Kocatepe Tıp Dergisi
Kocatepe Medical Journal
21:195-200/ Nisan/ 2020

ARAŞTIRMA YAZISI / RESEARCH ARTICLE

KRONİK BOYUN AĞRISI ŞİKAYETİ OLAN HASTALARDA SERUM D VİTAMİNİ SEVİYELERİ, AĞRI ŞİDDETİ VE SERVİKAL DİSK DEJENERASYONU İLİŞKİLİ MİDİR?

CERVICAL DISC DEGENERATION, SEVERITY OF PAIN AND VITAMIN D LEVELS IN PATIENTS WITH CHRONIC NECK PAIN: IS THERE ANY RELATIONSHIP?

Hilal ALTAŞ[1], Ali YILMAZ[2]

[1]Ordu Üniversitesi Tıp Fakültesi, Radyoloji Anabilim Dalı
[2]Ordu Üniversitesi Tıp Fakültesi, Beyin Cerrahi Anabilim Dalı

ÖZ

AMAÇ: Kemik metabolizması üzerinde D vitaminin etkileri uzun zamandır bilinmektedir. Çalışmamızda serum vitamin D seviyeleri ile intervertebral disk dejenerasyonu, disk yüksekliği ve ağrı şiddeti arasındaki ilişkiyi saptamayı hedefledik.

GEREÇ VE YÖNTEM: Beyin cerrahisi polikliniğine kronik boyun ağrısı şikayeti ile başvuran hastaların serum D vitamini seviyeleri, başvuru sırasındaki ağrı şiddeti (VAS) değerleri ve servikal MRG incelemeleri retrospektif olarak değerlendirildi.

BULGULAR: Çalışmaya 123 hasta dahil edildi. Vitamin D düzeylerine göre ayrılan gruplar arasında, VAS skorlarına göre anlamlı fark saptanmıştır (p=0.003). Vitamin D düzeylerine göre ayrılan gruplar arasında yapılan karşılaştırmalarda yaş (p=0.180), cinsiyet (p=0. 244/p=0.146) ve servikal C5-6 disk yüksekliği açısından (p= 0.299) istatistiksel olarak anlamlı bir ilişki bulunamamıştır.

SONUÇ: Çalışmamızda, servikal disk dejenerasyonu ve servikal lordoz kaybı olan hastalarda düşük serum vitamin D seviyeleri ile VAS arasında anlamlı fark saptanmıştır. Metabolik düzeyde D vitamini eksikliğinin, kronik boyun ağrısı ile başvuran, muayenede nörolojik bozukluğu ve disk hernisi olmayan hastalarda göz önünde bulundurulması gerektiğine inanıyoruz.

ANAHTAR KELİMELER: D vitamini, boyun ağrısı, servikal disk yüksekliği

ABSTRACT

OBJECTIVE: Effects of vitamin D on bone metabolism has been long known. We aimed to detect the relationship between vitamin D levels and intervertebral disc degeneration, disc height and severity of pain in patients with chronic neck pain.

MATERIAL AND METHODS: The data of patients who were admitted to neurosurgery polyclinic with chronic neck pain complaints were analyzed retrospectively, whom their vitamin D levels measured, pain severity (VAS) scores ware noted at the time of admission and were radiologically examined with cervical MRI.

RESULTS: Overall, 123 patients were included in the study. There was a significant relationship in terms of VAS scores between the groups divided on the basis of vitamin D levels (p=0.003). There was no statistically significant relationship in terms of age (p=0.180), gender (p=0. 244/p=0.146), and cervical C5-6 disk height (p= 0.299) in the comparison performed within the groups divided on the basis of vitamin D levels.

CONCLUSIONS: In the present study, it was shown that there is a significant relationship between low vitamin D levels and VAS in patients who had cervical disk degeneration and loss of cervical lordosis. We believe that vitamin D deficiency at a metabolic level should be considered in patients who are admitted with chronic neck pain, who do not exhibit neurologic deficits in the examination, and who do not have disc hernia.

