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KLİNİK ÇALIŞMA
 RESEARCH ARTICLE

Sleep disturbances in patients with lung cancer in Turkey

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SUMMARY

Sleep disturbances in patients with lung cancer in Turkey

Introduction: Sleep quality is known to be associated with the distressing symptoms of cancer. The purpose of this study was to analyze the impact of cancer symptoms on insomnia and the prevalence of sleep-related problems reported by the patients with lung cancer in Turkey.

Materials and Methods: Assessment of Palliative Care in Lung Cancer in Turkey (ASPECT) study, a prospective multicenter study conducted in Turkey with the participation of 26 centers and included all patients with lung cancer, was re-evaluated in terms of sleep problems, insomnia and possible association with the cancer symptoms. Demographic characteristics of patients and information about disease were recorded for each patient by physicians via face-to-face interviews, and using hospital records. Patients who have difficulty initiating or maintaining sleep (DIMS) is associated with daytime sleepiness/fatigue were diagnosed as having insomnia. Daytime sleepiness, fatigue and lung cancer symptoms were recorded and graded using the Edmonton Symptom Assessment Scale.

Results: Among 1245 cases, 48.4% reported DIMS, 60.8% reported daytime sleepiness and 82.1% reported fatigue. The prevalence of insomnia was 44.7%. Female gender, patients with stage 3-4 disease, patients with metastases, with comorbidities, and with weight loss > 5 kg had higher rates of insomnia. Also, patients with insomnia had significantly higher rates of pain, nausea, dyspnea, and anxiety. Multivariate logistic regression analysis showed that patients with moderate to severe pain and dyspnea and severe anxiety had 2-3 times higher rates of insomnia.

Conclusion: In conclusion, our results showed a clear association between sleep disturbances and cancer symptoms. Because of that, adequate symptom control is essential to maintain sleep quality in patients with lung cancer.

Key words: Lung cancer; sleep disturbance; insomnia; symptom; pain; dyspnea

ÖZET

Türkiye’de akciğer kanseri hastalarında uyku bozuklukları

Giriş: Uyku kalitesinin, kanser semptomlarının şiddetiyle ilişkili olduğu bilinmektedir. Bu çalışmada, Türkiye’de akciğer kanseri hastalarında uyku ile ilişkili sorunların prevalansı ve kanser semptomlarının insomnia üzerine etkisinin araştırılması amaçlandı.

Materyal ve Metod: Türkiye’de 26 merkezin katılımıyla gerçekleştirilen, akciğer kanserli olguların dahil edildiği çok merkezli bir çalışma olan ASPECT çalışması verileri, bu hastalarda görülen uyku sorunları, insomni ve bunların kanser semptomları ile ilişkisi yönüyle yeniden değerlendirildi. Hastaların demografik özellikleri ve hastalıkları hakkında bilgi, hasta ile yüz yüze görüşülerek ve hastane kayıtları aracılığıyla derlendi. Uykuyu başlatma ve sürdürme zorluğu (DIMS) ile gündüz artmış uyku hali veya yorgunluk tanımlayan olgular insomni olarak değerlendirildi. Gündüz uyku hali, yorgunluk ve akciğer kanseri semptomları Edmonton Semptom Değerlendirme Skalası kullanılarak kaydedildi.

Bulgular: Katılan 1245 olgunun, %48.4’ünde DIMS, %60.8’inde gündüz uyku hali ve %82.1’inde yorgunluk mevcuttu. Insomni prevalansı %44.7 olarak bulundu. Kadın cinsiyet, evre 3-4 hastalık, metastatik hastalık, komorbid hastalıklar ve kilo kaybı > 5 kg olan olgularda insomnia oranı anlamlı olarak daha yüksekti. Diğer yandan insomnisi olan hastalarda ağrı, bulantı, dispne ve anksiyete semptomları anlamlı düzeyde yüksek bulundu. Multivariate lojistik regresyon analizi, orta ileri şiddetli ağrısı ve dispnesi olan, ayrıca ciddi anksiyetesi olan hastalarda insomni sıklığının 2-3 kat fazla olduğunu ortaya koydu.

Sonuç: Çalışmamız, kanser semptomları ile uyku kalitesi arasında yakın bir ilişki olduğunu ortaya koymuştur. Bu nedenle, akciğer kanserli hastalarda kaliteli bir uyku için, kanser semptomların yeterince kontrol edilmesi gereklidir.

