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Evaluation of Neuropathic Pain Frequency and Related Factors in Patients with Chronic Low Back Pain

Kronik Bel Ağrısı Olan Hastalarda Nöropatik Ağrı Sıklığı ve İlişkili Faktörlerin Değerlendirilmesi

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ABSTRACT Objective: The aim of this study was to evaluate the prevalence of neuropathic pain in patients with chronic low back pain (LBP) using the PainDETECT questionnaire (PDQ) and to evaluate the relationship between neuropathic pain and physical disability, anxiety and depression. **Material and Methods:** Between June 2018 and December 2019, 141 patients with chronic LBP (35 males, 106 females; mean age: 49.4±12.0 years; range 20 to 65 years) were included in the study. Based on the PDQ, participants were classified into 2 groups: the neuropathic group and the non-neuropathic group. Socio-demographic characteristics and clinical data of the patients were recorded. Pain was evaluated with the visual analogue scale (VAS), disability with the Oswestry Disability Index (ODI), depression with the Zung Self-Rating Depression Scale (SDS) and anxiety with the Beck Anxiety Inventory (BAI). **Results:** In this study, neuropatic pain was detected in 21.3% of the patients with chronic LBP. Neuropathic pain was associated diabetes and pain radiation below the knee (p=0.002, p=0.003). However, there was no significant difference between the groups in age, gender, body mass index and smoking (p=0.06, p=0.9, p=0.4, p=0.4). VAS scores questioning current pain, mean pain in the last 4 weeks, and most severe pain in the last 4 weeks were significantly higher in the neuropathic pain group than in the non-neuropathic pain group (p=0.001, p<0.001, p=0.001). ODI, SDS, BAI scores were significantly higher in the neuropathic pain group than in the non-neuropathic pain group (p<0.001, p<0.001, p<0.001). **Conclusion:** Neuropathic pain is a major contributor to chronic LBP and its role should not be ignored.

Keywords: Chronic low back pain; neuropathic pain; PainDETECT questionnaire

ÖZET Amaç: Bu çalışmanın amacı, "PainDETECT ağrı anketi" kullanarak kronik bel ağrılı hastalarda nöropatik ağrı prevalansını ve nöropatik ağrı ile fiziksel özürlülük, anksiyete ve depresyon arasındaki ilişkiyi değerlendirmektir. **Gereç ve Yöntemler:** Haziran 2018-Aralık 2019 tarihleri arasında kronik bel ağrılı 141 hasta (35 erkek, 106 kadın; ortalama yaş: 49,4±12,0 yıl; dağılım 20-65 yıl) çalışmaya dâhil edildi. "PainDETECT ağrı anketine" dayanarak, katılımcılar 2 gruba ayrıldı: nöropatik grup ve nöropatik olmayan grup. Hastaların sosyodemografik özellikleri ve klinik verileri kaydedildi. Ağrı, görsel analog skala [visual analogue scale (VAS)] ile özürlülük, Oswestry Özürlülük İndeksi [Oswestry Disability Index (ODI)] ile depresyon, Zung Depresyon Ölçeği [Zung Self-Rating Depression Scale (SDS)] ile anksiyete, Beck Anksiyete Envanteri [Beck Anxiety Inventory (BAI)] ile değerlendirildi. **Bulgular:** Bu çalışmada kronik bel ağrılı hastaların %21,3'ünde nöropatik ağrı saptandı. Nöropatik ağrı, diyabet ve diz altına ağrı yayılımı ile ilişkiliydi (p=0,002, p=0,003). Ancak yaş, cinsiyet, beden kitle indeksi ve sigara kullanımı açısından gruplar arasında anlamlı fark yoktu (p=0,06, p=0,9, p=0,4, p=0,4). Mevcut ağrıyı, son 4 haftadaki ortalama ağrıyı ve son 4 haftadaki en şiddetli ağrıyı sorgulayan VAS skorları, nöropatik ağrı grubunda, nöropatik ağrı olmayan gruba göre anlamlı derecede yüksekti (p=0,001, p<0,001, p=0,001). ODI, SDS, BAI skorları nöropatik ağrı grubunda, nöropatik ağrı olmayan gruba göre anlamlı derecede yüksekti (p<0,001, p<0,001, p<0,001). **Sonuç:** Nöropatik ağrı, kronik bel ağrısına önemli katkıda bulunur ve rolü göz ardı edilmemelidir.

