Parasomnias and obstructive sleep apnea syndrome: in search for a parasomnia evaluating tool appropriate for OSAS screening


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Summary Background. Obstructive sleep apnea syndrome (OSAS) is the most common form of sleep-disordered breathing. It is also known as a major risk factor of parasomnias. 

Objectives. To verify if an additional diagnostic tool for parasomnia assessment might be useful in OSAS screening. Additionally, to investigate the possible relations of parameters measured during polygraphy evaluation and the severity/frequency of parasomnia episodes in order to find the pathophysiological background of increased frequency of parasomnias in OSAS cases.

Material and methods. Parasomnia evaluation with the Paris Arousal Disorder Severity Scale (PADSS) and OSAS evaluation with polygraphy in a group of 105 adult patients hospitalized for assessment of possible OSAS.

Results. According to the polygraphic evaluation, patients were divided into: non-OSAS (n = 19, 18.1%), mild OSAS (n = 31, 29.52%), moderate OSAS (n = 21, 20%) and severe OSAS (n = 34, 32.38%). Based on the recommended cut-off score of 13 points in PADSS, two groups of patients emerged after the parasomnia evaluation: with positive (n = 10) and negative (n = 95) results. PADSS achieved sensitivity of 10.9% and 92% specificity when used for moderate and severe OSAS screening. The positive predictive value (PPV) reached 60%, negative predictive value (NPV) - 48.4%. A statistically significant elongation of the percentage of estimated sleep time below 80% blood oxygen saturation emerged in patients with positive PADSS scores (p = 0.006). Focusing on the parasomnia frequency criterion did not significantly affect the results.

Conclusions. Due to low sensitivity, PPV and NPV PADSS cannot be used as a screening tool in possible OSAS assessment. Another tool with higher sensitivity should be developed, also including assessment of other parasomnias and sleep-related movement disorders. Cyclic intermittent hypoxia might be the cause of the higher frequency of arousal disorders in OSAS patients.

Key words: parasomnias, sleep apnea syndromes, sleep apnea, obstructive.

Background

Obstructive sleep apnea syndrome (OSAS) is the most common, but still underestimated, form of sleep-disordered breathing, characterized by the collapse of the upper airway leading to intermittent arterial oxygen desaturation, micro arousal-related deregulation of the sympathetic nervous system, oxidative stress, and chronic inflammation [1, 2], excessive daytime sleepiness causing automobile accidents and impaired functioning, among other symptoms [3].

One out of five adults suffers from at least a mild degree of OSAS, and the prevalence in adults 30–69 years of age is estimated at 17%, and 41–58% in obese patients. It was demonstrated that that 93% of females and 82% of males with moderate to severe OSAS had not been clinically diagnosed, despite access to healthcare [4–6]. OSAS has been independently associated with hypertension [7], stroke [8, 9], myocardial ischemia [10, 11], dyslipidemia [12, 13], impaired glucose tolerance [14, 15], and arrhythmias with an increased risk for sudden cardiac death [16].

OSAS is often the cause of impaired daytime functioning. Its symptoms include: daytime sleepiness, morning headache, attention disorders, impaired memory, decreased libido, affective disorders, fear of going to bed, snoring, increased sweating, heart palpitations, and dryness of the oral cavity during sleep and in the morning [17–19].

Nowadays, the diagnostic gold standard of OSAS is polysomnographic evaluation (PSG) – OSAS is classified based on the Apnea-Hypopneas Index (AHI), which describes the number of those nocturnal events per hour of sleep. According to the American Academy of Sleep Medicine, OSAS is classified as mild (AHI > 5), moderate (AHI > 15) or severe (AHI > 30) [20]. However, in this study only the polygraphic record without EEG registration was performed, due to technical limitations. Nevertheless, polygraphy was sufficient to determine basic respiratory parameters during sleep.

The occurrence of psychopathological symptoms in OSAS patients (mainly of moderate or severe level) suggests the possible cooperation of specialists in different fields of internal medicine, specialists and researchers with psychiatrists in order to improve the quality and effectiveness of diagnostic and therapeutic procedures.

