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SCREENING FOR SLEEP DISORDERED BREATHING IN THREE DISTINCT NEUROLOGICAL DISEASES IN THE BULGARIAN POPULATION

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Abstract

Sleep disordered breathing (SDB) is a common medical problem in the general population. Neurological disorders such as ischemic stroke (IS), myasthenia gravis (MG), or multiple sclerosis (MS) seem to be of higher risk of SDB. Nevertheless, the implementation of screening for SDB in such disorders has not been well studied. Therefore, the aim of this study was to explore screening parameters for SDB in IS, MG and MS, in our region.

We included prospectively patients with diagnosed IS, MG and MS. Psychometric tools such as the Epworth Sleepiness Scale (ESS), the STOP-BANG, and the Berlin questionnaire were implemented. For the respiratory screening portable recording device was used.

Seventy-two patients, 25 with IS (mean age 66.3 years), 24 with MG (mean age 47.9 years), and 23 with MS (mean age 40.1 years) were enrolled. Basic anthropometric parameters such as BMI, neck and waist circumference were higher in IS than in MG and MS ($p < 0.001$). The ESS scores were 5.5 ± 3.2 for IS, 5.6 ± 3.3 for MG, and 5.9 ± 4.5 for MS, but without significant difference between the groups. Contrariwise, STOP-BANG scores in IS were 4.8 ± 1.3, significantly higher ($p < 0.0001$) than both MG (2.1 ± 1.4) and MS (1.2 ± 0.9). A high risk for OSA in BQ was calculated in 68% of IS, much higher ($p < 0.0001$) than in MG (33.3%) and in MS (13%). In the respiratory screening, the mean apnea-hypopnea index in the IS group (20 ± 18.3) was statistically higher than in MG (8.1 ± 12.7, $p < 0.005$), and in MS patients (2.3 ± 4.9, $p < 0.001$). Oxygen

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desaturation index in IS (19.3 ± 19) differed statistically from the one in MG (8.1 ± 12.9, $p < 0.005$), and in MS (2.6 ± 5.5, $p < 0.001$). The oxygen saturation (SO2) showed difference only between IS and MS in all three measured values – baseline SO2 ($p < 0.001$), median SO2 ($p < 0.05$) and lowest SO2 ($p < 0.05$).

IS, MG and MS, as distinct neurological entities, show different clinical profiles with respect to screening for SDB. These should be taken into consideration in the individual evaluation for sleep disordered breathing.

Key words: sleep disordered breathing, screening, neurological diseases

Introduction. Obstructive sleep apnea (OSA), the commonest form of sleep disordered breathing (SDB), is a chronic disorder characterized by repeated episodes of partial or complete obstruction of the respiratory passages during sleep, resulting in recurrent nocturnal oxygen desaturation, fragmented sleep, major fluctuations in blood pressure, and increased sympathetic nervous system activity. OSA is a major health issue which leads to increased morbidity and mortality. Unfortunately, OSA remains underdiagnosed in more than 80% of the population [1]. This has raised the necessity of a reliable screening method for OSA. Neurological disorders such as ischemic stroke (IS) [2], myasthenia gravis (MG) [3] and multiple sclerosis (MS) [4] are generally of higher risk for SDB and OSA, despite their different underlying pathophysiological mechanisms. Nevertheless, the implementation of screening for SDB in such disorders is not properly defined.

IS and SDB are in clear bidirectional relationship [5]. As a consequence some efforts have been made to establish routine screening methods and predictive models for SDB in the acute phase of stroke [6]. MG, as a neuromuscular disorder, is also of higher risk for SDB [7]. Therefore, some authors justify the implementation of SDB home-screening in those patients [8]. Another well-known neurological condition, the MS is a demyelinating disorder of the central nervous system (CNS) which leads to severe disability. Studies have demonstrated that SDB in MS could complicate the disease course, especially with regards to fatigue [9].

Although the full-night polysomnography is still the gold standard in the diagnosis of OSA, its implementation in the clinical routine remains limited mostly to specialized sleep medical centres. This has led to the development of screening (AASM Type III) devices such as ApneaLink Plus™ (ALP) [10].

Since, to our knowledge, there is not a comparative study concerning SDB screening with portable device in hospitalized patients with distinct neurologic conditions, we formulated the main objective in this study: to compare patients' profiles in selected three neurological disorders – IS, MG and MS, with respect to screening parameters for SDB.