KEYWORDS: Vitamin D,neck pain, cervical disc height

Geliş Tarihi / Received: 18.10.2019
Kabul Tarihi / Accepted: 11.03.2020
Yazışma Adresi / Correspondence: Dr.Öğr.Üyesi Hilal ALTAŞ
Ordu Üniversitesi Tıp Fakültesi Radyoloji Anabilim Dalı
E-mail:hilalaltas@gmail.com
Orcid No: 0000-0001-5531-6764

INTRODUCTION

Vitamin D is a fat-soluble steroid vitamin, which is synthesized in the skin with exposure to an appropriate level of ultraviolet B (UVB) rays.

Calcitriol [1,25(OH)2D] is the active form of vitamin D and can be formed in several tissues at a local level (1-3).

25-Hydroxyvitamin D [25(OH)D] is the vitamin D form that can be measured in the serum. There is no consensus yet on the optimal serum 25(OH)D levels, although many sources define values under 20 ng/ml (50nmol/l) as deficiency (4). Serum 25(OH)D level ≤10 ng/ml is accepted as severe deficiency, 10–20 ng/ml is accepted as deficiency, 20–30 ng/ml is accepted as mild deficiency or insufficiency, ≥30 ng/ml is accepted as sufficient, 40–50 ng/ml is accepted as ideal, and >150 ng/ml is accepted as toxic (5).

Vitamin D deficiency prevalence is reported to be 38%–93% (6). Vitamin D has anti-inflammatory effects. In vitro studies it is shown that vitamin D inhibits prostaglandin E2 (PGE2) synthesis (7). Observational and interventional studies claim that vitamin D plays a role in the severity of pain and the management of pain in several clinical settings. The cervical intervertebral disc diseases are the second most common among all spinal intervertebral disc diseases. Cervical disc pain can be localized pain, referred pain or radicular pain. Some studies demonstrate that vitamin D levels are effective on non-specific musculoskeletal system pain (4-6).

Although several studies investigate epidemic D hypovitaminosis, only few studies have evaluated the relationship between serum vitamin D levels and the pain related with degenerative spinal diseases.

In the present study, the relationship between serum vitamin D levels, cervical disc height and Visual Analog Scale (VAS) scores were evaluated in patients admitted with non-specific neck pain that they have cervical disc degeneration and loss of cervical lordosis in imaging.

MATERIALS AND METHODS

The patients who were admitted to the neurosurgery department of our hospital between January and March 2018 complaining of neck pain with findings of cervical disc degeneration and loss of cervical lordosis in cervical spinal Magnetic Resonance Imaging (MRI) were enrolled the study. Their vitamin D levels at the time of admittance were reviewed, VAS scores was recorded.

Patients aged between 18–60 years with a vitamin D level < 40 ng/ml were included in the study. Patients were divided into four groups (Table I): severe deficiency group (patients with vitamin D level of <10 ng/ml) (group 1), deficiency group (patients with vitamin D level of 10–20 ng/ml) (group 2), insufficiency group (patients with vitamin D level of 20–30 ng/ml) (group 3), and sufficiency group (patients with vitamin D level of 30–40 ng/ml) (group 4).

Age; gender; body mass index (BMI); complaints at the time of admittance (duration of neck pain); calcium (Ca), phosphor (P), parathyroid hormone (PTH) and thyroid stimulating hormone (TSH) levels; sedimentation and C-reactive protein (CRP) values; and complete blood counts of the patients were recorded.

MRI examinations were performed using 1.5-T scanners (Magnetom Aera, Siemens, Erlangen, Germany) and included sagittal T1, T2-weighted and axial T2-weighted images. The intervertebral disc height was measured on the sagittal T2-weighted images from the midline of C5-6 intervertebral disc level, which is the level that cervical disc hernia secondary to the degeneration is most frequently observed.

Patients who have cervical disc hernia requiring surgery were not included, they were informed and prompted for surgery.

