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ORIGINAL ARTICLE

Subjective sleep quality in lung cancer patients before and after chemotherapy

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Abstract

Background: Sleep disturbances, such as difficulty in falling asleep, maintaining sleep, poor sleep efficiency, early awakening, and excessive daytime sleepiness, are common in patients with cancer. The aim of this study was to evaluate sleep characteristics in newly diagnosed lung cancer patients before and after three months of chemotherapy treatment.

Methods: Forty-nine patients with lung cancer, without brain metastasis, were included. Anthropometric and disease characteristics were collected. Upon diagnosis and after three months, a polysomnographic examination was conducted and the patients completed the Epworth Sleepiness Scale (ESS), the Pittsburgh Sleep Quality Index (PSQI), the Fatigue Severity Scale (FSS) and the Medical Research Council (MRC) dyspnoea scale.

Results: Before chemotherapy, the mean PSQI score was 7.1 $\pm$ 4, the FSS score was 3.92 $\pm$ 2, and the ESS score was 6.8 $\pm$ 4. The MRC score was low at 1.6 $\pm$ 1.1. A significant correlation between FSS and global PSQI was revealed ($r = 0.424$, $P < 0.01$), as well as with several of the PSQI components. After chemotherapy, no statistically significant change was observed in the PSQI (mean: 6.6 $\pm$ 4.5, t-score: 0.784, $P = 0.438$), or the FSS score (4.4 $\pm$ 2.2, t-score: -1.375, $P = 0.177$). Sleep efficiency was significantly reduced ($P = 0.008$), without any change in the distribution of sleep stages.

Conclusion: The perception of sleep quality is poor among newly diagnosed lung cancer patients and is correlated with fatigue. After chemotherapy, self-reported sleep impairment is present and sleep efficiency is reduced, without significant change in sleep architecture.

Background

Several studies have shown that sleep disturbances are common in lung cancer patients, indicating a significant association between these disturbances and health-related quality of life.[1–3] A wide spectrum of sleep disturbances may be present in cancer patients, including late sleep onset, early morning awakening, prolonged nocturnal waking periods, unrefreshing sleep, and daytime sleepiness.[4–6] Insomnia symptoms appear to have a varied distribution throughout the cancer course and may present shortly after the diagnosis or after the initiation of adjuvant therapy.[1,7] A study of 115 patients with lung cancer undergoing chemotherapy demonstrated that during the course of chemotherapy, poor sleep, assessed by the Pittsburgh Sleep Quality Index (PSQI), was reported by 52%, and was reduced to 45% of patients at the resting period.[7]

Various causes have been applied to explain sleep disturbances in cancer patients, such as psychological factors (depression or anxiety),[7] pain and the use of painkillers,[8–10]

hospitalizations,[11] cancer treatment and its side effects.[12,13] On the other hand, sleep/wake disturbances may also accentuate cancer symptoms like pain, depression, and fatigue.[14,15] Even though sleep disturbance is a common feature in cancer patients, with studies reporting sleep difficulties in 30% to 50% of patients with newly diagnosed or recently treated cancer, the importance of this symptom and its impact on the quality of life of these patients is frequently underestimated.[16]

Published data usually incorporates patients with different cancer types, but further studies isolating and evaluating sleep disturbances in each cancer type should be conducted. The purpose of this study was to evaluate sleep characteristics and quality – assessed subjectively in lung cancer patients, to whom brain metastasis was excluded by computed tomography scan – before chemotherapy and after three months under chemotherapy treatment at re-staging.

Patients and methods

Patients

A total of 49 patients (44 males and 5 females), with primary lung cancer diagnoses were included in the study. Treating physicians obtained demographic and clinical data, regarding age, sex, medications, and Eastern Cooperative Oncology Group (ECOG) performance status. Data concerning metastasis, stage, and therapy regimens, were also obtained from the patients' medical records and documented. The treatment regimen for non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) patients was carboplatin AUC 5.5 and paclitaxel 190 m^2.[17–19] None of the patients were candidates for radiotherapy. Exclusion criteria included brain metastasis and an inability to understand and answer the questionnaires that were distributed. The ethical committee and the oncology council of the hospital approved the study. Written informed consent was obtained from each patient before study enrollment.