Materials and methods. ***Patient sample, clinical and anthropometric assessments.*** All patients were recruited prospectively within 48 h after hospitalization. An informed consent was signed by each participant in the study. Basic anthropometric measurements such as neck and waist circumferences were

obtained, and the body mass index (BMI) was calculated. The initial clinical assessment was performed according to disease specifications: in IS – disease severity, assessed by The National Institutes of Health Stroke Scale (NIHSS), in MG – clinical severity, evaluated with Myasthenia Gravis Foundation of America Clinical Classification, in MS – disability assessment, using the Expanded disability status scale (EDSS).

The following exclusion criteria were implemented:

1. Alteration of consciousness that would impede the participant to follow the study protocol;
2. Baseline saturation lower or equal to 90%;
3. Respiratory recordings with less than 4 h recording time or with low quality;
4. Signs of respiratory failure or hypoventilation syndrome.

Questionnaires. Sleepiness was assessed using the Epworth sleepiness scale [11], where patients with scores equal or greater than 10 were considered sleepy. The STOP-BANG questionnaire (STB) [12] and the Berlin questionnaire (BQ) [13] were implemented for OSA detection. For the study purposes, we used STOP-BANG values as scale variables, and we did not categorize them. BQ scores were dichotomized to high or low risk for OSA.

Recording device. ApneaLink™ Plus (ALP) is a 3-channel portable testing device which records pulse, oxygen saturation and nasal airflow. ALP monitors the occurrence of apneas, hypopneas, flow limitations, snoring, blood oxygen saturation, as well as a possible periodic breathing (Cheyne–Stokes) pattern. The apnea was defined as a $\geq$ 90% reduction of airflow for more than 10 s, and the hypopnea as a 30–90% reduction of airflow for more than 10 s, in addition to a $\geq$ 4% reduction of oxygen saturation. The apnea-hypopnea index (AHI) was calculated as the total number of apnea plus hypopnea events divided by total recording time. Oxygen desaturation index (ODI) is a decrease in the mean oxygen saturation of $\geq$ 4% that lasts for at least 10 s [14]. According to AASM [10] ALP is categorized as Type III device, thus feasible for SDB screening. In patients with suspected SDB ALP has been proven to be reliable in the diagnosis of OSA, including for detection of central apneas [14].

Statistical analysis. For the statistical analysis we used IBM SPSS version 23 for Windows. A p-value of ≤ 0.05 was set as statistically significant. All subjects were described using descriptive statistics and frequency analysis. Chi-square test was used for the comparison of categorical frequencies. Parametric and non-parametric tests were implemented for the independent sample group comparison.

Results. In this prospective cross-sectional study, we recruited 72 patients, 25 with IS (mean NIHSS 2.6 ± 1.1), 24 with MG (87.5% below class III), and

23 with MS (mean EDSS 3.5 ± 1.8). The age of IS patients differed significantly from the rest ($p < 0.0001$). Male gender was also predominant in the IS group. BMI was statistically higher in IS patients than MG patients ($p < 0.05$) and this difference was even more obvious when compared to MS patients ($p < 0.005$). A statistical difference between the IS and other groups was observed in neck circumference ($p < 0.0001$ for both MG and MS) as well as in waist circumference ($p < 0.001$ for MG and $p < 0.0001$ for MS). A summary of the demographic and anthropometric data is presented in Table 1.

Table 1

Demographics and anthropometry BMI: body mass index

	IS	MG	MS
Age (years)	66.3 ± 9.6	47.9 ± 12.4	40.1 ± 7.5
Male (%)	76	37.5 ± 6.3	26.1 ± 5.1
BMI (kg/m^2)	29.3 ± 6	24.6	23.4
Neck circ. (cm)	42.8 ± 4.3	37.3 ± 3	36.1 ± 4.1
Waist circ. (cm)	107.9 ± 13.4	90.4 ± 14.6	85.8 ± 12.4

Whereas the level of sleepiness, measured by ESS, did not differ significantly among the groups, the subjective screening for OSA showed variations. In absolute values, IS subjects had a higher score compared to MG and MS participants ($p < 0.0001$) in the STOP-BANG score. A high risk for OSA in BQ was calculated in 68% of IS, 33.3% of MG, and in 13% of MS patients ($p < 0.0001$). The results from questionnaires and scales are shown in Table 2.

