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Original Article

The correlation between neuropathic pain incidence and vitamin D levels in patients with chronic low back pain

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Abstract

Aim: The present study aimed to investigate the correlation between neuropathic pain incidence and vitamin D levels in chronic mechanical low back pain.

Material and Methods: Sixty patients (36 females, 24 males) with chronic mechanical low back pain (CMLBP) were included in the study. Leeds Assessment Neuropathic Symptoms and Signs Scale (LANSS), Beck Depression Inventory (BDI), and Visual Analogue Scale (VAS) were applied to the patients. Patient vitamin D levels were measured.

Results: It was determined that the neuropathic low back pain incidence was 0.20. No statistically significant difference was determined between the neuropathic pain incidence in the group with subnormal vitamin D values and the group with normal vitamin D values ($p = 0.292$). The incidence of neuropathic pain was higher in the group with subnormal vitamin D levels when compared to the group with normal vitamin D values.

Conclusion: It was demonstrated that neuropathic low back pain was more frequent among CMLBP patients with subnormal vitamin D values when compared to patients with normal vitamin D levels, albeit not statistically significantly. Vitamin D deficiency should be reviewed in the evaluation of CMLBP, neuropathic component of which was not well defined, and its treatment and management requires a multidisciplinary approach, and vitamin D treatment should be considered when necessary.

Keywords: Low back pain; neuropathic pain; Vitamin D

INTRODUCTION

Low back pain, which is characterized by an increasing prevalence, socioeconomic burdens and high rate of labor loss, is an important musculoskeletal disorder. Previous studies reported that 20% of low back pain cases were chronic and the frequency of chronic low back pain was 30% in the population throughout life. Several factors play a role in the etiology of chronic low back pain (CLBP) characterized by a high level of disability, and specific diseases were identified in only about 10% of these cases. In most patients, functional instability, condition loss, abnormal posture and disc degeneration, arthritis, ligamentous hypertrophy could be listed as the causes (1-3).

Chronic low back pain includes three pain components: nociceptive pain, neuropathic pain and mixed-type pain. Nociceptive pain is induced by inflammation and biomechanical stress due to tissue damage in ligaments, joints, muscles, fascia and tendons. Neuropathic pain includes peripheral and central mechanisms induced by the disease or lesion in the somatosensory system. In the literature, the incidence of neuropathic pain in patients with low back pain was reported as 20-35% (4).

Vitamin D deficiency may occur due to insufficient daylight exposure, inadequate dietary intake, and absorption disorders. It was considered that vitamin D deficiency was associated with various pain syndromes (5,6). Vitamin D deficiency could lead to low back pain, non-inflammatory arthritis and stiffness in joints even in healthy individuals. Studies demonstrated that vitamin D

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had anatomical, neurological and immunological effects on pain treatment. Thus, vitamin D may play an active role in the etiology of chronic pain and in the treatment of chronic pain and resulting comorbidity (7,8).

The aim of this article is to investigate the relationship between neuropathic pain frequency and D vitamin levels in patients with chronic low back pain.

MATERIAL and METHODS

Sixty patients admitted to the outpatient clinic at Physical Medicine and Rehabilitation Center between January and July 2016 and diagnosed with CLBP were included in the study. Local ethics committee approval and patients' written informed consent were obtained before the study was conducted. All procedures were carried out in accordance with the ethical standards determined by the human experiments committee (institutional and national) and 1975 Helsinki Declaration, 2000 revision (9).

Patients with a history of lumbar region operation or fracture, patients under 30 years of age or older than 60 years, patients treated with osteoporosis, with rheumatologic low back disease, patients diagnosed with polyneuropathy and with malignancies were excluded from the study. Patient age, gender, body mass index (BMI), marital status, duration of low back pain (in months), smoking, alcohol, and drug addiction were determined.

Visual pain analogue scale (VAS) was used to assess pain. LANSS was used to diagnose neuropathic pain. LANSS is a 7-point pain scale that was developed to determine neuropathic pain symptoms, including sensory identification and sensory assessment developed with a simple scoring system. A score below 12 means that the patient symptoms were probably not neuropathic, while a score of 12 or above reflects the possibility that neuropathic mechanisms contributed to the patient's pain (10).

Beck Depression Inventory (BDI) was used to determine depression risk in patients. The threshold depression score was accepted as 17 (11).

