

Kronik Bel Ağrısı: Nöropatik Ağrı ve Özellikleri**Chronic Low Back Pain: Neuropathic Component and Its Characteristics**Esra Selimoğlu¹, Sadiye Murat², Selin Turan Turgut³, Afitap İçağasioğlu², Serap Yunsuroğlu Gürek⁴, Yasemin Yumusakhuyul²¹Erenköy Fizik Tedavi ve Rehabilitasyon Hastanesi, Fizik Tedavi ve Rehabilitasyon Kliniği, İstanbul, Türkiye²İstanbul Medeniyet Üniversitesi, Göztepe Eğitim ve Araştırma Hastanesi, Fizik Tedavi ve Rehabilitasyon Kliniği, İstanbul, Türkiye³Karaman Devlet Hastanesi, Fizik Tedavi ve Rehabilitasyon Kliniği, Karaman, Türkiye⁴Kayseri Eğitim ve Araştırma Hastanesi, Fizik Tedavi ve Rehabilitasyon Kliniği, Kayseri, Türkiye**Özet**

GİRİŞ ve AMAÇ: Kronik bel ağrısı hayatı tehdit eden bir hastalık olmamakla birlikte ciddi dizabiliteye neden olabilmektedir. Kronik bel ağrısı nöropatik veya nosiseptif kaynaklı olabilmektedir. Bu çalışmanın amacı kronik bel ağrılı hastalarda DN4 skalasıyla nöropatik ağrıyı saptamak; klinik ve demografik özelliklerini belirlemektir.

YÖNTEM ve GEREÇLER: Çalışmaya 20-75 yaş arası kronik bel ağrılı 224 hasta dahil edildi. Hastaların lomber bölge muayeneleri yapıp demografik özellikleri kaydedildi. Bütün hastalar DN4 skalasını doldurdular. Ağrı için görsel analog skala (VAS), dizabilite için Oswestry Dizabilite İndeksi (ODİ), yaşam kalitesi için SF-36, ve duygusal durum için Beck Depresyon İndeksi (BDİ) kullanıldı.

BULGULAR: DN4 skalasına göre hastaların %55,8'inde nöropatik ağrı bulunmaktaydı. Nöropatik ağrı sıklığı kadın cinsiyetle, radiküler ağrıyla ve duyu kaybıyla artmaktaydı. Nöropatik ağrılı hastaların VAS, ODİ ve BDİ puanları daha yüksekken, nosiseptif ağrılı hastaların SF-36 puanları tüm parametrelerde daha yüksek bulundu.

TARTIŞMA ve SONUÇ: Kronik bel ağrılı olgularda çoğunlukla nöropatik ağrı da vardır. Eğer hasta nöropatik ağrıyı iyi tanımlayabilirse ağrı daha iyi dindirilebilir, yaşam kalitesi artırılabilir, depresyon ve dizabilite düzeyi azaltılabilir.

Anahtar Kelimeler: kronik bel ağrısı, nöropatik ağrı, nosiseptif ağrı, DN4 skalası

Abstract

INTRODUCTION: Although chronic low back pain (CLBP) is not a life-threatening disease, it is characterized with high level of disability and is recognized to have both neuropathic and non-neuropathic origins. The aim of this study was to determine the prevalence of neuropathic pain component by DN4 scale in patients with CLBP and evaluate its relation with clinical and demographic characteristics.

METHODS: A total of 224 patients aged between 20-75 years with a history of CLBP were included in the study. The demographic data and lumbar region examinations were recorded. The patients filled out DN4 forms. The patients were evaluated for pain by visual analog scale (VAS), for disability by Oswestry Disability Index (ODI), for quality of life by SF-36 and for emotional status by Beck Depression Inventory (BDI).

RESULTS: According to the DN4 scale 55.8% of the patients had neuropathic pain. Neuropathic component was found to be associated with female gender, radicular pain and sensory deficit. The patients with neuropathic pain had higher VAS, ODI and BDI scores whereas the patients with nociceptive pain had higher scores for all the parameters of the SF-36.

