia might act as a physiological or neurobiological stressor that could impair brain function, thus contributing to the allostatic load, a process that compromises somatic health and stress resilience.

Keywords: *Stress-Induced Insomnia; Meta-Analysis; Allostatic Load; Somatic Health*

Introduction

The prevalence of hypertension has generally increased worldwide and is expected to rise to about 60% by 2025. Hypertension poses a huge economic burden on the healthcare systems of countries worldwide as it continues to be the most common cardiovascular disease in the world and contributes significantly to cardiovascular mortality and morbidity. The prevalence of insomnia has also increased significantly in the past decade making it the most common sleep complaint among the general population [1]. Insomnia is a disorder that is characterised by non-restorative sleep or difficulty in maintaining or initiating sleep followed by daytime consequences [2]. The latter is considered to be a public health crisis that affects up to 15% of the global population and up to 18% of the population in the Middle East. It is reported that the average duration of sleep among the general population has decreased as a result of a contemporary lifestyle.

Insomnia could be perpetuated by several physiological and psychological factors such as stressful events, the hyper-arousal of the central nervous system, age-related weakening of sleep homeostasis, and anxious-ruminative personality [3]. The observed reduction in sleep duration is marked in developed countries where people report sleeping for 2h less than was the case a century ago. Several researches have showed that the increased prevalence of hypertension could be associated with sleep deprivation and insomnia. It was proposed that the pathological and physiological mechanisms underlying the relationship between stress-induced insomnia and increased blood pressure are associated with the inappropriate arousal of the physiological mechanisms resulting from an alteration of stress system functions.

Sleep plays an important role in homeostatic functions including the suppression of stress system functions, while insomnia is related to the arousal of the central nervous system [4]. According to recent studies, sleep restriction or loss coupled with a worsening quality of sleep as observed in stress-induced insomnia irrespective of the origin could act as a physiological or neurobiological stressor [5]. The alteration of sleep quality could impair one's adaptation to stress by contributing to the allostatic load that increases blood pressure and compromises stress resilience [5].

The relationship between stress-induced insomnia and increased blood pressure is, however, complex. Other risk factors in the development of hypertension are age, gender, depression, alcohol consumption, and obesity making it difficult to determine whether there exists a cause–effect relationship of the two variables devoid of other risk factors [6]. The primary aim of this paper is to systematically review the available clinical evidence of the relationship between stress-related insomnia and increased blood pressure. The article will go further to discuss the potential physiological and pathological mechanisms that underlie this complex relationship.

Objectives and Justification of the Study

The objective of this study is to offer an in-depth analysis of the relationship between stress-induced insomnia and hypertension. The study also aims to describe the physiological and pathological consequences of stress-induced insomnia. The study systematically reviews various journals, articles, and books to achieve this objective. The prevalence of hypertension has increased drastically in the past decade and so has the rate of stress-induced insomnia [6]. The latter has mostly been precipitated by the modern lifestyle and stressful life events. The average sleep duration for individuals in the Middle East is currently 2h less than it was a century ago. The prevalence of hypertension is expected to rise to 60% by 2025. Both conditions have immense effects on the somatic health and neurobiological functioning of individuals. Comprehension of the relationship that exists between stress-induced insomnia and hypertension could lead to better approaches in managing the two conditions which could have significant impacts on the health of individuals.

Literature Review

Stress-induced insomnia is one of the most common sleep disorders among the general population who seek medical help. The condition has remained under-treated as it is under-recognized with up to 60% of the people affected failing to seek medical help [4]. The inadequate treatment and identification of stress-induced insomnia has had immense public health and medical implications as chronic insomnia can cause hypertension and impair quality of life. According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth

Edition (DSM-V), stress-induced insomnia is defined as problems with maintenance of sleep, initiation of sleep, non-restorative sleep, interrupted sleep, and early awakening. The significance of the condition is determined by the level of daytime function impairment, duration, frequency, and severity of the condition [7].

