Original paper

Sleep architecture and vitamin D in hypertensives with obstructive sleep apnea: A polysomnographic study

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Abstract

Background. Obstructive sleep apnea (OSA) and arterial hypertension (AH) are closely linked disorders with common pathophysiological features.

Objectives. The present study aimed to investigate the relationship between AH and OSA by examining sleep architecture, vitamin D concentration and electrolyte levels in patients with these coexisting conditions.

Material and methods. A total of 133 patients suspected of having OSA were recruited for examination. The participants were divided into 2 groups: hypertensives ($n = 52$); and normotensives ($n = 81$). One full-night polysomnographic examinations were conducted, followed by the statistical analysis of the collected data.

Results. Hypertensive individuals displayed increased apnea–hypopnea index (AHI), oxygen desaturation index (ODI), respiratory arousal index (RAI), and periodic limb movement index (PLMI) as compared to non-hypertensive individuals. Moreover, sleep efficiency (SE), the bruxism arousal index (BAI) and oxygen saturation (SpO_2) level were decreased in the hypertensive group. In terms of biochemical parameters, hypertensive individuals exhibited a lower magnesium (Mg) level, and higher levels of C-reactive protein (CRP), uric acid (UA) and glucose. Notably, there were no statistical differences in vitamin D concentration between hypertensive and normotensive individuals.

Conclusions. The study explored the potential influence of calcium (Ca), Mg, vitamin D, and UA concentrations on the sleep architecture of patients with comorbid AH and OSA. The findings revealed several notable associations. Firstly, sleep fragmentation correlated with Ca level, suggesting a potential role for both Ca and vitamin D in sleep arousals. Secondly, a higher UA concentration was linked to a higher AHI and increased sleep fragmentation. Additionally, alterations in Mg concentration were observed among hypertensive individuals with OSA. However, further research is needed to fully comprehend the potential impact of these factors on the sleep architecture of hypertensive individuals with apnea.

Keywords: uric acid, vitamin D, obstructive sleep apnea, hypertension, periodic limb movements of sleep

Cite as
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Introduction

Obstructive sleep apnea (OSA) is a highly prevalent sleep disorder that, based on rough estimates, may potentially impact nearly one billion adults globally, specifically those aged between 30 and 69 years. Within this population, approx. 425 million individuals are estimated to have moderate to severe OSA that requires medical intervention.[1] Patients with OSA commonly experience symptoms such as excessive daytime sleepiness, loud snoring, and witnessed pauses during breathing or awakenings from gasping for air after sleep events.[2] The signs of OSA include the repetitive collapse of the upper airway,[3] sleep fragmentation,[4] hypoxemia,[5] hypercapnia,[6] and increased sympathetic activity.[7] Furthermore, individuals with OSA may experience morning headaches, a dry mouth or a sore throat upon waking, difficulty with concentrating, and irritability.[8] The American Academy of Sleep Medicine (AASM) defines polysomnography (PSG) as the gold standard for diagnosing OSA.[9] Obstructive sleep apnea is associated with intermittent airflow obstruction leading to periods of a decreased oxygen level in the bloodstream.[10] These fluctuations in oxygen can have detrimental impact on various organs and systems, particularly the cardiovascular system. As a result, OSA has been associated with an increased risk of arterial hypertension (AH), heart disease, stroke, and other cardiovascular complications.[11]

Arterial hypertension, as defined by the American Heart Association (AHA) and other major guidelines, refers to a patient having a systolic blood pressure of 140 mmHg or higher and/or a diastolic blood pressure of 90 mmHg or higher upon repeated examination.[12] Arterial hypertension pathophysiology shares similarities with OSA, including the evidence of sympathetic nervous system activation[13] due to peripheral resistance,[14] renin–angiotensin system (RAS) involvement[15] and endothelial dysfunction.[16] Numerous studies have recognized an excessive sodium (Na) intake as a risk factor for hypertension, as it disrupts the balance of microelements in cellular fluids, leading to the contraction of vascular smooth muscles, a reduced blood flow and an increased blood pressure.[17] Besides changes in macroelements (Na and potassium (K)), studies have also shown plasma vitamin D alterations in hypertensive patients. Approximately 50% of the global population is affected by vitamin D insufficiency despite lifestyle and environmental factors.[18] Lower levels of vitamin D are associated with an increased risk of cardiovascular events, possibly due to its influence on blood pressure regulation.[19] One potential connection is the inverse association between serum vitamin D level and the renin–angiotensin–aldosterone system (RAAS) in patients with AH.[20,21] Furthermore, vitamin D plays a role in maintaining calcium (Ca) homeostasis through parathyroid hormone (PTH), and some studies have reported an association between PTH and hypertension.[22–24] Moreover, vitamin D has vasodilatory and antiatherosclerotic properties, influencing the vessel wall.[25,26] However, it is important to note that some research suggests that vitamin D may increase vascular resistance by enhancing sensitivity to vasoconstrictors.[27–29]