DISCUSSION AND CONCLUSION: CLBP cases are generally associated with a neuropathic component. If one differentiates neuropathic pain from non-neuropathic pain, than can reduce the pain, improve the quality of life, and decrease the level of disability and depression.

Keywords: chronic low back pain, neuropathic pain, nociceptive pain, DN4 scale

INTRODUCTION

Low back pain has been a serious health problem since the beginning of human history which currently affects 50-80% of people in Western countries at some point in their lives and stands as one of the major health issues causing workday loss, medical cost and injury (1). Chronic low back pain (CLBP) is defined as pain persists for at least 3 months (2). CLBP is not a life-

threatening disease, it is characterized with high level of disability (2, 3) and is recognized to have both non-neuropathic and neuropathic origins (4, 5). If a primary lesion or dysfunction in the nervous system causes the pain than it is called neuropathic pain (6).

Recent studies support the presence of mixed pain in CLBP cases. As the pain becomes more chronic, neuropathic component is observed to

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be more influential. When the pain continues after the normal healing period and it is accompanied by sensory, motor, autonomic and neurologic findings, one should think of neuropathy (4). However, the core shortcoming of this limited view was overlooking the neural tissues other than the ones localized in the nerve roots of the peripheral and central nervous systems (6).

The symptoms of neuropathic pain and severity of pain can be determined by using various pain scales (7). DN4 questionnaire is a screening tool for neuropathic pain which was recommended by the International Association for the Study of Pain (IASP). It is consisting of 10 items; 7 of them related to pain quality based on an interview with the patient, and 3 items based on the physical tests that are related to the presence or absence of touch or pinprick hypoesthesia and tactile allodynia (8). Bouhassira et al. conducted a review study about the neuropathic pain screening tests and found the sensitivity and specificity of DN4 as 83% and 90%, which made it the most specific screening test compared to the clinical diagnosis (9).

Epidemiologic studies have shown that patients with neuropathic pain have higher severity of pain, lower quality of life, and higher level of disability (10-12). However, the number of studies indicating a relationship between those parameters and presence of neuropathic component in patients with CLBP is very limited (13). In this study, we aimed to determine the prevalence of neuropathic pain component in patients with CLBP by using DN4 scale and to demonstrate the relation of neuropathic component with clinical and demographic characteristics such as severity of pain, quality of life, disability, and depression.

METHODS

The medical ethics committee of the İstanbul Medeniyet University Goztepe Training and Research Hospital approved the study and

written informed consent was obtained from all patients.

This was a cross-sectional, single blinded, prospective observational study. The patients were recruited from physical therapy and rehabilitation outpatient clinics of the İstanbul Medeniyet University Goztepe Training and Research Hospital. We enrolled 224 patients aged 20-75 years and diagnosed with CLBP by primary outpatient clinics doctor, who have been suffering pain for at least half the day during the past 3 months. To be included in the study patients have to get mechanical low back pain, but we neither assess the etiology of the CLBP nor done any radiologic imaging studies or laboratory tests to identify the diagnosis. The patients in whom CLBP was associated with acute fracture, neoplasia, infection, pain reflecting from abdominal or pelvic organs, or pregnancy were excluded from the study. All patients gave their written informed consent before entering the study.

Each patient filled out a questionnaire concerning the current therapy, low back pain extending to the legs, and history of other diseases. The patients were evaluated for pain by Visual Analog Scale (VAS), for disability by Oswestry Disability Index (ODI), for quality of life by Short Form 36 Health Survey (SF36), and for emotional status by Beck Depression Inventory (BDI). A physical medicine and rehabilitation specialist who was blinded to the results of the DN4 and other questionnaire, assessed all patients for general posture and physical examination involving the lumbar region and both hips, knees, and ankles. Motor system examination was performed to evaluate the muscle strength and reflexes. Muscle strength was assessed by applying manual muscle test to key motor points of both lower extremities, starting at the L2 level. Similarly, sensory system examination was performed from the key sensory points, starting at the L2 level.

