Psychiatr. Pol. 2017; 51(3): 483–494
PL ISSN 0033-2674 (PRINT), ISSN 2391-5854 (ONLINE)
www.psychiatriapolska.pl
DOI: https://doi.org/10.12740/PP/60420

Hypersomnia and cognitive impairment in a patient with bipolar disorder – a case report

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Summary

Aim. Obstructive sleep apnea (OSA) is a common clinical problem that can have serious health consequences and complicate the course of mental disorders. It is estimated that the prevalence of sleep apnea in patients with bipolar disorder can be 21–47.5%. Some symptoms of OSA are the same as the symptoms of depression: daytime drowsiness, cognitive dysfunction, decreased drive, apathy, depressed mood, anhedonia.

Method. We present a case of a patient whose depressive symptoms persisted despite repeated changes of pharmacological treatment and were exacerbated by severe sleep disorder. OSA was also the cause of serious respiratory complications and prolonged disorders of consciousness that occurred during ECT treatment.

Results. Based on test results of WatchPAT200 and polysomnography, the diagnosis of severe sleep apnea was established and Continuous Positive Airway Pressure (CPAP) treatment was introduced. Severe OSA led in this patient to almost total absence of REM sleep, a significant reduction of deep sleep as well as the reduction of total sleep time.

Conclusions. The presence of daytime sleepiness, unremitting despite the modification of treatment, indicates the need for diagnostic screening for OSA, which can mimic some of the symptoms of depression, increase the risk of complications during anesthesia, and can be one of the causes of drug resistance. In addition to the negative impact of obstructive sleep apnea on the course of bipolar disorder, OSA also causes significant cognitive impairment in terms of attention and vigilance, long-term semantic and visual memory as well as visual-spatial and executive functions.

Key words: treatment resistant depression, depression in bipolar disorder, obstructive sleep apnea

Introduction

A psychiatrist often interprets the symptoms as dependent on mental illness, personality traits or environmental factors. It is worth noting, however, that any mentally ill person may have comorbid somatic disorders which require careful exclusion. We present a case of a patient whose depressive symptoms were exacerbated by severe sleep disorder.

Medical history

A 23-year-old obese (BMI = 43.2 kg/m^2) patient with a diagnosis of bipolar disorder was admitted to a psychiatric day hospital because of another depressive episode.

The patient had been treated psychiatrically on an outpatient basis since the age of sixteen. As an 18-yer-old man, he was hospitalized with a diagnosis of a paranoid syndrome. Due to the occurrence of the manic and depressive phases in the course of the illness, the diagnosis was changed to bipolar disorder.

Ten months before admission to the ward another episode of depression appeared. Despite numerous changes in the treatment (including treatment with lithium carbonate, ziprasidone, aripiprazole, olanzapine, lamotrigine, quetiapine, escitalopram), no improvement was achieved. Therefore, the patient was referred to the psychiatric ward. During his stay the treatment with lamotrigine, aripiprazole and quetiapine was stopped and lithium carbonate and escitalopram was enrolled. Due to the lack of therapeutic effect, the treatment was changed later to reboxetine and phototherapy. After switching to lithium carbonate a slight improvement in mood and a relief in tearfulness were observed, but sadness, apathy and inactivity remained. The patient was referred to electroconvulsive therapy (ECT). During the first session, serious respiratory complications occurred: the difficulties in ventilation with the use of oropharyngeal tube, difficult intubation, a severe hypoxia, increased blood pressure after ECT and then, after waking, disorders in consciousness, which lasted for several hours. Due to those complications, the ECT treatment was abandoned. Lamotrigine at a dose of 50 mg/day and vortioxetine 20 mg per day were enrolled, and a gradual improvement of his mental state was observed. The dose of lithium was set at 1000 mg per day, serum level at discharge = 0.64 mmol/l). After two hospitalizations in the inpatient department (a total of 5 months of residence), the patient was discharged and sent for further treatment at the day ward. The improvement was described as incomplete.

