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Sleep disorders — risk factors and hypertension markers in young people with normal body weight

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Aim. To assess the relationship between different types of sleep disorders, sleep-related symptoms and hypertension (HTN).

Material and methods. This cross-sectional study based on the online survey of persons aged 18-39 years with a body mass index of 18-25 kg/m^2.

Results. According to the res ults, the HTN risk in persons aged 18-39 years with normal body mass index increases 2 or more times in the presence of various types of sleep disorders and related symptoms. The prevalence of HTGN depends on the patient's phenotype, i.e. from a combination of different types of sleep disorders and sleep-related symptoms.

Conclusion. Given the widespread prevalence of various sleep disorders, as well as the relationship between sleep disorders and hypertension in young people, it is necessary to develop preventive measures aimed at reducing the HTN risk by restoring healthy sleep. We also suggest that various sleep disorders may be the primary link in the development of essential HTN.

Keywords: hypertension, sleep disorders, snoring, sleep apnea, insomnia, restless legs syndrome.

Relationships and Activities. The work (data analysis) was carried out within the state assignment of the Lomonosov Moscow State University.

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Hypertension (HTN), despite hundreds of thousands of related studies and a wide range of antihypertensive drugs, remains the leading cause of death both in Russia [1] and in many countries of the world [2]. From 1998 to 2017, the prevalence of HTN in European Russia increased from 35,5 to 43,3% [3]. Due to wide prevalence of HTN, its prior probability is very high, while high predictive value of a positive result of routine blood pressure (BP) measurement makes its diagnosis perhaps one of the simplest ones. Despite this, the multifactorial nature of the problem, the complexity and long-term pathogenetic mechanisms do not allow to comprehensively solve it, often reducing the doctor's actions only to the appointment of antihypertensive therapy. It is well known that this problem is largely due reduced awareness among people with HTN, ignoring the problem by patients themselves, and their unwillingness to regularly take antihypertensive therapy. The situation is aggravated by the fact that factors contributing to HTN at an early age are often not considered. By the age of 40, when many people begin to think about maintaining health, hypertension may have already reached the stage where the correction of modifiable risk factors (RF) will no longer be as effective as before, and from secondary hypertension it can transform into essential or, more precisely, acquire its traits. This means that despite the cause elimination, BP may remain elevated. And in this case, the question arises whether this is a consequence of target organ, the presence of true essential hypertension, or is it still unrecognized one or several causes of the disease. There is also the gradient of essential HTN equal to 0, if the elimination of BP increase cause will lead to its complete normalization. Unfortunately, the theory by Yu. V. Postnov and S. N. Orlov "primary hypertension as the pathology of cell membranes" [4] did not on the march, but the question of the essential nature of HTN remains relevant to this day.

In 1997, we showed that obstructive sleep apnea (OSA) affects the HTN course, while the relief of OSA led to BP decrease, primarily at night. However, sleep disorders, in addition to respiratory ones, are represented by a wide range of insomnia and movement disorders, etc. Therefore, the analysis of sleep disorders in clinical practice is extremely important for identifying the causes of increased BP not only during sleep, but also during wakefulness. The pathogenetic mechanisms underlying this process are of fundamental importance for management of patients.

Material and methods

This study was performed in accordance with the Helsinki declaration and Good Clinical Practice standards. The research included data from an impersonal survey of visitors to somnology websites www.somnolog.ru and www.sleeplab.ru. In the period from June 2015 to June 2020, 5179 respondents responded to the survey. The survey included 42 questions to assess the presence of various sleep disorders and sleep-related symptoms (snoring, sleep apnea, insomnia, narcolepsy, restless legs syndrome (RLS), depression, anxiety) on a 5-point scale (0 — never, 1 — rarely, 2 — sometimes, 3 — often, 4 — almost always). All questions needed to be answered. The respondents also noted their age, sex, height, weight and place of residence. Before statistical analysis, duplicate data were removed, and respondents aged 18-39 years with a body mass index (BMI) of 18-25 kg/m^2 were selected. These categories are of interest due to absence of the effect of increased body weight and comorbidities, which are HTN RFs. As a result, for the statistical processing, the data of 2094 respondents were used.