Anahtar kelimeler: Akciğer kanseri; uyku bozukluğu; insomni; semptom; ağrı; dispne

INTRODUCTION

Sleep disturbances, such as difficulty falling asleep and maintaining sleep, early awakening, and excessive daytime sleepiness, are common in patients with cancer. Of the cancer patients, 30-75% report sleep problems, which is a rate about two times as high as in the general population (1). Specifically, in patients with lung cancer, 52% of newly diagnosed lung cancer patients were found to have insomnia (2). Sleep quality is known to be associated with the distressing symptoms of cancer (3). Inadequately controlled or uncontrolled cancer symptoms lead to disturbed and fragmented sleep which may contribute to poor quality of life and mood disorders, particularly depression (1).

Several studies have reported that there is a high prevalence of uncontrolled symptoms in patients with lung cancer (4,5). In a previous study, we have also shown that palliative treatment of lung cancer symptoms are mostly inadequate, and large number of patients continue to suffer from uncontrolled symptoms and unmet needs (6). Despite exiting data on association of sleep quality and symptoms in other cancer types, few studies, with limited number of patients, focused on this issue in lung cancer. We re-evaluated the results of this study to analyze the impact of cancer symptoms on insomnia and the prevalence of sleep-related problems reported by the patients with lung cancer in Turkey.

MATERIALS and METHODS

Study Design

Assessment of Palliative Care in Lung Cancer in Turkey (ASPECT) study is a prospective multicenter study conducted in Turkey (between March 2014-September 2014) with the participation of 26 centers, including all patients with lung cancer, who agreed to participate in the study (6). The study was approved by the local ethics committee and written informed consent was obtained from all patients. The results of ASPECT study were re-evaluated in terms of sleep disturbances and possible association with the cancer symptoms.

Patients and Setting

The study included all consecutive patients with lung cancer, whom disease was objectively confirmed histopathologically. Demographic characteristics of patients and information about disease were recorded for each patient by physicians via face-to-face interviews, and using hospital records.

Patients were questioned regarding whether or not they had difficulty initiating or maintaining sleep (DIMS): "Do you frequently have difficulty in falling asleep at night or waking up frequently during the night or getting back to sleep after waking during the night?" Patients with DIMS also expressed subjective reasons for DIMS as open ended questions. Daytime sleepiness, fatigue and lung cancer symptoms were recorded and graded using the Edmonton Symptom Assessment Scale (ESAS) (7). The ESAS symptom scores were categorized by severity as follows: none= 0; mild= 1-3; moderate= 4-6; and severe= 7-10. Patients who have DIMS and associated daytime sleepiness/fatigue were diagnosed as having insomnia.

Statistical Analysis

Data analysis was performed using SPSS software (Version 13.01; SPSS Inc., Chicago, IL, USA). The chi-square test was used to compare categorical variables. The parametric Student t-test was used for comparing mean or median values of normally distributed data, and the nonparametric Mann-Whitney U test was used to compare data that was not normally distributed. Demography and the symptoms that were potential predictors of insomnia were analyzed using logistic regression and multivariate logistic regression analysis was used as a stepwise descending method from predictive factors with a significance ≤ 0.05 in the univariate analysis.

RESULTS

Among 1245 cases (88.7% man) included, 48.4% (590/1218 pts) reported DIMS, 60.8% (742/1221 pts) reported daytime sleepiness and 82.1% (1002/1220) reported fatigue. The most frequent subjective reasons, reported by the patients, for DIMS were pain and dyspnea (Table 1).

The prevalence of patients with insomnia was 44.7% (541/1211 pts). Among demographic parameters,

Table 1. Subjective reasons for difficulty initiating or maintaining sleep cited by the patients with lung cancer

| Reasons (590 pts) | No (%) |
|---------------------------|------------|
| Pain | 220 (37.3) |
| Dyspnea | 164 (27.8) |
| Anxiety/stress/depression | 95 (16.1) |
| Nocturia | 70 (11.8) |
| Cough | 33 (5.6) |
| Other | 54 (9.1) |