Studies have revealed that, mostly due to the common pathomechanism in AH and OSA, approx. 30–40% of hypertensive patients also have OSA, while 50% of individuals with OSA have a history of AH.[30,31] Furthermore, OSA frequently coexists in patients with resistant hypertension,[32] which enhances the connection between these conditions. The primary pathophysiological mechanisms implicated in the changes induced by OSA include intermittent episodes of hypoxemia and reoxygenation, frequent arousals, and alterations in intrathoracic pressure.[33] These factors contribute to the development and progression of AH in individuals with OSA. The increasing prevalence of sleep disorders in the general population, particularly OSA, specifically among obese and hypertensive individuals, and those resistant to antihypertensive therapy, highlights the importance of implementing effective screening, diagnosis and treatment strategies for OSA to mitigate cardiovascular risks.

Patients with both OSA and AH are indeed at a heightened cardiovascular risk. Therefore, it is crucial to recognize all factors, including polysomnographic and biochemical markers, that can influence the effectiveness of sleep and contribute to a cardiovascular risk. Understanding the common pathomechanisms connecting sleep disorders, particularly OSA, and hypertension is essential for understanding the complex interplay between these conditions. By implementing comprehensive screening, diagnosis and treatment strategies, including PSG, and considering biochemical markers, healthcare professionals can effectively manage sleep disorders and hypertension. Such an approach mitigates associated cardiovascular risks, and ultimately improves overall patient outcomes.

The present study aimed to investigate the sleep architecture and vitamin D concentration in patients with coexisting AH and OSA as compared to normotensives. Furthermore, we aimed to assess the levels of electrolytes and explore their relationship with sleep parameters. By examining these factors, we sought to gain a comprehensive understanding of the interplay between AH, OSA and electrolyte levels, which could contribute to improving management strategies and reducing risks for affected individuals.

Material and methods

This prospective observational study involving 133 patients was conducted at the University Hospital in Wroclaw, Poland. The study was approved by the Wroclaw Medical University Bioethical Committee (No ID KB-407/2022) and adhered to the principles outlined in the Declaration

of Helsinki. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist (a combined checklist for cohort, case–control and cross-sectional studies) to ensure the transparency and comprehensiveness of the findings.[34] Before participation, all patients provided written informed consent, thereby affirming their comprehension of the objectives and procedures of the study, as well as potential risks and benefits.

Participants

The patients included in the study were referred to the Sleep Laboratory of the Department and Clinic of Internal Medicine, Occupational Diseases, Hypertension, and Clinical Oncology at Wroclaw Medical University, Poland. Eligible participants were aged 18 years and above and had suspected OSA. The study cohort comprised individuals of Caucasian ethnicity with an average age of 47.8 ±16.6 years who willingly agreed to participate in the examination. The exclusion criteria were established to ensure the validity of the study; they comprised severe mental disorders, active malignancy, active inflammation, secondary hypertension, recent myocardial infarction or stroke within 6 weeks, an estimated glomerular filtration rate (eGFR) of less than 30 mL/min, pregnancy, vitamin D supplementation in the past 6 months, and an inability to undergo a polysomnographic examination (Fig. 1). The characteristics of the study group are presented in Table 1. The patients were stratified into 2 groups – one consisting of patients diagnosed with hypertension (n = 52) and the other including patients without hypertension (n = 81). The hypertension diagnosis followed the guidelines provided by the European Society of Cardiology and the European Society of Hypertension (ESC/ESH).[35] In addition, a subgroup of normotensive individuals without sleep disorders (n = 34) was extracted for further analysis.