Current hospitalization

After a discharge from the inpatient department, the patient was admitted to the day ward and qualified for the therapy program for people with depressive disorders.

During the psychiatric examination the patient was in a good, logic contact, fully oriented. He denied suicidal ideations. The leading symptoms in the clinical picture were as follows: excessive daytime sleepiness, impaired drive, cognitive impairment, concerns about the future, periodically suicidal thoughts, lack of energy, listlessness, increased appetite. The patient showed no psychotic symptoms or formal thought disorders, and the mood was only slightly reduced.

In terms of comorbidities, the main problem was morbid obesity, with a BMI = 43.2 kg/m^2 (height 180 cm, weight 140 kg). Because of arrhythmias, and susceptibility to ventricular tachycardia, the patient received additional 25 mg of atenolol. The patient denied smoking, drinking alcohol or using other drugs.

During the hospitalization, it was possible to observe little activity, excessive daytime sleepiness and a periodic falling asleep during the psychological classes. During the periods, when the patient was vigil, we were also observing more and more often unsuited affection and weakened criticism, a tendency to respond to the statements of other patients during psychotherapy in the form of jokes. His mood was labile and oscillated between carefree and playful. These symptoms were initially interpreted as the beginning of the phase change.

The dose of lamotrigine was gradually increased to 100 mg/d, lithium to 1500 mg/d and the dose of vortioxetine was reduced to 10 mg/day. Individual (1x/week) and group (2x/week) cognitive behavioral psychotherapy with elements of schema therapy was implemented. There was some improvement in his mental status; daytime sleepiness, however, did not decrease. Psychologists interpreted falling asleep during classes as a low motivation for treatment. However, despite attempts to overwork this symptom, its intensity did not change. In view of the persisting daytime sleepiness despite the modifications in the therapy and the increase in the intensity of psychotherapeutic classes, it was decided to expand diagnostics.

Excessive daytime sleepiness

Excessive daytime sleepiness is a fairly common clinical problem. Epidemiological studies indicate that it is almost as common as the most common sleep disorder: insomnia. A severe excessive daytime sleepiness, which disrupts the functioning on a daily basis, occurs in about 5% of the general population in developed countries. A moderately severe excessive sleepiness, which affects the functioning of at least a few days a week, is present in approximately 15% of people [1]. Therefore, the presence of excessive daytime sleepiness should be assessed routinely during the mental state examination.

The differential diagnosis of excessive sleepiness can be difficult. Its most common causes can be, however, ruled out relatively simply by every doctor. There are many somatic diseases that cause drowsiness.

In the case of the above-mentioned patient, the tests excluded diabetes, kidney or liver disease, the presence of chronic inflammation, anemia and hypothyroidism. The duration of nocturnal sleep observed in the inpatient ward – which amounted to more than eight hours – led to exclusion of sleep deprivation as a cause of excessive sleepiness. Paying attention to the length of night sleep is very important because a chronic lack of sleep or irregular sleep are the most common causes of excessive sleepiness in developed countries. Other frequent causes include mental disorders, especially depression. That is why psychiatrists are very often confronted with excessive sleepiness. Prior to the recognition that an excessive sleepiness is a symptom of a mental illness, a doctor should also collect a history of primary sleep disorders.

The history of somatic diseases and physical examination indicated that the aforementioned patient met the criteria for high risk of sleep apnea, which is a common cause of excessive daytime sleepiness.

Obstructive sleep apnea (OSA) involves complete (apnea) or partial (shortness of breath) closing of the upper respiratory tract, which occurs many times during sleep. The subsequent episodes of stopped breathing cause frequent waking up, resulting in the impaired sleep pattern. With severity of the disease there also occur more hypoxic episodes, changes in cardiac rhythm and blood pressure fluctuations [2, 3].