Various factors such as socioeconomic status, age, and gender have all been associated with the prevalence of stress-induced insomnia. Stress-induced insomnia occurs more commonly in women, both in terms of daytime consequences and reported symptoms [3]. Menopause is proposed as a possible explanation for variations among middle-aged women and men even though other variables such as prevalence of depression and stress disorders in women are also significant [8]. Aging is also an important risk factor that is linked to the increased prevalence of stress-induced insomnia present in close to 50% of the individuals above 60 years. In socioeconomic terms, stress-induced insomnia is reported more commonly among the individuals who are widowed, divorced, or separated, particularly, in women or people with a lower economic or educational status.

Sleep Studies

Several studies have showed that stress-induced insomnia with objective short duration of sleep is related to a higher risk of developing hypertension due to the underlying mechanism of physiological hyperarousal [9]. This paper tested whether physiological hyperarousal with stress-induced insomnia as measured by the Multiple Sleep Latency Test (MSLT) was associated with an increased risk of developing high blood pressure [10]. The study included 96 normal sleepers and 119 chronic stress-induced insomniacs defined by the standardized sleep test that was based on a standard diagnostic criteria with consequences lasting for 6 or more months. All the participants underwent a one-night laboratory polysomnography test that was preceded by a standard MSLT. Hyperarousal was defined in the study by a median mean MSLT value of more than 14 minutes and a mean MSLT 75^{th} percentile value of more than 17 minutes. Hypertension was thus defined based on the positive diagnosis by the physician or on blood pressure measures.

After controlling for other variables such as caffeine use, alcohol consumption, cigarette smoking, diabetes mellitus, apnea-hypopnea index, body mass index, sex, and age, stress-induced insomnia combined with MSLT values of more than 14 minutes escalated the hypertension odds by 300 percent (confidence interval = 1.21 - 8.94, odds ratio = 3.27) while the values of stress-induced insomnia combined with MSLT further increased the odds of hypertension by 400 percent (confidence interval = 1.48 - 12.66) vis-à-vis normal sleepers who had MSLT values of 14 minutes or less. Stress-induced insomnia associated with hyperarousal of physiological functions is associated with a considerable increased risk of developing hypertension. Long values of MSLT could form reliable indexes of the biological severity and physiologic hyperarousal of chronic stress-induced insomnia.

Polysomnography

Polysomnography is a multi-parametric sleep test study that is often used in sleep medicine as a diagnostic tool [11]. The test comprehensively records the physiological and biological changes that take place during the sleep cycle. The test measures several body functions such as electrocardiogram and heart rhythm, skeletal muscle activation, eye movement, and the activity of the brain during sleep [5]. The test is often used in sleep medicine to rule out or diagnose several sleep disorders such as insomnia, sleep apnea, parasomnia, periodic limb movement disorders, idiopathic hypersomnia, and narcolepsy. A polysomnogram will typically record the ECG, airflow, the chin muscle tone, leg and eye movements, heart rate and rhythm, oxygen saturation as well as the movement of the chest wall and upper abdominal wall [12].

For a standard polysomnography test, the participants attend a sleep laboratory every evening where the diagnostic tool is connected by the sleep technician over the next few minutes to obtain multiple channels of data collection when the subjects fall asleep [5]. The technician observes the activities throughout the study by looking through the computer screen and the video monitor that displays the relevant information for every second. Generally, the subjects are discharged in the morning unless the MSLT is required to test their sleepiness during the day. It is important to note that the percentage of each sleep cycle varies according to the age of the participants

with a declining level of rapid eye movement and deep sleep among older individuals. The rapid eye movement normally occupies about a fifth to a quarter of total sleeping time [12].

Comparison of age groups in stress-induced insomnia

The significance that has been attached to the physiological attributes of individuals such as their inadequate coping mechanisms and certain personality traits have become vulnerability factors that enhance the susceptibility to stress-induced insomnia leading to considerable neglect of the biological and physiological changes that affect the pathogenesis of stress-induced insomnia. Recent studies have showed that aging, among other physiological factors, could enhance vulnerability to stress-induced insomnia.

