ARAŞTIRMA / RESEARCH

Changes in sleep quality and geriatric-8 (G8) score with chemotherapy in older patients with multiple myeloma

Uyku kalitesi ve geriatrik 8 (G8) skorunun multiple myelomlu yaşlı hastalarda kemoterapi ile değişimleri

Mahmut Bakır Koyuncu[1] , Çağatay Çavuşoğlu[2] , Anıl Tombak[3] , Mehmet Ali Uçar[4] ,
Aydan Akdeniz[3] , Eyüp Naci Tiftik[3]

[1]Adana City Research and Training Hospital, Department of Hematology, Adana, Turkey
[2]Şanlıurfa Mehmet Akif İnan Research and Training Hospital, Department of Geriatrics, Sanlıurfa, Turkey
[3]Mersin University, Department of Hematology, Mersin, Turkey
[4]Cukurova University, Department of Hematology, Adana, Turkey

Abstract

Purpose: The aim of this study was to evaluate the sleep quality of older patients with multiple myeloma before and after chemotherapy and investigate factors affecting sleep quality.

Materials and Methods: A total of 108 patients with newly diagnosed multiple myeloma were included in the study. Geriatric 8 (G8) and Pittsburgh Sleep Quality Index scores were calculated for the patients at the time of diagnosis, and the changes in these scores were evaluated after three cycles of chemotherapy.

Results: At the time of diagnosis, 63 (58.3%) of the patients had sleep disturbances. The sleep disturbance rate decreased to 41.7% after chemotherapy. There was no statistically significant difference in the total G8 score before and after treatment. In logistic regression analyses, the serum calcium level, pre-treatment G8 score, and response to chemotherapy were predictors of sleep quality. Increases in sleep quality were significantly higher in patients with good responses to chemotherapy.

Conclusion: Sleep disturbances are a common problem in older patients with multiple myeloma. Our study demonstrated that sleep quality increased with chemotherapy, and patients with low sleep quality had worse responses to treatment. Therefore, there is a need for measures and treatments to increase the sleep quality of these patients.

Keywords:. Multiple myeloma, sleep quality, geriatric scores

Öz

Amaç: Bu çalışmada multipl miyelomlu yaşlı hastaların kemoterapi öncesi ve sonrası uyku kalitesini değerlendirmeyi ve uyku kalitesini etkileyen faktörleri araştırmayı amaçladık.

Gereç ve Yöntem: Yeni tanı konmuş Multipl miyelomlu toplam 108 hasta çalışmaya dahil edildi. Hastaların tanı anında Geriatrik 8 (G8) ve Pittsburgh Uyku Kalitesi İndeksi skorları hesaplandı ve bu skorlardaki değişiklikler üç kür kemoterapi sonrası değerlendirildi.

Bulgular: Hastaların 63'ünde (%58,3) tanı anında uyku bozukluğu vardı. Kemoterapiden sonra uyku bozukluğu oranının %41.7'ye düştüğü görüldü. Tedavi öncesi ve sonrası toplam G8 skorunda istatistiksel olarak anlamlı bir fark yoktu. Lojistik regresyon analizlerinde serum kalsiyum düzeyi, tedavi öncesi G8 skoru ve kemoterapiye yanıtın uyku kalitesinin belirleyicileri olduğu görüldü. Kemoterapiye iyi yanıt veren hastalarda uyku kalitesindeki artış anlamlı olarak daha yüksekti.

Sonuç: Uyku bozuklukları, multipl miyelomlu yaşlı hastalarda yaygın bir sorundur. Çalışmamız kemoterapi ile uyku kalitesinin arttığını ve uyku kalitesi düşük hastaların tedaviye yanıtlarının daha kötü olduğunu gösterdi. Bu nedenle bu hastaların uyku kalitesini artıracak önlemlere ve tedavilere ihtiyaç vardır.

Anahtar kelimeler: Multipl miyelom, uyku kalitesi, geriatrik skorlar

INTRODUCTION

Multiple myeloma (MM) accounts for 1-2% of all cancers, and the median age at the time of diagnosis varies between 65 and 74. Geriatric evaluation is recommended before treatment in patients with MM. The time-consuming nature of the comprehensive geriatric assessment (CGA) and the requirement of trained personnel to perform it limits its use[1]. Therefore, the Geriatric 8 (G8) screening test, which can be performed more quickly and practically, was developed and used in cancer patients[2]. A significant relationship between the CGA and the G8 screening test has been shown in many types of cancer[3]. However, there are few published studies about using the G8 screening test in patients with MM.

