Does Neuropathic Pain Affect the Quality of Sleep?

Nöropatik Ağrı Uyku Kalitesini Etkiler mi?

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ABSTRACT

Objective: We aimed to evaluate the quality of sleep (QoS) in patients with neuropathic pain (NP) and to investigate the association between possible QoS impairment and NP characteristics.

Materials and Methods: Patients with NP and controls were examined. Age, sex, NP duration, NP cause (central, peripheral, or mixed), and pain intensity (with a Likert-type scale and visual analog scale) were recorded. NP was screened with Douleur Neuropathique 4 questions (DN4), and QoS was evaluated using the Pittsburg Sleep Quality Index (PSQI). Mann-Whitney U test and regression analysis were performed to evaluate the data.

Results: Seventy patients with NP and 30 age- and sex-matched controls were included. The mean age of the patients and controls were 45.04±10.21 years and 39.00±19.23 years, respectively. Significantly higher scores of sleep latency (p=0.002), sleep duration (p=0.003), sleep efficiency (p=0.002), sleep disturbance (p<0.000), daytime dysfunction (p=0.04), and PSQI total were observed in patients with NP than in controls (p<0.000). In addition, 80% of patients with NP and 37 % of controls were classified as having poor QoS (p<0.000). Female sex, pain intensity, and NP duration were found to be factors related to having poor QoS in patients with NP (p=0.026, p=0.006, and p<0.000, respectively).

Conclusion: In our study, 80% of patients with NP had poor QoS regardless of the NP cause. Female sex, pain severity, and NP duration were found to be factors correlated with poor QoS. Treatment strategies that target not only NP itself but also better QoS may contribute to the overall success of management.

Keywords: Neuropathic pain, quality of sleep, pain

ÖZ

Amaç: Bu çalışmanın amacı nöropatik ağrı (NA) tanısı alan hastalarda uyku kalitesini değerlendirmek uyku kalitesindeki bozulma ile NA'nın özellikleri arasındaki olası ilişkileri incelemekti.

Gereç ve Yöntem: Bu çalışmaya NA'lı hastalar ve sağlıklı kontroller dahil edildi. Yaş, cinsiyet, NA süresi, NA nedeni (santral, periferik veya mikst) ve ağrı yoğunluğu (görsel analof skala ve Likert tipi skala ile) kaydedildi. NA (Douleur Neuropathique4 (DN4) anketi ile, uyku kalitesi ise Pittsburg uyku kalitesi indeksi (PUKİ) ile değerlendirildi. Mann-Whitney U testi ve regresyon analizi uygulandı.

Bulgular: Bu çalışmaya NA'lı 70 hasta (54 kadın, 16 erkek) ile yaş ve cinsiyet olarak benzer 30 kontrol dahil edildi. Hastaların ve kontrollerin ortalama yaşları sırasıyla 45,04±10,21 ve 39,00±19,23 yıl idi. Hastalarda semptom süresi 24,8±18,2 olarak kaydedildi. NA'lı hastalarda sağlıklılara göre PUKİ bileşenlerinden uykuya geç geçiş (p=0,002), uyku süresi (p=0,003), uyku etkinliği (p=0,002), uyku disturbansı (p<0,000), gündüz disfonksiyonu (p=0,04) ve total PUKİ skoru (p<0,000) anlamlı şekilde daha yüksek tespit edildi. Ayrıca NA'lı hastaların %80'inin ve kontrollerin %37'sinin kötü uyku kalitesine sahip oldukları kaydedildi (p<,000). NA'lı hastalarda kadın cinsiyet, ağrı yoğunluğu ve semptom süresi kötü uyku kalitesi ile ilişkili faktörler olarak tespit edildi (p=0,026, p=0,006 ve p<0,000).

