ORIGINAL RESEARCH

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Sleep Quality of Cancer Patients Receiving Systemic Treatment: A Cross-Sectional Study

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ABSTRACT Objective: The present research was designed with the aim to detect insomnia in cancer patients and to determine the factors responsible for the development of insomnia through patient information and to provide suggestions for any contribution. **Material and Methods:** The cross-sectional study was conducted on 264 patients including 132 females and 132 males who attended the Outpatient Therapy Unit of Medical Oncology Department of Medical Faculty Hospital within Ankara University and accepted to take part in the research. The questionnaire prepared by the researchers was implemented through personal interview technique and information was collected from the patient files. The questionnaire form includes demographic information, Pittsburgh Sleep Quality Index (PSQI), and Beck's Depression Inventory. **Results:** Higher prevalence of insomnia was detected in cancer patients (54.4%). Depression negatively affects the sleep quality and the problem of insomnia in the patients, who were diagnosed with depression before, was remarkable. Furthermore, the female participants were more prone to develop insomnia and depression (61.36%, 25.76%, respectively). The sleep duration was found to be affected positively in patients receiving cisplatin containing regimens (p=0.029) whereas those receiving other platin group drugs were affected negatively (p=0.017). The use of pyrimidine and folic acid group drugs positively affected sleep quality (p=0.031). **Conclusion:** It can be said that sleeping and mental problems of the patients visiting the oncology clinics should be monitored and cared closely.

Keywords: Cancer; insomnia; sleep disorders; depression; psycho-oncology

An increase in the complexity of the cancer therapeutics may lead to the development of various functional problems among the patients. Novel surgical procedures developed to protect organ function employ minimally invasive procedures. However, complex therapies including radiotherapy and chemotherapy are often provided to the patients. Multidisciplinary treatment approaches in cancer patients affect a number of functional fields including physical, psychosocial, and economic areas.[1]

The primary objective of cancer therapeutics in palliative settings for metastatic patients is to enhance the quality of life of the patients. Rehabilitation interventions help to combat with the morbidities encountered in patients due to cancer therapy and to increase the functional state.[1]

Sleep is a reversible and active regeneration process. It is a state of immobility enabling both the mind and body to rest.[2] Sleep is one of the essential activities influencing the quality of life and health of the individuals. Sleep comprises of physiological, psychological, and social components.[3] One of the basic and vital needs of humans for health and enriched quality of life is sleep.[4] A secondary cancer prevention study conducted by the American Cancer Society investigated the sleep duration and death hazard of the participants. The most ideal sleep duration for health was considered to be 7 h, as reported in this study.[5]

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The present research was designed with the objective to study the prevalence of insomnia among cancer patients and to determine the factors responsible for the onset of insomnia through information gathered from patients and to develop suggestions for any contribution.

MATERIAL AND METHODS

The present cross-sectional study was designed to determine sleeping problems and associated factors in cancer patients attending the Outpatient Therapy Unit of Medical Oncology Department of Medical Faculty Hospitals in Ankara University. The present research was conducted among Outpatient Therapy Units of Medical Oncology Departments within Cebeci Hospital and Ibni Sina Hospital of Ankara University, Faculty of Medicine. The study was conducted between January and May 2016 by screening 264 randomly selected patients out of 1500 cancer patients receiving systemic treatment, the inclusion criteria being age above 18 years and patients who gave consent by signing the Informed Consent Form.

The following forms and scales were implemented to the patients creating the sample during the therapy session.

The Questionnaire Form: The questionnaire form signed by the researchers comprised of 22 questions investigating demographic data, comorbid diseases, travel history, use of drugs such as sleeping drugs/antidepressant agents as well as history and behaviors of insomnia.

The Information Form to be obtained from the Patient Files: This form was filled in by the researchers based on the information obtained from the patient files. Questions pertaining to the type of cancer, stage of cancer, existence of metastasis, treatment type received, therapeutic regimen prescribed, existence of surgical treatment, existence of radiotherapy, and time of diagnosis which were considered relevant to sleep quality, were extracted from the patient files.

Pittsburgh Sleep Quality Index (PSQI): It was developed by Bussy et al. in 1989.[6] Although a number of insomnia inventories are available in the literature, the aforesaid is one of two valid and reliable scales.[6-9] The scale consisted of 24 questions including 19 self-notification questions. The response of the other 5 questions was provided by the spouse or roommate. Such 5 questions were used for clinical information only; the last self-notification question was related to having a roommate or spouse and was excluded from the scoring system.