The aim was to assess the relationship between different types of sleep disorders, sleep-related symptoms and HTN.

Statistical analysis was performed using IBM SPSS Statistics 25 software.

Results

The clinical characteristics of participants are presented in Table 1.

The dependent variable "I have high BP" was converted into a binary variable: 0 — never and 1 — all other answers (1-4).

All independent variables indicating the sleep disorders and sleep-related symptoms were transformed as follows. As already noted, the assessment of sleep disorders in the questionnaire was initially carried out using 5-point scale (0-4). Such a scale ranks the response categories well among themselves, but does not allow measuring how the category values differ among themselves. It is a well-known fact that when using such a scale, different respondents tend to overestimate or underestimate values.

To solve this problem, we calculated the average score for all questions for each respondent. Further, for each question, the difference between the answer score and this average was calculated. For further statistical analysis, we used the deviation for each question from the typical answer of a respondent [5, 6]. This made it possible to solve the abovementioned problem.

Further, to assess the effect of independent variables, the optimized categorization algorithms in the SPSS package was applied, which was based on the following optimization criteria: maximization of the relationship measure between the created

Table 1

Clinical characteristics of participants (n=2094)

Parameter	Value
Sex	m — 553 (26,4%); f — 1541 (73,6%)
Age, years	25,8±6,0
Height, cm	169,3±8,7
Weight, kg	61,0±8,9
BMI, kg/m^2	21,2±1,9

Abbreviation: BMI — body mass index.

Table 3

Prevalence of HTN in clusters

Cluster number	Sample		Presence of HTN, %
	n	%	
I	334	16,0	35,6
II	1345	64,3	38,6
III	412	19,7	46,1
Total	2091	100,0	39,6

Abbreviation: HTN — hypertension.

Table 2

Characteristics of the relationship between HTN and sleep disorders*

Variable/wording in the questionnaire	Cramer coefficient	Information Value (IV)	OR (95% CI)
Snoring — "I was told that I snore"	0,13	0,07	1,97 (1,56-2,49)
Apnea — "I was told that I have sleep apnea"	0,17	0,12	2,23 (1,84-2,77)
Insomnia — "I wake up earlier in the morning than I would like"	0,11	0,05	2,34 (1,68-3,27)
Cataplexy — "When I am angry or surprised, I feel muscle weakness"	0,11	0,05	0,62 (0,51-0,75)
Daytime sleepiness — "I can fall asleep while driving"	0,19	0,14	2,43 (1,97-2,98)
Cough — "I wake up at night coughing and wheezing"	0,16	0,10	2,11 (1,71-2,60)
Heartburn — "I feel heartburn"	0,12	0,06	2,14 (1,64-2,80)
Choking — "At night I wake up unexpectedly with a feeling of choking"	0,16	0,10	2,03 (1,67-2,46)
Cramps — "I have cramps or pain in my legs at night"	0,14	0,07	2,66 (1,93-3,67)

Note: * — all parameters have a significant effect on HTN (p<0,001, Pearson chi-squared test).
Abbreviations: HTN — hypertension, CI — confidence interval, OR — odds ratio.

categorical independent variable and the created binary dependent variable (entropy was used as the relationship measure) and minimization of created intervals' number. As a result, the effect of the following variables on HTN was found (Table 2). For the created categorical variables, the chi-squared test and the Cramer's coefficient were used, as well as the Information value and the odds ratio were calculated.