Anahtar Kelimeler: Kronik bel ağrısı; nöropatik ağrı; painDETECT ağrı anketi

Low back pain (LBP) is the pain of the region between the 12th rib and the inferior gluteal fold and is a musculoskeletal problem that causes significant disability in industrial societies.[1] While 90% or more of LBP heals within the first 3 months, the remaining 10% of the pain heal more slowly and become chronic. Studies have shown that chronic LBP causes a high level of disability by negatively affecting daily life and work life.[2]

Previously, chronic pain was thought to arise via two sources: nociceptive, which is associated with tissue damage and neuropathic, caused by injury or

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disease affecting the nervous system.[3] Chronic LBP covers a spectrum of different types of pain, including nociceptive pain, neuropathic pain and in some cases, nociplastic pain, which is caused by amplification of pain in the central nervous system.[4] Although the cause of pain in chronic LBP has disappeared, the chronic pain may become neuropathic as a result of the persistence of the lesion in the somatosensory system. Although it varies depending on the method used in the studies, the prevalence of neuropathic pain in chronic LBP was found to be 16%-55%.[5] In chronic LBP, the neuropathic component is significantly associated with socio-economic loss. It has been shown that the neuropathic component is responsible for 96% of the total expenditures in chronic LBP.[6] The role of neuropathic pain in chronic LBP is often overlooked, but early diagnosis and treatment of the neuropathic component is very important.

The negative effect of chronic LBP on quality of life is well known. There are very few studies investigating the effect of neuropathic pain component on quality of life and disability in chronic LBP. In this study, we aimed to determine the frequency of neuropathic pain component in chronic LBP using the painDETECT questionnaire (PDQ) and to determine the effect of neuropathic pain on pain intensity, disability, anxiety and depression.

MATERIAL AND METHODS

This study was designed as a cross-sectional study and conducted at Ankara University, Faculty of Medicine, Department of Physical Medicine and Rehabilitation, between June 2018 and December 2019. A total of 141 patients were included.

The inclusion criteria were: 1) patients between 20 and 65 years of age, 2) LBP lasting more than 3 months. Patients were excluded if they have 1) history of low back surgery, 2) inflammatory diseases, spine infection, tumors, 3) active psychiatric illness, 4) pregnancy or breastfeeding. Informed consent was provided from all the participants.

The study was approved by Ankara University Faculty of Medicine Clinical Research Ethics Committee (date: June 12, 2017, no: 11-621-17) and all procedures were performed in compliance with the Helsinki Declaration.

Demographics of the patients including age, gender, height, weight, history of smoking, presence of diabetes mellitus and presence of pain radiation below the knee were recorded.

Severity of pain was assessed by using the visual analogue scale (VAS) with a range of 0-10 (0=no pain, 10=worst pain imaginable) to portray the current pain, the maximum pain during the past 4 weeks, and the average pain for the past 4 weeks.

The PDQ was used to determine the presence of neuropathic pain. PainDETECT questions the pattern, the severity and the presence of radiation of the pain.[7] Classification by score is done as follows: ≥19: neuropathic pain possible, 13-18: result uncertain, ≤12: neuropathic pain unlikely. In our study, those with possible neuropathic pain according to PDQ have neuropathic group, those with neuropathic pain as uncertain and unlikely were included in the non-neuropathic group.

The disability related to LBP was evaluated with Oswestry Disability Index (ODI). It consists of 10 questions. There are 6 options in each question, and the options are scored between 0 and 5. The evaluation is made based on answered questions. As the total score increases, the individual's disability level increases.[7]

The Zung Self-Rating Depression Scale (SDS) was applied to determine the level of depression. SDS includes 20 items exploring symptoms related to depressive episodes (two items for affective symptoms, eight for cognitive, eight for somatic symptoms and two for psychomotor symptoms); there are ten positive and ten negative questions. Scores on the test range from 20 to 80 and the scores are divided into four ranges that determine the severity of depression. SDS scores are classified as normal (<50), mild depression (50 to 59), moderate to marked major depression (60 to 69) and severe to extreme major depression (>70).[8] Beck Anxiety Inventory (BAI) was used to determine the level of anxiety experienced by the patients. BAI consists of 21 items with a Likert scale ranging from 0 to 3 and raw scores ranging from 0 to 63. The BAI scores are classified as

minimal anxiety (0 to 7), mild anxiety (8 to 15), moderate anxiety (16 to 25), and severe anxiety (26 to 63).[9]