Patient vitamin D levels were measured by Thermo Scientific High-Performance Liquid Chromatography® device in the study. Patients with 20 ng/mL and lower serum 25(OH)D levels were considered to have vitamin D deficiency, with 21-29 ng/mL serum 25(OH)D level were considered with vitamin D insufficiency and with 30 ng/mL and above serum 25(OH)D levels were considered to have normal vitamin D levels (7).

Statistical Analysis

SPSS 16.0 (IBM SPSS for Windows version 16, IBM Corporation, Armonk, New York, United States) was used in data analysis. Quantitative data were given in mean ± standard deviation values. Normal distribution of the data was tested by Kolmogorov-Smirnov test. Student t-test was used for the analysis of independent paired groups and Pearson correlation analysis was conducted to analyze intra-group correlations. Data were analyzed at 95% confidence level; a p value smaller than 0.05 was considered significant.

RESULTS

Of the 60 CLBP patients included in the study, 36 were female (60%) and 24 were male (40%). The patient age ranged between 16 and 55 (mean 33.08 ± 7.93). Mean age, BMI, duration of low back pain, VAS, BDI, and LANSS scores, and vitamin D levels of the subjects are presented in Table 1.

Table 1. Participant demographics

	Age (year)	BMI (kg/m²)	LBPD (month)	VAS (cm)	BDI score	LANSS score	Vitamin D (ng/ml)
Female	31.97±8.23	28.81±5.99	35.38±3.20	6.63±1.68	12.06±8.01	7.58±5.61	14.43±1.58
Male	34.75±7.30	26.41±3.06	30.95±4.02	6.19±1.75	11.12±7.76	6.08±5.06	19.84±1.28
Total	33.08±7.93	27.85±5.13	33.61±3.52	6.46±1.71	11.68±7.86	6.98±5.41	16.59±1.48

BMI: Body mass index, LBPD: Low Back Pain Duration, VAS: Visual analog scale, BDI: Berg depression inventory, LANSS: Leeds assessment of neuropathic symptoms and signs scale

Table 2. Neuropathic pain distribution based on gender

	Neuropathic pain	No Neuropathic pain	Total
Female	9 (%15)	27 (%45)	36 (%60)
Male	3 (%5)	21 (%35)	24 (%40)
Total	12 (%20)	48 (%80)	60 (%100)

Neuropathic pain (NP) rate was determined as 20% and 75% of the patients with neuropathic pain were women. The incidence of neuropathic pain was 25% among females, while it was lower among male patients (12.50%) (Table 2).

While the mean vitamin D level in female patients with neuropathic pain was 9.00 ± 1.06, the same figure was 26.82±1.31 in males (Table 3).

When the cases were analyzed based on neuropathic pain incidence and vitamin D levels (Table 4), no statistically significant difference was determined between the groups (p = 0.747, p <0.05). Neuropathic pain was present in 16.66% of patients with normal vitamin D levels, while 20.83% of patients with vitamin D deficiency suffered from neuropathic pain. Vitamin D levels were normal in 16.66% of patients with neuropathic pain, while vitamin D levels were below normal in 83.34% of the same group of patients.

Comparison of the patients with and without neuropathic pain demonstrated no statistically significant difference based on mean BMI, BDI and vitamin D levels (p=0.331, p=0.198, p=0.309, p<0.05) (Table 5).

Table 3. Distribution of patients with neuropathic pain based on gender

	# of cases	BMI (kg/m²)	LBPD (months)	VAS (cm)	BDI score	LANSS score	Vitamin D (ng/ml)
Female	9	29.11±5.81	29.55±3.60	7.68±1.60	13.11±8.90	14.66±2.00	9.00±1.06
Male	3	27.80±2.30	5.00±1.00	6.43±2.22	17.67±7.37	16.00±1.73	26.82±1.31

BMI: Body mass index, LBPD: Low Back Pain Duration, VAS: Visual analog scale, BDI: Berg depression inventory, LANSS: Leeds assessment of neuropathic symptoms and signs scale

There was a statistically significant difference between the groups based on VAS scores and low back pain duration (p=0.049, p=0.048, p<0.005, respectively).

Comparison of the patients based on vitamin D levels demonstrated no statistically significant differences between BMI, low back pain duration, VAS, BDI and LANSS scores of the normal and low vitamin D groups (p=0,753, p=0,162, p=0.631, p=0.690, p=0.292, p <0.05) (Table 6).

