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Sleep disorders in cancer patients during systemic therapy

Zaburzenia snu u pacjentów z chorobą nowotworową w trakcie leczenia systemowego


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Abstract

Aim: The aim of this study was to investigate the frequency, quantity and quality of subjective sleep problems, and their correlation with accompanying factors in cancer patients undergoing systemic therapy. **Materials and methods:** The study included 100 patients – 50 females and 50 males – undergoing oncological treatment who filled out an anonymous questionnaire specifically designed for this research. **Results:** 88% of the respondents reported the duration of sleep in the range of 5 to 9 hours. 48% of the respondents declared a deterioration in the quality of sleep after the diagnosis of cancer. Following the onset of sleep problems, 66% of respondents did not pursue any treatment. Among the examined patients, symptoms of insomnia were reported by 18%, and symptoms of hypersomnia – by 6%. Mixed sleep disorders were reported by 11% of respondents. The patients undergoing surgical treatment reported a statistically significantly lower quality of sleep compared to the patients not undergoing surgery (median score in the quantitative scale 6 vs. 7 on a scale of 1–10, where 1 indicated the worst quality of sleep and 10 indicated the best quality of sleep; $p = 0.04$). A very small percentage of patients sought pharmacotherapy or specialist help for sleep disorders, which precludes drawing statistically significant conclusions about the impact of these interventions on sleep quality. **Conclusions:** Sleep problems are often reported by patients during oncological treatment (48%). The main sleep-related complaints were advanced sleep phase disorders. Due to the frequent occurrence of sleep disorders among patients, it is important to conduct a thorough medical interview to diagnose them and implement appropriate treatment.

Keywords: sleep disorders, cancer, insomnia

Streszczenie

Cel: Celem pracy było zbadanie częstości występowania oraz specyfiki zaburzeń snu i czynników towarzyszących u pacjentów onkologicznych w trakcie leczenia systemowego. **Materiał i metody:** Do badania zostało włączonych 100 pacjentów – 50 kobiet i 50 mężczyzn w trakcie leczenia onkologicznego, którzy wypełnili anonimową ankietę. **Wyniki:** 88% respondentów deklarowało długość snu w przedziale 5–9 godzin. 48% respondentów relacjonowało pogorszenie jakości snu po rozpoznaniu choroby nowotworowej. Po pojawieniu się problemów ze snem 66% respondentów nie stosowało żadnego leczenia. 18% badanych pacjentów zgłaszało objawy bezsenności, objawy opóźnionej fazy snu, 6% – objawy hipersomnii; 11% ankietowanych zaznaczyło kilka odpowiedzi, wskazując na występowanie mieszanych zaburzeń snu. Pacjenci poddani leczeniu chirurgicznemu zgłaszali statystycznie istotnie niższą jakość snu w porównaniu z pacjentami niepoddanymi leczeniu chirurgicznemu (mediana ocen 6 vs 7 w skali ilościowej 1–10, gdzie 1 oznacza najgorszą, a 10 – najlepszą jakość snu; $p = 0,04$). Niewielki odsetek pacjentów szukał pomocy w postaci farmakoterapii lub konsultacji specjalistycznych w zakresie zaburzeń snu, co uniemożliwia wyciągnięcie statystycznie istotnych wniosków dotyczących wpływu tych interwencji na jakość snu. **Wnioski:** Zaburzenia snu są częstym problemem zgłaszanym przez pacjentów w trakcie leczenia onkologicznego (48%). Najczęstszymi zaburzeniami wskazywanymi przez chorych były zaburzenia o charakterze przyspieszonej fazy snu. Ze względu na częste występowanie zaburzeń snu u pacjentów istotne jest odpowiednie przeprowadzenie wywiadu lekarskiego w celu ich zdiagnozowania i wdrożenia odpowiedniego leczenia.

Słowa kluczowe: zaburzenia snu, nowotwory, bezsenność

INTRODUCTION

Sleep is an essential functional state in human physiology. It consists of a complex set of physiological and behavioural processes. Disruptions of these processes can lead to problems with sleep induction and, consequently, a deterioration in the quality of life. It has been shown that sleep disorders, which are essential for regeneration, negatively impact the immune system and are associated with an increased risk of cancer recurrence, cognitive decline, worsened wound healing, social dysfunction, the risk of drug abuse, and increased healthcare costs (Khemiri et al., 2019; Miladinia et al., 2018).