The patients also completed a DN4 questionnaire. This questionnaire is consisted of 10 items about the neuropathic pain. First 7 questions are based on an interview with the patient, whereas the remaining 3 are based on clinical examination. First 3 questions defines the characteristics of the pain (burning, painful cold, electric shocks). The next 4 questions inquires presence of paresthesia/dysesthesia over the pain site (tingling, pins and needles, numbness, itching). 8th and 9th items aims to reveal a possible presence of sensory deficit in the painful area (hypoesthesia to touch, hypoesthesia to pinprick). 10th item determines whether brushing causes pain or increases an already existing pain. The patient answers the questions as 'Yes' or 'No'. Total score is calculated by giving a score of 1 to each 'Yes' and a score of '0' to each 'No'. The cut-off value for the diagnosis of neuropathic pain is a total score of 4/10 (8). The study population was split into two groups based on the DN4 scale as follows: those who scored less than 4 (non-neuropathic group) and those who scored ≥ 4 in the DN4 scale (neuropathic group). These two groups were compared in terms of severity of pain, quality of life, disability, and depression.

Statistical analyses were performed with NCCS (number cruncher statistical system) 2007 & PASS (power analysis and sample size) 2008 statistical software (Utah, USA). Study data were evaluated by descriptive statistical methods (mean, standard deviation, median, frequency, and ratio), Student's t-test was used for the intergroup comparison of normally distributed parameters and Mann-Whitney U test was used for the intergroup comparison of non-normally distributed parameters. Qualitative data were analyzed by Chi-square test and Fisher's exact test. The relationship between the scale scores were evaluated with Pearson's and Spearman's correlation analysis. Significance was determined as $p < 0.05$ with 95% confidence interval.

RESULTS

Our study was performed on a total of 224 patients. The neuropathic group consisted of 55.8% (n=125) and the non-neuropathic group consisted of 44.2% (n=99) of the patients. Definitive characteristics relative to the groups are shown in Table 1.

Tablo 1. Definitive Characteristics

		Total (n=224)	GROUPS		*p	
			Non-neuropathic Group (n=99)	Neuropathic Group (n=125)		
			Mean±SD	Mean±SD		
Age		47,50±13,18	46,74±14,45	48,10±12,39	0,445	
Gender	Female	169 (75,4%)	60 (60,6%)	109 (87,2%)	0,001**	
	Male	55 (24,6%)	39 (39,4%)	16 (12,8%)		
Smoking status	Never smoker	138 (61,6%)	61 (61,6%)	77 (61,6%)	0,958	
	Smoker	46 (20,5%)	21 (21,2%)	25 (20,0%)		
	Quitter	40 (17,9%)	17 (17,2%)	23 (18,4%)		
Comorbidity	None	136 (60,7%)	70 (70,7%)	66 (52,8%)	0,006**	
	Diabetes	19 (8,5%)	5 (5,1%)	14 (11,2%)	0,162	
	++Hypothyroidism	10 (4,5%)	4 (4,0%)	6 (4,8%)	1,000	
	++Depression	9 (4,0%)	2 (2,0%)	7 (5,6%)	0,305	
	Hypertension	22 (9,8%)	8 (8,1%)	14 (11,2%)	0,580	
	Other	28 (12,5%)	10 (10,1%)	18 (14,4%)	0,466	
Neurologic Deficit	Motor	+	11 (4,9%)	3 (3,0%)	8 (6,4%)	0,246
		-	213 (95,1%)	96 (97,0%)	117 (93,6%)	
	Sensory	+	33 (14,7%)	5 (5,1%)	28 (22,4%)	0,001**
		-	191 (85,3%)	94 (94,9%)	97 (77,6%)	
Treatment	No treatment	88 (39,3%)	50 (50,5%)	38 (30,4%)	0,002**	
	NSAID+Muscle Relaxant	90 (40,2%)	32 (32,3%)	58 (46,4%)	0,033*	
	Antiepileptic	8 (3,6%)	3 (3,0%)	5 (4,0%)	1,000	
	Other	38 (17,0%)	14 (14,1%)	24 (19,2%)	0,316	

Student's t-Test *p<0,05 +Chi-square Test **p<0,01 ++Fisher's Exact Test

The mean VAS score of the neuropathic group was significantly higher than that of the non-neuropathic group ($p < 0.01$).