OSAS is also a major risk factor of parasomnias [21–23]. Parasomnias are defined as undesirable physical or experiential...
events that accompany sleep [21, 24, 25]. They usually include abnormal motor activity, perceptions, emotions, autonomic nervous system dysfunctions and dreaming [21]. They can be disorders of arousal but also of sleep-stage transition and sleep/wake transition events [22, 23]. Some of them are known to occur only in a specific sleep stage. NREM parasomnias include confusional arousals, sleepwalking and sleep terrors. Conversely, REM sleep behavior disorder (RBD), nightmares and isolated sleep paralysis emerge from the REM stage. Other parasomnias (like enuresis, sleep talking or exploding head syndrome) may occur during different stages or at sleep/wake transition [25]. Catathrenia was also included in this group of disorders in the International Classification of Sleep Disorders 2nd edition (ICSD-2), but in the 3rd edition it was moved to the group of Sleep-related Breathing Disorders (SBD) [24, 25].

Many studies have so far presented pathophysiological theories explaining the causes of these events. Most parasomnias may result from incomplete dissociation of wakefulness, NREM and REM sleep [22, 26, 27, 39]. Sleep is not a global process, and does not manifest in the same way in different brain parts. Parasomnia might occur when two different sleep stages overlap or take place simultaneously. But this process is sometimes insufficient for disorders to occur – several studies state that other factors contribute to arousal events, especially including motor activity [23]. Those factors include: activation of locomotor centers (cortical and thalamocortical pathways [28, 29]), sleep inertia [30, 31] and sleep state instability (cyclic alternating pattern, representing the NREM instability) [32–34]. It is presumed that comorbidities leading to cortical arousals, promoting sleep inertia and affecting sleep microstructure (like OSAS and sleep-related movement disorders) may lead to intrusions of some sleep/wakefulness stages into others [35]. Subsequently, it leads to different parasomnia events [36, 37]. However, according to our knowledge, there are very limited data regarding the prevalence and frequency of parasomnias in the group of OSAS patients. Whether the theoretical model described above has a clinical meaning in OSAS is still to be determined. Other parasomnia risk factors also contribute to the stimulation of those mechanisms (psychoactive substances, drugs, sleep deprivation, shift-working, emotional stress, and genetic factors) [23, 38]. However, much research still needs to be performed in order to discover the exact mechanisms of sleep stage transition and the neuronal dysfunctions mentioned above.

Objectives

This study was designed as a cross-sectional study in order to estimate parasomnia presence in OSAS-suspected patients at the moment of first polygraphic evaluation. The basic goal of this study was to adapt PADSS in Poland, and to verify if it might prove useful as an additional screening tool in the group of related breathing disorders. This tool was developed mainly in order to assess and evaluate the presence, severity and frequency of parasomnias with nocturnal arousals, specifically somnambulism and sleep terrors, though some items contained in the scale also refer to other parasomnias. It has been used in several studies in groups of patients presenting sleepwalking, sexsomnia and sleep terrors [41, 63]. According to our knowledge, PADSS has not been used so far in other studies concerning OSAS patients. PADSS consists of three main parts – the first contains questions about the patient’s activity during sleep and symptoms, the second determines their frequency, and the third specifies the daytime symptoms and their influence on the quality of life. Examination with the scale takes about 5–10 minutes, which is important in the case of OSAS patients as they often suffer from attention disorders. PADSS has been not used in Poland before, so translation into Polish was performed and checked with back translation done by a professional translator.

Material and methods

Participants

Patients of the Department and Clinic of Internal Medicine, Occupational Diseases, Hypertension and Clinical Oncology of Wroclaw Medical University subsequently hospitalized for the assessment of possible obstructive sleep apnoea were enrolled, after receiving informed consent. Inclusion criteria consisted of adult age and suspicion of developing OSAS in patients who had not been diagnosed with OSAS before. OSAS suspicion was based on clinical symptoms and/or increased risk of OSAS shown by the STOP BANG and Berlin questionnaires. A total number of 128 patients were recruited and evaluated with polygraphy. All of them had indications for this diagnostic procedure. In n = 19 patients it was impossible to get necessary data via polygraphic evaluation due to technical issues, and those patients did not come back for the second examination. N = 4 patients refused to fill in the PADSS before the polygraphic evaluation. Finally, 105 patients were included in the statistical analysis.