Sleep disorders during oncological treatment are among the disorders most frequently reported by patients. In the conducted study, sleep disorders during oncological treatment were examined with a focus on advanced sleep phase syndrome and delayed sleep phase syndrome. They affect 30–75% of patients, and according to some sources, insomnia is the most common symptom reported by patients during systemic treatment, affecting 59% of patients (Ancoli-Israel et al., 2001; Berger et al., 2005; Grond et al., 1994; Mogavero et al., 2021). Sleep disorders, apart from pain and weakness, are important factors influencing the well-being and general condition of patients.

Despite the growing interest in sleep disorders, there is still a lack of reliable data on the incidence of these disorders in cancer patients and the impact of the therapy used. Additionally, the issue is often overlooked by physicians, who rarely inquire about the quality of sleep in their patients. The aim of this study was to investigate the frequency of subjective sleep disorders and to find potential correlations between sleep problems and accompanying factors in cancer patients. A fuller understanding of the issue of sleep disorders in the group of cancer patients and the methods of counteracting these ailments may prove helpful in cancer therapy. Further research using validated tools and objective sleep quality assessments, such as actigraphy and polysomnography, is necessary.

MATERIALS AND METHODS

The study included 100 patients ($N = 100$; 50 females and 50 males) undergoing oncological treatment in the Clinical Oncology Department from January to June 2021, who agreed to fill in an anonymous questionnaire consisting of 17 questions. Of the 100 patients studied, 60% received combination therapy; postoperative treatment was used in 27%, and treatment for recurrence or dissemination was used in 34%. Out of all the questions, 4 related to patient demographic data (age, education, place of residence, marital status), 5 – clinical data (location of neoplastic lesions, method and duration of treatment), 4 – sleep quality parameters [sleep duration in hours per day, subjective assessment of sleep quality on a scale from 1 to 10 (where 1 indicates the poorest sleep quality and 10 indicates the

Variable	Result
Age	60.1
Gender	Females – 50% Males – 50%
Education	Primary – 6% Secondary – 30% Vocational – 32% Higher – 32%
Place of residence	City – 75% Village – 25%
Marital status	In a relationship – 78% Single – 22%
Diagnosis	Gastrointestinal neoplasms – 63.0% Neoplasms of the genitourinary system – 7.0% Central nervous system neoplasms – 4.0% Lung cancer – 9.0% Head and neck tumours – 9.0% Other – 8.0%
Treatment method	Surgical treatment – 46 people, 46.0% Radiotherapy – 17 people, 17.0% Chemotherapy – 97 people, 97.0% Immunotherapy – 2 people, 2.0% Hormonotherapy – 3 people, 3.0%

Tab. 1. Study participant demographics

best sleep quality), type of recorded sleep disorder, and impact of cancer diagnosis and treatment on sleep quality], 4 – sources of learning about sleep disorders, and how to deal with existing ailments (specialist consultations, pharmacotherapy). The questions comprised an exploratory set specifically designed for this study. Details of the questionnaire are included in the Supplementary Material. Tab. 1 presents the demographic data of the study participants.

The Mann–Whitney U test for comparing two groups or the Kruskal–Wallis ANOVA test for multigroup comparisons was used to compare the quantitative variables describing sleep quality. The relationships between the quantitative variables were analysed using the Spearman's rank correlation coefficient. The analysis was performed using the STATISTICA 13 software (TIBCO software). The $p < 0.05$ values were considered significant.

RESULTS

The median sleep quality satisfaction on a scale from 1 to 10 was 6.5 ($M = 6.5$, $SD = 2.34$, interquartile range, IQR = 4–8, $N = 100$). The median duration of sleep ranged from 5 to 6 hours per day, with most respondents declaring a sleep duration in the range of 5 to 9 hours.

48% of the respondents reported a deterioration in satisfaction with sleep quality after the diagnosis of cancer, while in 45% of the cases, the quality of sleep did not change, and 7% of the respondents declared an improvement in the quality of sleep.