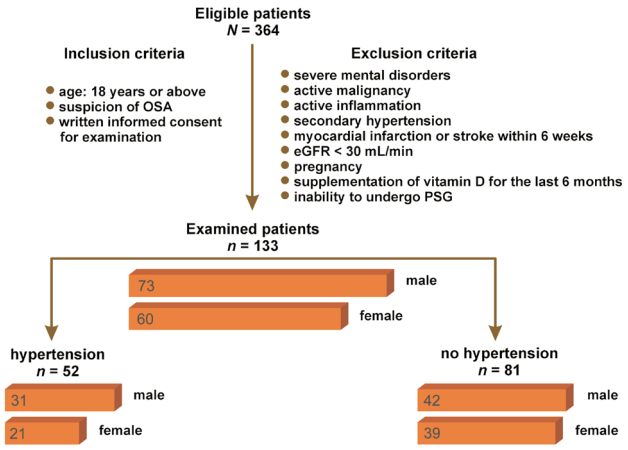

Fig. 1. Study inclusion and exclusion criteria

OSA – obstructive sleep apnea; eGFR – estimated glomerular filtration rate; PSG – polysomnography.

Table 1. Characteristics of the entire study group (N = 133)

Characteristics		Statistics
Comorbidities *n* (%)	AH	52 (39.1)
	prior myocardial infarction	7 (5.3)
	prior stroke	6 (4.5)
	diabetes	24 (18.0)
	ischemic heart disease	10 (7.5)
PSG parameters *M* ±*SD*	AHI	19.83 ±23.42
	ODI	18.21 ±21.25
	snore [%]	20.82 ±21.11
	PLMI	8.02 ±17.24
	SL [min]	15.16 ±11.17
	REM latency [min]	101.01 ±77.81
	WASO [min]	65.83 ±61.39
	SE [%]	81.46 ±14.30
	N1 [%]	6.17 ±4.87
	N2 [%]	48.61 ±18.33
	N3 [%]	26.19 ±24.81
	REM [%]	22.58 ±9.72
	av SpO_2 [%]	92.73 ±4.34
	min SpO_2 [%]	82.16 ±8.87
	SpO_2 < 90% duration [%]	10.11 ±16.30

Data presented as number (percentage) (n (%)) or as mean ± standard deviation (M ±SD). AH – arterial hypertension; AHI – apnea–hypopnea index; ODI – oxygen desaturation index; snore [%] – snore percentage during sleep; PLMI – periodic limb movement index; SL – sleep latency; REM latency – rapid eye movement sleep latency; WASO – wakefulness after sleep onset; SE – sleep efficiency; N1 – sleep stage 1; N2 – sleep stage 2; N3 – sleep stage 3; REM [%] – REM sleep stage percentage of the total sleep time; av SpO_2 – average oxygen saturation; min SpO_2 – minimal oxygen saturation; SpO_2 < 90% duration [%] – percentage of the average oxygen saturation below 90%.

To determine the minimum required sample size, a sample size calculator (https://www.calculator.net/sample-size-calculator.html) was utilized. The parameters used for the calculation included a population size of 3,000,000 (representing the population size of the Lower Silesian Voivodeship), a confidence level of 95% (default value), a maximum error of 5%, and a population proportion of 8%. Based on these calculations, a minimum sample size of 114 individuals was determined and achieved for the study.

During the admission of the participants to the Sleep Laboratory, blood samples were collected from all individuals into polyethylene terephthalate plastic tubes containing K2EDTA (Becton, Dickinson and Company, Franklin Lakes, USA) via venipuncture. After collection, the samples were stored at –70°C until they were ready for analysis. All blood and urine samples were analyzed at the Main Laboratory of Wroclaw Medical University, following the standard laboratory protocols of the Wroclaw Medical University Teaching Hospital. The plasma concentrations of C-reactive protein (CRP) [mg/dL], Na [mmol/L], K [mmol/L], Ca [mg/dL], magnesium (Mg) [mg/dL], and vitamin D [ng/mL] were determined using appropriate laboratory techniques.