Also patients who had infectious disease, endocrine pathology (thyroid disorders, diabetes mellitus, and hyperparathyroidism), inflammatory rheumatologic disease or myopathy, patients undergoing oncologic treatment, patients on replacement treatment due to vitamin D deficiency, patients who had undergone cervical disc surgery, smokers, patients diagnosed with osteomalacia/osteoporosis, and patients aged <18 years or >60 years were excluded from the study.

ETHICS COMMITTEE

All patients provided written informed consent, and the study protocol was approved by the hospital's Ordu University local ethics committee (number / date: 70 / 05.04.2018) in accordance with the Helsinki Declaration and Good Clinical Practice Guidelines.

ISTATISTICAL ANALYSIS

Statistical analyses were performed using IBM SPSS Statistics 23.0 for Windows (SPSS Inc., Chicago, IL, USA). Data were presented using descriptive methods. VAS scores of the study subgroups with severe deficiency, deficiency, insufficiency, and sufficiency were analyzed using t-test and ANOVA with post hoc Tukey test. A value of $p < 0.05$ was considered statistically significant.

RESULTS

Overall, 123 patients were included in the study; 71 were female (57.7%) and 52 were male (42.3%). The mean age of the patients was 35.9 years. Thirty patients (24.4%) were in the severe deficiency group (Group 1), with the mean VAS score of 5.83 ± 12.08. Thirty-one patients (25.2%) were in the deficiency group (Group 2), with the mean VAS score of 5.12 ± 1.33. Thirty-one patients (25.2%) were in the insufficiency group (Group 3), with the mean VAS score of 2.48 ± 1.02. Thirty-one (25.2%) patients were in the sufficiency group (Group 4), with the mean VAS score of 1.87 ± 0.82. In the comparison of the groups carried out according to the measurement of the C5-6 disc height and vitamin D levels, the average disc height of the first group was 4.52 ± 0.83, the average disc height of the second group was 4.24 ± 1.03B, the average disc height of the third group was 4.10 ± 0.83, and the average disc height of the fourth group was 4.09 ± 84. There was a significant relationship in terms of VAS scores between the groups divided into four on the basis of vitamin D levels (p=0.003). There was no statistically significant relationship in terms of age, gender, and cervical C5-6 disc height in the comparison performed within the groups divided on the basis of vitamin D levels (p levels respectively; p=0.180; p=0. 244 /p=0.146; p= 0.299) **(Table 1)**.

Table 1: Groups of vitamin D levels

	Group 1	Group 2	Group 3	Group 4	P value
Sex ,female (n, %)	20(66)	17 (54)	16(51)	18(58)	0.244
Age (years)	36.1±8.0	34.0±9.4	34.7±10	31.1±8.0	0.180
VAS Score	5.83±12.08	5.12±1.33	2.48±1.02	1.87±0.82	0.003
Disc height	4.52±0.83*	4.24±1.03	4.10±0.83	4.09±84*	0.299

VAS: Visual Analog Scale, *Disk height Group 1vs group 4 p=0.05

The mean calcium (Ca) level in the severe deficiency group (Group 1) was 7.1±1.2, in the deficiency group (Group 2) it was 8.1±1.1 , in the insufficiency group (Group 3) it was 8.9±1.4, in the sufficiency group (Group 4) it was 9.1±1.1.

There was a statistical relationship in terms of Ca levels between groups (p=0.049). There was no statistically significant relationship between groups in terms of body mass index (BMI), duration of neck pain, Phosphor (P) levels, Parathyroid Hormone (PTH) levels, Thyroid Stimulating Hormone (TSH) levels, sedimentation levels and C-reactive protein (CRP) levels. Detailed data is given at **(Table 2)**.