The average predictive power was noted for the following predictor variables: apnea, excessive daytime sleepiness, cough at night, shortness of breath at night. Other predictor variables has low predictive power. It should be noted that of the predictor variables indicated in Table 2, only 'cataplexy' had an inverse relationship with HTN (odds ratio, <1). However, in our opinion, this symptom was associated not with cataplexy as such, but with BP decrease and more closely resembles vasovagal syncope in hypertensive people. In this case, it becomes clear why this symptom had a feedback with hypertension.

Next, we created a logistic regression model predicting the HTN in respondents using the independent variables shown in Table 2. However, we did not receive a model with a sufficient number of significant independent variables in the equation and a high predictive power (Gini coefficient >0,3). Apparently, this is due to the fact that the above predictor variables are a manifestation of various diseases, which, on the one hand, can affect the quality of sleep, on the other hand, are observed in different phenotypes or clusters of patients. Therefore, they do not merge into a common model.

In this regard, we decided to conduct a cluster analysis for 19 quantitative independent variables, calculated on a deviation scale.

Hierarchical agglomerative clustering was applied, while the squared Euclidean distance was chosen as a relationship measure of objects. The clusters were divided according to the Ward method.

Clustering revealed 3 clusters of respondents (Table 3). We have arranged the clusters in the order of increasing HTN prevalence. The prevalence of HTN in the first (n=334, 16,0%), second (n=1345, 64,3%) and third (n=412, 19,7%) clusters was 35,6%, 38,58% and 46,1%, respectively. The relationship between the HTN presence and belonging to the resulting

Table 4

Clinical characteristics and relative score of answers in deviations from the total mean depending on clusters

Parameter	Me [Q1; Q3]			p-value (Kruskal-Wallis test)
	Cluster I	Cluster II	Cluster III	
Age, years	25 [21; 30]	26 [21; 31]	22 [19; 27]	<0,001
BMI, kg/m^2	20,95 [19,72; 22,53]	21,08 [19,71; 22,58]	20,81 [19,61; 22,53]	0,78
Snore	-0,61 [-1,26; 0,26]	-0,93 [-1,30; 0,11]	-1,26 [-1,67; 0,67]	<0,001
Apnea	-1,04 [-1,41; -0,70]	-1,19 [-1,48; -0,89]	-1,48 [-1,78; -1,19]	<0,001
Insomnia	0,16 [-0,32; 0,72]	1,34 [0,88; 1,83]	0,84 [0,43; 1,20]	<0,001
Daytime sleepiness	0,57 [0,19; 0,91]	-0,11 [-0,37; 0,17]	0,57 [0,33; 0,85]	<0,001
RLS	-0,15 [-0,81; 0,85]	0,04 [-0,89; 1,07]	0,41 [-0,67; 1,15]	0,008
Depression	0,85 [0,19; 1,52]	1,07 [0,48; 1,74]	1,56 [0,93; 2,00]	<0,001
Anxiety	0,52 [-0,19; 1,26]	1,67 [0,96; 2,22]	1,48 [0,74; 2,04]	<0,001

Note: insomnia — all symptoms of the questionnaire characterizing insomnia are grouped; daytime sleepiness — all the symptoms of the questionnaire characterizing daytime sleepiness are grouped; RLS — "Sometimes at night I cannot find a place for my legs, I want to move them all the time in order to feel comfortable"; depression — "I often feel sad and depressed"; anxiety — "I am constantly worried about different things and cannot relax".
Abbreviations: BMI — body mass index, RLS — restless legs syndrome.