Polysomnography

The polysomnograms were analyzed using the Nox A1 Noxturnal system (Nox Medical, Reykjavik, Iceland). The recorded data was divided into 30-second epochs and scored according to the sleep scoring criteria outlined in the AASM Manual for the Scoring of Sleep and Associated Events, v. 2.6.[36] Various physiological signals were recorded during the study by using numerous techniques and devices, including electroencephalography (EEG) to measure brain activity, electrooculography (EOG) to detect eye movements, electromyography (EMG) to assess muscular tension (recorded from the chin and tibial electrodes), a nasal pressure sensor to measure airflow, and inductive plethysmography to evaluate chest and abdomen movements. In addition to these recorded signals, the patient's body position and bilateral masseter EMG were also captured. Episodes of bruxism were classified according to the AASM standards, distinguishing between phasic, tonic and mixed forms. Arousals were categorized as spontaneous, respiratory, bruxism, and periodic limb movement (PLM) arousals. The manual scoring and the analysis of the collected data were conducted by a qualified physician (H.M.) from the Sleep Laboratory of Wroclaw Medical University, following the guidelines provided by AASM.

Statistical analysis

Statistical analysis employed Dell™ Statistica™, v. 13 (Dell Inc., Austin, USA). Descriptive statistics, including the mean (*M*), standard deviation (*SD*) and range (minimum and maximum) values, were calculated for the estimated parameters in the study groups. Correlation analysis was conducted to identify any associations between the variables of interest. Statistical significance was determined based on a two-sided *p*-value of less than 0.05.

Results

The study participants were divided into 2 groups – hypertensive and normotensive – and comparisons were made between them. Several PSG parameters exhibited statistically significant differences between the 2 groups (Table 2). Among hypertensive patients, the apnea–hypopnea index (AHI) was significantly higher (28.87 ±26.23 vs. 13.95 ±19.41; $p < 0.05$) as compared to the non-hypertensive group. Similarly, the oxygen desaturation index (ODI) was higher in the hypertensive group (27.39 ±24.27 vs. 12.24 ±16.64; $p < 0.05$). The periodic limb movement index (PLMI) and the snore percentage were also significantly higher among patients with hypertension (11.74 ±24.88 vs. 5.61 ±8.84; $p < 0.05$, and 31.12 ±22.44% vs. 14.13 ±17.29%; $p < 0.05$, respectively). Differences were also observed in the distribution of sleep stages, with a significantly lower duration of rapid eye movement (REM) sleep among hypertensive patients (20.58 ±8.73% vs. 23.89 ±10.15%; $p < 0.05$).

Table 2. Polysomnography parameters of the examined groups

Parameter	Hypertension	No hypertension	*p*-value
AHI	28.87 ±26.23	13.95 ±19.41	<0.05*
ODI	27.39 ±24.27	12.24 ±16.64	<0.05*
Snore [%]	31.12 ±22.44	14.13 ±17.29	<0.05*
PLMI	11.74 ±24.88	5.61 ±8.84	<0.05*
SL [min]	21.45 ±28.86	15.98 ±13.82	0.77
REM latency [min]	99.13 ±80.02	102.21 ±76.85	0.78
WASO [min]	74.30 ±65.79	60.32 ±58.11	0.09
SE [%]	78.36 ±16.50	83.48 ±12.36	<0.05*
N1 [%]	7.62 ±6.61	6.27 ±6.09	0.26
N2 [%]	47.27 ±12.27	51.21 ±26.5	0.96
N3 [%]	24.53 ±8.64	27.26 ±31.13	0.40
REM [%]	20.58 ±8.73	23.89 ±10.15	<0.05*
AI	8.28 ±7.82	6.59 ±5.77	0.34
RAI	4.90 ±7.80	2.42 ±5.31	<0.05*
RERAs	0.44 ±0.69	0.22 ±0.38	<0.05*
BAI	0.61 ±0.85	1.11 ±1.28	<0.05*
PLMAI	0.12 ±0.29	0.19 ±0.55	0.88
SAI	2.21 ±1.65	2.58 ±2.25	0.46
BEI	4.23 ±3.99	4.10 ±3.41	0.83
RDI	29.47 ±26.03	13.19 ±18.06	<0.05*
Apneas/h	15.49 ±20.25	6.72 ±12.85	<0.05*
Hypopneas/h	13.39 ±11.85	7.34 ±11.34	<0.05*
av SpO_2 [%]	91.82 ±2.18	93.33 ±5.22	<0.05*
min SpO_2 [%]	79.81 ±9.07	83.69 ±8.45	<0.05*
SpO_2 < 90% duration [%]	17.20 ±20.14	5.50 ±11.15	<0.05*