It is worth noting that some of the symptoms of obstructive sleep apnea coincide with some depressive symptoms, such as daytime sleepiness, cognitive impairment, reduction in drive, apathy, depressed mood. Symptoms of sleep apnea can also be misinterpreted as those resulting from schizophrenia or mania/hypomania in bipolar disorder [4]. In severe sleep apnea, hypoxia and hypercapnia caused by impaired breathing during sleep lead to the symptoms resembling a mild frontal lobe syndrome with the injury of the supraorbital parts. The reduction or lack of higher emotionality, disinhibition, unsuited affect, weakened criticism, lack of insight, labile mood, a tendency to vulgar jokes and stories with erotic content can be observed.

There are studies showing that the prevalence of sleep apnea in patients with bipolar disorder can be 21–47.5% [5]. The presence of risk factors for sleep apnea, such as, for example, obesity is associated with a worse course of bipolar disorder [6]. Like other exogenous reasons for reducing the number of hours of sleep, such as shift work or sleep disorders associated with the change of time zones (jet lag), sleep apnea can contribute to changing the phase in bipolar disorder [7, 8].

Obesity, male sex and daytime sleepiness are the risk factors indicating the necessity of screening for sleep apnea (Figure 1).

SCREENING SCALES:

An effective way to memorize a risk factors for obstructive sleep apnea is a mnemonic STOP-BANG technique, created by anesthesiologists to assess the risk of respiratory complications in the postoperative period. Developing a shortcut STOP: S – snoring loudly (loud snoring), T – tired in the daytime (daytime fatigue), O – observed stops in breathing (seen during sleep), P – blood pressure (hypertension). BANG: B – BMI > 35 kg/m^2, A – age (age > 50 years), N – neck circumference (neck circumference > 41cm for women and > 43cm for men), G – gender (male). The presence of three or more of these eight factors indicates a high risk of obstructive sleep apnea [9].

Another way to assess the risk of sleep apnea is the Berlin Questionnaire, which measures the risk of sleep apnea using three categories. If the result is positive in at least two categories, the risk for OSA is assessed as significant [10]. A study comparing the two scales for people without psychiatric disorders demonstrates the superiority of the STOP-BANG method, however, none of the scales has been validated for the population of the mentally ill people yet [11].

Figure 1. **Screening scales**

In addition, the patient's collar circumference was 47 cm, and the history revealed snoring and pauses in breathing during the night. This meant the presence of up to six risk factors. It was decided to execute the WatchPAT200 examination. It is a portable device used for screening for sleep apnea in an outpatient setting. The basis of the study is to measure the peripheral arterial tension, that is, PAT signal (Peripheral Arterial Tone). A recently published meta-analysis has demonstrated that the measurement of PAT is the right alternative, if considered as the gold standard in the evaluation of sleep apnea, for polysomnography.[12]

The test for sleep apnea

The screening for sleep apnea showed significantly increased rates of respiratory events (RDI 100.9/h, the standard up to 10/h), apnea and hypopnea (AHI 100.6/h, the standard 5/h) and desaturation (ODI 86.0/h, the standard up to 5/h). The respiratory disorders resulted in significant decreases in blood oxygen saturation. The average blood oxygen saturation was 84%, the lowest recorded value was 58%, the mean of the lowest values was 80%. Estimated total sleep time was only 3 hours and 53 minutes; there was no REM sleep present.

The most important parameter associated with the above-mentioned description is the indicator of apnea and hypopnea – AHI (Apnea-hypopnea Index). The result 5–15/h indicates a mild form of sleep apnea, result 15–30 indicates moderate OSA, and the AHI greater than 30/h – severe sleep apnea

With the AHI 100.6/h, the patient fulfills the criteria for severe sleep apnea, and this result is away from the cut-off point for the severity, which thus indicates a very serious disorders. The patient's respiratory disorders led to the almost total lack of

