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The impact of sleep disorders in the development of hypertension

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Abstract

Hypertension is one of the most common chronic non-communicable diseases in the world. Risk factors, methods of prevention and treatment of hypertension have been sufficiently studied. However scientists are still looking for pathogenetic mechanisms of its development. At the same time, 36.9% of patients with hypertension had different sleep disorders. Patients with insomnia have a 21% higher risk of developing hypertension compared with those who have quality sleep. Hypnotics are given up to 15% of patients with hypertension. Hypnotics have been shown to increase the risk of cardiovascular events. As much as 44.1% of patients with established diseases of the cardiovascular system have problems with the quality or duration of sleep. At this time, hypertension and sleep disorders are considered mutually aggravating diseases.

Key words: hypertension; sleep disorders; insomnia

Introduction

Hypertension is primarily associated with adverse cardiovascular outcomes, such as heart failure, stroke, myocardial infarction, and death. The global pandemic of hypertension is increasing due to an aging population and an increasing prevalence of obesity and it is estimated to affect one third of the world's population by 2025. Adverse outcomes are exacerbated by mechanical hemodynamic changes, arterial stiffness, neurohormonal and vegetative disturbances, dysregulation and reduced kidney function. This review highlights current evidence and summarizes the latest information on the relationship between hypertensive disease and sleep disorders. In our opinion, prevention and treatment of hypertension should begin with non-drug lifestyle interventions to diminish the risk of hypertension and as adjunctive therapy to reduce the need for drugs. Given the burden of hypertension on the economies and public health of countries around the world, it is imperative to change the lifestyles of the younger generation to prevent hypertension as they age.

The aim of our narrative review was to comprehensively summarize the relationship between hypertension and sleep disorders. We incorporated evidence from only human studies that assessed epidemiology, clinical characteristics, and pathomechanisms underlying this link. Furthermore, we have discussed the evidence gaps and potential areas for further research such as the effect of antihypertensive therapy on sleep disorders.

We searched PubMed using the terms: “hypertension” AND “sleep disorders” or “hypertension” AND “insomnia”. Our initial search yielded 3618 reports published in the previous 10 years, which we narrowed by excluding studies not reported in the English language and duplicate reports. We further selected studies according to the strength of the design and the publication date (preferring the most recent reports). Nevertheless, we included older studies (preferring high-ranking journals) in the case of seminal studies or when few studies were available for a specific topic. Of the studies retained, we included 92 that were most specific to sleep disorders in patients with hypertension.

Healthy sleep is necessary for the full functioning of the brain, memory, regulation of metabolic processes, and muscle recovery. In addition, during this period, most of the repair processes take place. But all functions are not fully defined.

Normal sleep architecture consists of four to five cycles lasting approximately 90 minutes, alternating between deep sleep (NREM — non rapid eye movement) and short (REM — rapid eye movement) sleep. At the same time, NREM sleep predominates at the beginning of the night, while the duration of REM sleep increases during the last sleep cycle [1, 2].

Sleep disturbance is one of the most common “non-cardiac” complaints among patients with cardiovascular diseases. According to Taylor et al., almost 40% of patients with defined

diseases of the cardiovascular system have problems with the quality or duration of sleep [3], whereas in the overall population, according to the data, this diagnosis is made only in 10–13% of the population [4, 5]. Moreover, scholars consider sleep disturbances as a separate risk factor for hypertensive disease. In order to characterize the possible relationship between sleep disorders and hypertension, a definition and existing classifications of disturbances should be imaged.

Insomnia can have important consequences for patients and it can affect health, work, and quality of life. There are the increased use of insurance [6, 7] and the increased risk of road accidents [8] among the negative social consequences. Ford et al. and Quera-Salva et al. found a prevalence of insomnia ranging from 10% to 48% [9, 10]. According to other authors, the prevalence of insomnia among the adult population in the world reaches 33–50% [11]. According to an estimate of the incidence of insomnia, accidents, and injuries, the United States spends approximately 5,000 USD per person affected per year [12].

Insomnia is associated with an increased prevalence of somatic disorders, especially cardiovascular ones [13]. Studies using polysomnography have demonstrated higher nighttime systolic blood pressure in normotensive patients with chronic insomnia [14].

Using multivariate statistical analysis, a crossover study of 49,405 Australian adults aged 45 to 65 found that decreased sleep was associated with increased hours of work, lower education levels, and more single people than married people, increased social habits (smoking, alcohol consumption), obesity, depression, or anxiety [15].