The scale comprised of 18 questions for scoring. The scale consisted of 7 components reflecting subjective sleep quality, sleep latency, sleep duration, adopted sleep activity, sleeping disorders, use of sleeping pills and day functions.[10] Some of the components were indicated by a single question and others were obtained by grouping several questions. Each component was evaluated over 0 to 3 points. Scoring was done as follows: 0 if none during last month; 1 if less than once a week; 2 if once or twice a week; 3 if three times or more in a week.[11] Summation of the scores of the 7 components demonstrated the total scale score and the range varied between 0 and 21. Bad sleep quality was indicated by a total score greater than 5. Diagnostic sensitivity was 89.6% and specificity was 86.5%.[12,13] The validity and reliability study of PSQI specific to Turkey was performed by Agargun et al. in 1996.[14]

Beck's Depression Inventory: Beck's depression inventory (BDI) was developed in 1961 by Beck et al. to measure the severity of Depression and to monitor the treatment efficiency in adolescents and adults.[15] The behaviors and symptoms induced by depression were defined with different expressions on the scale. The patients were asked to identify the expression which defined their situations best within last week including today.[16] The questionnaire included twenty-one items. Each question was scored between 0 and 3, according to the severity. The total score was interpreted as follows: 0-9=Minimal; 10-16=Mild; 17-29=Moderate; 30-63=Severe.[17] The score ranged between 0 and 63. The reliability study of the scale in Turkish was performed by Tegin in 1980; and the validity study was conducted by Hisli in 1989.[18-20] The advantages of BDI were being filled in by the patient, having a simple language and easy scoring.[21] In the validity and reliability study conducted by Hisli (1989), the cut-off point was determined as 17; the BDI scores at and over 17 were reported to differentiate a depression which required treatment by an accuracy rate of 90%.[10,11,17,19-21]

The questionnaire was implemented to the participants older than 18 years of age through personal interview method during their therapy sessions in the outpatient therapy unit. The duration of the questionnaire took about 25 minutes. The participants were informed that the information would be kept confidential and used for scientific purposes only. Each participant signed the Informed Consent Form. All procedures complied with the Helsinki Declaration.

The ethical approval (No: 72189195-050.03.04/E.674) was obtained from the Ethical Committee of Pre-Graduate Student Research in the Medical Faculty of Ankara University on January 5, 2016.

DATA EVALUATION

The data obtained were analyzed statistically through SPSS (Statistical Package for the Social Sciences) software for Windows 11.5 package program. Chi-Square test, Fisher's Exact test, Student's t-test, Mann-Whitney test, and one Way Variance Analysis were used for evaluation. Categorical data frequency and percentage were referred to as descriptive data whereas arithmetic average ±standard deviation (SD) was used for quantitative data. The statistical significance level was accepted as 0.05.

RESULTS

The present cross-sectional study comprised 264 randomly selected patients including 132 (50%) females and 132 (50%) males who were referred to the Outpatient Therapy Unit of Medical Oncology Department Ankara University Faculty of Medicine and consented to participate in the study. The demographic characteristics of the patients were represented in Table 1. A significantly higher PSQI (p=0.008) and Beck's Depression scores (p=0.017) of the female participants were revealed during the gender-based estimation. The rate of bad sleep quality was 61.36% for the female subjects, whereas 47.72% for the male participants (Figure 1).

The age of the participants ranged from 19 years to 88 years. The average age of the study population was 57.3 years. However, no significant association was observed between age and insomnia (p>0.05).

TABLE 1: Demographic characteristics of patients attending to work.

	Number of pts	%
Gender		
Male	132	50,0
Female	132	50,0
Education		
Literate	74	28,0
Primary School	80	30,3
Secondary School	65	24,6
High School	42	15,9
University	3	1,1
Marital Status		
Single	47	17,8
Married	217	82,2
Residing		
Ankara	184	69,7
Out of Ankara	80	30,3

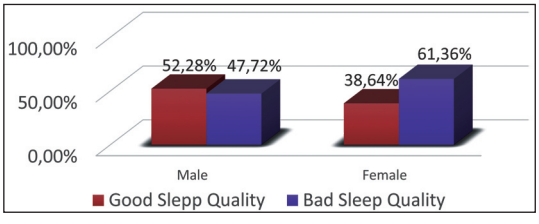

FIGURE 1: Gender-sleep quality relationship.