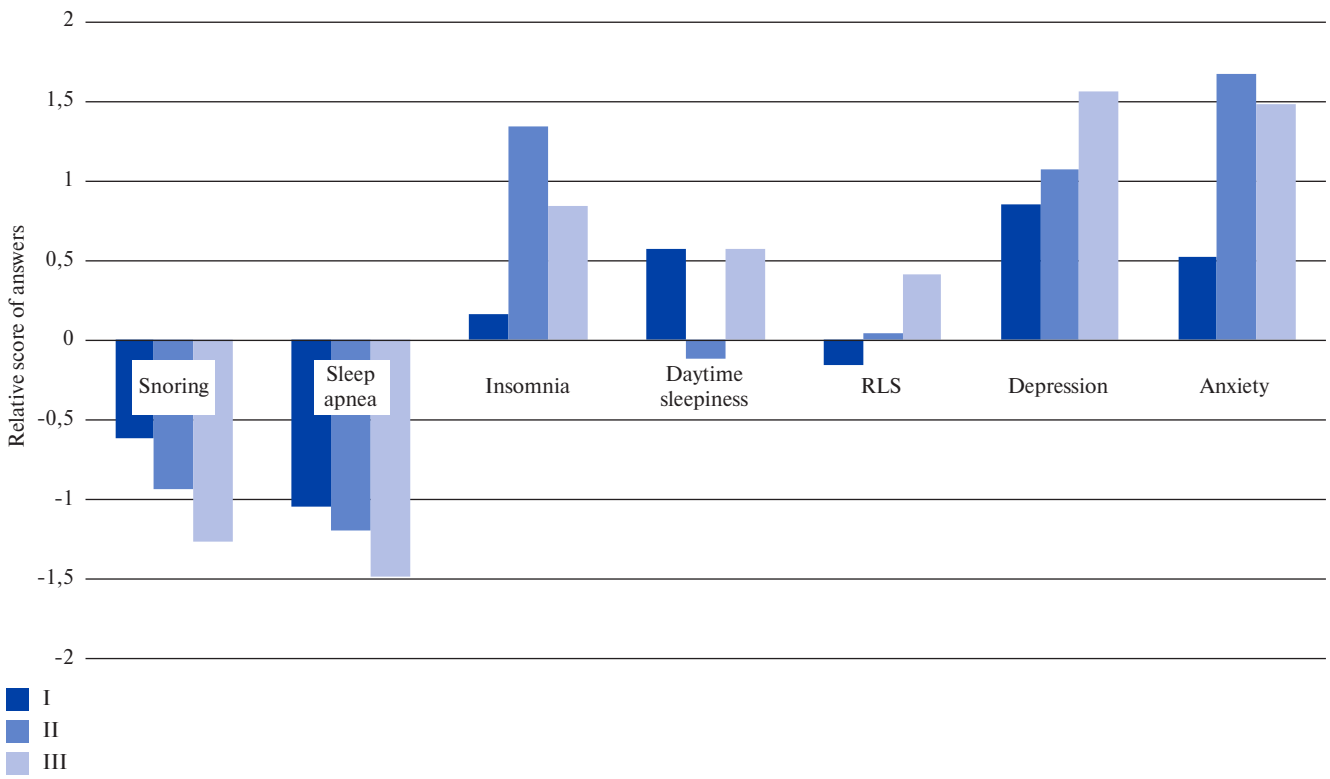

Figure 1. Distribution of the relative score* of answers depending on clusters for snoring, sleep apnea, insomnia, daytime sleepiness, RLS, depression, anxiety.
Note: * — more negative values correspond to a greater severity of symptoms/conditions.
Abbreviation: RLS — restless legs syndrome.

cluster is significant (χ^2=10,09, p=0,006). Pairwise comparison of HTN proportions between clusters using the z-test yields a significant difference only in the third cluster with the highest HTN proportion (p<0,05), i.e. the proportions of 35,6% and 38,6% do not differ significantly. By sex, the categories did not differ significantly (χ^2=4,57, p=0,102).

Clinical characteristics and relative score of answers in deviations from the total average score for each cluster are presented in Table 4.