Table 4. Distribution of vitamin D levels based on the presence of neuropathic pain

	Vit. D <30ng/ml	Vit. D >30ng/ml	Total
Neuropathic pain	10 (16.64%)	2 (3.33%)	12 (20%)
No Neuropathic pain	38 (63.33%)	10 (16.64%)	48 (80%)
Total	48 (80%)	12 (20%)	60 (100%)

Table 5. Correlations between neuropathic pain and low back pain duration, VAS, BDI and vitamin D levels

	BMI (kg/m²)	LBPD (months)	VAS (cm)	BDI score	Vitamin D (ng/ml)
NP	28.78±5.09	23.41±3.26	7.37±1.75	14.25±8.47	13.45±1.34
No NP	27.62±5.17	36.16±3.57	6.23±1.64	11.04±7.65	17.38±1.51
P*	0.331	0.048	0.049	0.198	0.309

* p<0,005
NP: Neuropathic pain, BMI: Body mass index, LBPD: Low Back Pain Duration, VAS: Visual analog scale, BDI: Berg depression inventory

Table 6. Correlations between vitamin D levels and BMI, LBPD, VAS, BDI and LANSS scores

	BMI (kg/m²)	LBPD (months)	VAS (cm)	BDI score	LANSS score
Vitamin D <30ng/ml	27.89±5.03	37.27±3.81	6.40±1.75	11.62±8.00	6.68±5.66
Vitamin D >30ng/ml	27.67±5.75	19.00±1.26	6.70±1.61	11.92±7.57	8.16±4.21
P*	0.753	0.162	0.631	0.690	0.292

* p<0.005
NP: Neuropathic pain, BMI: Body mass index, , LBPD: Low Back Pain Duration, VAS: Visual analog scale, BDI: Berg depression inventory, LANSS: Leeds assessment of neuropathic symptoms and signs scale

DISCUSSION

In this study, we investigated the interaction between vitamin D levels and the frequency of neuropathic pain in chronic low back pain. Although the incidence of neuropathic pain was higher in women than in men, no statistically significant difference was found between the groups when the cases were analyzed according to the incidence of neuropathic pain and vitamin D levels. There was a statistically significant difference between the groups according to VAS scores and low back pain duration. According to vitamin D levels, no statistically significant difference was observed between BMI, low back pain duration, VAS, BDI and LANSS scores of normal

and low vitamin D groups. Patients with low vitamin D levels had a higher incidence of neuropathic pain.

Previous studies demonstrated that vitamin D deficiency was common among patients with CLBP and that vitamin D deficiency could lead to chronic low back pain, myasthenia, balance dysfunction, gait disorder, diffuse musculoskeletal pain, regional pain, and fibromyalgia-like pain (12-15).

It was observed that neuropathic pain incidence was 20% among the study patients. In a study conducted by Kaki et al. with LANNS, it was found that neuropathic pain incidence was 54.7%, and neuropathic pain incidence was 37% in a study conducted by Freynhagen et al. with Pain Detect neuropathic pain scale (16). In another analysis, it was emphasized that the neuropathic pain incidence in low back pain was 20-35% (17). In the present study, the relatively low neuropathic pain incidence when compared to other findings in the literature may be due to patient sample and comprehensive exclusion criteria.

Previous studies demonstrated that chronic mechanical low back pain was more common among women (18). It was found in the present study that the incidence of neuropathic component in chronic low back pain was 25% in women and 12.5% in men. In studies on neuropathic component in chronic low back pain, it was reported that the neuropathic component was significantly higher among females compared to male patients (19,20). In the present study, the number of patients with neuropathic pain was not adequate for a statistical analysis based on gender. Thus, no gender comparison was conducted. However, it was determined in our study that it was 2 times more common in females when compared to males. In a study, a positive correlation was determined between neuropathic pain and VAS score (19). We also identified a significant correlation between VAS and neuropathic pain ($p = 0.049$).