Sleep quality evaluation

All patients completed self-report questionnaires the day before initiation of treatment and three months after. Daytime sleepiness was evaluated using the Greek version of the Epworth Sleepiness Scale (ESS).[20] The ESS assesses daytime sleepiness over the last three months in eight usual circumstances. The range of scoring in each question is from zero (would never doze) to three (high chance of dozing) and the maximum possible score is 24. For the Greek population, the cut-off point, indicating excessive daytime sleepiness, is set at 10.

Sleep quality was assessed using the Greek version of the Pittsburgh Sleep Quality Index (PSQI).[21] The PSQI is composed of 19 self-rated questions grouped into seven domains (subjective sleep quality [SSQ], sleep latency [SL], sleep duration [SDU], habitual sleep efficiency [HSE], sleep disturbances [SDI], use of sleeping medication [SM] and daytime dysfunction [DD]), over the last month before treatment initiation. Each item is rated on a zero to three scale to provide a global sleep quality PSQI score that varies from zero (high quality of sleep) to 21 (low quality of sleep). A global sum of five or greater indicates a poor quality of sleep, with higher scores indicating a decreasing quality of sleep.

Fatigue was assessed using the Greek version of the Fatigue Severity Scale (FSS).[22] The FSS is a nine item self-report questionnaire with a seven-point response format, created to investigate the severity of fatigue in different situations (e.g. in motivation, in physical functioning, in duties and responsibilities, in work, family and social life etc.), during the last seven days before treatment initiation. Each item is rated with a score from one to seven, where one indicates strong disagreement and seven indicates strong agreement. The final FSS score is extracted by the mean value of the nine items, and a score greater than four is considered to be indicative of fatigue.

Sleep quality was objectively evaluated by an attended overnight polysomnography (PSG) (Alice 3, Respironics), using a standard montage of electroencephalogram (EEG), electrooculogram, electromyogram (EMG) and electrocardiogram (ECG) signals, together with pulse oximetry and airflow detected using combined oronasal thermistors. Thoracic cage and abdominal motion were recorded by inductive plethysmography. EEG recordings were manually scored according to standard criteria.

The presence and grade of dyspnea was evaluated using the Medical Research Council (MRC) scale, which consists of a five-point graded system that quantifies the disability associated with breathlessness by identifying that breathlessness occurs when it should not (Grades 1 and 2) or by quantifying the associated exercise limitation (Grades 3–5).[23] There is an almost 98% agreement between observers recording MRC breathlessness scores. The score correlates well with the results of other breathlessness scales, lung function measurements, and with direct measures of disability, such as walking distance.

Statistical analysis

Analyses were carried out with the SPSS statistical software package (SPSS version 17.01; SPSS, Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation (SD) or median (with interquartile ranges), depending on the normality of distribution. For categorical variables, the percentages of patients in each category were calculated and a chi-squared test was performed. The paired samples *t*-test was used in normally distributed parameters to compare the mean values in patients before and after chemotherapy.

Table 1 Patients' demographic and clinical characteristics (n = 49)

Age (years)	
Mean (±SD)	60.78 (±9.31)
Range	38–75
BMI (kg/m^2)	
Mean (±SD)	27.14 (±5.47)
Range	15–53
Sex	
Male	44 (89.7%)
Female	5 (10.2%)
Type/Staging of Cancer	
SCLC	18 (36.7%)
Limited	4 (22.2%)
Extensive	14 (77.8%)
NSCLC	31 (63.2%)
IIIb	9 (29%)
IV	22 (71%)
Histology of NSCLC	
Adenocarcinoma	21 (40.8%)
Squamous cell carcinoma	7 (14.3%)
Large cell carcinoma	3 (6.1%)

NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer.

Pearson's correlation was performed in order to explore possible correlations, and the correlation coefficient (r) was displayed in each case. A P-value of less than 0.05 indicated statistical significance.

Results

General characteristics

Patient age varied between 38 and 75 years. In the majority (n = 31), NSCLC was diagnosed, with adenocarcinoma being the most prevalent histologic type, followed by squamous cell carcinoma. Eighteen patients were diagnosed with SCLC. Anthropometric characteristics and disease classification are reported in Table 1. All patients were smokers or ex-smokers, except one, with a mean use of 81.3 ± 42.3 pack years. The mean MRC scale score was 1.6 ± 1.1 for all patients. The majority of patients (75.5%) reported an ECOG functional capacity of zero (indicating that the patient is fully active and able to carry on all pre-disease performance), while the remaining patients' score (24.4%) was one (indicating that the patient was restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature).