Insomnia was reported by 54.5% of the participants. The average (±SD) PSQI score was found to be $\overline{\chi}$±SD=5.70±3.81. During the study duration, twenty (7.6%) patients used sedatives. A significant association was determined between the consumption of sedatives and bad sleep (p=0.017). Furthermore, the history of insomnia was recorded among at least one family member of 24 (9.1%) participants. According to the study outcomes, a significant correlation was detected between bad sleeping experience and family history of insomnia (p=0.011). Insomnia was detected before the onset of cancer in 39 (14.8%) patients. The statistical evaluation also portrayed a significant relationship between the previous history of insomnia and bad sleeping conditions during the treatment period (p=0.002) (Table 2).

Chronic comorbid diseases were documented among 182 (68.9%) out of 264 participating patients. Hypertension (27.7%), diabetes (21.2%), Chronic

TABLE 2: Distribution of answers regarding the sleep habits of patients.

Questions		n	(%)
Do you use sedative?	Yes	20	7,6
	No	244	92,4
Does any one have a sleeping disorder in the family?	Yes	24	9,1
	No	240	90,9
Was there any insomnia problem before your illness?	Yes	39	14,8
	No	225	85,2
Have you ever been diagnosed with depression?	Yes	39	14,8
	No	225	85,2
Have you used antidepressants before?	Yes	45	17,0
	No	219	83,0

Obstructive Pulmonary Disease (COPD 6.4%), heart failure (3.8%), and thyroid diseases (3%) were the commonly observed concomitant chronic disorders among the study population.

Patients suffering from all types of cancer were included in the present study. Cancer types were divided into subgroups for statistical analysis. The cancers were classified as cancers of the gastrointestinal system and oral region (25.8%), respiratory system (24.6%), breast (23.5%), mesothelium (6.1%), genitourinary system (14.4%), and others (5.5%). A significant association was absent between cancer type and PSQI score. No significant association was obtained between cancer type and BECK's depression score ($p>0.05$).

The study population was treated with a number of therapy protocols. The therapies were, therefore, divided into 6 subgroups as immunotherapy only (6.1%), chemotherapy only (61.7%), immunotherapy and radiotherapy (3%), immunotherapy and chemotherapy (6.1%), radiotherapy and chemotherapy (22.3%), and triple treatment (0.8%) (Table 3).

TABLE 3: Distribution of treatment types.

	n	(%)
Chemotherapy	163	61,7
Immunotherapy	16	6,1
Chemotherapy + Immunotherapy	16	6,1
Immunotherapy + Radiotherapy	8	3
Chemotherapy + Radiotherapy	59	22,3
Chemotherapy + Immunotherapy + Radiotherapy	2	0,8

The study subjects were not selected based on the type of medication administrated. A wide range of drugs are used in oncology and they are often prescribed by the physicians in different combinations. The participants were classified based on these combinations. The medications were grouped in 6 categories in terms of their main toxicities as follows: cisplatin (26.1%), taxanes+vinca alkaloids (31.8%), etoposide+topoisomerase I inhibitors+adriamycin (16.3%), other platinum+alkylating agents (33.3%), purine/pyrimidine antagonists (antimetabolites) (33.7%), zoledronate+monoclonal antibodies (20.5%). It was observed that the patients receiving cisplatin slept more than other patients; a significant and positive correlation was detected with a sleeping duration which is one of PSQI subtypes (Figure 2). A significant and negative association was obtained between the platin group and the others ($p=0.017$). A significant association was also shown in sleep latency between the patients receiving pyrimidine/purine antimetabolites and those not receiving these medications ($p=0.031$).

The patients were grouped as single drug receivers and multiple drug receivers. Insomnia was also found to be significantly related to the number of drugs within the treatment ($p>0.05$).