Krueger and Friedman found that factors such as low education and cardiovascular disease were associated with both reduced sleep duration and prolonged sleep (more than nine hours). Shorter sleep duration was associated with older age, social habits (smoking or alcohol consumption), overweight, or obesity. The risk group also included patients who had small children [16].

Thus, the social consequences of insomnia are quite significant, but the consequences for each individual suffering from sleep disturbances can be even more dramatic.

Risk factors for sleep disturbances

Research from Finland by Kronholm et al. found that gender, marital status, occupation, and physical activity were the main factors of REM sleep. According to the study, men are more likely to experience a reduction in sleep duration than women [17].

According to the data of Japanese authors who investigated risk factors for decreased sleep duration associated with the workplace, it was found that factors such as stress at work, quantitative workload, and interpersonal conflicts lead to a decrease in the sleep duration [18].

Psychosocial factors such as stress, state anxiety, and depressive symptoms have also been associated with decreased sleep duration. Furthermore, discrimination, work-life balance, high job demands, and social insecurity have been associated with an increased prevalence of sleep problems [19]. In addition, medication, chronic pain, frequent jet lag, nighttime eating habits, night and shift work, and breastfeeding can also be risk factors for sleep disturbances.

The impact of sleep disturbances on the human body

There is compelling evidence that both insufficient sleep and excess sleep can have negative consequences. Epidemiological evidence suggests that sleep duration and poor sleep are associated with the risk of premature death, as well as a wide variety of adverse health effects [20]. The Sleep Heart Study, which enrolled 4,994 participants with an average age of 64.0 ± 11.1 years, was conducted to determine the relationship between sleep disorders, including insomnia or poor quality sleep, the predominance of REM sleep over non-REM sleep, and the risk of developing cardiovascular diseases, as well as the risk of cardiovascular disease and mortality in the overall population. The study has shown that the risk of developing cardiovascular disease was 29% higher in patients who had insomnia or decreased sleep, compared with the control group. Thus, the researchers have concluded that objectively measured REM sleep was associated with a greater risk of developing cardiovascular disease [21].

One of the most threatening conditions resulting from sleep disturbances is the risk of premature death. According to Hafner et al., it has been shown that reduced sleep increases the risk of premature death. It was found that people who slept less than six hours had a 10 times higher risk of premature death than those who had seven to nine hours of sleep [22].

Sleep loss can have adverse effects on mood and behavior control. Irritability and low mood are the most commonly reported symptoms in individuals with sleep deprivation [23]. It is known that with insomnia, overexcitement signs appear in the cognitive-emotional and behavioral spheres, as well as in the autonomic or central nervous systems [24]. This is manifested in an increase in heart rate and a decrease in heart rate variability during the day, an increase in body temperature, an increase in the ACTH and cortisol (the main mediators of the stress response) secretion planes, especially in the evening. An increase in high-frequency electroencephalographic activity during slow wave sleep indicates an increased activity of the sympathetic nervous system and hyperactivation of the hypothalamus-pituitary-adrenal axis during sleep and wakefulness. It is assumed that physiological deregulation of these systems is the main cause of the development of insomnia. The same mechanisms of pathogenesis are inherent in the development of hypertension [25].

Using neuroimaging methods (positron emission tomography), it was revealed that in patients with insomnia, compared with healthy volunteers, is observed an increased activity in the 2nd stage of sleep in the following areas of the brain: the ascending reticular formation, hypothalamus, thalamus, cerebellar amygdala, hippocampus, insular and anterior cingulate gyrus and medial prefrontal cortex. This fact suggests that hyperactivity and disturbances in the activity of these structures responsible for the regulation of emotional and cognitive functions are one of the pathophysiological factors in the development of insomnia.

First of all, this leads to a decrease in volitional qualities and, as a direct consequence, to the inability to control such behavioral risk factors for hypertension and type 2 diabetes mellitus as inappropriate nutrition (overeating, night meals, excessive carbohydrate and fatty foods), smoking, alcohol consumption.

Scholars also identify individual genes whose mutations lead to insufficient sleep — Clock, Bmal1, Per1, Per2, Per3, Cry2, and Rev-Erbα [26]. Sleep loss disrupts the level of Bmal1 expression, which manifests itself in a strong decrease in amplitude (≈70%) and loss of rhythmicity. The circadian clock also shows a strong decrease in amplitude with sleep deprivation (≈40%) [27]. The level of Rev-Erbα expression also decreases after a period of reduced sleep duration [26].