Table 2: Group of vitamin D levels and demografic characteristics of patient

	Group 1	Group 2	Group 3	Group 4	P Value
BMI	26.6±1.23	26.3±1.18	25.9±1.06	26.1±1.24	0.265
Neck Pain Duration (Mounth)	8.3 ±1.3	6.2±1.1	7.2±1.2	7.7±1.3	0.452
Ca	7.1±1.2	8.1±1.1	8.9±1.4	9.1±1.1	0.049*
P	3.9±1.1	3.8±1.4	4.0±1.1	4.1±1.1	0.372
PTH	36±1,4	35.9±1.1	36.1±1.2	35.9±14	0.246
TSH	1.2±1.0	1.3±1.1	1.2±1.1	1.2±1.3	0.446
Sedim	8±1	7±1	8±1	9±1	0.596
CRP	0.73±0.01	0.75±0.07	0.69±0.03	0.72±0.01	0.489

BMI: Body mass index , P: Phosphor, PTH: Parathyroid Hormone, TSH: Thyroid Stimulating Hormone, CRP: C-reactive protein *Ca level Group 1vs group 4 p=0.049

DISCUSSION

Vitamin D can be taken via diet as well as simultaneously synthesized in the skin with exposure to UVB rays. The paracrine effect of vitamin D is explained by the ability to produce calcitriol, the active form of vitamin D, at a local level and the presence of vitamin D receptors in almost all tissues in the body (3).

Intervertebral disc degeneration is a natural part of aging process which can be accounted for mostly a genetic predisposition and partly by environmental factors. Environmental factors such as heavy physical activity can trigger a cascade of molecular events and can accelerate disc degeneration at a younger age. The vitamin D plays an important role in the molecular processes of musculoskeletal system. Its receptors are expressed in osteoblasts, chondrocytes, annulus fibrosus and nucleus pulposus cells of the discs (7, 8).

Also, it has been demonstrated that vitamin D is effective on the proliferation and functional regulation of these cells and their production of certain proteins and cytokines in vitro.

Many studies shown that patients with chronic pain complaints have low vitamin D levels (9-12). Turner et al. were examined vitamin D insufficiency prevalence and its relationship with chronic pain complaints. The rate of vitamin D deficiency was 26% in their study population.

They were stated that the rate of using opioid-type drugs was reportedly higher in the vitamin D deficiency group, as it was mentioned by other studies before (12). This situation was explained by skeletal pain developing secondary to the negative effects of vitamin D deficiency on bone mineralization (13). In addition, it has been reported that vitamin D receptors are present in muscle tissues and low vitamin D levels may also lead to proximal muscle weakness (12, 14). In a randomized-controlled study on patients with back pain by Lodh et al. (15), it is stated that vitamin D levels of the patients in the experiment group were statistically lower than that in the control group. It was reported in the study that vitamin D levels should be checked in individuals with chronic pain complaints at the early period and that treatment should be initiated if necessary.

It is believed that sufficient active vitamin D at cellular level has a protective effect on cell functions and decreases inflammation (14). As a result, it is deemed that low vitamin D levels increase pain by increasing inflammation (16, 17).

Therefore, it can be suggested that low vitamin D levels may lead to increased inflammation and chronic pain in the patients complaining neck pain, who have degeneration findings on MRI and no surgical indications for cervical disc hernia.

The annulus fibrosus is the more vascular part of intervertebral disc in which vitamin D receptors are located is directly exposed to vitamin D metabolites in cerebrospinal fluid (10, 11). Gruber et al. (18) showed that administration of 24-, 25-, or 1.25-dihydroxy vitamin D calcitriol leads dramatic downregulation of monocyte chemo attractant protein-1, interferon-γ, and interleukin (IL) 8. These are proinflammatory mediators that increases chemotaxis or monocyte activity and also they have been detected at herniated disc tissue. In some musculoskeletal system studies, it has been shown that lack of vitamin D receptor stimulation give rise to proinflammatory macrophage influx to the diseased joints and also increase monocyte expression, serum TNF-α, IL-1β, IL-6 and IL-8 levels (19).