Regarding the SF-36 Health Survey, the non-neuropathic group had higher physical functioning, physical role functioning, bodily pain, general health perceptions, social functioning, vitality, emotional role functioning and mental health scores as compared with the

neuropathic group ($p<0.01$) (Figure 1).

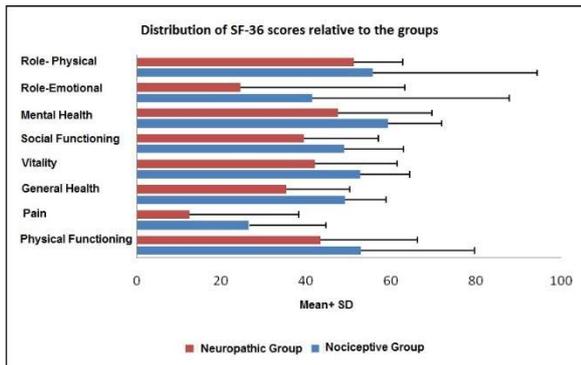


Figure 1. Distribution of SF-36 scores relative to the groups

Neuropathic group was observed to have higher mean ODI total score, ODI percentage score, and disability grade, as compared with the non-neuropathic group ($p<0.01$) (Table 2).

Table 2. Evaluation of Oswestry Disability Index relative to the groups

	Total (n=224)	Groups		p
		Non-neuropathic Group (n=99)	Neuropathic Group (n=125)	
		Mean±SD (Median)	Mean±SD (Median)	
ODI Total	22,37±8,23	18,59±7,65	25,37±7,42	0,001**
ODI Percentage	44,74±16,46	37,17±15,30	50,74±14,85	0,001**
ODI Grade	2,67±0,87 (3,00)	2,28±0,79 (2,00)	2,98±0,81 (3,00)	0,001**

** $p<0,01$

The BDI scores were higher in the neuropathic group than in the non-neuropathic group ($p<0.01$) (Figure 2).

By assessing the DN4 questionnaire we saw that the 4th question got the highest number of “Yes” response (64.3%), whereas the 10th question got the lowest number of ‘Yes’ response (15.2%). The distribution of the responses relative to the groups are shown in Table 3.

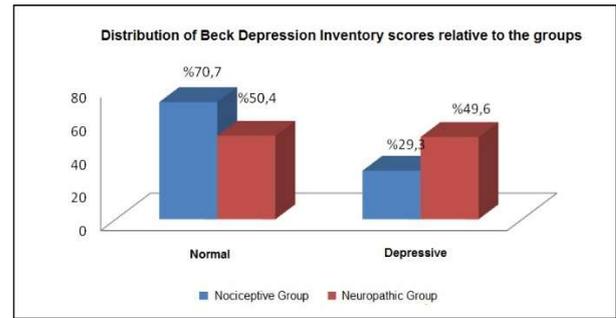


Figure 2. Distribution of Beck Depression Inventory scores relative to the groups

Table 3. Distribution of DN4 Survey questions relative to the groups

DN	Total (n=224)	Groups	
		Non-neuropathic Group (n=99)	Neuropathic Group (n=125)
		n (%)	n (%)
DN1	123 (54,9%)	30 (30,3%)	93 (74,4%)
DN2	88 (39,3%)	17 (17,2%)	71 (56,8%)
DN3	79 (35,3%)	13 (13,1%)	66 (52,8%)
DN4	144 (64,3%)	31 (31,3%)	113 (90,4%)
DN5	136 (60,7%)	27 (27,3%)	109 (87,2%)
DN6	90 (40,2%)	10 (10,1%)	80 (64,0%)
DN7	38 (17,0%)	3 (3,0%)	35 (28,0%)
DN8	83 (37,1%)	10 (10,1%)	73 (58,4%)
DN9	82 (36,8%)	18 (18,4%)	64 (51,2%)
DN10	34 (15,2%)	9 (9,1%)	25 (20,0%)