Kaki et al. found that patients with neuropathic pain based on the LANSS scale were older when compared to those with nociceptive pain (21). Freynhagen et al. reported that patients with neuropathic pain were younger when compared to patients with nociceptive pain (16). In the present study, we did not determine a significant correlation between neuropathic pain and LANSS score based on age. This may be due to the fact that the age range in the present study was between 16 and 55, since we predicted that vitamin D metabolism may change with age, due to diseases with increased risk with age such as osteoporosis. Studies demonstrated that the effect of vitamin D on target tissues changes with increased age, and vitamin D receptor resistance is altered by the changes and decreases in Vitamin D receptor expression (22).

In the present study, we investigated whether there was a correlation between the neuropathic component in CLBP and vitamin D deficiency. The mean vitamin D level was 16.59 ± 1.48. In forty-four patients (73.34%), vitamin D levels were <20 ng / ml and these were included in the deficiency group. Vitamin D level was between 20 and 30 in 4 (6.66%) subjects and these patients were considered as the low vitamin D group. In 12 patients (20%), vitamin D level was ≥30 and within normal range.

In a study conducted on chronic low back pain and vitamin D levels, 243 patients with low back pain were examined, and it was observed that 83% of the patients had vitamin D levels below 30 ng/ml (15). In a study conducted on patients with diffuse musculoskeletal pain, it was reported that the prevalence of vitamin D deficiency was 71.7% (23). Based on the above-mentioned findings, the incidence of vitamin D deficiency in the present study was consistent with the literature. In another study on chronic low back pain, 275 female and 24 male patients with low back pain were examined and it was found that 83% of the patients experienced low vitamin D levels. In the same study, vitamin D supplements were administered to patients with vitamin D deficiency and it was demonstrated that the pain of about 95% of the patients, whose vitamin D levels increased to normal levels, disappeared or decreased (12). In another study, vitamin D supplementation regulated muscle strength and improved balance, and falling risk decreased (24). It was reported in a study conducted in India that vitamin D deficiency could be clinically observed as chronic low back pain and the clinical findings could be improved by the removal of the deficiency (13).

Although the results on neuropathic pain and vitamin D levels were not statistically significant in the present study, neuropathic pain incidence rate was higher in patients with low vitamin D levels. The prevalence of both Vitamin D deficiency and neuropathic pain component in low back pain among women could be an indicator of the role vitamin D deficiency could play in neuropathic pain induced by chronic low back pain. Also, in studies conducted with CLBP and vitamin D, it was found that there were no correlations between vitamin D and neuropathic low back pain due to the analysis of the pain character of the patients with CLBP without distinction between neuropathic and nociceptive pain components. In studies on neuropathic pain, it was reported that vitamin D deficiency may be a risk factor especially in the development of diabetic neuropathy and it was found that vitamin D administration reduced the pain in diabetic neuropathy (25-28).

LIMITATION

In our study, the number of cases was limited due to the exclusion of diabetic patients and patients without neuropathic pain and because of the limited age range. In addition, the lack of power analysis at the beginning is an important shortcoming. Selective inclusion of a higher number and wide range of cases will contribute to the literature.

CONCLUSION

Although vitamin D levels were not statistically significant in CMLBP patients, neuropathic pain incidence was

higher among patients with low vitamin D levels. Vitamin D deficiency should be reviewed in the evaluation of CMLBP, neuropathic component ow which was not well defined, and treatment and management of which require a multidisciplinary approach, and vitamin D treatment should be considered when necessary.

Competing interests: The authors found that the conflict of interest did not fully coincide.