Thus, sleep disorders have a complex effect; they can have both psychological and social consequences and lead to significant changes in the physiology of the body, namely, to the activation of the sympathoadrenal system, increased adrenocorticotropic hormone secretion, eating disorders and carbohydrate metabolism.

Sleep disturbance and hypertensive disease

The role of cortisol in the development of sleep disturbances

As mentioned above, sleep disturbance leads to the activation of the sympathoadrenal system. Several pathological links can be noted that link sleep disorders with hypertension and type 2 diabetes mellitus.

One of the most potent counterinsular hormones is cortisol. It is a steroid produced by the hypothalamic-pituitary-adrenal axis. In the blood serum, 85–95% of cortisol is bound to carriers such as GCS-binding globulin and albumin and the remaining 5–15% is free, unbound cortisol, which can be easily measured in saliva and blood serum [28, 29]. Increased blood cortisol levels counteract insulin, suppress the immune system, and promote the metabolism of carbohydrates, fats, and proteins. Long-term exposure to increased cortisol levels is associated with many adverse physiological effects, including body weight gain, development of abdominal obesity, decreased bone mineral density, impaired short-term memory, increased risk of cardiovascular

disease, and increased blood pressure and glucose. Many studies have found a negative association of cortisol with poor sleep quality or REM sleep [30]. Moreover, some studies have found that moderately increased levels of fasting morning cortisol are also associated with the presence of cardiovascular risk factors in adults [31]. Thus, Reinher and Andler found an association between serum cortisol levels and fasting insulin levels in obese patients, and the levels of both hormones decreased after weight loss [32]. In two Latin American studies involving overweight young patients with a family history of type 2 diabetes mellitus, it was shown that higher fasting cortisol levels were in those with greater insulin resistance [33, 34].

Difficulties in investigating the relationship between cortisol and essential hypertension and type 2 diabetes mellitus are associated with the fact that it follows the daily pattern. Peak nighttime levels are usually found during the second half of sleep, with daytime peak levels occurring about 30 minutes after waking up. After this initial peak, cortisol declines steadily throughout the rest of the day [35]. In the absence of stress or other pathological factors, the hypothalamic-pituitary-adrenal axis follows a circadian rhythm. In conditions of violations, an increase in the level of cortisol is determined. A meta-analysis by Van Cauter et al. examined the daily pattern of cortisol secretion among persons aged 18–83 years (n = 90). It has been shown that older age decreases the amplitude and increases the circadian activity of increasing cortisol levels, which can be considered as one of the factors in the etiology of sleep disturbances [36].

Experimental studies have shown which sleep characteristics are associated with nighttime or daytime cortisol levels. These studies were carried out in sleep laboratories, usually among young people whose quality or duration of sleep were artificially altered. There is evidence that poor sleep quality and sleep disturbances are associated with increased cortisol at night [37]. Several studies have found that after significant sleep restriction, such as 4 hours at night, or afternoon and evening sleep, cortisol levels are also increased [38]. A study of 3,100 men with an average age of 76.6 years found that the longer the usual duration of sleep, the lower level of cortisol in the 24-hour urine [39]. In the Whitehall II study, patients kept a sleep diary, and it was found that patients who had higher evening cortisol levels reported less sleep the night before and more sleep disturbances than usual [40].

Several studies have established associations between increased serum cortisol levels and decreased brain volume [41–43]. And some studies suggest that changes in brain volume correlate with decreased cognitive function and they are associated with cortisol levels [44]. According to The Framingham Heart Study, increased cortisol levels were associated with impaired visual memory and perception. Also, increased cortisol has been associated with numerous areas of microstructural changes in the brain, especially in the splenium of the corpus callosum. The association of cortisol with total cerebral volume varied by gender: increased

cortisol levels were associated with cerebral volume in women, while no such association was found in men [45].

Insomnia, as a rule, is accompanied by an increase in the cortisol level, and this is one of the mechanisms of the development of hypertension and type 2 diabetes mellitus.

The role of prolactin in the development of sleep disturbances

One of the factors explaining how sleep disorders can lead to the formation of pathology in glucose metabolism and blood pressure regulation may be prolactin. This hormone is multifunctional and it has more than 300 biological effects, including its effect on reproductive function, the function of the immune system, regulation of appetite, adipose tissue, synthesis and secretion of insulin [46]. Prolactin was discovered in 1928; since then every year new data on this hormone have appeared. It has now been established that an increase in prolactin levels is not necessarily associated with lactation or pituitary adenoma, it can also be observed with excessive protein intake, and it is of particular importance in stress. Moreover, anaerobic exercise promotes the additional prolactin release. In the context of studying the pathogenesis of type 2 diabetes mellitus, it is important that hypoglycemia through exposure to the central nervous system is a powerful stimulus for increased prolactin secretion [47, 48].