Parasomnia evaluation

Usually, almost every parasomnia is diagnosed based on medical history (REM-sleep Related Behavior Disorder needs PSG confirmation) [25]. Still, not many well described tools with verified research history are available regarding parasomnia diagnosis and screening [40]. It was difficult to obtain a single tool that would meet all criteria (range of parasomnia symptoms, simplicity and multiple verification in research history). Finally the Paris Arousal Disorder Severity Scale (PADSS) was chosen [41]. This tool was developed mainly in order to assess and evaluate the presence, severity and frequency of parasomnias with nocturnal arousals, specifically somnambulism and sleep terrors, though some items contained in the scale also refer to other parasomnias. It has been used in several studies in groups of patients presenting sleepwalking, sexsomnia and sleep terrors [41, 63]. According to our knowledge, PADSS has not been used so far in other studies concerning OSAS patients. PADSS consists of three main parts – the first contains questions about the patient’s activity during sleep and symptoms, the second determines their frequency, and the third specifies the daytime symptoms and their influence on the quality of life. Examination with the scale takes about 5–10 minutes, which is important in the case of OSAS patients as they often suffer from attention disorders. PADSS has been not used in Poland before, so translation into Polish was performed and checked with back translation done by a professional translator.

Polygraphic evaluation

All patients underwent a standardized overnight, single night polygraphy as a reference standard for the diagnosis of OSAS [42]. The following parameters were obtained: AHI (the number of apneas and hypopneas per hour of estimated sleep time), oxygen desaturation index (ODI; the number of oxygen desaturations > 3% per hour of estimated sleep time), average and minimal blood oxygen saturation and percentage of estimated sleep time below 90% and 80% oxygen saturation. Abnormal respiratory events were evaluated according to the standard criteria of the American Academy of Sleep Medicine Task Force [43]. Additionally, all patients filled out a short survey containing questions about their age, body mass and height.

Statistical analysis

Statistical analysis was performed with the Statsoft Statistica 12 software. The analysis of the results included Shapiro–Wilk testing (normality of the distribution) with histogram analysis, non-parametrical testing (the U Mann–Whitney test) and correlation calculation (ρ Spearman testing).

Results

The study group finally consisted of 105 patients, 35 women (33.3%) and 70 men (66.6%), aged from 21 to 77 years (mean = 56, SD = 12.8).
Based on the polygraphy results, participants were divided into four groups according to the recommendations of the American Academy of Sleep Medicine (mild OSAS – AHI = 5, moderate – AHI > 15 or severe – AHI > 30): non-OSAS (n = 19, 18.1%), mild OSAS (n = 31, 29.52%), moderate OSAS (n = 21, 20%) and severe OSAS (n = 34, 32.38%). From a clinical perspective, mild OSAS treatment includes only elimination of risk factors (mainly body mass reduction and lifestyle changes) and further observation. In these patients clinical symptoms are often very subtle or absent. Proper treatment with CPAP is recommended for some patients with moderate OSAS (if they present severe clinical symptoms like increased daytime sleepiness or cardiovascular risk factors) and all patients with severe OSAS [44, 65]. Thus, it was primarily verified if PADSS is a proper tool for diagnostics of moderate or severe OSAS.

Based on the recommended cut-off score of 13 points [41], two groups of patients emerged: with positive (n = 10) and negative (n = 95) results. Compared to the polygraphy evaluation, PADSS achieved very low sensitivity (10.9%) and high specificity (92%) when used for moderate and severe OSAS screening. The positive predictive value (PPV) reached 60%, negative predictive value (NPV) – 48.4%. Comparatively, when used for the screen-positive predictive value (PPV) reached 60%, negative predictive value (NPV) – 92% when used for moderate and severe OSAS screening. The PADSS achieved very low sensitivity (10.9%) and high specificity (92%) when used for moderate and severe OSAS screening. The positive predictive value (PPV) reached 60%, negative predictive value (NPV) – 48.4%. Comparatively, when used for the screening of any OSAS severity level, PADSS achieved a sensitivity of 10.46% and a specificity of 94.73%. The low sensitivity level eliminates the possibility of using PADSS for screening purposes with the recommended cut-off level.