These results supported that calcitriol act as an anti-inflammatory mediator that decrease TNF production by T cells and secretion of IL-1β and TNF by mononuclear cells (3, 20). Both of which have been widely implicated in disc disease pathogenesis. Current literature findings suggest that these exacerbated inflammatory processes plays an important role in chronic pain complaints without disc hernia and non-specific severe pain pathogenesis developing after disc surgery (21).

In the study by Geoffrey E. Stoker et al. (22) stated that, there was a significant relationship between low vitamin D levels and cervical disc hernia. In our study, severity of neck pain was evaluated using VAS score in patients who did not have disc hernia but had disc degeneration and loss of lordosis. It is shown that in our data, there was a significant relationship between vitamin D deficiency and non-specific chronic pain.

Some studies show that there is a relationship between neck pain and loss of cervical lordosis (10-12, 23). However, there are also studies showing that the changes in cervical lordosis do not have any prognostic or diagnostic value (2, 14).

Grob et al. (24) stated that performed measurements on 54 patients with neck pain using Tangent method and demonstrated that neck pain was not associated with cervical angle. On MRI studies decrease of intervertebral disc height due to dehydration is considered as an early indicator of disc degeneration. Statistically, cervical intervertebral disc degeneration and hernia mostly occurs at the level of cervical 5-6 intervertebral disc. In our study, there isn't a significant relationship between C5-6 disc height and vitamin D levels.

Cervical spinal pain may have many different etiologic reasons, as it is more mobile and prone to trauma than other parts of the spine. Because acute neck pain usually resolves without requiring any treatment, imaging is not performed. As chronic neck pain rarely improves spontaneously, imaging is required to determine the underlying pathology. Degenerative changes usually develop starting from the age of 30 (25). MRI is helpful in confirming the diagnosis for patients suspected for cervical disc hernia, radiculopathy or cervical spondylotic myelopathy during physical examination.

Cervical disc diseases range widely from diseases that can regress with simple, conservative treatment to diseases with severe conditions that require emergent surgical interventions. The correct diagnosis and treatment of these conditions require combined use of adequate knowledge of anatomy, detailed physical examination, and appropriate diagnostic methods.

In the present study, it was shown that there is a significant relationship between low vitamin D levels and pain severity (VAS) in patients who had cervical disc degeneration and loss of cervical lordosis, who were admitted with non-specific neck pain complaints and who did not require surgical treatment. We believe that the evaluation of vitamin D levels would be an appropriate clinical approach in the presence of non-specific chronic pain complaints that are not consistent with cervical MRI and neurologic examination findings. Our study has limitations. First, the number of patients is relatively low.

Second, the potential effects of increased spondylotic changes observed in later ages couldn't be evaluated because of the age range of patients being 18–60. Third, due to retrospective pattern of our study, after vitamin D replacement therapy chronic neck pain VAS scores and efficacy of vitamin D couldn't be evaluated. As a result; neck pain is a clinical condition developing because of many factors.

Detailed history and physical examination are essential in terms of diagnosis and differential diagnosis. In light of the results of our study, we suggest that vitamin D deficiency should be considered in the differential diagnosis during the evaluation of patients with chronic non-specific neck pain. However, further prospective studies with larger, multi-centered, randomized, controlled data are needed.

REFERENCES

1. Bikle DD. Vitamin D and immune function: understanding common pathways. Current osteoporosis reports2009 ;7(2):58-63.

2. Zehnder D, Bland R, Williams MC,et al. Extrarenal expression of 25-hydroxyvitamin D3-1α-hydroxylase. The Journal of ClinicalEndocrinology&Metabolism2001;86(2):888-94.

3. Tuffaha M, El Bcheraoui C, Daoud F,et al. Deficiencies under plenty of sun: Vitamin D status among adults in the kingdom of Saudi Arabia. North American journal of medical sciences 2015;7(10):467-75.

4. Heidari B, Shirvani JS, Firouzjahi A, et al. Association between nonspecific skeletal pain and vitamin D deficiency. International journal of rheumatic diseases 2010;13(3):340-6.