Depression was previously diagnosed among thirty-nine (14.8) participants. Forty-five (17%) individuals used antidepressants before. The existence of depression during the study period was estimated by Beck's depression scale. As a result, the average Beck's Score was found to be 11.25±7.32. Signifi-

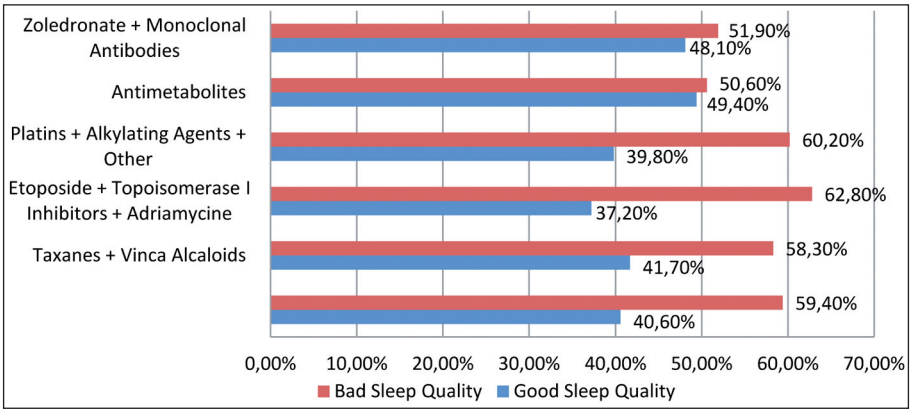

FIGURE 2: Chemotherapy variety-sleep quality relationship.

cantly higher Beck's depression score was recorded among the women participants in the study population (p=0.017). Depression was experienced by 25.76% of female participants and 13.64% of male participants. The overall depression rate was 19.70%.

A statistically significant correlation was evident between depression and all PSQI subtypes as well as total score (p<0.0001). A significant association was also apparent between Pittsburgh Sleep Score and Beck's Depression Score (Pearson's Correlation Coefficient: 0.453; p<0.0001) (Figure 3). Furthermore, a significant relation was perceived between the previous diagnosis of depression and PSQI score (p=0.002). In addition, a significant association was found between previous use of antidepressant agents and bad sleep (p=0.034).

The regression analysis accomplished with the data of the present study revealed a direct association between Beck score and PSQI score.

However, no significant correlation was witnessed between the presence of metastasis treatment period, BMI (Body Mass Index), smoking, alcohol use, tea-coffee intake, number of the children and their ages, day-trip for treatment, and quality of sleep (p>0.05).

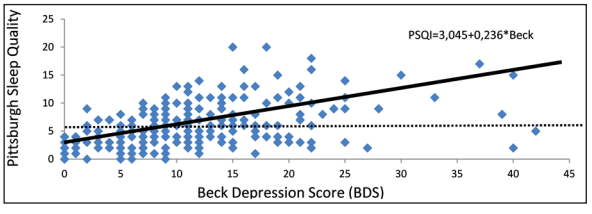

FIGURE 3: PSQS-BDS relationship.

DISCUSSION

Cancer patients are often found to suffer from severe sleeping disorders. Therefore, the present study aimed to highlight the severity and possible causes of a sleeping disorder. Sleeping disorders such as difficulty falling asleep, problems to continue sleeping, ineffective sleep, early awakening, oversleeping during the day, etc. are frequent observations among cancer patients.[13] Insomnia is a common problem in cancer patients.[25,29] Different studies reported the incidence of sleeping disorders affecting 5% to 35% of the overall population whereas such rate was detected between 30% and 50% among the cancer patients.[23,26,27] The present study documented the rate of bad sleep in cancer patients as 54.5%. The higher rate when compared with the population may be explained with the following factors; sleep quality of the cancer patients, biochemical changes caused by neoplastic growth and antineoplastic treatment, pain, exhaustion, and depression.[13]

On a gender-based evaluation, female patients exhibited higher PSQI and Beck's Depression scores with a statistically significant difference. Patients suffering from bad sleep accounted for 61.4% in females and 47.7% in males. No significant association between insomnia and gender was observed in a previous study.[28] This study also stated that pharyngeal and supraglottic airway resistance is more common in men as compared to women. The cause underlying

the sex-based difference in resistance has not been elucidated properly. However, the central pattern of androgenic fat distribution in the body, triggering the effect of masculine hormones as well as the protective effect of feminine hormones are suggested to be the responsible factors.[31] Prevalence of obstructive sleep apnea syndrome was reported to be two-fold more in males at 40 to 65 years of age when compared with females.[30,31] Observations from the present study corroborated that the rate of the patients with bad sleep varied between male and female, however, the cause was not investigated.