Materials and Methods

In a recent study conducted in Saudi Arabia that examined the impacts of the administration of CRH, a hormone with arousing effects on young men versus their middle-aged counterparts found that the degree of wakefulness increased considerably in the middle-aged group, an increase that was more pronounced during the first half of the night. The administration of the hormone, moreover, caused a significant decline in the wakefulness levels among the young men [10]. The findings of the study found that the middle-aged men were more vulnerable to the arousing effects of the hormone as compared to the young men. The increased prevalence of stress-induced insomnia among the middle-aged participants could result from the declining sleep mechanisms that are associated with the increased sensitivity to CRH rather than to life stressors that were enhanced at the time.

A separate study was conducted in Beijing, China between May 2012 and August 2015 to determine the impacts of improvement of insomnia on the blood pressure of hypertensive patients. A total of 404 respondents were randomly selected for the study. The respondents were basically hypertensive patients and insomniacs. A treatment group comprising of 202 respondents were treated with standard antihypertensive medications with Estazolam tablets, while the control group with the same number of respondents were treated with standard antihypertensive medications with placebo [13]. The sedentary systolic and diastolic blood pressure was determined prior to the treatment and during the seven days of the test. The Hamilton Depression Scale 17, Hamilton Anxiety Rating Scale, and the Pittsburg Sleep Quality Index were used to assess the levels of anxiety, levels of depression and the quality of sleep of the participants.

At the end of the study, the Hamilton Depression Scale 17, the Hamilton Anxiety Rating scale, and the Pittsburg Sleep Quality Index scores of the treatment group were considerably lower than that of the control group. The efficacy of Estazolam treatment for insomniacs in the treatment group was 66.3%, significantly higher than the control group which stood at 52.4%. The blood pressure of the respondents in the treatment group showed significant improvement throughout the study [13]. By Day 21, the decline of sedentary systolic and diastolic blood pressures in the treatment group was considerably greater than that of the control group. The target blood pressure compliance rate was 73.6% with Estazolam, while the compliance rate was 51.2% in the control group ($P < 0.001$). The findings of the study thus indicate than an improvement of insomnia can lower the blood pressure of hypertensive patients significantly.

Another study conducted in Japan indicated that persistent stress-induced insomnia was a predictor of increased blood pressure among Japanese male workers [14]. The study aimed to assess the effects of stress-induced insomnia on the development of high blood pressure. Eligible participants were selected using a Japanese telecommunication company annual health examination database. The eligible middle-aged male respondents in the 2009 health examination were followed through until 2013 or rather until the development of high blood pressure. The impacts of insomnia were also assessed by the difficulty initiating sleep (DIS) dataset. The DIS dataset (n = 6 698) included persistent-DIS (n = 208) and non-DIS (n = 6 578) subjects.

The difficulty maintaining sleep (DMS) parameters were determined by the DMS dataset (n = 6, 484), including persistent-DMS (n = 283) and non-DMS (n = 6, 176) subjects. The incidence of hypertension was considerably lower among the non-DIS at 32% compared to the persistent-DIS at 40.3%. The incidence of hypertension was significantly lower among the non-DMS at 30.1% as compared to the persistent-DMS group which stood at 41.8%. After controlling the confounding factors such as alcohol drinking, smoking, body mass index, and age, the persistent complaints of DMS and DIS were considerably associated with a higher risk of hypertension.

In a separate study conducted in Greece between April 2010 and November 2014 on the characterization of insomnia among patients with hypertension, an association was indicated between chronic insomnia and development of hypertension. The study was aimed at describing the association between insomnia and different biochemical and clinical parameters among hypertensive clients [4]. The study selected 432 participants, made up of 179 females and 253 males. The participants were hypertensive patients who were screened for insomnia prior to participation through the Athens Insomnia Scale (AIS). Other variables that were analysed in the study included the use of alcohol, smoking status, coexisting disorders, left ventricular mass index, creatinine, and body mass index, known duration of hypertension, sex, and age. The ambulatory blood pressure measurements (ABPM) of the respondents were measured on a daily basis.