The importance of sleep both in the normal geriatric population and in elderly patients with cancer is increasingly being recognized. Sleep disturbances increase cancer risk and significantly affect the treatment process and quality of life in patients with cancer[4]. The frequency of sleep disturbances in malignant diseases is approximately 50%[5]. Although many scales can be used to measure sleep quality, the Pittsburgh Sleep Quality Index (PSQI) is the most common[6]. Although only a few published studies have described sleep quality in patients with MM, no studies using the PSQI were found[7,8].

Many factors that affect sleep quality in patients with cancer have been identified. Depression, pain, anxiety, cancer-related fatigue, and performance status are among these factors[9]. In addition, chemotherapy has been shown to worsen sleep quality in various types of cancer[10]. Studies have shown that patients with poor sleep quality have lower survival rates. Sleep disturbances occur in 10-50% of elderly individuals without cancer[11]. In studies conducted with the CGA in the normal elderly population, sleep disturbances were correlated with coronary artery disease, chronic pain, anorexia, malnutrition, depression, and cognitive disorders[12].

This study aimed to reveal the prevalence of sleep disturbances at the time of MM diagnosis in older patients, to investigate geriatric evaluation after diagnosis and treatment using the G8 screening test, to show changes in the total PSQI scores from the time of diagnosis to after treatment in patients with MM, and to investigate factors that may affect these scores.

MATERIALS AND METHODS

This study was conducted with patients over 65 years of age diagnosed with MM after applying to the hematology outpatient clinics of Mersin University, Çukurova University, and Adana City Training and Research Hospital between March 2020 and March 2021. To minimize the biases associated with chemotherapy protocols, patients started on the CyBorD chemotherapy protocol (weekly bortezomib, cyclophosphamide, and dexamethasone), which is the most frequently used first-line protocol in Turkey, were included in the study[13] Patients younger than 65 years of age, patients who did not receive chemotherapy, patients who received other than Cybord chemotherapy in the first-line treatment, and patients who could not cooperate in terms of the reliability of the answers given to the scales were excluded from the study. Of 138 patients, six refused to participate in the study. Three patients died before completing three cycles of chemotherapy. Four patients were lost to follow-up. Hearing loss was present in two patients. Three patients had previously applied to the geriatric outpatient clinic and undergone the G8 screening test there. Dementia was present in 12 patients. The remaining 108 patients were included in the analysis.

Procedure

The G8 screening test and PSQI questionnaire were administered to all patients by face-to-face interviews at the time of diagnosis. After three cycles of chemotherapy, the G8 screening test and PSQI questionnaire were re-administered while evaluating the treatment responses. This study was approved by the Mersin University ethics committee (2020/205) and conducted in accordance with the Declaration of Helsinki. Written informed consents of all patients were obtained.

Measures

Demographic form

The sociodemographic characteristics, educational status, comorbid diseases, medication histories, hemogram parameters at the time of diagnosis, serum calcium, and creatinine levels, and bone involvement status of the patients were recorded. Bone marrow biopsy and serum and urine immunofixation electrophoresis were used to evaluate patients' responses after the third cycle of chemotherapy.

When the G8 and PSQI evaluations were performed after the third cycle of chemotherapy, the patients' responses to chemotherapy were unknown.

G8 screening test

Bellera et al. developed G8 screening test for older individuals with oncological diseases[14]. This test includes eight items: food intake in the last three months, weight loss in the previous three months, mobility, neuropsychological problems, body mass index, intake of more than three medications, general health status, and age. The total score for this test is between 0 and 17 points. The CGA is recommended if a total G8 score of 14 or less is detected. The translation of this test to Turkish and studies of its validation and reliability in older individuals without cancer were carried out by Cavusoglu et al[15].

Pittsburgh Sleep Quality Index

PSQI was developed by Buysse et al. and consists of 24 questions. Of these questions, 19 are answered by the patient, and five are answered by a partner who sleeps in the same room. However, questions answered by the partner are not included in the total score. There are seven items in this index: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping medications, and daytime dysfunction. The total score is obtained by summing the scores of these seven items. Each item is scored between 0 and 3, and the total score is between 0 and 21[6]. A total score of five or above indicates sleep disturbances.

Statistical analysis

Statistical analysis was performed with SPSS 21. The Kolmogorov–Smirnov test, histograms, and probability plots were used to determine the distribution of numerical data. Normally distributed numerical data are expressed as mean±SD, and non-normally distributed data are expressed as median (minimum-maximum). Categorical data are expressed as frequencies and percentages. The chi-square test was used to compare categorical data. The t-test and Mann–Whitney U test were used to compare continuous data for comparisons between groups. The Kruskal–Wallis test was performed to compare more than two variables, and posthoc analysis was performed to determine which groups had significant differences. Bonferroni correction was applied to calculate the p-value of multiple variables. Logistic regression analysis was performed to evaluate independently correlated factors related to sleep

quality. Variables with p<0.05 in pairwise comparisons were included in the logistic regression analysis. The backward stepwise method was used in the logistic regression analysis, and the Omnibus p was <0.005. In the correlation analysis of numerical data, Spearman or Pearson correlation was used according to the data distribution.