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REFERENCES

1. Bigos JS, Müller G. Primary care approach to acute and chronic back problems: Definitions and care. In: Looser JD, ed. Bonica's management of pain Philadelphia: Lippincott Wiliams & Wilkins 2001:1509-28.
2. İnanıcı F. Bel Ağrısı Nedenleri ve Muayenesi. In: Beyazova M, Gökçe Kutsal Y (eds). Fiziksel Tıp ve Rehabilitasyon. Güneş Tıp Kitapevleri 2011;2053-66.
3. Krismer M, van Tulder M; Low Back Pain Group of the Bone and Joint Health Strategies for Europe Project. Strategies for prevention and management of musculoskeletal conditions. Low back pain (non-specific). Best Pract Res Clin Rheumatol 2007;21:77-91.
4. Baron R, Binder A, Attal N, et al. Neuropathic low back pain in clinical practice. Eur J Pain 2016;20:861-73.
5. Kocyigit BF, Akyol A. Vitamin D levels in patients with ankylosing spondylitis: Is it related to disease activity? Pak J Med Sci. 2018;34:1209-14.
6. Shipton EA, Shipton EE. Vitamin D and Pain: Vitamin D and Its Role in the Aetiology and Maintenance of Chronic Pain States and Associated Comorbidities. Pain Res Treat. 2015;2015:904967.
7. Holick MF. Vitamin D deficiency, N Engl J Med 2007;357:266-81.
8. Özçelik DÇ, Koçer H, Kasım İ, et al. D Vitamini. Turkish Medical J 2012;6:2
9. Riis P. Perspectives on the Fifth Revision of the Declaration of Helsinki. JAMA 2000;284:3045-6.
10. Bennett M. The LANSS Pain Scale: the Leeds assessment of neuropathic symptoms and signs. Pain 2001;92:147-57.
11. Hisli N. Beck Depresyon envanterinin geçerliliği üzerine bir çalışma. Türk Psikoloji Dergisi 1989;22:118-26.
12. Faraj SE, Mutairi KE. Vitamin D deficiency and chronic low back pain in Saudi Arabia. Spine 2003 15;28:177-9.
13. Rao R, Maruthi W. Study of Beneficial Role of Vitamin D in Chronic Low Back Pain. Paripex Indıan J Research 2015; 4: 7.
14. Sarıfakıoğlu B, Yalbuz ŞA, Güzelant AY, et al. D Vitamini ile İlişkili Kas-İskelet Sistemi Bulguları. Turk J Osteoporos 2015;21:113-7.
15. Siddique SA, Malik YM. Frequency of Vitamin D Deficiency in Patients of Low Backache. Ann. Pak. Inst. Med. Sci. 2011;7:208-12.
16. Freynhagen R, Baron R, Gockel U, et al. Pain-DETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. Curr Med Res Opin 2006;22:1911-20.
17. Tüzün Ş. Diskopatilere Bağlı Nöropatik Ağrı. Türkiye Klinikleri J PM&R-Special Topics 2012;5:32-7.
18. Sinaki M, Mokri B. Low back pain and disorders of the lumbar spine. In: Braddom RL, Buschbacher RM, Dumitru D, Johnson WE, Sinaki M, editors. Physical Medicine and Rehabilitation. Philadelphia: W.B Saunders Company 1996;813-50.
19. Çalık Y, Çalık AF. Kronik Bel Ağrılı Hastalarda Nöropatik Ağrının Fonksiyonel Yetersizlik Üzerine Etkisinin Değerlendirilmesi. Turk J Osteoporos 2015;21:122-6.
20. Haliloğlu S, İçağasıoğlu A, Çarlıoğlu A, ve ark. Kronik Bel Ağrısının Nöropatik Komponenti. Yeni Tıp Dergisi 2013;30:148-51.
21. Kaki AM, El-Yaski AZ, Youseif E. Identifying neuropathic pain among patients with chronic low-back pain: use of the Leeds Assessment of Neuropathic Symptoms and Signs pain scale. Regional Anesthesia and Pain Medicine2005:30;422-9.
22. Bischoff-Ferrari HA, Borchers M, Gudat F, et al. Vitamin D receptor expression in human muscle tissue decreases with age. Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research 2004;19:265-9.
23. Çiğdem M, Kara S, Sarı H, et al. Yaygın kas-iskelet ağrısı olan hastalarda D vitamini eksikliği prevalansı ve risk faktörleri. Journal of Clinical and Experimental Investigations 2013;4:488-91.
24. Bischoff-Ferrari HA. Relevance of vitamin D in muscle health. Reviews in endocrine & metabolic disorders 2012;13:71-7.
25. Shehab D, Al-Jarallah K, Mojiminiyi OA, et al. Does Vitamin D deficiency play a role in peripheral neuropathy in Type 2 diabetes? Diabet Med 2012;29:43-9.
26. Basit A, Basit KA, Fawwad A, et al. Vitamin D for the treatment of painful diabetic neuropathy. BMJ Open Diabetes Res Care. 2016;4:148.
27. Özkan B, Döneray H. D vitamininin iskelet sistemi dışı etkileri. Çocuk Sağlığı ve Hastalıkları Dergisi 2011; 54: 99-119.
28. Lee P, Chen R. Vitamin D as an analgesic for patients with Type 2 Diyabetes and neuropathic pain. Arch İntern Med., 2008;168:1629-37.