It is known that the rate of mortality in cancer patients is enhanced by sleep disorders.[32,33] Despite these adverse consequences, insomnia may be ignored in cancer patients. The present study substantiated a significant association between the use of sleeping drugs and bad sleep. Such an outcome was in accordance with a previous study.[34] Despite the treatment for insomnia, the persistence of sleeping problems in patients may be attributed to insufficient drug doses or types.[35]

A significant association was detected between the experience of bad sleep by the patients already suffering from insomnia and the experience of bad sleep by the patients who had a history of insomnia before the treatment period. Detection of sleeping problems among different family members may be explained by similar sleep hygiene. Furthermore, the possibility of hereditary for sleeping patterns might contribute to such similarity. In-depth research in genetics is essential to analyze such findings.

The present study failed to establish any significant association between cancer type and PSQI. Contrary to this result, a large-scale study detected a significant association between breast cancer and insomnia.[24] Therefore, more comprehensive studies are essential to make a general conclusion. Though the present study portrayed an insignificant association between treatment protocols and sleep quality, however, significant differences were detected between insomnia scores among the patients receiving chemotherapy and the patients receiving single or multiple chemotherapy cycles.[36] Published reports investigating the therapy types and sleep quality were not available in the literature. In the present study, the patients receiving cisplatin group drugs sleep more than the others and PSQI subtypes were found to possess a positive relationship with sleep duration. A negative correlation in terms of sleep latency was observed between the patients taking other platin group drugs and those not consuming such medications. A negative relation also existed in terms of sleep latency between patients using antimetabolites and those not using antimetabolites.

Adverse effects induced by various antineoplastic agents used in cancer therapy may be responsible for the significant association between treatment types and PSQI scores. Sleep quality may also be affected by adverse events such as nausea, vomiting, exhaustion, tiredness, infection, constipation, anemia, sexual dysfunction, pain, etc. Furthermore, antiemetic agents, non-steroid anti-inflammatory drugs, steroids, antihistaminic agents, prescribed concomitantly with antineoplastic agents are used as supportive drugs. Such drugs administrated with chemotherapy may alter the side effects of antineoplastic agents as well as sleep quality by reducing patient symptoms.[22] In the present study, lack of knowledge of the wide variety of drugs used as a supportive treatment and the doses and durations of these drugs, the relationship of these drugs to sleep quality has not been examined.

Literature studies have mentioned that anxiety and depression during the diagnosis and treatment process would adversely affect the quality of life of cancer patients and reduce treatment compliance.[37] The present study emphasized a statistically significant association between depression, all PSQI subtypes, and total score. There are many studies pertaining to depression and sleep disorders.[38-41] Contrary to the study where no linear association was found in the study data, in our study a direct association was found between Beck score and PSQI.[35] Furthermore, a significant association between the previous diagnosis of depression and PSQI score as well as the significant association between the use of antidepressant drugs and bad sleep authenticated the association between sleep quality and depression.

A previous study determined major depressive disorder incidence in 11.3% of the cancer patients.[42] Another study reported that 15% to 25% of cancer patients affected by depression.[43] It was detected in this study that 19.7% of the patients experienced depression. Higher rates of psychiatric problems in female patients, those who were aware of their disease and exhibited the previous history of any psychiatric disorder, was documented in a different study.[42] Such observations were in line with the outcomes of the present study. Another study mentioned that 66% of cancer patients experienced anxiety and depression.[44] This was also in accordance with the results obtained from our study.

CONCLUSION

In conclusion, it can be said that sleeping and mental problems of the patients visiting the oncology clinics should be monitored and cared closely. It should be noted that the response to cancer treatment and good sleep are complementary to each other. Special attention should be taken to assess the sleep process of patients. Large-scale studies with different groups would be useful to elucidate the factors responsible for the sleep disorder. Insomnia in cancer patients may be ignored by the physician and the patient. However, sleep quality may be a healing factor for the patients that provides the strength to fight cancer and enhance the efficiency of chemotherapy. Therefore, the care and importance of the healthcare staff on this issue cannot be ignored. Oncology patients should be treated and followed by a multi-disciplinary approach. More studies are required on this topic.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

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