Discussion

In recent years, more and more data have appeared on the relationship of various sleep disorders with cardiovascular diseases and, above all, hypertension. Our study identified a number of sleep-related factors that are associated with hypertension. Sleep disorders such as OSA, the clinical manifestation of which is snoring, already belong to the RFs for HTN and are dominant among other sleep disorders, which was also confirmed in our study. Early, unplanned awakening is a sign of chronic insomnia and may be a manifestation of a depressive disorder. Excessive sleepiness, one of the extreme manifestations of which is drowsy driving, is most often a manifestation of disturbed sleep at night due to respiratory and movement disorders, or the presence of chronic insomnia. The night cough and heartburn may indicate the chronic obstructive pulmonary disease, asthma, gastroesophageal reflux disease and also lead to sleep fragmentation. Moreover, these conditions are often combined with OSA. Awakening with a shortness of breath is a fairly characteristic sign of panic disorder and can be a manifestation of a wide range of anxiety disorders, but it can also be observed in patients with OSA.

Clustering allowed us to characterize the phenotypes of patients.

Considering that the prevalence of HTN in cluster III is the highest (46,11%), while the age in this cluster is significantly even less than in clusters I and II, and also that BMI and sex do not significantly differ between clusters, it remains to consider the differences by the presence of sleep disorders and sleep-related symptoms. The relationship between central sleep-related disorders and symptoms is shown in Figure 1.

The differences between the clusters consist in an increase in snoring and sleep apnea from cluster I to cluster III, while the presence of RLS and depression symptoms also decreased from cluster I to cluster III. The fact is that, according to our results, sleep apnea and periodic limb movements (PLM) during sleep, which is often combined with RLS, are competing conditions. This means that, mainly with PLM manifestations, we do not observe OSA, sometimes only central sleep apnea. Moreover, OSA can transform into PLM without changing the phase and/or stage of sleep, body position and without micro-awakening. Apparently, this is due to the fact that in the brain there is a single central mechanism for the implementation of both PLM, which is well known, and OSA. However, their intermittent manifestation is probably associated with a change in conduction pathways from a common central regulator to the periphery.

The decrease in depression prevalence from cluster I to cluster III may be due to the fact that patients with snoring and sleep apnea have a more pronounced pressure for sleep. Therefore, the duration of their sleep is longer, which may contribute to a decrease in the manifestation of depression. Another possible mechanism is associated with partial deprivation of rapid eye movement (REM) sleep phase, which is often observed in patients with OSA, and it is known that sleep deprivation, especially REM phase, is used as a temporary but effective method to reduce the manifestations of depressive disorder. There is also a decrease in anxiety in clusters II and III compared to cluster I, which indicates an inverse relationship with OSA severity.

Thus, among all sleep disorders in young people with normal body weight, snoring and sleep apnea are the earliest factors determining the HTN development. And this is not surprising, since the likelihood of chronic insomnia, RLS, and other age-related sleep disorders in this age group is minimal.

When developing methods for preventing the hypertension by restoring healthy sleep, it is necessary to take into account the phenotype of a patient with snoring and sleep apnea. On the one hand, this is a 'classic' patient with snoring and sleep apnea without or with a minimal concomitant sleep disturbances and symptoms of mental disorders but with a high risk of hypertension (cluster III). On the other hand, a patient with snoring and sleep apnea in various combinations with chronic insomnia, RLS, depression, and anxiety (cluster II), in whom daytime sleepiness is most pronounced. The third group of patients with mild snoring and sleep apnea but with a predominant chronic insomnia in various combinations and without concomitant sleep and mental disorders (cluster I).

The study limitations include the use of a non-validated questionnaire. However, the data obtained will help to determine the tasks for future studies and focus on the suspected RFs of HTN.

Conclusion

Thus, the HTN risk in people aged 18-39 years with a normal BMI increases 2 or more times in the presence of various sleep disorders and sleep-related symptoms, which must be taken into account both for creating measures for HTN prevention and in clinical practice. The prevalence of hypertension depends on the patient's phenotype, i.e. from a combination of different types of sleep disorders and related symptoms. We also suggest that various sleep disorders may be the primary link in the development of essential HTN.

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