Nevertheless, statistically higher PADSS scores in patients with elongation of the percentage of estimated sleep time below 80% blood oxygen saturation (p = 0.097) and percentage found in minimal oxygen saturation (p = 0.03). A weaker trend was observed in PADSS-positive patients (n = 17 PADSS-positive patients after cut-off lowering). The statistical relationship of the percentage of estimated sleep time below 80% blood oxygen saturation in the group with positive PADSS scores was again confirmed (p = 0.068) in patients with positive PADSS score.

Lowering the cut-off level down to 10 points did not significantly affect sensitivity – 20% in patients with moderate/severe OSAS, specificity 88% (n = 17 PADSS-positive patients after cut-off lowering). The statistical relationship of the percentage of estimated sleep time below 80% blood oxygen saturation in the group with positive PADSS scores was again confirmed (p = 0.03). A weaker trend was observed in PADSS-positive patients and AHI value (p = 0.074), which did not occur in the positive group with the recommended cut-off value.

Finally, participants were divided based only on the frequency of their reported parasomnia symptoms (second section of PADSS), ignoring their qualitative complaints. Group 0 contained patients who did not report any parasomnia events (n = 66). Patients in group I confirmed rare occurrence of symptoms, less than once a week (n = 20), while patients in group II reported frequency of at least once a week (n = 9). Group III reported parasomnia events to occur every night (n = 10). Parasomnia events happening at least once a week determine the positivity of answers may depend on apnea severity, and it is worth mentioning that those questions also refer to typical OSAS symptoms (fatigue, mood disorders, daytime sleepiness), while only a few questions refer to other parasomnias (like sexomnia, enuresis, and sleep-related eating disorder). A few symptoms especially often reported by patients with OSAS are not included in PADSS (catathrenia, sleep talking, and sleep paralysis), as they usually do not lead to arousals. We assume that another tool with a wider range of questions concerning different disorders could be much more sensitive in this group of patients.

Due to technical limitations, the evaluation of sleep microstructure was impossible, and this is why no data regarding this subject were presented. Changes of NREM and REM microstructure in OSAS are well known [45]. The research team is currently in an advanced stage of research concerning this issue, and is testing a new parasomnia and sleep-related movement disorders screening tool that may be valid for OSAS patients.

Probably the greatest impact of OSAS on brain function is based on cyclical intermittent hypoxia [46]. Lim describes three ways in which this process affects the blood-brain barrier (BBB) and thus brain functioning during sleep: promoting oxidative stress, inducing so-called “hypoxia inducible factors” (HIFs) in cells, and finally causing chronic inflammation in the BBB area. Oxidative stress in neurons is a known factor of neurodegeneration in many demetive diseases, and is a possible cause of neurodegeneration in long-suffering OSAS patients leading to cognitive dysfunctions [47, 48]. Such degeneration was even observed in neuroimaging studies [49–51]. HIFs act as transcription factors in brain cells, promoting genes responsive for hypoxia reaction like glucose metabolism, erythropoietin production, and angiogenesis [52–54]. Chronic inflammation in some studies seems to affect the BBB much more in OSAS patients with obesity than those with BMI < 30 [55, 56]. Lim and Pack describes studies that lead to the conclusion that those three processes impair the microvessel permeability of the BBB, although it is still too early to determine whether this impairment is a sufficient factor in causing neuronal morphologic changes or synaptic dysfunctions [46].

This study delivers data that somehow support this theory. We have shown a statistically significant relation of percentage of total estimated sleep time below 80% blood oxygen saturation with arousal disorder severity (measured with PADSS) in OSAS patients. We could not determine if the patients already had morphological changes in the brain without the use of neuroimaging techniques. However, the presence of parasomnia...
may suggest abnormalities in sleep microstructure on a sufficiently deep level to cause REM/NREM and wakefulness intrusions in different sleep stages that lead to parasomnia events. Nevertheless, some of the PADSS high-scoring patients did not have significantly elongated sleep time with lowered saturation level, so other factors have to contribute to parasomnia events in this group (possibly changes in sleep microstructure and arousals due to apnea events [23, 35], which were not evaluated in our study). Whether intermittent hypoxia is a sole risk factor of parasomnia is yet to be determined. It is also worth noting that we did not obtain any strong evidence that AHI is significantly higher in those patients. This supports the theory that AHI does not truly show the impact of OSAS on blood oxygen saturation and brain hypoxia risk. Lim and Pack came to similar conclusions [46]. Vgontzas observed that the association between AHI and daytime sleepiness symptoms is rather weak, and AHI alone may not represent the severity of OSAS [57]. Anyway, the results suggest that patients with increased AHI do not have statistically higher PADSS scores or increased frequency of arousal disorders.