STATISTICAL ANALYSIS

Continuous variables were expressed in mean±standard deviation, or median (minimum-maximum), while categorical variables were expressed in number and frequency. The Shapiro-Wilk test was used to evaluate the normal distribution of data. Chi-square and Fisher's exact probability tests were used to test for associations between categorical sociodemographic variables. Independent samples t-test was used to explore the mean difference in normally distributed continuous variables and the Mann-Whitney U test was used for nonparametric continuous data. The relationship between variables was evaluated using Pearson and Spearman correlation analysis. All statistical analyses were carried out using SPSS software version 21.0 (IBM Corp., Armonk, NY, USA), and a significance level of $p \leq 0.05$ was used.

RESULTS

A total of 141 patients were included. Of these, 106 (75.2%) were women. Mean age was 49.41 years (range 20-65 years). The average body mass index (BMI) of this study population was 28.95±5.85 kg/m^2. Based on the PDQ, 30 (21.3%) were classified as having likely neuropathic LBP, 35 (24.8%) uncertain, and 76 (53.9%) unlikely neuropathic pain. Those who were found to have likely neuropathic pain were included in the neuropathic group. Those with uncertain and unlikely neuropathic pain were included in the non-neuropathic group. Thus, the neuropathic group consisted of 30 patients (21.3%) and the non-neuropathic group consisted of 111 patients (78.7%).

All demographic and clinical characteristics of the patients are presented in Table 1. Table 2 presents the results of comparison of demographic and clinical parameters between the patients with and without neuropathic pain.

Gender distribution of the patients with and without neuropathic pain was similar (p=0.9). Age, BMI, smoking status were not significantly associated with the occurrence of neuropathic pain compared with the non-neuropathic group (p=0.06, p=0.4 and p=0.4). The VAS scores, ODI score, SDS score, BAI score were significantly increased in the neuropathic group. Pain radiation below the knee and diabetes were significantly increased in the neuropathic group (p=0.003 and p=0.002).

TABLE 1: Demographic and clinical characteristics of the 141 patients with chronic low back pain.

Age (years)[a]	49.41±12.03
Gender	
Female	106 (75.2%)
Male	35 (24.8%)
BMI (kg/cm^2)[a]	28.95±5.85
Smoking	
Yes	38 (27%)
No	103 (73%)
Diabetes mellitus	
Yes	23 (16.3%)
No	118 (83.7%)
VAS (present)[a]	4.90±1.90
VAS (average)[a]	5.39±1.74
VAS (maximum)[a]	7.63±1.53
Pain radiation below the knee	
Yes	82 (58.2%)
No	59 (41.8%)

[a]Mean±standard deviation; BMI: Body mass index; VAS: Visual analogue scale.

There were statistically significant positive correlations between PDQ score and ODI score (r=0.566 p<0.001), between PDQ score and SDS score (r=0.342, p<0.001), between PDQ and BAI score (r=0.362, p<0.001), and between PDQ and VAS scores (r=0.361, p<0.001, r=0.456, p<0.001, r=0.455, p<0.001). Binary correlation of patients with chronic LBP are shown in Table 3.

DISCUSSION

Our study showed that 21.3% of the patients with chronic LBP have neuropathic pain as screened by the PDQ. Neuropathic pain was associated with diabetes and pain radiation below the knee (p=0.002, p=0.003). However, there was no significant difference between the groups in age, gender, BMI and smoking (p=0.06, p=0.9, p=0.4, p=0.4). VAS scores questioning current pain, mean pain in the last 4

TABLE 2: Comparison of demographic and clinical characteristics between the groups.