Sleep and fatigue characteristics

Upon diagnosis, 12 patients (24.5%) had an ESS score that exceeded the cut-off point of 10, indicating excessive daytime sleepiness, with a mean ESS score being among the normal range (6.8 ± 4.3). After treatment, this percentage was 16.3%, but this change was not considered statistically significant (P = 0.163). On the contrary, most of the patients (59.1%) had an abnormal global PSQI score, indicating poor sleep quality (mean global PSQI score 7.1 ± 4). After treatment, the percentage of patients with abnormal scores was 51.2% (P = 0.054). Regarding FSS, 16 patients (32.7%) exhibited a score exceeding the cut-off point of four, which indicates fatigue was observed, with a mean FSS score being 3.9 ± 2.

After three months of chemotherapy, no statistically significant change after chemotherapy was observed in global PSQI (mean: 6.6 ± 4.5, t-score: 0.784, P = 0.438) or FSS score (4.4 ± 2.2, t-score: −1.375, P = 0.177). PSQI global score, its components, and the FSS score before and after treatment, are shown in Table 2.

A significant relationship was observed between FSS and PSQI before and after treatment (r = 0.424, P < 0.002 and r = 0.478 P = 0.003, respectively). Moreover, a significant association between FSS and several PSQI components before and after treatment was revealed (Table 3). A statistically significant correlation was also revealed between FSS and ESS (r = 0.311, P = 0.030), establishing the interaction between fatigue and subjective sleepiness. In comparison, no association was revealed between PSQI and ESS (P = 0.238).

The Cronbach's alpha score of the questionnaire before and after chemotherapy enforced the results of our study. Indeed, the Cronbach's alpha score for the global PSQI was 0.770 before chemotherapy and 0.793 after chemotherapy, which is comparable to results previously reported in other studies of cancer patients.[19,24–27]

Polysomnography results

Upon diagnosis, the sleep efficiency of the patients was 72.5 ± 15%, while after three months it was significantly

Table 2 Pittsburgh Sleep Quality Index (PSQI) global, PSQI components and Fatigue severity scale (FSS) scores before and after chemotherapy treatment (n = 49)

	Before treatment		After treatment			
	Mean ± SD	Range	Mean ± SD	Range	t-value	P
SSQ	1.39 ± 0.81	0–3	1.18 ± 0.88	0–3	1.462	ns
SL	0.88 ± 1.01	0–3	0.69 ± 1.08	0–3	1.482	ns
SDU	1.29 ± 1.10	0–3	1.28 ± 1.27	0–3	0	ns
HSE	0.84 ± 0.94	0–3	1.05 ± 1.3	0–3	−1.290	ns
SDI	1.73 ± 0.76	0–3	1.36 ± 0.49	1–2	1.239	ns
SM	0.22 ± 0.74	0–3	0.08 ± 0.35	0–2	1.226	ns
DD	0.88 ± 0.86	0–3	0.79 ± 0.95	0–3	0.279	ns
PSQI	7.16 ± 4.01	1–17	6.62 ± 4.51	1–17	0.785	ns
FSS	3.92 ± 2.03	0–7	4.43 ± 2.18	0–7	−1.375	ns

DD, daily dysfunction; FSS, Fatigue severity scale; HSE, habitual sleep efficiency; ns, not significant; PSQI, Pittsburgh Sleep Quality Index; SDI, sleep disturbances; SDU, sleep duration; SL, sleep latency; SM, sleep medication; SSQ, subjective sleep quality.

Table 3 Correlation of Fatigue severity scale (FSS) score with Pittsburgh Sleep Quality Index (PSQI) global and PSQI components score before and after chemotherapy treatment

	Before treatment		After treatment	
	r	P	r	P
PSQI	0.424	0.002	0.478	0.003
SSQ	0.524	<0.001	0.432	0.006
SL	0.135	ns	0.286	ns
SDU	0.366	0.010	0.376	0.018
HSE	0.157	ns	0.394	0.013
SDI	0.178	ns	0.437	0.005
SM	0.193	ns	–0.060	ns
DD	0.359	0.011	0.433	0.006

DD, daily dysfunction; FSS, Fatigue severity scale; HSE, habitual sleep efficiency; PSQI, Pittsburgh Sleep Quality Index; SDI, sleep disturbances; SDU, sleep duration; SL, sleep latency; SM, sleep medication; SSQ, subjective sleep quality.