Table 2. Demographic parameters according to the patients with/without insomnia

| Variables | Patients without insomnia No (%) | Patients with insomnia No (%) | p |
|-----------------------------------------|-------------------------------------|----------------------------------|---------|
| Age (mean ± SD) | 61.82 ± 9.45 | 61.76 ± 9.34 | 0.920 |
| Gender | | | |
| -Man | 610 (91.0) | 467 (86.3) | 0.009 |
| -Woman | 60 (9.0) | 74 (13.7) | |
| BMI (mean ± SD) | 24.80 ± 4.50 | 24.48 ± 4.63 | 0.119 |
| Histopathologic type | | | |
| -Small | 123 (18.4) | 111 (20.5) | 0.344 |
| -NSCLC | 547 (81.6) | 430 (79.5) | |
| Time from diagnosis (mean ± SD, months) | 8.99 ± 14.47 | 9.13 ± 13.27 | 0.794 |
| Comorbidity | | | |
| -No | 387 (58.2) | 263 (48.7) | 0.001 |
| -Yes | 278 (41.8) | 277 (51.3) | |
| Family cancer history | | | |
| -No | 468 (70.6) | 347 (65.6) | 0.066 |
| -Yes | 195 (29.4) | 182 (34.4) | |
| Weight loss > 5 kg | | | |
| -No | 381 (57.2) | 231 (42.8) | < 0.001 |
| -Yes | 285 (42.8) | 309 (57.2) | |
| Disease stages | | | |
| -Stage 1-2 | 140 (21.5) | 58 (11.0) | < 0.001 |
| -Stage 3-4 | 510 (78.5) | 469 (89.0) | |
| Metastases | | | |
| -No | 357 (53.7) | 189 (35.1) | < 0.001 |
| -Yes | 308 (46.3) | 350 (64.9) | |

female patients, patients with stage 3 and 4 disease, patients with metastases, with comorbidities, and with weight loss more than 5 kg had higher rates of insomnia (Table 2). Also, lung cancer symptoms were clearly associated with insomnia. Patients with insomnia had significantly higher rates of pain, nausea, dyspnea, and anxiety (Table 3). Multivariate logistic regression analysis showed a clear association between insomnia and symptoms: pain, dyspnea and anxiety. Especially patients with moderate to severe pain and dyspnea and severe anxiety had 2 to 3 times higher rates of insomnia (Table 4).

DISCUSSION

Insomnia is a sleep disorder characterized by repeated difficulty initiating sleep, difficulty maintaining sleep, or waking up to early which results in daytime impairment despite adequate time and opportunity for sleep (8). Estimations of the insomnia prevalence depend on the criteria used to define insomnia; however a general consensus has developed from population-based studies that approximately 6-10% of patients have insomnia (9). The results of this study showed that a

Table 3. Distribution of symptoms according to the patients with/without insomnia

| Symptoms | Patients without insomnia No (%) | Patients with insomnia No (%) | p |
|------------|-------------------------------------|----------------------------------|---------|
| Pain | | | |
| -No | 295 (44.0%) | 122 (22.6%) | < 0.001 |
| -Yes | 375 (56.0%) | 417 (77.4%) | |
| Nausea | | | |
| -No | 418 (62.5%) | 244 (45.3%) | < 0.001 |
| -Yes | 251 (37.5%) | 295 (54.7%) | |
| Dyspnea | | | |
| -No | 272 (40.7%) | 100 (18.9%) | < 0.001 |
| -Yes | 397 (59.3%) | 439 (81.4%) | |
| Depression | | | |
| -No | 405 (60.5%) | 186 (34.5%) | < 0.001 |
| -Yes | 264 (39.5%) | 353 (65.5%) | |
| Anxiety | | | |
| -No | 358 (53.4%) | 154 (28.6%) | < 0.001 |
| -Yes | 312 (46.6%) | 385 (71.4%) | |

Table 4. Multivariate logistic regression analysis of demography and symptoms predicting insomnia