n=141	Neuropathic group (n=30)	Non-neuropathic group (n=111)	p value
Age (years)[a]	53.30±9.22	48.35±12.51	0.06
Gender			0.9
Female	22 (20.7%)	84 (79.3%)	-
Male	8 (22.8%)	27 (77.2%)	-
BMI (kg/cm²)[a]	30.05±6.42	28.65±5.68	0.4
Smoking			0.4
Yes	6 (15.7%)	32 (84.3%)	-
No	24 (23.3%)	79 (76.7%)	-
Diabetes mellitus			0.002
Yes	11 (47.8%)	12 (52.2%)	-
No	19 (16.1%)	99 (83.9%)	-
VAS (present)[a]	5.93±1.68	4.63±1.87	0.001
VAS (average)[a]	6.40±1.63	5.11±1.67	<0.001
VAS (maximum)[a]	8.40±1.27	7.43±1.53	0.001
Pain radiation below the knee			0.003
Yes	25 (30.4%)	57 (69.6%)	-
No	5 (55.5%)	4 (44.5%)	-
Oswestry Disability Index[a]	54.40±12.00	41.58±12.45	<0.001
Zung Self-Rating Depression Scale[a]	55.77±9.87	45.46±9.95	<0.001
Beck Anxiety Inventory[a]	19.00±7.25	13.41±8.52	<0.001

[a]Mean±standard deviation; BMI: Body mass index; VAS: Visual analogue scale.

TABLE 3: Binary correlation of patients with chronic low back pain.

	r value	p value
PDQ score-ODI score	0.566	<0.001
PDQ score-SDS score	0.342	<0.001
PDQ score-BAI score	0.362	<0.001
PDQ score-VAS (present)	0.361	<0.001
PDQ score-VAS (average)	0.456	<0.001
PDQ score-VAS (maximum)	0.455	<0.001

PDQ: PainDETECT questionnaire; ODI: Oswestry Disability Index; SDS: Zung Self-Rating Depression Scale; BAI: Beck Anxiety Inventory; VAS: Visual analogue scale.

weeks, and most severe pain in the last 4 weeks were significantly higher in the neuropathic pain group than in the non-neuropathic pain group (p=0.001, p<0.001, p=0.001). ODI, SDS, BAI scores were significantly higher in the neuropathic pain group than in the non-neuropathic pain group (p<0.001, p<0.001, p<0.001). A positive correlation was observed between PDQ and ODI, SDS, BAI, VAS scores.

Chronic LBP is a complex, heterogeneous condition that might have nociceptive, neuropathic, and nociplastic components.[3] Nociceptive LBP is understood to be pain arising from the vertebral column or its adnexa, evoked by noxious stimulation of structures in the lumbar spine, or from the deep soft tissues of the back.[10] Neuropathic LBP describes pain arising from injury or disease directly affecting the nerve roots that innervate the spine and lower limbs, and pathological invasive innervation of the damaged lumbar discs. In chronic LBP, neuropathic pain may be caused by lesions of nociceptive sprouts within a degenerated disc, by mechanical compression of the nerve root or by the effects of inflammatory mediators arising from a degenerative disc that results in inflammation and damage to the nerve roots.[11]

In 2017, nociplastic pain is defined by the International Association for the Study of Pain as "pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain."[12] Nociplastic pain is defined as distinct from nociceptive pain caused by ongoing inflammation and tissue damage and neuropathic pain caused by nerve damage.[3] The

mechanisms underlying this type of pain are not fully understood but in which the principal mechanism is sensitization of the nervous system.[13]

In studies aiming to determine the prevalence of neuropathic pain in patients with LBP, a wide range of 19.3%-65.3% is stated.[14,15] This difference may be due to the duration of LBP (acute, subacute, chronic), the patient population included in the studies (ethnicity, rural or urban residents), the screening test used, the center where the study was conducted (primary, secondary, tertiary).

Freynhagen et al. aimed to provide an appropriate scale to determine the neuropathic pain and its prevalence in patients with chronic LBP.[16] For this purpose, they compared the PDQ they developed with other screening questionnaires (Leeds assessment of neuropathic symptoms and signs pain scale, Douleur Neuropathique 4 Questions, Neuropathic Pain Scale) developed for neuropathic pain. They revealed that it shows similar specificity and sensitivity, is applied in a short time and easily by the patient, and is important in early and appropriate treatment. In this multicenter study with 7,772 LBP patients, neuropathic (PDQ>19) pain was found in 37.0% of patients and nociceptive (PDQ<12) was found in 35.3% of the patients.

In our study, the mean age of the neuropathic group was higher than non-neuropathic group but it was not statistically significant (p=0.06).

Many studies have found a significant relationship between age and neuropathic pain.[4,15] Kesikburun et al. included the patients with chronic LBP between the ages of 18-65 in their study and found that neuropathic pain increases with age.[17]

In our study, there was no significant difference between the 2 groups regarding sex and BMI (p=0.9 and p=0.4).