In the case of deterioration in satisfaction with sleep quality, 15 (15%) respondents talked to a doctor about their sleep disorders, and 6 (6%) respondents benefited from the help of a specialist (neurologist, psychiatrist, psychologist or

Pair of correlated variables	N	R	p
Age and sleep quality assessment	100	-0.02	0.86
Age and mean declared sleep time		0.20	0.04
Age and subjective change in sleep quality after cancer detection		-0.30	0.00
Treatment time and sleep quality assessment		-0.05	0.59
Treatment time and mean declared sleep time		0.06	0.55
Treatment time and subjective change in sleep quality after cancer detection		0.05	0.59

Tab. 2. Correlations between age and treatment duration and sleep quality among the respondents (Spearman's R correlation)

		Number of study participants	Median (treatment duration in months)	Q1	Q3	p
Have you consulted a sleep disorder specialist?	No	94	5.0	2.0	8.0	0.199
	Yes	6	8.0	4.0	12.0	
Have you discussed your sleep problems with your oncologist or radiotherapist?	No	85	5.0	2.0	8.0	0.702
	Yes	15	4.0	3.0	10.0	
Have you been looking for information on sleep problems during cancer on the Internet?	No	88	4.0	2.0	8.0	0.111
	Yes	12	6,5	4.5	15.5	
What methods do you use in case of sleep problems?	Drugs	19	4.0	2.0	8.0	0.480*

Tab. 3. Relationships between treatment duration and patient behaviour related to sleep disorders (U – Mann-Whitney test, * Kruskal-Wallis ANOVA)

		n	Median (sleep quality assessment)	Q1	Q3	p
Surgical treatment	No	54	7.00	5.00	8.00	0.04
	Yes	46	6.00	4.00	8.00	
Radiotherapy	No	83	6.00	4.00	8.00	0.34
	Yes	17	7.00	6.00	8.00	
Chemotherapy	No	97	7.00	4.00	8.00	0.44
	Yes	3	5.00	4.00	7.00	
Immunotherapy	No	98	6,50	4.00	8.00	0.97
	Yes	2	6,50	6.00	7.00	
Hormonotherapy	No	97	7.00	4.00	8.00	0.19
	Yes	3	5.00	4.00	5.00	

Tab. 4. Relationship between sleep quality and applied therapy (U – Mann-Whitney test)

		n	Median (sleep quality assessment)	Q1	Q3	p
Have you consulted a sleep disorder specialist?	No	94	6,50	5.00	8.00	0.30
	Yes	6	5.00	1.00	8.00	
Have you discussed your sleep problems with your oncologist or radiotherapist?	No	85	7.00	5.00	8.00	0.01
	Yes	15	5.00	3.00	6.00	
Have you been looking for information on sleep problems during cancer on the Internet?	No	88	7.00	4,50	8.00	0.47
	Yes	12	6.00	3,50	8.00	
What methods do you use in case of sleep problems?	Drugs	19	5.00	3.00	6.00	0.01
	Herbs	9	7.00	4.00	8.00	
	None	66	7.00	5.00	8.00	
	Other	4	4.00	2,50	6.00	

Tab. 5. Relationship between patients' behaviour related to sleep quality disorders and its quality (U – Mann-Whitney test)

psycho-oncologist). The Internet was the source of information on sleep disorders in 12 respondents (12%).

After diagnosing sleep problems, 66% of respondents did not use any treatment methods, 19% indicated pharmacological methods, 9% herbal medicine, and 4% – other methods. Two people incorrectly answered the question about coping with sleep disorders.

Among the examined patients, symptoms of early sleep phase disorder were reported by 26%, symptoms of insomnia – 18%, symptoms of delayed sleep phase disorder – 18%, hypersomnia – 6%; mixed sleep disorders were

shown by 11% of respondents. Mixed sleep disorders were classified if a patient reported at least two types of sleep disorders.

Tab. 2 shows the correlation between the age of patients and the studied quantitative variables. There was a significant positive correlation between the age and sleep duration of the respondents ($R = 0.20$; $p = 0.04$), and a negative correlation between age and the change in sleep quality associated with cancer ($R = -0.30$; $p = 0.00$).

No statistically significant differences in patients' behaviour related to the duration of oncological treatment were observed (Tab. 3).

Surgical patients reported a statistically significantly lower quality of sleep compared to non-surgical patients (median scores 6 vs. 7; $p = 0.04$). There were no such differences with other treatments (Tab. 4).