Table 2

Scores form questionnaires
(ESS – Epworth sleepiness scale, BQ – Berlin questionnaire)

	IS	MG	MS
ESS	5.5 ± 3.2	5.6 ± 3.3	5.9 ± 4.5
STOP-BANG	4.8 ± 1.3	2.1 ± 1.4	1.2 ± 0.9
BQ – high risk (%)	68	33.3	13

The AHI in the IS group was significantly higher than in the MG ($p < 0.05$) and in the MS ($p < 0.001$) group. The same statistical difference was calculated for ODI. Based on the formal AHI categorization, the IS group had the highest share of severe sleep apnea whereas in the MS group there was the highest quantum of patients without sleep apnea (Fig. 1).

There was a statistical difference of hypopneas per hour only between IS and MS ($p < 0.005$) patients. Unlike hypopneas, there were significant differences in the number of obstructive events (apneas) per hour between IS and MG ($p < 0.005$) and between IS and MS ($p < 0.001$). No statistical significance was reached regarding central and mixed apneas between the groups of patients.

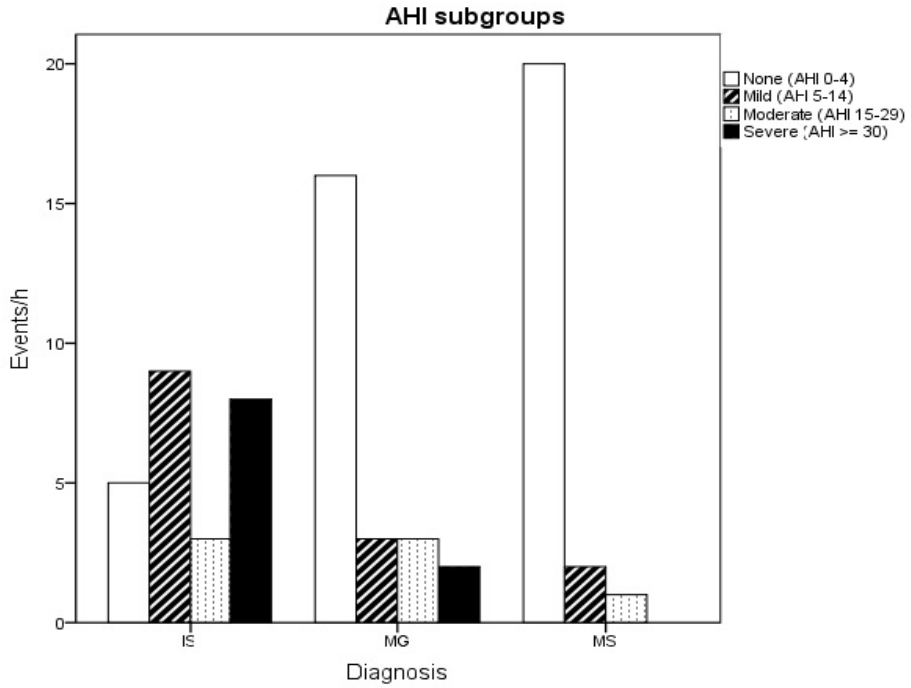


Fig. 1. Shares of patients according to AHI in each group

The oxygen saturation (SO2) showed difference only between IS and MS in all three measured values – baseline SO2 ($p < 0.001$), median SO2 ($p < 0.05$) and lowest SO2 ($p < 0.05$). The maximal values of heart rate were statistically significant only between IS and MS ($p < 0.05$). The ALP respiratory and cardiac values are presented in Table 3.

Discussion. In this study, we explored the presence of OSA in three pathologically different neurological disorders which are very frequent in our daily practice. Since an exclusively clinical evaluation for SDB in neurological patients apparently leads to its underdiagnosis [15], we implemented a combination of subjective and objective evaluation of signs and symptoms which may be related to SDB.

Regarding demography, on the imaginary axis IS-MG-MS we observe certain shift: from older towards younger patients, from male to female gender share, but also from higher to lower BMI and circumferences. This constitutional shift is mainly due to disease-specific clinical profiles of the patients which also to certain extent predetermine the occurrence of SDB in those subjects. This shift is well visible in the subjective SDB screening tools, in this case the STOP-BANG and the BQ, and more importantly, it goes along with the AHI and ODI changes, reported by the ALP. The STOP-BANG was able to differentiate statistically the OSA risk between the three explored groups which confirms its reliability,

Table 3

Respiratory and cardiac assessments
(AHI – apnea-hypopnea index, ODI – Oxygen Desaturation Index,
O – obstructive, C – central, M – mixed, HR – heart rate)