El Sissi et al. found that older age and being female were significantly associated with the presence of neuropathic pain. The ratio of females with neuropathic pain was 2% higher than the ratio of males with neuropathic pain.[18]

In many studies, a significant relationship was found between neuropathic pain and higher BMI.[19,20] In our study, VAS, ODI, SDS, BAI scores were found to be significantly higher in the group with neuropathic pain compared with the group without neuropathic pain.

Freynhagen et al. found that the higher the PainDETECT score, the higher the VAS score was. They found that VAS 7 and above was 43% in neuropathic pain and 24% in nociceptive pain.[16] They found a close relationship between the neuropathic component and the frequency and severity of different comorbidities (depression, panic/anxiety, sleep disorders). Kew et al. in their study including 210 patients with LBP, detected neuropathic pain in 12.4% of patients according to PDQ.[19] Pain severity scores at all the three time points (at the time of interview, on its average and at its strongest, in the preceding four weeks), the level of disability, anxiety and depression were found to be significantly higher in the neuropathic pain group. In the study conducted by Kaki et al. in 1,169 patients with chronic LBP, smoking was found to be significantly higher in the group with neuropathic pain compared to those without.[15] The reason for this is that nicotine in cigarettes causes the release of neuradrenaline, accelerates neuropathic pain by increasing sympathetic activity by vasoconstriction, as in complex regional pain syndrome, or accumulating in peripheral arteries to cause atherosclerosis and ischemia.

Due to the smaller number of patients included in our study, a relationship between neuropathic pain and smoking couldn't be detected. Similarly, there are studies that did not find a significant relationship between smoking and neuropathic pain.[17,18] In our study, a significant positive relationship was found between neuropathic pain and diabetes mellitus. Diabetes mellitus is an important cause of neuropathic pain that affects the sensory, motor or autonomic nerves in different ways, creating a heterogeneous clinical picture.[21]

In our study, a positive significant relationship was found between pain radiating below to the knee and neuropathic pain. In the study by Kew et al., leg pain radiating down to the knee was found to be significantly higher in the neuropathic group.[19] However, it has been noted that radicular leg pain does not consistently differentiate neuropathic LBP from non-neu-

ropathic LBP.

In the study conducted by El Sissi et al., disc prolapse was found to be significantly higher in patients with neuropathic pain. On the other hand, traumatic, inflammatory and degenerative causes were found to be significantly lower in patients with neuropathic pain.[18] In the study conducted by Hiyama et al., lumbar disc herniation was the most prevalent diagnosis in the neuropathic pain group, while non-specific LBP was most prevalent in the nociceptive pain group.[22] In the study of Kew et al., the etiology of LBP in the neuropathic pain group was investigated 76.9% of the patients had lumbar spondylosis, 42.3% had spinal canal stenosis, 19.2% had spondylolisthesis, 15.4% had disc prolapse, 7.7% had myofascial pain syndrome, and 3.8% had spinal trauma. However, no significant difference was found between the group with and without neuropathic pain in terms of disease etiology. In addition, patients were evaluated with magnetic resonance imaging (MRI), and nerve root compression was not found to be significantly higher in the neuropathic pain group in MRI. With these results, it was concluded that conditions were typically associated with nerve root compression, such as lumbar spinal stenosis, intervertebral disc prolapse, spondylolisthesis, and conditions associated with nerve root compression on MRI and evidence of nerve root compression on MRI are not always correlated with neuropathic pain.[19]

Our study has several limitations. In our study, we used PDQ for neuropathic pain diagnoses although that has high sensitivity and spesifity, it is known that it can not differentiate neuropathic and nociceptive on biological bases. Although screening tests guide the clinician about neuropathic pain, they can not be an alternative to clinical examination. The other limitation might be the patients in our study were taken from an institution providing tertiary health services in a single center in a metropolitan city.

Bouhassira et al. and Torrance et al. reported that neuropathic pain is more prevalent in unemployed rural dwellers and those with a lower professional or educational status.[23,24]

The last limitation might be that the etiology of LBP in our patients was not differentiated.

CONCLUSION

As a result of this study, we found that patients had higher scores for pain intensity, anxiety, depression and disability in the presence of neuropathic pain in chronic LBP. For this reason, it is necessary to investigate the presence of neuropathic pain while evaluating patients with chronic LBP. It should be kept in mind that presence of neuropathic pain would have a negative effect on LBP.

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

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