Among the study participants, 47.9%, represented by 207 respondents, had AIS scores of above 14 and, thus, were categorized as insomniacs. Insomnia was found to be more common in women at 60.9% compared to men who stood at 37.8%, and was also more commonly reported among patients with underlying coronary heart disease. The insomniacs were generally of more advanced age and with longstanding hypertension. The ABPM parameters were generally the same for both insomniacs and non-insomniacs. There was a significant relationship between insomnia frequency and the number of antihypertensive drugs. There also existed correlations between the duration of hypertension ($r = 0.23$; $p < 0.001$) and the AIS score and age ($r = 0.22$; $p < 0.001$).

There were negative correlations between night fall and the AIS score for diastolic and systolic blood pressure in the sub-group of untreated hypertensive patients. The study showed that insomnia was more prevalent among hypertensive patients and also indicated a relationship between insomnia and the number of antihypertensive drugs taken, known duration of hypertension, and gender [11]. The study concluded that essential hypertensive insomniacs who were untreated were characterised by a lower nocturnal fall in both diastolic and systolic blood pressure as compared to hypertensive non-insomniacs.

Selection of Articles

The meta-analysis of the study assumed several preliminary steps that included the development of specific meta-data. The study performed a systematic review of articles in PsychInfo, EMBASE, and MEDLINE. The initial search was conducted in January 2010 and a final search was conducted in April 2016. The search strategies utilised MeSh headings and the keywords “stress-induced insomnia” or “insomnia” or “sleep disorders” and “blood pressure” or “hypertension”. The searches were limited to studies conducted on adult participants and those conducted in the English language.

The articles included in the study were those that involved participants above 18yrs, case-control, cross-sectional and longitudinal studies, meta-analyses, systematic reviews, articles that analysed the relationship between sleep, hypertension, insomnia and sleep duration, and those published between 1975 to 2016. The articles that were excluded from the study were those that did not control for confounding factors such as psychiatric disorders, metabolic disease, disordered breathing, other sleep disorders, coronary heart diseases, stroke, and history of diabetes, alcohol use, body mass index, cigarette smoking, education, and sex. Articles were also excluded if they failed to analyse data stratifies by age and race, if they were unavailable in full text via library access, and if they were unavailable in English language.

Results and Discussion

In a study conducted in West China Hospital of Sichuan University at the Sleep Medicine Center, individuals with stress-induced insomnia and normal sleepers were matched for sex and age to comprise the study sample. The inquiry was approved by the Institutional Review Board of the University and informed consent was obtained from all participants prior to their participation in the study. The participants were all above 18 years and selected consecutively between January 2010 and July 2014 form the Sleep Medicine Center of West China Hospital of Sichuan University. The normal sleepers were selected from among the University’s students, technical and medical staff, and visitors of the healthcare institution with posted announcements.

Physical examination and a comprehensive medical history were obtained from the participants including a mental status assessment. The respondents were then interviewed with the aid of a comprehensive questionnaire. The questionnaire deciphered the participants' medication use, general health status, and complaints of sleep. The stress-induced insomniacs met the DSM-V criteria for primary insomnia. In addition to ascertaining the severity and chronicity of their condition, the participants with stress-induced insomnia were supposed to report a six-month or more duration of insomnia symptoms instead of the one-month period that is required according to the DSM-V.

The normal sleepers were adults who had no major psychiatric or medical conditions according to the findings of the comprehensive physical assessment and complete medical histories and also reported no sleep problems. The insomniacs and normal sleepers who were excluded from the study included those with major psychiatric conditions such as depression and anxiety, chronic sleep disruptive medical conditions, past or current use of hypnotics, psychotropic medication, antidepressants, and anxiolytics, and those with evidence of sleep apnea [15]. Other participants that were excluded from the study included those with evidence of sleep-related movement disorders translating to a periodic limb movement of 15 or more, individuals with evidence of hypersomnia disorder with values of 8 minutes or less, 2 or more sleep onset REM periods or a cumulative Epworth Sleepiness Scale score of less than 10, and any other sleeping disorder as per the interviews.