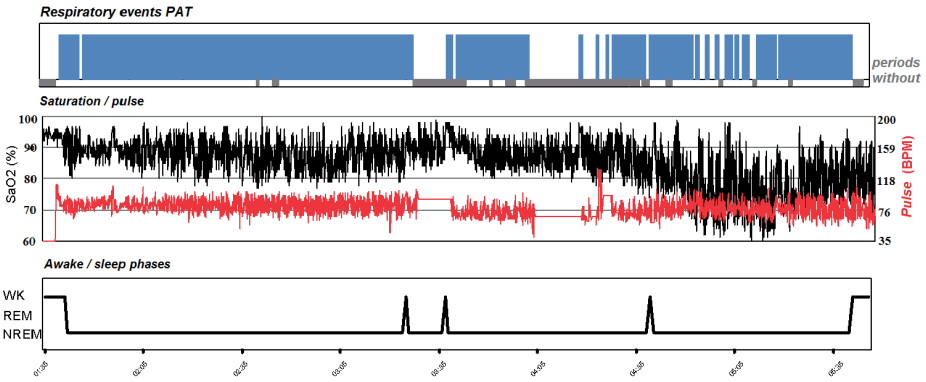

Figure 2. **Selected parameters registered during WatchPAT2000 test**

The respiratory events chart shows periods with numerous respiratory events which occurred during almost the whole time of the test. The saturation and pulse graph shows the saturation declines (lowest recorded saturation: 58%) and concomitant pulse oscillations. The sleep phases chart shows almost total lack of REM sleep.

REM sleep and significantly reduced the amount of deep sleep and thus reduced the total sleep time (Figure 2 – Watch PAT testing results).

Recommendations

The patient was discharged from the hospital with a moderate improvement and the treatment with lamotrigine 100 mg/d, lithium carbonate 1500 mg/d, vortioxetine 10 mg/d was recommended. Lithium serum level controlled prior to discharge from the hospital was only 0.44 mmol, although the dose of lithium carbonate was, in comparison to the treatment in inpatient department, about 500 mg/d higher (and then the lithium level was 0.64 mmol/l). This was interpreted as a result of lower than in the inpatient ward supervision of medication, which could lead to forgetting by patient about evening doses. For this reason and due to the concomitant therapy with other mood stabilizer, the dose of lithium carbonate was not increased. The main principles of treatment with lithium carbonate were one more time discussed with the patient and dose optimization in outpatient setting was recommended.

In connection with the diagnosis of obstructive sleep apnea, the patient received further recommendations:

1. ENT consultation, to assess the patency of the nose, tonsils, palate and posterior pharyngeal wall.
2. Avoiding alcohol and sleeping pills.
3. Reduction in body weight – a consultation with a nutritionist was recommended

4. The patient was urgently referred to a center specialized in the treatment of breathing disorders during sleep – to confirm diagnosis with polysomnography, then consider the indications for treatment with continuous positive airway pressure (CPAP).

After a discharge from hospital, the patient is continuing the treatment in the outpatient clinic. What is more, polysomnography performed in the center specializing in the OSA treatment confirmed the diagnosis substituted on the basis of the screening. Since August 2015, the patient has been receiving the treatment with CPAP.

Before the implementation of CPAP treatment pharmacotherapy was optimized in an outpatient settings. Due to the symptoms of mood elevation, vortioxetine was discontinued, the dosage of the lithium carbonate was raised to 1750 mg/day (serum level = 0.65 mmol/l), lamotrigine was maintained at a dose of 100 mg/day. The stabilization of mood was observed, notwithstanding daytime sleepiness, apathy and lack of motivation remained. Epworth sleepiness scale has shown 14 points – no change since the moment of discharge from the day ward has been observed (cut-off point for excessive daytime sleepiness is at least 8 points). Despite attempts to keep dietary recommendations, patient's weight did not change.