Data presented as *M* ±*SD*. AI – arousal index; RAI – respiratory arousal index; RERAs – respiratory effort-related arousals; BAI – bruxism arousal index; PLMAI – periodic limb movement arousal index; SAI – spontaneous arousal index; BEI – bruxism episode index; RDI – respiratory disturbance index; * statistically significant.

Sleep efficiency (SE) was reduced in the hypertensive group as compared to the non-hypertensive group (78.36 ±16.50% vs. 83.48 ±12.36%; $p < 0.05$). Moreover, the average oxygen saturation (SpO_2) level was lower in the hypertensive group as compared to the normotensive group (91.82 ±2.18% vs. 93.33 ±5.22%; $p < 0.05$), while the minimal SpO_2 level was also significantly lower in the hypertensive group (79.81 ±9.07% vs. 83.69 ±8.45%; $p < 0.05$). Additionally, the time spent with SpO_2 below 90% was significantly higher in patients with hypertension (17.20 ±20.14% vs. 5.50 ±11.15%; $p < 0.05$), as shown in Table 2.

The examination of electrolyte concentration levels revealed several significant differences between the hypertensive and non-hypertensive groups (Table 3). Among hypertensive patients, there was a decrease in Mg concentration (1.87 ±0.24 mg/dL) as compared to non-hypertensive individuals (2.01 ±0.16 mg/dL) ($p < 0.05$). Vitamin D concentration in the hypertensive group (30.24 ±11.07 ng/mL)

Table 3. Blood test parameters among the examined patients

Parameter	Hypertension	No hypertension	*p*-value
CRP [mg/dL]	2.78 ±2.58	2.46 ±5.00	<0.05*
ESR [mm/h]	10.97 ±12.13	6.58 ±5.54	<0.05*
UA [mg/dL]	5.67 ±1.26	5.07 ±1.42	<0.05*
Glucose [mg/dL]	117.94 ±39.12	97.27 ±20.12	<0.05*
Na [mmol/L]	139.69 ±2.22	140.07 ±2.00	0.69
K [mmol/L]	4.27 ±0.34	4.31 ±0.28	0.38
Ca [mg/dL]	9.34 ±0.29	9.32 ±0.32	0.53
Mg [mg/dL]	1.87 ±0.24	2.01 ±0.16	<0.05*
Vitamin D [ng/mL]	30.24 ±11.07	34.17 ±18.05	0.40

Data presented as *M* ±*SD*. CRP – C-reactive protein; ESR – erythrocyte sedimentation rate; UA – uric acid; Na – sodium; K – potassium; Ca – calcium; Mg – magnesium. * statistically significant.

was similar to that in normotensive individuals (34.17 ±18.05 ng/mL) ($p > 0.05$). Interestingly, when comparing vitamin D levels between hypertensive and normotensive individuals without sleep disorders, a significant difference was observed (30.24 ±11.07 ng/mL vs. 39.42 ±24.70 ng/mL; $p < 0.05$) (Fig. 2). Additionally, hypertensive patients exhibited a higher level of CRP (2.78 ±2.58 mg/dL) as compared to non-hypertensive individuals (2.46 ±5.00 ng/mL) ($p < 0.05$). The erythrocyte sedimentation rate (ESR) was also higher in the hypertensive group (10.97 ±12.13 mm/h) than in the non-hypertensive group (6.58 ±5.54 mm/h) ($p < 0.05$). Furthermore, uric acid (UA) concentration was elevated in hypertensive individuals (5.67 ±1.26 mg/dL) as compared to non-hypertensive individuals (5.07 ±1.42 mg/dL) ($p < 0.05$) (Table 3).