DISCUSSION

One of the most frequently reported chronic pain conditions is low back pain and it is a well recognized fact that CLBP is characterized with nociceptive, neuropathic, or both pain properties (14). Clinical practice guidelines classify patients with LBP into; LBP associated with an underlying disease (1–2% of cases); LBP associated with a neurological condition (about 5%); and nonspecific LBP (more than 90%) (15). However, the prevalence of neuropathic pain in CLBP reported differently in various studies and is not exactly known. In this study, we aimed to determine the prevalence of neuropathic pain by using DN4 scale and investigate conditions associated with it.

Kaki et al. (16) studied the prevalence of neuropathic pain in 1169 patients with CLBP by using LANSS pain scale and found that 54.7% of the patients had neuropathic pain, while 45.3% had non-neuropathic pain. Another prospective,

multicenter study (17) evaluated 1134 patients based on the LANSS pain scale and found that 55% had results consistent with neuropathic pain component. Freynhagen et al. (18) developed a new scale for determining neuropathic pain component in patients with CLBP which was called as Pain Detect, and they detected neuropathic pain in 37% of their patients. In one other prevalence study (19), 49.5% of the 107 patients were observed to have a DN4 scale ≥ 4 . Our study was consistent with previous data which determined neuropathic pain prevalence by using LANSS pain scale. 55.8% of the patients had neuropathic pain and 44.2% had non-neuropathic pain.

There are studies in the literature investigating the association between neuropathic pain component and various sociodemographic data. Quedro et al. (20) split patients in neuropathic and non-neuropathic groups based on the DN4 evaluation and found no significant difference between them with regard to mean age; female gender was more predominant in the neuropathic group but the difference was not significant. Hassan et al. (21) found higher mean age in the non-neuropathic group, however, the groups presented no significant difference relative to gender. In the present study, we observed no significant difference between the groups relative to mean age. Furthermore, significantly higher number of female cases were observed in the neuropathic group ($p < 0.05$).

Although smoking poses an elevated risk for low back pain, the reports in the literature appear to be contradictory on this subject. In their study, Kaki et al. (16) observed higher rates of neuropathic pain among smokers and associated this finding with the fact that nicotine triggers noradrenaline release which in turn accelerates the disease development. Quedrago et al. (19) did not include the factor of smoking in their study, however, they noted that smoking could contribute to the development of neuropathic pain component in patients with CLBP via axonal degeneration. Here we found no relationship between smoking status and neuropathic pain. Neuropathic pain occurs after a disease affecting the somatosensory system. As in other chronic types of pain, various comorbidities such as sleep disorders, depression, and anxiety may have an

influence over disease process and response to treatment. A close relationship has been shown between neuropathic component and prevalence and severity of different comorbidities (22). El Sissi et al. (17) found a significantly high prevalence of neuropathic component associated with diabetes and diabetes and hypertension in patients with CLBP. Kaki et al. (16) evaluated diabetes and hypertension separately in patients with CLBP and found no significant relationship with them and neuropathic component, however, the prevalence of diabetes and hypertension coexistence was found to be strongly correlated. Hassan et al. (21) did not find any significant relationship of neuropathic component with diabetes or hypertension. There was no statistically significant relationship between the groups with regard to comorbidity rates in our study.

Neuropathic mechanisms are believed to have an important role in the extension of low back pain to the leg (22). Nonetheless, there is no exact definition of neuropathic low back pain, with no consensus over its clinical signs (23). In a study (24), the degree of neuropathic pain was found to be consistent with the extension to distal leg, however, the presence of neuropathic component was observed to be possible among patients with proximal extension. Beith et al. (25) confirmed the association between clinical leg pain and neuropathic component, however, since the pain was extended to the leg in the non-neuropathic group of their study as well, they noted that low back pain extending to leg was a sensitive, but not a specific finding relative to neuropathic pain component. In our study, the rate of patients with a low back pain extending to the leg was significantly higher in the neuropathic group than in the non-neuropathic group ($p < 0.05$).