After initiation of CPAP treatment patient described his state as follows: "After these few days sleeping with CPAP I feel a difference, especially in efficiency/vitality, the sleepiness has decreased, during one or two days I didn't feel it at all. I feel my mood has improved and it's easier for me to organize. Finally I started to feel a need to pass the exams". The patient's mood remained stable. During a control visit he filled in Epworth scale, yielding 8 points. Among inconvenience associated with the use of CPAP the most important for the patient was the need to put on the mask carefully and some discomfort during sleep. Still, faced with the great improvement of symptoms this inconvenience had little meaning for the patient.

Not only effective treatment for sleep apnea, but also optimization of treatment with lithium carbonate should be considered as a cause of mood improvement. Against this thesis are, however, two arguments. Firstly, the therapeutic lithium level which was achieved in the inpatient department was not associated with complete remission of the symptoms. Secondly, in the patient's opinion the implementation of CPAP caused an immediate improvement of cognitive function and drive. This change also made him optimistic about therapeutic possibilities, and thus, caused further mood improvement.

Discussion

This case report points to the frequent clinical problem – drug resistance and persistence of depressive episodes in bipolar disorder. The willingness to help the patient in his suffering results in attempts to use drugs that have proven antidepressant

efficacy in recurrent depression or schizophrenia, however, are not recommended for the treatment of bipolar depression. Both the Polish [13] and international [14] standards for the treatment of bipolar disorder show a prominent role of effective, optimal treatment with mood stabilizers. The drug level in blood serum should be monitored, appropriately type of drug and dosage should be used, and there should be also good cooperation with the patient. This is not always easy, as shown in the described case. In addition, the patient was treated with various drugs, wherein some of them, for example, ziprasidone, aripiprazole, escitalopram, reboxetine and vortioxetine, have no proven therapeutic efficacy in this diagnosis. The legitimacy of the use of these drugs is indeed not established, but especially regarding to the use of antidepressants, has many advocates among experienced clinicians. Experts of the World Federation of Societies of Biological Psychiatry (WFSBP), in the commentary to the guidelines of 2013, also declared that despite significant progress made in the treatment of bipolar disorder, there is still a lot of uncertainty in terms of prevention of depressive episodes and optimal long-term treatment [14].

The most important issue which we wanted to mention is not the pharmacological aspect, but the multiplicity of aspects of bipolar depression treatment. Psychiatrists often perceive the causes of persistence of depressive symptoms in the incorrect psychiatric treatment or in psychological and environmental factors. Too little attention is devoted to the somatic causes of depressive symptoms. One of the causes may be sleep apnea – disorder, which is most often overlooked in the differential diagnosis of depression, and which, because of the frequent occurrence in the population of mentally ill patients and many negative health consequences, should be always taken into account [4].

The third important aspect are problems and risks associated with conducting ECT treatment in the population of mentally ill patients with concomitant OSA. Although there is no data on the prevalence of obstructive sleep apnea among patients treated with ECT, it can be assumed that it is not lower than in the general population. OSA is a condition that requires the involvement of doctors of various specialties, both in terms of diagnostics, health consequences, possible complications, and the methods of treatment. Notwithstanding their severity, the symptoms and complications that are caused by OSA are often underestimated. Obstructive sleep apnea is one of the most important risk factors for severe respiratory problems during anesthesia. According to the guidelines of the American Society of Anesthesiologists [15], the preparation of a patient suffering from OSA to surgery under general anesthesia is associated with a need for increased monitoring in the periprocedural period, the need for intubation due to difficulties in conducting mechanical ventilation with the use of oropharyngeal tube, extubation in semi-sitting position carried out only after the patient wakes up, leaving the patient during the postoperative period in semi-sitting position with the possibility of monitoring. The anesthetic team should also be prepared for the pos-

sibility of difficulties in intubation [16, 17] resulting, in individual cases, even in the use of the tracheostomy tube [15].