There has been a connection between some antihypertensive drugs and impaired prolactin secretion. For example, verapamil causes both short-term and long-term increases in basal prolactin secretion by blocking the secretion of dopamine in the hypothalamus [49, 50]. Alpha-methyldopa leads to moderate development of hyperprolactinemia by inhibiting the enzyme decarboxylase, which is responsible for the conversion of L-DOPA to dopamine and independently acts as a false neurotransmitter of dopamine [51]. Reserpine, an antihypertensive drug, causes hyperprolactinemia in about 50% of patients, probably interfering with the deposition of catecholamines in the hypothalamus [52]. However, no such relations have been established for ACE inhibitors and IRB.

The secretion of prolactin, like cortisol, has certain circadian rhythms throughout the day. So, the increase in prolactin levels begins 60–90 minutes after falling asleep without connection with the sleep phase. In this case, it does not matter what time of day the sleep came. After waking up, the prolactin level drops sharply and closer to noon, it gradually begins to rise again. [53]. It follows that prolactin levels are directly related to the sleep-wake cycle.

Experimental studies have shown prolactin impact on appetite and satiety, weight gain and insulin resistance by inhibiting adiponectin and IL-6 production in adipose tissue [54], which can lead to the development of type 2 diabetes. On the other hand, experimental studies have also shown that prolactin affects the growth of pancreatic β-cells, lowers the threshold for insulin

secretion in response to glucose stimulation, and thus, it may be involved in the onset or development of type 2 diabetes mellitus [55, 56].

Studies in humans with high serum prolactin levels caused by antipsychotic medication or prolactinoma suggest that increased prolactin levels may have adverse metabolic effects leading to type 2 diabetes mellitus [57]. Furthermore, bromocriptine, a well-known dopamine agonist, suppresses serum prolactin levels, effectively improves insulin sensitivity, and has been approved for the treatment of type 2 diabetes in the United States [58].

Several studies have shown different results. In particular, according to Ruiz-Herrera et al., it has been shown that higher prolactin levels are associated with increased insulin sensitivity, decreased glucose and lipid levels [59], and lower prevalence of diabetes and metabolic syndrome [60]. A possible relationship between prolactin and metabolic parameters looks like a G-curve.

However, studies of serum prolactin levels within the physiological range have shown rather conflicting results. Several studies have found positive associations between prolactin levels and metabolic parameters, hypertension [61], waist circumference [62], aortic stiffness [63], and mortality [64].

Since prolactin levels are regulated differently depending on gender [65], any association between prolactin levels and any other factors should be assessed separately for women and men. However, most authors estimate prolactin levels separately for men and women [61–63]. Several studies have demonstrated gender-specific associations between serum prolactin levels and insulin release induced by oral glucose administration [66], cardiac remodeling [67], and metabolic syndrome [68]. So, in a crossover Japanese study, where only men who did not have diabetes took part, associations between the prolactin level in the physiological range and the glucose level were established. A direct correlation between the HOMA index and the level of prolactin in the blood serum below 12.4 ng/mL, which indicates that higher levels of prolactin in the physiological range are associated with insulin resistance in men, was found [69].

The role of sleep disorders in the development of hypertension

The sympathetic nervous system decreases its activity with the onset of deep sleep (NREM—non-rapid eye movement) [70]. Using heart rate variability analysis, it has been demonstrated that NREM sleep is indeed characterized by a predominance of vagal regulation, with a decrease in sympathetic activity. As a result, blood pressure and heart rate decrease during the deep sleep phase, whereas during REM sleep, blood pressure varies greatly and it can be compared to the wakefulness phase. This physiological setting allows the hypothesis that the regulation of nighttime blood pressure may be related to sleep characteristics. Any disturbance in

the quantity or quality of sleep can contribute to the development of hypertension or an increase in its severity.

More data on the relationship between sleep disorders and hypertension comes from obstructive sleep apnea syndrome studies. Currently, this condition is considered to be a separate risk factor for resistant hypertension [71]. Obstructive sleep apnea syndrome is well studied, unlike other sleep disorders. Most of all in the modern literature data the effect of sleep duration on the development and course of hypertension.