5. Pfeifer M, Begerow B, Minne H. Vitamin D and muscle function. Osteoporosis International2002;13(3):187-94.

6. Plotnikoff GA, Quigley JM. Prevalence of severe hypovitaminosis D in patients with persistent,nonspecific musculoskeletal pain.Mayo clinic proceedings2003;78(12):1463-70.

7. Lane NE, Gore LR, Cummings SR,et al. Serum vitamin D levels and incident changes of radiographic hip osteoarthritis: a longitudinal study. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology1999;42(5):854-60.

8. Royce PM(Editör).Connective tissue and its heritable disorders: molecular, genetic, and medical aspects. John Wiley & Sons,2003:159-62.

9. Bunout D, Barrera G, Leiva L,et al. Effects of vitamin D supplementation and exercise training on physical performance in Chilean vitamin D deficient elderly subjects. Experimental Gerontology2006;41(8):746-52.

10. Singh S, Cuzick J, Mesher D, et al. Effect of baseline serum vitamin D levels on aromatase inhibitors induced musculoskeletal symptoms: results from the IBIS-II, chemoprevention study using anastrozole.Breast cancer research and treatment 2012;132(2):625-9.

11. Straube S, Moore AR, Derry S, et al.Vitamin D and chronic pain. Pain 2009;1(41):10-3.

12. Tetlow LC, Smith SJ, Mawer EB, et al. Vitamin D receptors in the rheumatoid lesion: expression by chondrocytes, macrophages, and synoviocytes. Annals of the rheumatic diseases1999;58(2):118-21.

13. Turner MK, Hooten WM, Schmidt JE, et al. Prevalence and clinical correlates of vitamin D inadequacy among patients with chronic pain. Pain Medicine 2008;9(8):979-84.

14. Knutsen KV, Madar AA, Brekke M,et al. Effect of vitamin D on musculoskeletal pain and headache A randomized, double-blind, placebo-controlled trial among adult ethnic minorities in Norway.Pain2014;155(12):2591-8.

15. Lodh M, Goswami B, Mahajan RD, et al. Assessment of vitamin D status in patients of chronic low back pain of unknown etiology. Indian Journal of Clinical Biochemistry 2015;30(2):174-9.

16. Glover T, Goodin B, Horgas A, et al. Vitamin D, race, and experimental pain sensitivity in older adults with knee osteoarthritis. Arthritis Rheumatism 2012;64(12):3926-35.

17. Mauck MC, Linnstaedt SD, Bortsov A,et al. Vitamin D insufficiency increases risk of chronic pain among African Americans experiencing motor vehicle collision.Pain 2020;161(2):274-280.

18. Gruber HE, Hoelscher G, Ingram JA, et al. 1, 25 (OH) 2-vitamin D3 inhibits proliferation and decreases production of monocyte chemoattractant protein-1, thrombopoietin, VEGF, and angiogenin by human annulus cellsin-vitro. Spine 2008;33(7):755-65.

19. Werina K, Baum W, Axmann R, et al. Vitamin D receptor regulates TNF-mediated arthritis. Annals of the rheumatic diseases 2011;14(6):23-31.

20. Stoffels K, Overbergh L, Giulietti A, et al. Immune regulation of 25 hydroxyvitamin D3 1α hydroxylase in human monocytes. Journal of Bone and Mineral Research2006;21(1):37-47.

22. Stoker GE, Buchowski JM, Bridwell KH, et al. Preoperative vitamin D status of adults undergoing surgical spinal fusion. Global Spine journal2013;38(6):507-15.

24. Grob D, Frauenfelder H, Mannion A. The association between cervical spine curvature and neck pain. European Spine Journal2007;16(5):669-78.

25. Wynne-Davies R, Walsh W, GormleyJ. Achondroplasia and hypochondroplasia. Clinical variation and spinal stenosis. The Journal of bone and joint surgery1981;63(4):508-15.