Sonuç: Çalışmamızda NA'lı hastaların %80'inin NA'nın sebebinden bağımsız şekilde kötü uyku kalitesi sergilediği gözlendi. Kadın cinsiyet, ağrı yoğunluğu ve ağrı süresi kötü uyku kalitesi ile ilişkili faktörler olarak tespit edildi. NA'lı hastaların tedavi stratejisinde daha iyi bir uyku kalitesinin de hedeflenmesi tedavinin başarısına katkıda bulunacaktır.

Anahtar Kelimeler: Nöropatik ağrı, uyku kalitesi, ağrı

Introduction

Chronic pain because of several factors, as a widespread problem, has been estimated to affect 19% of the European population [1, 2]. Within this population, neuropathic pain (NP) is of particular interest because they have a greater comorbidity profile than age- and sex-matched controls. NP is currently defined as "pain arising as a direct consequence of a lesion or disease

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affecting the somatosensory system" and its estimated prevalence has been accepted to be approximately 7% in general population [3, 4]. Several factors can damage the central or peripheral nervous system and cause NP, which is generally more difficult to manage than many other types of chronic pain. NP has various symptoms such as spontaneously or trigger-induced chronic pain, characteristic burning, stabbing, electric-like shocks, sharp, shooting, lancinating or sometimes as dull, aching, pressure, squeezing, deep, cold pain, and neuropathic itch [5].

It was demonstrated that cases with NP define pain-related interference in health-related quality of life (HRQoL) and experience several adverse consequences such as depression, fear, and sleep disturbances [6, 7]. Although previous studies have reported QoL impairment because of NP, whether NP similarly affects the quality of sleep (QoS) has been rarely investigated. This study aimed to evaluate QoS in NP and to investigate associations between possible QoS impairment and NP characteristics.

Materials and Methods

Patients

This investigation was planned as a cross-sectional study and was approved by the local Ethics Committee. Written informed consent was obtained from the participants. Seventy patients with NP (aged 18-64 years) and 30 age- and sex-matched controls were included in the study. NP was screened with Douleur Neuropathique 4 questions (DN4), and patients with a score of ≥4 were accepted as presenting NP. Age, sex, NP duration, and NP cause (central, peripheral or mixed) were recorded. Drug use for NP or any drug having potential effect on sleep was accepted as exclusion criteria. Furthermore, patients with thyroid disorders, infections, and other chronic diseases such as heart and renal failure and those with a history of serious psychiatric disorders were excluded from the study.

Evaluations

Pain intensity was evaluated using a Likert-type scale (6-point scale) and a visual analog scale (VAS; 100 mm).

NP was screened with DN4, which is a recent scale developed by the French Neuropathic Pain Group to distinguish NP from non-NP, and it is a valid and reliable instrument [8]. It has been translated into many languages and has been also validated for the Turkish population [5]. A cutoff score of 4 has a predictive value of 86%, sensitivity of 82.9%, and specificity of 89.9% [8].

QoS was evaluated using the Pittsburg Sleep Quality Index (PSQI), which evaluates the individual's self-reported QoS during the last month [9]. This 19-item index assesses seven components of QoS: subjective QoS, sleep latency, sleep duration, sleep efficiency, sleep disturbances, drug use for sleep, and daytime dysfunction. A total PSQI score is the total of individual scores from the seven components (range, 0-21). A score of ≥6 is considered to be indicative of poor QoS. The validation of PSQI in Turkish was performed by Agargun et al. [10].

Statistical analysis

All the statistical analyses were performed using the Statistical Package for the Social Sciences version 21.0 software package program (IBM Corp., Armonk, New York, USA). Descriptive statistics are presented as mean±standard deviation (SD). Mann-Whitney U test was used to compare the data between groups, and regression analysis was performed to evaluate the factors related to QoS. Statistical significance was determined as a p value of ≤0.05.