		<i>n</i>	Median (sleep duration in hours)	Q1	Q3	<i>p</i>
Have you consulted a sleep disorder specialist?	No	94	5–6	2.00	3.00	0.44
	Yes	6	5–6	1.00	3.00	
Have you discussed your sleep problems with your oncologist or radiotherapist?	No	85	5–6	2.00	3.00	0.21
	Yes	15	5–6	1.00	3.00	
Have you been looking for information on sleep problems during cancer on the Internet?	No	88	5–6	2.00	3.00	0.77
	Yes	12	5–6	2.00	3.00	
What methods do you use in case of sleep problems?	Drugs	19	5–6	1.00	2.00	0.15
	Herbs	9	5–6	2.00	3.00	
	None	66	5–6	2.00	3.00	
	Other	4	5–6	1.50	3.00	

Q1, Q3 – first and third quartiles.

Tab. 6. Relationship between patients' behaviour related to sleep problems and sleep duration

Patients who used pharmacotherapy for sleep disorders and patients who sought specialist help had a statistically significantly lower assessment of their sleep quality (Tab. 5). No statistically significant impact of patient interventions in the event of sleep disorders on sleep duration was observed (Tab. 6).

There was a statistically significant positive correlation between sleep duration and sleep quality ($R = 0.51$; $p = 0.00$).

DISCUSSION

Current views on the aetiology and pathogenesis of sleep disorders indicate the interdependence of various biological factors – related to the disease and its course, psychogenic, as well as environmental and professional (Pysz-Waberski et al., 2020).

After the diagnosis of cancer, patients experience fear related to the diagnosis, and depressed mood or depression, which may predispose them to sleep disorders. Later, additional factors that can trigger insomnia arise, including physical symptoms associated with the disease or side effects of the therapy. Poor quality of sleep in cancer patients is a risk factor for fatigue during therapy and reduced functional performance (Fox et al., 2020; Papadopoulos et al., 2019). Greater mental strain causes sleep disorders, such as insomnia and obstructive sleep apnoea, and contributes to increased fatigue in patients undergoing systemic therapy. These sleep disorders can lead to other side effects, which may result in a deterioration in the quality of life of patients and negatively affect the outcomes of the treatment itself.

The incidence of sleep disorders in cancer patients varies widely, from 24% to even 95% (Al Maqbali et al., 2022; Davidson et al., 2002; Sarna, 1993). However, researchers agree that the above disorders are more common in the population of cancer patients than in the general population, and cancer is an independent risk factor for sleep disorders. Independent analyses also indicate that individuals who have completed effective radical cancer treatment experience severe sleep disorders even for many years after the end of therapy (Clevenger et al., 2013; Fortner et al., 2002; Gonzalez and Lu, 2018).

The prevalence of sleep disorders in the Polish population is estimated at approximately 50% according to Nowicki et al. (2016). Their study, covering 2,413 adults (1,245 women and 1,168 men aged 18–79 years), was part of the national NATPOL cardiovascular disease risk factor research programme. In the study population, difficulties with falling asleep were most often indicated (60.2%), and age and gender had an influence on the frequency of sleep disorders (the incidence of disorders increased with age, and women reported problems with falling asleep more often than men). In other studies (Szelenberger and Skalski, 1999) concerning sleep disorders, problems with falling asleep concerned 24% of respondents. Other sleep disorders were related to difficulties in maintaining sleep (29% of respondents), premature waking up in the morning (24%), and non-restful sleep (27%) (Kiejna et al., 2003; Szelenberger and Skalski, 1999). Patients experiencing sleep disorders during oncological treatment were not specifically identified in these studies.

In our study, as many as 81% of patients reported sleep disorders. This finding, although high, is consistent with previous reports. Other studies assessing sleep quality in cancer patients showed a reduction in sleep quality in 52% of adult lung cancer patients, 34% of patients diagnosed with malignant neoplasm, and 51% of patients with a 5-year survival after the diagnosis of breast or prostate cancer (Papadopoulos et al., 2019; Slade et al., 2020; Strollo et al., 2020). The literature has repeatedly described the deterioration of sleep quality in patients after cancer diagnosis, and a negative impact of anticancer therapy on the quality of sleep. Belloumi et al. (2020) compared sleep quality in patients with lung cancer before and after systemic treatment, observing a decrease in sleep quality in over 30% of subjects. Tuyan İlhan et al. (2017) described the influence of selected treatment methods (surgery, chemotherapy, and radiotherapy) on the quality of sleep in patients with endometrial cancer, and found that the incidence of poor-quality sleep increased from 28% to 79% after oncological treatment. The above observations are consistent with the results of the present study, in which as many as 48% of patients reported a reduction in the quality of sleep after cancer

diagnosis and treatment. Poorer quality of sleep after oncological treatment is associated with both side effects of the therapy itself and with additionally triggered stress – related to doubts as to the effectiveness of the therapy, uncertain future, and side effects of treatment.