The role of sleep duration in the development of hypertensive disease

According to Kronholm et al., sleep duration has decreased in the overall population over the past 30 years [72]. In the United States, the National Sleep Foundation reported a decrease in average sleep duration from 9 hours/night in 1910 to 7.5 hours in 1975 and 6.8 hours in 2005. Two main cohort studies in humans, the Sleep Heart Health Study (SHHS) [73] and the National Health and Nutrition Examination Survey (NHNES) [74], were the first to report an association between sleep duration and hypertension.

Most of the studies used subjective self-reported sleep duration data; however, Knutson et al., in a follow-up study of the coronary artery risk (CARDIA), found a significant association between REM sleep duration and the prevalence of hypertension using actimetry to obtain objective measurements of sleep duration [75].

Moreover, there is a significant correlation between sleep duration assessed by subjective questionnaires and objective actimetry [76], suggesting that questionnaire-only studies are informative enough.

It was also found that the association between self-reported sleep duration and hypertension differed by age and sex [77], as well as by location. In a meta-analysis of 17 crossover studies (n = 105 432) and six longitudinal studies (n = 9 959), short sleep duration was associated with a 20% increase in the risk of hypertension, especially among patients of both sexes under 65 years of age and women [Wang Q, Xi B, Liu].

A meta-analysis by Guo et al. [60] included 27 studies: 21 transverse and 6 longitudinal. The studies included men and women between the ages of 18 and 106 in the Americas, Europe, Asia, and Australia. Pooled analyzes of crossover studies showed a significant association of both short sleep duration and increased sleep duration with prevalence of hypertension, whereas the studies showed associations only between short sleep duration and hypertensive situations. It was also found that there is no significant association between sleep duration and hypertension in the European population. According to other authors, no relationship between sleep duration and the risk of hypertension for the European Region has been established.

Haack et al. suggested that increasing sleep duration may be an effective behavioral strategy for lowering blood pressure. The patients were randomized into 2 groups. The first group consisted of patients who had an artificially increased sleep duration and increased bed time by 1 hour daily over a 6-week intervention period. The second group included patients who adhered to the usual duration of sleep. Systolic and diastolic blood pressure during 24-hour monitoring significantly decreased in relation to the initial level in patients of the first group. It has also been found that lengthening sleep is associated with increased daily activity as assessed by actigraphy [78].

The role of sleep deprivation in the development of hypertensive disease

The literature contains data characterizing not only the quantitative characteristics of sleep, but also its quality. So, in a study among persons experiencing short-term awakening during sleep, changes in heart rate and blood pressure were demonstrated, namely: compared with undisturbed sleep quality and duration, sleep deprivation nights were associated with increased systolic and diastolic blood pressure, increased heart rate between 9:00 p.m. and 2:00 a.m., and these symptoms persisted throughout the next morning [79].

Tochikubo et al. conducted 24-hour blood pressure monitoring among men who had regular overtime work. Monitoring was performed during a typical workday (average sleep period — 8 hours) and during the day with periods of sleep deprivation (average sleep period— 3.6 hours). Systolic, diastolic blood pressure and heart rate increased on the day after sleep interruption compared to the day when sleep was not disturbed. It was also found that after sleep deprivation, urinary excretion of noradrenaline increases [80]. Thus, it can be concluded that interrupted sleep may be associated with an increase in blood pressure and heart rate through activation of the sympathoadrenal system.

Likewise, activation of the sympathetic nervous system was reported by Dettoni et al. in a study in healthy European men with poor sleep quality. Study participants spent five nights at home with undisturbed sleep and five nights at home with 1.5 hours of sleep interruption. This moderate sleep deprivation did not alter heart rate or blood pressure, but did lead to a significant increase in plasma noradrenaline [81].

The role of insomnia in the development of hypertensive disease

In the modern literature, there is not enough data characterizing the relationship between insomnia and hypertension. Although short sleep duration and insomnia are classically related, they are different sleep disturbances that result in different complications. Insomnia leads to dissatisfaction with the quality of sleep and daytime consequences that cannot always be

attributed to reduced sleep duration. Individuals with short sleep durations do not necessarily suffer from insomnia.

Fernandez-Mendoza et al. found that the prevalence of hypertension increased by 3.5 times against the background of a decrease in sleep duration from 6 to 5 hours. The prevalence of hypertension has increased 5.1-fold when the duration of sleep was less than 5 hours at night. Accordingly, chronic insomnia with short sleep duration (less than 6 hours) is associated with an increased risk of hypertension [82].