	IS	MG	MS
AHI (/h)	20 ± 18.3	8.1 ± 12.7	2.3 ± 4.9
ODI 4% (/h)	19.3 ± 19	8.1 ± 12.9	2.6 ± 5.5
O Apnea (/h)	8.7 ± 10.1	1.6 ± 3.1	0.4 ± 0.7
M Apnea (/h)	0.1 ± 0.2	0.33 ± 0.14	0.004 ± 0.2
C Apnea (/h)	3 ± 6.8	0.4 ± 1.4	0.05 ± 0.1
Hypopnea (/h)	8.1 ± 9.1	6.1 ± 10.1	1.7 ± 4.5
SO2 baseline	93.6 ± 1.6	94.4 ± 1.6	95.4 ± 1.5
SO2 median	91.2 ± 1.9	91.6 ± 3.7	92.7 ± 1.9
SO2 lowest	82.4 ± 7.1	82.8 ± 11.6	87.7 ± 4.7
Sat 90%	32.2 ± 26.7	20.3 ± 26.8	8.6 ± 21
Sat 88%	11.6 ± 17.2	8.1 ± 19.8	3.8 ± 10.1
HR median	61.8 ± 7.6	61.3 ± 10	67.6 ± 11.9
HR max	92.1 ± 12.8	101 ± 17.9	102.7 ± 14.6
HR min	51.8 ± 7	49.3 ± 6.1	51.9 ± 14.6

shown also in other studies [12]. The mean STOP-BANG score in the IS group corresponds to a moderate risk for OSA, which we did not find in the MG and in the MS groups. Based on BQ stratification for OSA risk, we found a greater share of the high-risk group (68% vs. 53%) than in other studies with stroke patients [16], probably due to different study populations. Interesting, however, is the relatively low level of subjective sleepiness in all three groups which does not show statistical difference among them. Nevertheless, there is a slightly higher ESS score in MS patients compared to the other two groups. This might be due to the incomplete understanding of the difference in the terms fatigue and sleepiness, as fatigue is generally present in patients with MS, and even higher in those with MS and SDB [4].

As already mentioned, the AHI and the ODI, which are still the most used markers for the severity grade of OSA, show differences between the investigated neurological entities. Further analysis showed significant differences between the groups in the count of hypopneas, but it was not able to demonstrate differences in apneas.

The mean AHI in the IS group was higher, compared to other studies [17,18]. This is probably due to the more extended signal acquisition of ALP, compared to a single-channel ApneaLink, which allows more precise interpretation of the data. Despite the current rather skeptical opinion on the benefit of routine OSA screening in IS [19], we see a clear difference between the share of severe OSA in IS patients, compared to the other two investigated groups. Such finding justifies at least more careful clinical reasoning in the evaluation of the potential usefulness of the currently available simple screening tools in stroke.

We found OSA in 1/3 of the MG patients which is lower than in some studies where the definitive SDB is present in over 40% of patients with MG [8,20]. Given the study sample, we do not find this difference to be critical and inconsistent with other studies. The share of MS patients with positive SDB screening (i.e. AHI $\geq$ 5/h) was equal to studies with polysomnography-diagnosed SDB [21], but lower than in other, questionnaire-based studies where the SDB prevalence reaches almost 40% [22]. Additionally, our data show overall lower ESS and STOP-BANG scores in the MS group compared to other authors [9], which may contribute to the non-apnea profile of the MS patients on the IS-MG-MS axis and might be due to the smaller number examined MS patients.

Limitations. This study has certain limitations. Despite our findings, the examined patient groups cannot be representative for the entire clinical range in each of the explored pathologies. The exclusion of patients with more complicated disease course, mainly due to their inability to follow the study procedures, leads to a certain selection bias, and therefore our data cannot be conclusive about this group of patients. In order to implement a simple screening tool, we chose a device that has certain diagnostic limitations, which some authors find concerning. This fact, however, should be always taken into consideration when such monitoring devices are used.

Conclusions. Our results clearly show the necessity for individualized approach, in order to evaluate the need for respiratory screening in neurological diseases. As expected, the underlying pathology is the most significant factor in this clinical reasoning. Such SDB screening applies for patients with IS and obviously to a much lesser extent for MS. The third explored pathology, the MG, stands between the other two, which of course warrants the individual approach in the assessment of each patient. Nevertheless, studies with greater sample are needed to further investigate this interesting topic.

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