Table 1. Demographic features, pain scores, and NP causes (central, peripheral, and mixed) of the patients

	Patients with NP	Controls	P values
Ages (years)	45.04±10.21	39.00±19.23	NS
Sex (female/male)	54/16	22/8	NS
NP duration (months)	24.8±18.2		
Pain; Likert-type scale (0-5)	3.5±1.3		
Pain; VAS (0-100 mm)	77.4±22.3		
NP cause (central, peripheral, and mixed) n (%)	13/4/53 (19, 6, and 75)		

NP: neuropathic pain; NS: not significant; VAS: visual analog scale

Table 2. Comparison of the sleep quality components, total PSQI scores, and poor sleep quality distribution between patients and controls (mean±SD)

	Patients with NP (n=70)	Controls (n=30)	P values
Subjective sleep quality	1.54±0.89	1.38±0.75	0.106
Sleep latency	1.64±0.90	1.11±1.03	0.002
Sleep duration	1.17±1.04	0.7±0.5	0.003
Sleep efficiency	0.98±0.57	0.46±0.15	0.020
Sleep disturbance	2.01±0.69	1.30±0.61	0.000
Drug usage for sleep	0.95±0.38	0.19±0.03	0.073
Daytime dysfunction	1.50±1.04	1.19±1.09	0.040
PSQI total	8.82±3.50	5.69±2.70	0.000
Poor sleep quality (PSQI≥6) n (%)	56 (80)	11 (37)	0.000

NP: neuropathic pain; PSQI: Pittsburgh sleep quality index; SD: standard deviation

Results

Seventy patients with NP (54 females and 16 males) and 30 age- and sex-matched controls (22 females and eight males) were included in our study. The mean age of the patients and controls were 45.04±10.21 years and 39.00±19.23 years, respectively. NP duration of the patients was 24.8±18.2 months. The demographic features, pain scores (Likert scale and VAS), and NP causes (central, peripheral, and mixed) are shown in Table 1.

In our study, we evaluated the NP subcategories regarding its cause (central, peripheral, or mixed) and found similar poor QoS patterns among these groups (data were not shown).

While comparing PSQI domains of the participants, significantly higher scores of sleep latency (p=0.002), sleep duration (p=0.003), sleep efficiency (p=0.002), sleep disturbance (p<0.000), daytime dysfunction (p=0.04), and PSQI total were observed in patients with NP than in controls (p<0.000). Moreover, 80% of patients with NP and 37 % of controls were classified as having poor QoS (p<0.000). The comparison of QoS components, total PSQI scores, and poor QoS distribution between patients and controls are summarized in Table 2.

Table 3. Regression analysis for the poor sleep quality in patients with NP

	Unstandardized Coefficients		Standardized Coefficients		
	B	Std. Error	Beta	t	p
Age	-0.003	0.007	-0.067	-0.440	0.664
Sex	-0.461	0.193	-0.327	-2.385	0.026
NP duration	0.019	0.004	0.730	4.775	0.000
Pain; VAS	-0.005	0.004	-0.224	-1.260	0.221
Pain; Likert-type scale	0.085	0.069	0.249	1.229	0.006

VAS: visual analog scale; NP: neuropathic pain

Regression analysis revealed that sex (worse in female patients than in male ones), NP duration, and pain intensity were factors related to having poor QoS in patients with NP (p=0.026 and p<0.000). These data are shown in Table 3.

Discussion

QoS can be affected by several factors such as coexisting diseases, clinical symptoms, psychological disorders, and many painful conditions. It has been suggested that >70% of patients with chronic pain report sleep disturbances [11]. It is reasonable that similar to other types of chronic pain, patients with NP may present with sleep disturbances, which can cause treatment difficulties and reduce the likelihood of a successful management. In previous studies, it has been found that more than half of the patients with painful diabetic neuropathy reported substantial sleep interference [12]. Similarly, sleep disturbance has been reported to be a common comorbid condition in patients with postherpetic neuralgia, leading to depression and anxiety and both of which can contribute to pain and sleep interference [7, 12]. In our study, while investigating the quality component of sleep in patients with NP, 80% of patients with NP presented with poor QoS. Our results may contribute to the general perception of sleep disturbances in NP by adding a poor QoS component to these patients.