RESULTS

The general characteristics of the patients and their total PSQI scores and PSQI sub-scores are summarized in Table 1.

When PSQI scores before and after chemotherapy were compared with G8 scores, the improvement in the sleep quality of patients after chemotherapy was statistically significant, but the change in G8 was non-significant (Table 2).

A significant negative correlation was found between the pre-treatment PSQI score and the pre-treatment G8 score (r: -0.485, $P < .001$) and between the post-treatment PSQI score and the post-treatment G8 score (r: -0.598, $P < .001$).
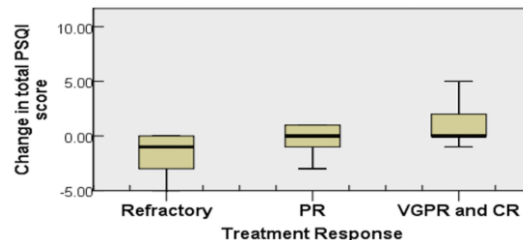

Figure 1.   Changes in the total PSQI score after treatment according to treatment response

PR: Partial response, VGPR: very good partial response
The Kruskal–Wallis test was used in pairwise comparisons, and the significant difference was due to the VGPR and CR group.

When examining the relationship between response to chemotherapy and PSQI score before treatment, patients with a very good partial response (VGPR) and complete response (CR) had significantly lower PSQI scores than patients with other response levels. No significant difference was found in G8 scores before chemotherapy in terms of response to treatment.

The parameters that were included in the multivariate analysis to identify factors that were independently associated with sleep quality were serum calcium level, age, total G8 score, gender, and response to chemotherapy. The last backward stepwise model is

presented in Table 3. Serum calcium level, pre-treatment G8 score, and response to chemotherapy were predictors of sleep quality. Patients with VGPR and CR demonstrated significant changes in their total PSQI scores before and after chemotherapy, and sleep quality improved (*P* = .003) (Figure 1).

Table 1. General characteristics of the patients

Variable	
Age, year, median (min-max)	74 (65-91)
Female, n (%)	60 (55.6)
Sleep disturbance by total PSQI score (pre-treatment)	
Yes, n (%)	63 (58.3)
No, n (%)	45 (41.7)
Average scores by PSQI domains at diagnosis (mean±SD)	
Subjective sleep quality	1.12±0.78
Sleep latency	1.40±0.97
Sleep duration	0.83±0.98
Habitual sleep efficiency	1.06±0.97
Sleep disturbances	1.44±0.67
Use of sleeping medication	0.14±0.55
Daytime dysfunction	0.60±0.91
Response to chemotherapy	
Refractory, n (%)	11 (10.2)
PR, n (%)	24 (22.2)
VGPR and CR, n (%)	73 (67.6)
Sleep disturbance by total PSQI score (post-treatment)	
Yes, n (%)	45 (41.7)
No, n (%)	63 (58.3)

PSQI: Pittsburgh Sleep Quality Index, SD: standard deviation, PR: partial response, VGPR: very good partial response, CR: complete response

Table 2. Total PSQI and G8 scores before and after chemotherapy

	Pre-treatment, median (min-max)	Post-treatment, median (min-max)	p-value
Total PSQI score	6 (0-17)	4 (0-19)	0.002
G8 score	13 (6-17)	14 (6-17)	0.073

PSQI: Pittsburgh Sleep Quality Index, G8: Geriatric 8 screening test

Table 3. Factors independently associated with sleep quality (before chemotherapy) according to the multivariate analysis

	B	SE	Wald	P-value	OR	95% CI for OR	
						Lower	Upper
Serum calcium level	-0.718	0.331	4.702	0.03	0.488	0.255	0.933
G8 score before chemotherapy	-0.313	0.101	9.494	0.002	0.731	0.599	0.892
Status of treatment response	2.676	0.575	21.690	<0.001	14.522	4.71	44.776

B: Coefficients, SE: standard error, OR: odds ratio, CI: confidence interval

DISCUSSION

This is the first study showing the changes in PSQI and G8 test scores in patients with MM before and after chemotherapy. In older patients with MM, sleep disturbances at the time of diagnosis are common, and a statistically significant improvement in sleep quality was observed after chemotherapy. Sleep scores in patients with poor responses to treatment are worse at diagnosis, and sleep scores in patients with good responses to treatment significantly improve.