In order to assess the risks of anesthesia associated with OSA, the Society of Anesthesiologists has recommended the routine evaluation of each patient before anesthesia with the STOP-BANG scale (Figure 1). Score of 3 or more points on a STOP-BANG scale is a risk factor for difficult intubation [16]. In the group of patients who achieved at least 6 points on a STOP-BANG scale life-threatening respiratory complications resulting in hospitalization in the intensive care unit occurred twice as often as in patients whose risk was rated for 2 or fewer points in this scale [18]. The score of more than 5 points in this scale is correlated with a fivefold increase in the risk of periprocedural complications such as hypoxia, failed intubation, fractures of the teeth, laryngospasm, bronchospasm, cardiac arrhythmia, increase in blood pressure [17].

In the described patient, 6 risk factors for respiratory complications in the perioperative period (STOP-BANG – 6 points) were present. The inability of effective ventilation with oropharyngeal tube, difficult intubation, hypoxia and increase in blood pressure that occurred during ECT session and were the reason for the discontinuation of the following treatments indicate the importance of screening for OSA in the group of patients referred to ECT [19, 20].

The comorbidity of mental illness and such a severe a respiratory disorder explains why the modification of the treatment of bipolar disorder was not sufficiently effective in the case of the described patient. The use of continuous positive airway pressure (CPAP) for a period of 1–2 weeks prior to ECT can reduce the risk of respiratory complications immediately after the session. [15, 19].

The data collected from the literature indicate the need for caution when initiating the therapy with CPAP in patients with bipolar disorder. There have been described the cases of mania induced by treatment with CPAP, which also concerned the patients in stable mental states treated continuously with mood stabilizers [21]. This is probably due to the rapid normalization of sleep architecture with a significant increase in REM sleep (REM sleep rebound), leading to a change in the balance between monoaminergic and cholinergic systems in the brain.

Conclusions

We have noted the important issue for patients with depressive symptoms – excessive daytime sleepiness unremitting despite treatment modification. Sleepiness is often interpreted as a lack of motivation to treatment, or a resistance to change. Of course, one must consider all the possible causes of the symptom and, as shown in the above-mentioned case, in practice the patients' problems are often dependent upon various factors. What is needed before an unequivocal classification of the symptoms is the consideration of all possible causes – the somatic ones as well.

Screening for the obstructive sleep apnea is not difficult. The scales described in the article can be used in the course of a few minutes examination of the patient. Diagnostic devices for OSA screening are also becoming more accessible.

Further diagnostics probably spared the described patient further modifications of treatment and prolonged hospitalization. In addition to the postulated negative effects of breathing disorders during sleep caused by bipolar disorder, sleep apnea can also cause significant cognitive impairment (attention and vigilance, semantic and visual long-term memory, visual-spatial and executive functions) [16]. It is important to note that the patient complained of some of these symptoms, which were explained as a result of bipolar disorder (perhaps that was partly right considering that in many patients with bipolar disorder without OSA, cognitive dysfunction is resistant to pharmacological treatment). In this case, the respiratory disorders during ECT and prolonged disturbance of consciousness after ECT were also observed (short-term disturbances of consciousness occur frequently after ECT and are not regarded as a complication). Sleep apnea significantly increases the risk of such complications. The patients with sleep apnea must be particularly carefully monitored for any respiratory impairment during and after general anesthesia.

Although the available data indicate that initiation of the treatment for obstructive sleep apnea with CPAP leads to a rapid resolution of excessive daytime sleepiness and improvement in cognitive functioning, it is important to note that in some patients an effective treatment period must last at least several months until some improvement is observed [22]. During this period, the patient should be motivated not to become prematurely discouraged to therapy. The data from the literature confirm that the implementation of CPAP therapy may cause a reduction of depressive symptoms and the improvement of quality of life [23, 24].

It is worth noting that the mentally ill people are interested in the treatment of obstructive sleep apnea and cooperate in the therapy, as the patient described in this article. Among patients with schizophrenia, who are often considered as a group of patients with the highest risk of possible non-cooperation, as many as 71% of patients showed an interest in performing a study assessing breathing during sleep [25], which, of course, does not necessarily mean complying with all of the recommendations.

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