In this study, we observed significant correlations between blood and sleep parameters. There was a negative correlation between Mg concentration and AHI ($r = -0.25$; $p < 0.05$), indicating that a lower Mg level was associated with a higher severity of sleep apnea. Similarly, we observed a negative correlation between Mg concentration and ODI ($r = -0.26$; $p < 0.05$). Furthermore, we found a negative correlation between Ca concentration and the arousal index (AI) ($r = -0.26$; $p < 0.05$), as well as correlations between UA concentration and AHI ($r = 0.27$; $p < 0.05$), ODI ($r = 0.28$; $p < 0.05$) and the average SpO_2 ($r = -3.34$; $p < 0.05$). Additionally, there were correlations between vitamin D concentration and AHI ($r = -0.18$; $p > 0.05$) and the average SpO_2 ($r = 0.21$; $p < 0.05$).

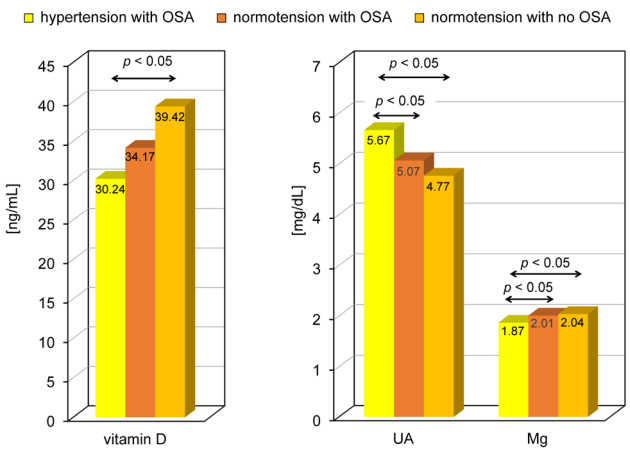

Fig. 2. Statistical differences in blood test parameters among the examined patients

Discussion

The prevalence of AH in individuals with OSA is significantly higher in comparison with the healthy population.[37] In this study, we aimed to compare sleep architecture parameters, including sleep fragmentation, inflammatory and metabolic markers, and vitamin D concentration, between hypertensive and normotensive individuals with OSA. Additionally, we aimed to assess different types of arousal in hypertensives in comparison with normotensives to better understand sleep fragmentation as a novel cardiovascular risk factor.

Our findings revealed increased respiratory parameters (AHI, respiratory effort-related arousals (RERAs) and snoring) and altered SpO_2 parameters (ODI, average SpO_2 and minimal SpO_2) in hypertensive individuals with OSA, which is consistent with previous studies.[38] Furthermore, we observed sleep architecture differences between hypertensive and normotensive individuals.

Sleep architecture

Sleep architecture consists of 2 main stages: REM sleep; and non-REM sleep. In hypertensive individuals with OSA, we found a decrease in REM sleep duration, while non-REM sleep duration was similar in both groups. Rapid eye movement sleep is characterized by REMs, low-voltage EEG[39,40] and muscle atonia.[41] It is also associated with the occurrence of dreams, as discovered by Aserinsky and Kleitman.[42] A decrease in REM sleep duration accompanied by longer N1 sleep duration has been previously observed in OSA patients,[43] which aligns with our results. Additionally, it has been observed that OSA patients experience a decrease in both REM sleep and slow-wave sleep (SWS) duration.[44] However, a recent study reported no changes in sleep architecture and the total sleep time (TST) in hypertensive individuals with OSA,[45] which partially aligns with our results of similar TST duration in hypertensives and normotensives.

Notably, this study contributes by showing, for the first time, a decrease in REM sleep duration among hypertensive individuals with OSA. Sleep architecture studies often yield inconsistent findings or contradict the existing literature regarding hypertension. Recently, Ren et al. showed that decreased SWS duration was associated with higher odds of hypertension in OSA, but not in primary snoring, although they did not investigate the relationship between REM sleep and hypertension.[46]

The function of REM sleep is complex and not fully understood, though it is widely recognized as a crucial period for memory consolidation and emotional processing.[47] One hypothesis suggests that REM sleep may serve as a "gate" for wakefulness,[48] as most spontaneous awakenings occur during REM sleep.[49,50] Therefore, the observed reduction in REM sleep among hypertensives with OSA may be a defensive response to increased sleep fragmentation. However, further research is needed to explore this hypothesis.