Sleep quality directly affects the quality of life. Especially in cancer patients, patients' quality of life substantially deteriorates due to their disease and treatment. The patients' social lives, mood, mental health, and the treatment process can be markedly affected[9,10]. While sleep disturbances are observed in approximately 15% of the general population, studies show that the rate of sleep disturbances reaches 65% in patients with cancer[16]. In addition, sleep disturbances increase with age, and the prevalence of sleep disturbances varies between 10% and 50% in the elderly population[11]. In our study population, the rate of sleep disturbances at the time of diagnosis was 58.3%. When evaluating this rate, it should be kept in mind that our patients had two essential risk factors: cancer and older age. Sleep quality screening at the time of diagnosis is crucial since the sleep disturbance rate is high in older patients with MM at diagnosis.

Although sleep disturbances have been shown to increase with chemotherapy in most types of cancer, our study demonstrated that the incidence of sleep disturbances decreased to 41.7% after chemotherapy[10,17,18]. Disease burden and pain due to bone involvement, which is common in patients with MM, are considered the leading causes of sleep disturbances at diagnosis. Sleep quality increases due to decreases in bone pain and disease burden after chemotherapy. In addition, the standard CyBorD chemotherapy regimen used in this patient group is better than the chemotherapy used in solid cancers in terms of adverse effects. CyBorD chemotherapy includes high-dose steroids (40 mg of dexamethasone per week). Previous studies have shown that steroid therapy increases the sleep quality of patients with hematological malignancies, prolongs sleep duration at night, and decreases nighttime awakenings[19]. Therefore, the high-dose steroids used in our patients may also have had a role in reducing sleep disturbances. However, studies are needed to demonstrate the relationship between steroids and sleep quality in patients with MM.

One of the essential characteristics of this study is that it revealed the relationship between sleep quality and response to chemotherapy. Patients with poor sleep quality at diagnosis have worse responses to treatment, raising the question of whether sleep quality affects treatment success. There is a need for studies investigating the relationship between sleep quality and chemotherapy response. Perhaps more effective sleep treatments and interventions will be provided for these patients to increase chemotherapy

responses in the future. The fact that the patients with good responses to chemotherapy in our study had improved sleep scores supports this hypothesis. However, sleep scores may have improved because of the good responses to chemotherapy (and the more significant reduction in disease burden) observed in these patients.

Although there was no statistically significant difference in pre-treatment and post-treatment G8 scores, there was a correlation between G8 scores and sleep quality. In addition, the G8 score was a factor that affected sleep quality in the logistic regression model created to evaluate factors affecting the PSQI score at the time of diagnosis. In this respect, both geriatric assessment and evaluation of sleep quality are critical in older patients with MM.

Many methods that may be useful in correcting sleep disturbances in cancer patients have been described in the literature. Studies have shown that aerobic exercise can be beneficial in treating insomnia in older individuals[20]. However, intense exercise may not be suitable for older patients since most older patients with MM have bone involvement. The positive effects of yoga on sleep quality have been demonstrated previously, and yoga can be tried in this patient group[21]. In addition, intravenous vitamin C may be beneficial in increasing sleep quality and appetite and reducing the symptoms of depression and fatigue in patients with breast cancer[22]. The concept of sleep hygiene is becoming increasingly important in the treatment of sleep disturbances. 'Sleep hygiene' means habits that help you have a good night's sleep. In the current guidelines of the American Academy of Sleep Medicine, cognitive behavioral therapies are strongly recommended in primary care to increase sleep hygiene in the treatment of chronic insomnia[23]. Intermittent sleep hygiene training significantly improves sleep quality in cancer patients[24]. In light of this evidence, behavioral sleep therapy may also be preferred to sleeping medications, which have many adverse effects, in older patients with MM, especially during the chemotherapy process.

Our study had limitations. Our patient population was small. Sleep quality was evaluated with the PSQI instead of more objective methods, such as polysomnography. However, polysomnography is not an easily accessible and practical method. There is a need for studies in which sleep quality is evaluated by polysomnography. In addition, the CGA could not be included in the analyses because it could not

be performed in all patients with a G8 screening test score of ≤14. Our failure to evaluate for depression and chronic pain, which are known to affect sleep quality, may have led to inaccurate results. If we could have evaluated patients with depression and pain scales before and after treatment and include the results in a logistic regression analysis, we could have defined the factors affecting sleep more clearly. In addition, we would like to evaluate the effect of increased sleep quality on quality of life, especially after chemotherapy. Based on all these points, we hope to assess the factors affecting sleep in this patient group more clearly by designing new studies in which all these factors are evaluated together.

In conclusion, sleep disturbances are a common roblem in older patients with MM. Our study demonstrated that sleep quality increased with chemotherapy, and patients with low sleep quality had worse responses to treatment. Therefore, there is a need for measures and treatments to increase the sleep quality of these patients.

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