The recruitment period was between January 2010 and July 2014 during which 843 consecutive stress-induced insomniacs and 116 normal sleepers were studied in a sleep laboratory by the sleep laboratory technician. After a polysomnography test that lasted overnight preceded by a standard MSLT study, a total of 313 individuals were selected for the study. Two hundred and eighteen of the individuals were stress-induced insomniacs while 95 of them were normal sleepers, all of whom met the selection criteria for the study. The insomniacs and the normal sleepers had similar age and gender compositions and were all evaluated for one night in light temperature-controlled and sound-attenuated sleep laboratories. The subjects were monitored continuously with polygraphs consisting of 16 channels that analysed the sleep parameters enabling recording and scoring of the findings.

Another study conducted at Tel Aviv University in Israel on the impacts of stress on sleep and health took place between February 2013 and April 2015. The main objective of the prospective quasi-experimental study was to assess the role of stress on sleep vis-à-vis the development of hypertension. The sleep of 36 students was analysed by the use of daily logs and actigraphy during high stress periods and low stress periods [1]. The low stress period was a normal academic session period while the high stress period was the week when the university students were undergoing their evaluations for acceptance to the clinical psychology graduate programs. The coping skills of the students were also assessed in the study. The study revealed that higher scores for highly emotion-focused coping predicted the reduction of sleep time during the high and low stress periods and also significantly increased the blood pressure of the participants.

Multiple Sleep Latency Test

The MSLT study was performed by the sleep laboratory technician one day after the polysomnography test that lasted overnight. The study was comprised of 4 sets of 20-minute sleep periods at intervals of 2h. The technical staff closely monitored the subjects in between the sleep periods to prevent unplanned sleep episodes. Any sleep stage necessitated a sleep onset so long as it lasted for more than 30 seconds [9]. If the participants failed to sleep, the trial was stopped at 20 minutes and assigned a sleep latency period of 20 minutes. Blood pressure readings were recorded at two different intervals; approximately two hours before starting polysomnography in the evening and in the morning after the procedure were completed just before getting out of bed.

The study used pneumoelectric microprocessor-controlled instruments with an accuracy of ± 3 mmHg. Three different blood pressure readings were obtained at intervals of 5 minutes and the average determined. Hypertension was defined as a systolic blood pressure of 140mmHg or more and a diastolic blood pressure of 90 mmHg or more, a physician positive diagnosis of hypertension as per the medical history, or the present use of anti-hypertensive medications.

Proposed guidelines

Data for the meta-analysis was presented as the mean, standard deviation for frequency, continuous variables, and percentages for categorical variables. The independent association of hypertension and insomnia were compared to normal sleep using logistic regression. Two logistic regression models were used to analyse the relationship between hypertension and insomnia on various levels of hyperarousal states measured by the MSLT values.

Limitations of the study

A major limitation was that limited studies have been conducted on the relationship between stress-induced insomnia and hypertension in the Middle East. The analysis had to rely largely on surveys conducted outside the region. Most articles reviewed for the meta-analysis were limited to large hospitals and universities which may not be a clear reflection of the overall situation in the country and region.

Conclusions

Stress-induced insomnia is associated with increased blood pressure and an increased risk of developing hypertension. Sleep loss, particularly as a result of sleep deprivation, could precipitate a sustained increase in blood pressure among hypertensive, pre-hypertensive, and normotensive patients, both young and old and of both genders [9]. The lack of sleep could also create a surge in blood pressure as a result of psychological stress. Stress-induced insomnia might favour the development or the maintenance of hypertension.

Insomnia appears to be associated with an increased risk of developing hypertension among middle-aged individuals after controlling for other confounding variables. The effects of this could be more pronounced when complaints about sleep are linked to short durations of sleep with variations in age [16]. Further studies are required to elucidate the degree of stress-induced insomnia required to develop hypertension vis-à-vis the roles of confounding factors. The pathological and physiological mechanisms underlying the association could be related to inappropriate arousal of the physiological parameters of insomniacs. Insomnia could act as a chronic stressor that precipitates systemic inflammation and activates the sympathetic nervous system.

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