reduced to 67.4 ± 2.2%, (P = 0.008). However, the sleep stage distribution did not change: Stage 1: from 21.9 ± 14.6% to 15.9 ± 13% (P = 0.235); Stage 2: from 39.4 ± 14.7% to 41.6 ± 16.4% (P = 0.731); Slow Wave Sleep (SWS): from 25.7 ± 19.4% to 36.7 ± 20.8% (P = 0.094); and REM: from 10 ± 5% to 8.3 ± 8.2% (P = 0.645). Additionally, no change was observed in the average SpO_2 (from 92.1 ± 1.98% to 91.9 ± 2.4%, P = 0.758) or in the minimum SpO_2 (from 84.7 ± 3.7% to 84.5 ± 3.7%; P = 0.521) during sleep.

Discussion

The main finding of this study is that the sleep quality of newly diagnosed lung cancer patients is poor, it is associated with daytime fatigue, and it is not affected by chemotherapy treatment. This finding is in accordance with Le Guen *et al*.[1] who evaluated sleep quality, daytime alertness, and quality of life in 29 newly diagnosed lung cancer patients, in comparison to 14 controls, using questionnaires and actigraphy. Lung cancer patients had poorer sleep quality, excessive daytime sleepiness, and impaired quality of life compared to the control group.

The results of the present study are similar to that of the study by Chen *et al*.,[7] in which 115 patients with lung cancer underwent chemotherapy. They reported that during chemotherapy, 52% of patients were poor sleepers versus 45% of patients at the resting period, while in our study 59.1% reported poor sleep before chemotherapy and 51.2% after chemotherapy. In another study, including 102 cancer patients (22 with lung cancer), the mean global PSQI was higher than that in our study, depicting the poor sleep of cancer patients.[28] The most affected component was sleep latency, followed by sleep duration, while the component with the lowest score was use of sleep medication. In a study comprising 982 patients with cancer, lung cancer patients (n = 112) reported the highest prevalence of fatigue (56.1%), sleepiness (39.5%), use of tranquillizers/sleeping pills (40.4%), and the second highest prevalence of insomnia (36.8%), compared to other types of cancer.[4] Finally, in a study including 102 patients with advanced cancer, the global PSQI was high. Poor sleep quality was most influenced by the sense of hopelessness (P = 0.003), interference of pain with mood (P < 0.005), and the use of strong opioids (P = 0.010).[29]

Dyspnea is a major symptom in patients with chronic lung diseases that may affect both daytime function and sleep quality. However, poor sleep quality could not be attributed to dyspnea in our study, since in our sample of patients the mean MRC scale score was low. Additionally, no relationship was found between the MRC score and sleep quality.

Reduced sleep duration could explain poor sleep quality, as insomnia is the most common sleep disturbance in lung cancer patients, with a major impact on quality of life.[4,24–26] Interestingly, in our patients no daytime sleepiness was reported, despite poor sleep duration and efficiency. No correlation was observed between daytime sleepiness and sleep quality, assessed by the global PSQI score or any of its components.

On the contrary, fatigue was initially associated with sleep quality and with the following of its components: subjective sleep quality, sleep duration, and daily dysfunction. These findings are in accordance with previous studies.[21,28–30] After three months of chemotherapy, these correlations remained significant and fatigue was additionally correlated with habitual sleep efficiency and sleep disturbances.

Cancer related fatigue is a common symptom and its prevalence reaches 80 to 90% among cancer patients under treatment.[31] Fatigue symptoms are often under-diagnosed and under-treated by health care practitioners, despite the fact that they have a significant impact on patients' quality of life and daytime activities. Numerous mechanisms implicating the effects on the central nervous system, muscle metabolism, circadian rhythm, inflammatory and stress mediators, immune system activation and hormonal alteration, have been proposed in order to explain the relationship between cancer and fatigue occurrence.[27] The limitations of the present study are the small sample size, and the small rate of women in this sample.

Conclusion

Sleep quality of lung cancer patients, subjectively evaluated, is poor both before and after chemotherapy, while sleep efficiency, objectively measured, deteriorates during the course of chemotherapy. Fatigue is the major symptom associated with sleep quality in these patients. Sleep quality in patients with lung cancer should be evaluated in large-scale, prospective studies, including PSG, in order to obtain a better

understanding of the mechanisms of poor sleep and its contribution to daily fatigue. In addition, every clinical physician should bear in mind that sleep impairment is common in lung cancer patients, affecting their general status in daily activities.

Disclosure

No authors report any conflict of interest.

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