In this study, there was no significant difference between the motor deficit rates of the groups, however, the difference between the sensory deficit rates was significant. The rate of sensory deficit was significantly higher in the neuropathic group than in the non-neuropathic group.

As CLBP is recognized to have both non-neuropathic and neuropathic origins (16, 21, 25,

26), combined use of antidepressant and/or anticonvulsants with opioids, NSAIDs, or muscle relaxants are recommended in the treatment (3, 13, 27). In the study of Quedroago et al. (19), 9 of the 53 patients with neuropathic component were found to be receiving a therapy confirmed to be effective in neuropathic pain. In the study of El Sissi et al. (17), 11.4% of the patients with CLBP having neuropathic component (55.4%) were found to be under proper medical therapy. In the present study, the percentage of patients receiving no treatment was significantly higher in the non-neuropathic group, whereas the number of cases receiving NSAID and muscle relaxant therapy was significantly higher in the neuropathic group. Despite the presence of neuropathic component in 55.8% of the patients, only 3.6% of the patients were under a therapy with confirmed efficacy in neuropathic pain, while there was no one receiving combination therapy. In light of these findings, we associate the inadequate response in patients with CLBP with failure to recognize the pain as of mixed nature, ignoring of the neuropathic component and thus application of an insufficient treatment.

In many studies, patients with neuropathic pain have been shown to have higher level of pain, poorer quality of life, and increased disability (9-11, 30). Bouhassira et al. (9) determined higher level of pain and lower quality of life in patients with neuropathic pain than in patients without neuropathic pain. Smith et al. (12) observed higher level of pain and poorer quality of life in patients with chronic neuropathic pain. In the study of Beith et al. (25), patients with CLBP who were included in the neuropathic pain group demonstrated higher severity of pain relative to VAS, higher disability relative to Rolland Morris Disability Index, higher anxiety and depression relative to Hospital Anxiety and Depression Scale, and significantly lower quality of life relative to SF-36 Health Survey. In the present study, patients with CLBP having neuropathic pain exhibited higher severity of pain in VAS, lower quality of life in all subparameters of SF-36 survey, higher disability in ODI, and higher depression points in BDI.

Neuropathic pain symptoms are comprised of negative sensorial symptoms such as numbness, hypoalgesia, and hypoesthesia; and positive

sensorial symptoms such as paresthesia, dysesthesia, needles and pins, burning pain, sharp pain, pain similar to electric shock, allodynia, and hyperalgesia. These symptoms and severity of pain can be determined by various pain scales (6). We applied DN4 scale in the present study. The highest number of "Yes" responses were obtained for 'tingling', whereas the lowest number of 'Yes' responses were obtained for 'brushing'. Unal et al. (30) conducted a study by using DN4 scale and obtained highest number of 'Yes' for 'tingling' and lowest number of 'Yes' response for 'itching'. Quedroago et al. (19) found 'Yes' response was most common for 'numbness' and least common for 'painful cold' among the patients with CLBP. The mechanisms underlying the symptoms of neuropathic pain vary. Accurately defining the symptoms and determining the clinical characteristics in detail may be helpful in revealing the underlying mechanisms and pathology, thus enable the physician to choose the best treatment strategy.

Our study has some its own limitations. Our data was collected from a tertiary clinic in which all patients were referred, one may ask whether the data obtained from this center would also have been found in a more general LBP population. New multicenter future studies should be performed to generalize the results.

One should always bear in mind that CLBP is of mixed nature. Findings from this paper endorse that CLBP cases are generally associated with a neuropathic component. The DN4 screening tool can quickly and correctly differentiates neuropathic pain from non-neuropathic pain and allow the physician to apply proper treatment, thus can reduce the pain, improve the quality of life, and decrease the level of disability and depression.

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