Several studies showed that sleep fragmentation and sleep efficiency do not contribute directly to increased daytime sleepiness, and other factors have to be found in the OSAS patient group [17]. Some possible associations of daytime sleepiness, fatigue and daily mood disorders (the third section in PADSS) with minimal blood oxygen values, as well as the percentage of estimated sleep time below 80% blood oxygen saturation were observed. Such results may support the hypothesis that cyclical intermittent hypoxia may affect daytime functioning, which was previously described by Miliauskas and Sakalauskas and Jacobsen et al. [58, 59]. What is once again worth noting is that no association between the symptoms reported in the last section of PADSS and AHI was found. So again, AHI turned out not to be an efficient marker for blood oxygen saturation evaluation. Taking into account the fact that most of the patients giving positive answers in this section (16 out of 19) belonged to groups II and III of parasomnia events frequency, we can assume that parasomnia disorders may contribute to impaired daytime functioning in OSAS patients. Zadra et al., based on several studies, came to the conclusion that somnambulism itself may be characterized by excessive daytime sleepiness, even after nights without arousal episodes [60]. Zhou et al. described several studies which stated that many patients, even with severe OSAS, do not report excessive daytime sleepiness or other daytime functioning impairments [17, 61, 62]. The results suggest that parasomnia may contribute to the further impairment of daytime functioning, which may be a priori worsened by the OSAS itself. However, our study has its limitations – the evaluation of daytime sleepiness with other tools was not performed.

Some other weaker trends that were observed (including associations between minimal oxygen saturation, percentage of sleep time below 90% blood oxygen saturation and parasomnia severity) together with the previously described results could also support the statement that parasomnia events may somehow be evoked by cortical arousals typical for OSAS superimposed on intermittent hypoxia and sleep deprivation [22]. However, the data still do not have sufficiently strong statistical power to clearly support those hypotheses, mainly due to the small number of PADSS-positive patients, and lack of EEG monitoring during polygraphic diagnostics. Further research is needed, including focusing on microstructural sleep disturbances and neuroimaging in OSAS patients with parasomnias, including tools with higher sensitivity, and possibly including other sleep complaints like sleep-related movement disorders or catathrenia [24]. It is also worth mentioning that patients with OSAS often report insomnia-like complaints, which are generally a common problem in Polish primary care [63]. This is why family doctors should always consider OSAS as a possible cause of insomnia and increased daytime sleepiness.

Limitations of the study

We are aware that this study has some limitations. Our study provides limited statistical power to confirm the hypothesis that cyclic intermittent hypoxia might be the cause of higher frequency of arousal disorders in OSAS patients. According to our knowledge, PADSS has not been validated in OSAS – our study is the first to use PADSS in this group of patients. Due to technical limitations, we were not able to assess the patients with full polysomnographic evaluation, so polygraphy was performed instead. The sample size in this study is relatively small and the results are partially under-powered. This limitation is determined due to lack of financial support, which hampered the possibility of further recruitment. Such studies very often meet some sample or time limitations, and we are aware of this fact. However, we believe that this study indicates some directions for future research, including bigger samples and better methodology (including other questionnaires and full polysomnographic evaluation), and the results obtained in this study are sufficient to justify the cautious conclusions included in the text. Currently, another study regarding parasomnias in OSAS is being carried out by this team.

Conclusions

- Due to low sensitivity, PPV and NPV PADSS cannot be used as a screening tool in possible OSAS assessment. Another tool with higher sensitivity should be developed, also including the assessment of other parasomnias and sleep-related movement disorders.
- Cyclic intermittent hypoxia might be the cause of the higher frequency of arousal disorders in OSAS patients. However, our study did not provide sufficient statistical power to fully confirm this hypothesis. Further studies concerning this topic are needed.
- High AHI value does not directly increase the frequency of arousal disorders.

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References


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