| Variables* | OR | 95.0% CI | p |
|------------------------------|-------|---------------|---------|
| Gender | 1.273 | 0.829 - 1.954 | 0.270 |
| Comorbidity | 1.176 | 0.897 - 1.542 | 0.239 |
| Weight loss > 5 kg | 1.301 | 0.989 - 1.710 | 0.060 |
| Stage 3-4 disease | 1.311 | 0.852 - 2.018 | 0.218 |
| Metastasis | 1.319 | 0.966 - 1.802 | 0.081 |
| Pain | REF | | |
| Mild | 0.904 | 0.628 - 1.303 | 0.589 |
| Moderate | 2.520 | 1.732 - 3.666 | < 0.001 |
| Severe | 3.354 | 2.207 - 5.098 | < 0.001 |
| Nausea | REF | | |
| Mild | 0.980 | 0.688 - 1.397 | 0.913 |
| Moderate | 1.245 | 0.827 - 1.873 | 0.294 |
| Severe | 1.622 | 0.968 - 2.717 | 0.066 |
| Dyspnea | REF | | |
| Mild | 1.354 | 0.929 - 1.974 | 0.115 |
| Moderate | 2.060 | 1.402 - 3.028 | < 0.001 |
| Severe | 2.888 | 1.921 - 4.341 | < 0.001 |
| Depression | REF | | |
| Mild | 1.081 | 0.686 - 1.704 | 0.737 |
| Moderate | 1.286 | 0.748 - 2.213 | 0.363 |
| Severe | 1.597 | 0.838 - 3.045 | 0.155 |
| Anxiety | REF | | |
| Mild | 0.979 | 0.624 - 1.534 | 0.925 |
| Moderate | 1.115 | 0.659 - 1.888 | 0.685 |
| Severe | 2.145 | 1.174 - 3.920 | 0.013 |

*Only variables, derived from predictive factors with a significance ≤ 0.05 in the univariate analysis, were included.

significant percentage of patients with lung cancer had poor sleep quality; insomnia (44.7%), daytime sleepiness (60.8%) and fatigue (82.1%). Ginsburg et al. reported similar results of insomnia in (52%) newly diagnosed lung cancer patients (2). Also, the prevalence of insomnia was reported to be as 31% among women patients with lung cancer (10). Chen et al. reported that about half of all lung cancer patients, receiving chemotherapy, were poor sleepers (11).

In current study, we found a significant correlation between insomnia and some demographic parameters. Female gender, patients with stage 3 and 4 disease, with metastases, with comorbidities, and patients with weight loss more than 5 kg had higher rates of insomnia. Again, we found that patients with insomnia had significantly higher rates of pain, nausea, dyspnea, and anxiety/depression. However, multivariate logistic regression analysis showed that only moderate to severe pain and dyspnea, and severe anxiety were the parameters predicting insomnia among lung cancer patients. Pain, dyspnea and anxiety/depression were also the most frequent subjective reasons of DIMS as reported by the patients. The relationship between sleep quality and the distressing symptoms of cancer is not surprising and several studies showed that some demographic parameters (including patients' gender, age, previous sleep history, cancer stage) and symptoms (due to cancer, chemotherapy and radiotherapy) were associated with the sleep problems in general cancer patients (3,12-14). The association between sleep quality and the lung cancer symptoms has also been studied in a few studies and they emphasized a relationship between sleep quality and pain, vomiting, fatigue and dyspnea and cough (11,15,16). Despite we found significantly higher rates of nausea in patients with insomnia, logistic regression analysis failed to show this association. On contrary, Akyüz et al. reported a significant correlation between sleep quality and nausea and fatigue (15). The difference between both studies might be associated with limited number of patients in the study by Akyüz et al. (15). Despite we found a relation between insomnia and distressing cancer symptoms, it is a complex process and each of these symptoms can aggravate the others, for example; unresolved symptoms, such as pain, dyspnea, fatigue etc. can lead to depression, anxiety and impaired quality of life which in turn can cause sleep disturbances and insomnia.

This study has some limitations. First of all, the results of this study primarily based on self-reported sleep disturbances with no objective measures, such as polysomnography or actigraphy. Second, we did not evaluate the effect of medications and treatment on sleep. Finally diagnosis of insomnia limited to those with DIMS and daytime sleepiness and fatigue. However in addition to daytime sleepiness and fatigue, other parameters leading daytime impairment such as attention/concentration/memory impairment, mood disturbance or irritability, motivation/energy reduction etc. were not questioned (8). Because of that, the rate of insomnia in this study might be a little bit higher than we found.

We concluded that high percentage of patients with lung cancer suffer from sleep disturbances, such as insomnia, daytime sleepiness and fatigue. Sleep disturbances in lung cancer patients were associated with cancer symptoms and especially pain, dyspnea and anxiety. Because there was a clear association between sleep disturbances and cancer symptoms, adequate symptom control is essential to maintain sleep quality in patients with lung cancer. We also conclude that, patients with lung cancer should be routinely evaluated for cancer symptoms: pain, dyspnea, and anxiety to restore sleep problems.

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