Although most analyses show a decrease in the quality of sleep in patients during systemic treatment of cancer, it is possible to counteract the decrease in sleep quality. These methods of improving sleep should be an integral part of supportive care in cancer therapy.

However, only about 30% of those suffering from insomnia consult a doctor about the problem (Dudzińska et al., 2015), and in our population this percentage was much lower (15%). The results of our analysis are consistent with the previous reports – the majority of patients (66%), despite the occurrence of sleep disorders, do not use any methods of improving the quality of sleep. According to the available literature, the most commonly employed method of treating sleep disorders is the use of hypnotic drugs (sleeping pills). In the study by Strollo et al. (2020), 28% of patients used pharmacological methods, and in the study by Paltiel et al. (2004), 25.7% took sleeping pills. Moore reports that as many as 46% of breast cancer patients benefited from pharmacological methods of treating sleep disorders (Moore et al., 2011). The above observations show that the use of sleeping pills is less frequent – only 19% of patients used them, and the second most common type of intervention aimed at improving the quality of sleep was based on medicinal herbs (9%), followed by other methods (4%).

According to experts, non-pharmacological methods that increase sleep hygiene, based on relaxation and visualisation techniques and psychotherapy, without which pharmacological treatment is unlikely to be successful, are also extremely important in the management of insomnia (Moore et al., 2011).

In their randomised study, Zengin and Aylaz (2019) demonstrated a significant improvement in the quality of sleep of patients during chemotherapy by introducing the principles of sleep hygiene and reflexology, which resulted in a lower level of fatigue with therapy. An et al. (2020), in a study of 301 patients undergoing chemotherapy for breast cancer, demonstrated significant effectiveness of aerobic and passive resistance exercise in improving sleep quality, reducing therapy fatigue, and enhancing treatment outcomes. In our population, only 4% of respondents used non-pharmacological relaxation techniques, sleep hygiene rules, and physical activity to improve sleep quality. For this reason, there is a need to educate patients on the principles of proper sleep hygiene and non-pharmacological treatment methods, and if they prove ineffective – on the need to implement pharmacotherapy.

Consistent with the reports of other authors, our study revealed a positive correlation between sleep duration and the age of respondents. Sleep duration in the general population shows a decline with age (Li et al., 2018). The Pittsburgh Sleep Quality Index (PSQI) is a commonly accepted questionnaire for determining sleep quality (Buysse et al., 1989). However, researchers dealing with specific subgroups of patients, such as those with malignant neoplasms, point to its lack of objectivity (Chen et al., 2015; Fujisawa et al., 2019; Parker et al., 2008). Therefore, in the present study, the authors used an original research questionnaire, which was prepared with a view to optimising mental and somatic observations related to sleep induction, quality and quantity in the population of oncological patients. Another reason for using an original non-validated questionnaire was the fact that it was specifically prepared for patients undergoing systemic therapy and included the impact of cancer treatment on sleep quality.

In the literature, there are studies assessing the sleep quality of patients depending on the location and type of cancer. The groups of oncological patients distinguished by the researchers as different from the rest of the population of oncological patients include people in advanced stages of cancer, patients with severe negative symptoms, and patients after completed oncological treatment (Khemiri et al., 2019; Miladinia et al., 2018; Musarezaie et al., 2014; Silberfarb et al., 1993). In this study, patients who underwent surgical procedures during their therapy were a distinguished group. They assessed their sleep quality as statistically lower compared to other patients.

CONCLUSIONS

Sleep disorders are a common problem among patients during oncological treatment, but patients rarely report these symptoms and seek specialist help. Unfortunately, they also occasionally engage in behaviours that worsen sleep quality. The most commonly reported disorder by patients was early sleep phase disorder. Improving the quality of sleep can be achieved by improving the awareness of patients and collaborating within a multidisciplinary team.

Conflict of interest

Authors declare no conflict of interest.

Author contribution

Original concept of study: DPW. Collection, recording and/or compilation of data: DPW. Analysis and interpretation of data: DPW, JW, ŁP. Writing of manuscript: DPW, JW, ŁP, OW. Critical review of manuscript: DPW, OW. Final approval of manuscript: DPW.

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