The present study also revealed decreased SE and increased wakefulness after sleep onset (WASO) duration in hypertensive individuals, indicating poor sleep quality. We further investigated the specific causes of arousals by assessing different types of arousal. Respiratory arousals were the most commonly observed in both groups, though hypertensives exhibited more respiratory arousals than normotensives, highlighting sleep fragmentation. There were no statistically significant differences in spontaneous and PLM arousals between the study groups.

Interestingly, normotensive individuals experienced a higher incidence of arousals related to bruxism episodes despite a similar bruxism episode index (BEI) in the hypertensive and normotensive groups. Previous studies have suggested that individuals with mild apnea experience more bruxism events than those with severe apnea.[51] However, non-apneic hypertensives have been found to exhibit more bruxism episodes than normotensives.[52] The occurrence of bruxism episodes can be influenced by various factors, such as age, OSA severity, arousals, sympathetic activity, and hypertension, which may explain why BEI was similar in hypertensives and normotensives in this study. Our findings suggest that in hypertensive individuals, bruxism episodes may not commonly lead to arousals, unlike in normotensive individuals.

The most prevalent type of arousal observed in this study was respiratory arousal. Recent studies associated respiratory events with poor sleep quality, excessive daytime sleepiness and an increased cardiometabolic risk.[53] Although arousal scoring is not mandatory according to the AASM guidelines, omitting arousals may result in failing to identify patients who could benefit from OSA treatment. These patients, typically female, younger and non-obese, may experience respiratory events causing sleep fragmentation, even without significant oxygen desaturation.[54] Recurrent arousals result in sympathetic activation, inflammation, oxidative stress, and metabolic dysfunction, leading to cardiometabolic disturbances and cardiovascular diseases.[55] Animals exposed to long-term sleep fragmentation for 12 weeks demonstrated the initiation of mild hypertension, endothelial dysfunction and early structural vascular changes.[56] Moreover, repetitive arousals have been associated with repetitive blood pressure rises,[57,58] indicating that sleep fragmentation may contribute to AH. Interestingly, it has been observed that only respiratory arousals lead to blood pressure surges.[59]

Notably, respiratory arousals were the most common type of arousal observed in this study. To the best of our knowledge, we have demonstrated, for the first time, the significance of different types of arousal in AH among individuals with OSA.

Movement disorders

Limited data is available on the relationship between the PLM disorder (periodic limb movements of sleep – PLMS) and AH. However, a recent meta-analysis indicated an increased risk of hypertension among individuals with PLMS.[60] While PLMS is often associated with OSA, the current criteria set by AASM do not score limb movements if they occur within 0.5 s before or after a respiratory event. A recent study demonstrated a strong correlation between PLMS and a lower threshold for a respiratory arousal.[61] The analysis of the European Sleep Apnea Database (ESADA) revealed an association between PLMS and an increase in systolic blood pressure, regardless of AHI, and independent of other clinical and sociodemographic factors.[62] The authors concluded that individuals with a PLMS phenotype might be at an increased risk of cardiovascular diseases in the presence of OSA.[62]

Consistent with previous findings, this study also found a higher prevalence of PLMS in hypertensive individuals as compared to normotensive individuals. However, a retrospective hospital-based study in a Korean population found no association between coincidental hypertension and PLMS and related arousals.[63]

Electrolyte concentrations

The present study suggests a potential relationship between sleep fragmentation and fluctuating electrolyte and vitamin D levels. A notable finding is the decreased Mg concentration observed in hypertensives as compared to normotensives. Additionally, there was an important decrease in vitamin D levels in hypertensives as compared to normotensives without OSA, although no significant difference was observed between hypertensives and normotensives.