There has been a common consideration that normal aging changes interfere with QoS. However, an increasing age was not a factor related to poor QoS in our patients with NP. This may be because of the poor QoS pattern, which was also presented by younger patients with NP. Pain severity was another factor correlated with poor QoS in our study. In a previous study on patients with diabetic peripheral neuropathy, patients with severe pain reported more sleep problems [13]. Moreover, it has been reported that the majority of patients with chronic pain reported "pain" to be the main reason for their sleep disturbance [14]. Poor QoS was found to be related to NP duration in our study. This result appears to be in parallel to those reported in previous studies that demonstrated the higher prevalence of sleep problems in patients with chronic pain [15, 16].

In our study, the patients had significantly worse scores than the controls in five components of QoS: sleep duration, sleep latency, sleep disturbance, sleep efficiency, and daytime dysfunction. It has been previously reported that patients with NP often experience difficulties in initiating sleep and remaining asleep, and most patients reported suboptimal sleep durations [12]. It can be considered that NP has multidimensional effects on sleep. Furthermore, previous studies on NP showed that patients may present with impairments in all aspects of HRQoL, one of which is sleep disturbance that is reported by 88% of patients [17, 18]. Because comorbid sleep disturbances in patients with NP have an impact on QoL, a comprehensive evaluation of patients with NP should include an assessment of QoS, an important component of QoL.

The association between sleep disturbances and NP may be accepted as a complex process. Poor QoS may exacerbate pain, and in turn, pain may exacerbate the poor QoS. In an experimental animal model of NP, Narita et al. [19] revealed a decrease in the non-rapid eye movement sleep and an increase in wakefulness under a NP-like state. They concluded that NP-like stimuli can suppress γ-aminobutyric acid (GABAergic) transmission with increased GABA transporters located on activated astrocytes in the cingulate cortex related to sleep disturbance. In another experimental study, it was shown that sleep deprivation makes rats more vulnerable to nerve injury-induced NP probably because of associated lower melatonin levels [20]. Although these observations, at least in part, might explain the sleep disturbances in patients with NP, there appears to be a need for clarifying this association.

In our study, we evaluated the NP subcategories regarding to its cause (central, peripheral, or mixed) and found similar poor QoS patterns in both the groups. This observation may lead to a consideration that the quality component of sleep is impaired in most patients with NP, regardless of its causative factor.

The efficacy of anticonvulsants and antidepressants in improving NP and its impact on QoL and mood disturbances have been demonstrated [11]. Because of the similarities in the pathophysiology of NP, treatments used in NP may also theoretically improve sleep and reduce anxiety besides reducing pain. In a previous study that investigated the beneficial effects of pregabalin on HRQoL, sleep, and pain, pregabalin-related improvements in QoS and HRQoL were found to be marginally related to reductions in pain intensity in patients with NP [21]. In this study, although improvement in QoS was as a significant predictor of better HRQoL, pain reduction was not found to be a related factor. Thus, it is suggested that treatments that can address not only pain relief but also QoS improvement in patients with NP may represent viable management options for the population with NP.

In our study, while investigating the quality component of sleep in patients with NP, 80% of patients with NP presented poor QoS regardless of NP cause. Female sex, pain severity, and NP duration were found to be factors correlated with poor QoS in our study. Compared with our controls, our patients had significantly worse scores in five components of QoS: sleep duration, sleep latency, sleep disturbance, sleep efficiency, and daytime dysfunction. This observation suggests that poorer QoS should be considered for the management of patients with NP.

In conclusion, QoS should be assessed as a part of the diagnostic work-up in patients with NP, and strategies that target not only NP itself but also better QoS may contribute to the overall success of management.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Atatürk University School of Medicine Clinical Research Ethic Comitee (20.03.2014/ B.30.2.ATA.0.01.00/31).

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