The role of movement disorders associated with sleep in the development of hypertensive disease

Changes in the quantity or quality of sleep due to movement sleep disorders are thought to be associated with the prevalence of hypertension [83].

In a Swedish study of 4,000 men between the ages of 18 and 64, the aim was to determine the relationship between movement disorders associated with sleep and the presence of bodily diseases. A disadvantage of the study was that sleep disturbances were diagnosed using a questionnaire that included a question about sleep habits, symptoms of daytime sleepiness, and somatic and neuropsychiatric complaints. Four questions on the symptoms of movement sleep disorders adopted as the minimum diagnostic criterion by the International Restless Legs Syndrome Study Group were also included. It was found that patients with movement sleep disorders more often reported depressive mood [odds ratio (OR): 2.6; 95% CI: 1.8–3.8) and more often complained of decrease in libido (OR: 2.2; 95% CI: 1.4–3.3). Patients with movement sleep disorders were more likely to have hypertension (OR, 1.5; 95% CI, 0.9–2.4) and other cardiovascular diseases (OR: 2.5; 95% CI: 1.4–4.3) [84].

Winkelman et al., in the Wisconsin sleep cohort study of 2,821 patients, found a high prevalence of hypertension among patients with movement disorders associated with sleep [85].

Lindner et al. conducted a study that randomized 100 patients after kidney transplantation and 50 patients on hemodialysis. Polysomnography was used to diagnose sleep disorders. They assessed the 10-year risk of coronary heart disease and the 10-year risk of stroke for all patients using the Framingham Risk Score and its modified version. High physical activity during sleep is an independent predictor of higher cardiovascular risk in patients with chronic kidney disease, namely, it was diagnosed in 27% of patients after transplantation and in 42% of patients on dialysis ($p = 0.094$). Patients with sleep disorders had a higher 10-year estimated risk of stroke in the post-transplant group [10 (7–17) *vs.* 5 (4–10); $p = 0.002$] and a higher risk of coronary heart disease at 10 years in both the post-transplant group [18 (8–22) *vs.* 7 (4–14); $p = 0.002$] compared to the hemodialysis group [11 (5–18) *vs.* 4 (1–9); $p = 0.032$] [86].

Patients with more than 35 movements per hour as determined by polysomnography had greater left ventricular hypertrophy [87].

Thus, many data support the relationship between sleep duration and sleep quality and hypertension and type 2 diabetes mellitus. But neither sleep duration nor sleep quality are clinical diagnoses. While insomnia, which necessarily includes daytime symptoms, is a diagnosis and needs correction, there are practically no studies examining the relationship between insomnia and hypertension and type 2 diabetes mellitus.

The role of antihypertensive therapy in the development of sleep disorders

One of the complex and important questions is the relationship between antihypertensive therapy and sleep disorders. Many studies have found a link between sleep characteristics and blood pressure and hypertension. Moreover, hypertensive patients may require changes in antihypertensive therapy after some time, depending on the achieved level of blood pressure [88]. In another study, it was found that patients with hypertension are more likely to use sleeping pills [89].

Data presented in a prospective cohort study that included 752 hypertensive patients with an average age of 69.9 years is of particular interest. It was found that the regular use of sleeping pills was associated with an increased risk of an increase in the amount of antihypertensive drugs. It's important that this relationship was observed regardless of the duration and quality of sleep, body mass index, diet, or physical activity [90].

A pharmacoepidemiological research was carried out by Japanese authors Tanabe et al. to investigate the incidence of insomnia in hypertensive patients and to determine how different antihypertensive therapies can affect the quality and duration of sleep. For the analysis, they used post-marketing observation databases. The incidence of insomnia in hypertensive patients receiving antihypertensive therapy was 0.77/100 person-time. Factors contributing to the onset of insomnia were α-blockers (OR: 2.38; 95% CI: 1.14–4.98), β-blockers (OR: 1.54; 95% CI: 0.99–2.39), calcium channel blockers (OR: 0.62; 95% CI: 0.43–0.90), angiotensin-converting-enzyme inhibitors (OR: 1.76; 95% CI: 1.27–2.44). This study has identified potential factors that can help predict the occurrence of insomnia in hypertensive patients on antihypertensive therapy [91, 92].

Conclusions

It is generally accepted that sleep disturbances are a risk factor for hypertensive disease and significantly worsen its course. However, many mechanisms of the relationship between these states are not fully understood and require further research.

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