Vitamin D metabolism

Vitamin D is primarily recognized for its role in maintaining Ca homeostasis and bone metabolism.[64] Animal studies indicated that vitamin D deficiency could lead to increased activity of RAAS and subsequent blood pressure elevation, suggesting a potential role for vitamin D as an antihypertensive agent. However, the results regarding the relationship between vitamin D and hypertension development remain contradictory.[65] A recent study involving 491 healthy middle-aged participants demonstrated a significant association between low vitamin D levels and non-optimal blood pressure, high-normal blood pressure and the development of hypertension over an 8-year follow-up period.[66] Additionally, physiological doses of vitamin D have been found to enhance Mg absorption.[67]

Magnesium and calcium metabolism

Mild to moderate hypomagnesemia has been associated with hypertension,[68] metabolic syndrome[69] and type 2 diabetes mellitus.[70,71] It is worth noting that Mg serves as a cofactor for 325 enzyme systems, including specific vasoactive mediators.[72] Intracellular Mg helps regulate vascular tone, while extracellular Mg influences Ca channels,[73] thereby impacting Ca metabolism. In the present study, Ca concentration was similar among the analyzed groups of patients. However, there was a correlation between Ca concentration and AI. Previous studies also showed a relationship between Ca signaling and the arousal state.[74] The thalamic T-type Ca channel is known to play a crucial role in blocking the transmission of arousal signals and promoting sleep stability.[75] Therefore, sleep fragmentation is associated with alterations in Ca metabolism and, indirectly, Mg and vitamin D metabolism in hypertensives with OSA.

Vitamin D deficiency is associated with increased OSA severity.[76,77] In this study, we observed a negative correlation between vitamin D concentration and AHI, as well as between vitamin D and the SpO_2 parameters, suggesting that hypoxemia may impact vitamin D concentration. However, it is important to note that there have been inconsistent findings regarding the relationship between vitamin D and sleep apnea, indicating the need for further studies to better understand this association.[78]

Uric acid metabolism

Studies consistently show that individuals with OSA tend to have higher levels of UA, which can be attributed to the hypothesis that the hypoxia associated with OSA leads to the breakdown of adenosine triphosphatase into xanthine, resulting in an elevated UA concentration.[79] According to a study conducted by Hira et al., the average level of serum UA was significantly higher in the group with OSA as compared to the control group and the standard laboratory reference value, and the association remained consistent after adjusting for factors such as sex, age and obesity.[80] These results align with previous research investigating UA levels in individuals with OSA.[81,82] It is important to note that serum UA level is also linked to hypertension, suggesting that UA may play a contributory and potentially causal role in primary hypertension.

The rise in the hypertension rates over the past century has been linked to increased sugar and salt consumption, and other components of the Western diet that can impact intracellular urate levels.[83] Hyperuricemia is a significant independent predictor of hypertension, with individuals experiencing a higher risk of developing hypertension within 5–10 years.[84,85] This study is consistent with previous research, as we observed significant differences in UA concentration between hypertensive patients with OSA and normotensive patients. However, further research is necessary to explore the underlying causes and mechanisms in greater detail.

In summary, individuals with hypertension have more severe OSA, an elevated frequency of PLMs, altered sleep architecture, sleep fragmentation, decreased sleep quality, a lower Mg concentration, and a higher UA concentration as compared to normotensive individuals.

Conclusions

Sleep architecture is altered in hypertensives with OSA. There is a reduction in the duration of REM sleep, an increase in WASO and a decrease in SE in comparison with normotensives.

Individuals with hypertension and OSA have an increased RAI, indicating sleep fragmentation. Calcium levels have been implicated in sleep fragmentation, suggesting a potential role for Ca and vitamin D in arousals. However, further studies are needed to investigate this relationship. Hypertension does not affect vitamin D concentration in patients with OSA, but a correlation between vitamin D and OSA severity has been established.

Uric acid and glucose concentrations are higher in hypertensives than in normotensives with OSA. Along with elevated AHI and sleep fragmentation, these factors contribute to an increased cardiovascular risk.

The periodic limb movement index is increased in hypertensives with OSA as compared to normotensives. However, PLMAI is similar in normotensives and hypertensives, suggesting no significant sleep fragmentation due to PLMs in hypertensives with OSA.

Magnesium concentration is decreased in hypertensives as compared to normotensives in OSA subjects. Therefore, hypertensives with OSA should be investigated for Ma insufficiency, and if present, supplementation should be considered.

Ethics approval and consent to participate

The study was approved by the Wroclaw Medical University Bioethical Committee (No. ID KB-407/2022) and adhered to the principles outlined in the Declaration of Helsinki. All patients provided written informed consent for the participation in the study.

Data availability

The datasets generated and analyzed during the current study are available from the corresponding author on request.

Consent for publication

Not applicable.

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