

The Relationship between Vitamin D Deficiency and Nonspecific Shin Pain in the Elderly; A Case-control Study

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J Babol Univ Med Sci; 19(3); Mar 2017; PP: 15-20

Received: Jan 10th 2017, Revised: Jan 25th 2017, Accepted: Feb 14th 2017.

ABSTRACT

BACKGROUND AND OBJECTIVE: Lower extremity pain is an important cause of impaired physical activity and the incidence of disability in the elderly. Since vitamin D plays a role in bone metabolism, the present study aims to investigate the relationship between vitamin D deficiency and shinbone pain and sensitivity in the elderly.

METHODS: This case-control study was conducted among patients who referred to the hospital because of nonspecific pain localized to the anterior surface of shin for 6 weeks and above and aged 50 years and above. The problem was confirmed during clinical examination with the examiner's finger pressure on the Tibia. The same-age control subjects were chosen from among patients without shin pain. The level of 25-hydroxyvitamin D (25OHD) was measured using ELISA method and 25OHD<20 ng/ml was considered deficiency.

FINDINGS: In this research, 80 patients with mean age of 61±8.2 years and 59 control subjects with mean age of 62.3±9.1 years were studied. The level of 25OHD in patients was lower than control subjects (21±16 versus 37.4±21.6 ng/ml) (p=0.001), while BMI in patients was significantly higher than control subjects (p=0.001). Moreover, a significant relationship was observed between vitamin D deficiency and shin pain (OR=15.3 [8.5-40]), which was more severe among men.

CONCLUSION: According to the results of the resent study, the elderly patients with local pain and unexplained shin pain need to be examined in terms of vitamin D status and need to be treated in case of deficiency.

KEY WORDS: Elderly people, Shin pain, Vitamin D deficiency.

Please cite this article as follows:

Babaei M, Esmaili Jadidi M, Heidari B, Gholinia H. The Relationship between Vitamin D Deficiency and Nonspecific Shin Pain in the Elderly; A Case-control Study. J Babol Univ Med Sci. 2017;19(1):15-20.

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Introduction

Vitamin D deficiency is common among all age groups, particularly the elderly (1–3). The prevalence of this problem varies based on age, gender, geographical region and the type of nutrition in different populations (1, 3). The prevalence of this problem in the geographical region of this study ranges from 36 to 70% (1, 4–7).

Not only vitamin D plays a role in bone metabolism, but is also associated with metabolic, extraskeletal, musculoskeletal, inflammatory and non-inflammatory diseases (8–15). Vitamin D deficiency is associated with incidence, escalation and progress of osteoarthritis and rheumatoid arthritis in the elderly (16–18). Vitamin D deficiency weakens the strength of quadriceps and as a result causes knee pain in osteoarthritis of the knee and improving vitamin D deficiency through strengthening the quadriceps leads to knee pain reduction (19,20).

The type of musculoskeletal pain in patients with vitamin D deficiency is different from localized bone pain and diffuse musculoskeletal pain without specific localization (4, 8, 12, 19–22). Studies have shown that the association between vitamin D deficiency and skeletal pain is more prominent in regard with shin (8) and knee joint pain in the elderly has responded to treatment with vitamin D (23, 24). Vitamin D deficiency increases sensitivity to pain (25) and even a slight decline in this vitamin intensifies pain in patients with osteoarthritis of the hip and knee (26), whereas modification of this vitamin relieves pain (18).

Pain in lower extremity in the elderly is of great importance, since it is an important factor for disability and weakness, which is often associated with osteoarthritis (15), whereas other factors such as shinbone (tibia) pain, joint instability, paresis, recurrent pain, neuropathy and osteomalacia may cause lower extremity pain and intensification of disabilities, either alone or along with knee osteoarthritis. Identification of modifiable factors of lower extremity pain in the elderly and modifying them can prevent the incidence and progress of pain (27).

Although several studies have been dedicated to the relationship between vitamin D deficiency and musculoskeletal pain, there is not enough information regarding the relationship between vitamin D deficiency and shin pain. This pain in the elderly is important since it is the main cause of immobility in these people and thus is a predisposing factor in the incidence of disability. Considering the high prevalence of vitamin D deficiency in the society and

the role of lower extremity pain in the incidence of disability in the elderly, the present study aims to investigate the relationship between shin pain and vitamin D deficiency in the elderly.

Methods

After receiving permission with code of MUBABOL/REC.1394.311 from the ethics committee of Babol University of Medical Sciences, this case–control study was conducted consecutively and prospectively from September 2015 to February 2016 among patients admitted to Rheumatology Clinic of Ayatollah Rouhani Hospital (Babol, Iran) with shin pain and were diagnosed with shin pain based on the patients' remarks and clinical examination. The problem was confirmed during clinical examination with the examiner's finger pressure on the anterior surface of tibia until the fingernail became white and the patient reacted (8). The level of finger pressure on shin was the same for patients and control subjects. Diagnostic accuracy and persistence of pain was confirmed by re-examination, at least two weeks after the first examination.

Patients with pain according to the abovementioned specifications for at least 6 week and age of 50 or above were included in the study. Patients were excluded from the study in cases of symptomatic osteoarthritis, knee joint instability, history of surgery or trauma in shin area, sciatic pain, recurrent pain in hip, congenital and hereditary neurological disorders, use of medicines such as vitamin D, calcium, corticosteroids and medicines that are involved in the metabolism of vitamin D. Symptomatic osteoarthritis in knee or spine was confirmed according to examination, medical history or by radiography if necessary. The serum level of 25-hydroxyvitamin D (25OHD) was measured using ELISA method and 25OHD lower than 20 ng/ml was considered as deficiency, 20–30 ng/ml was considered as inadequate level and higher than 30 ng/ml was normal vitamin D level (2). Demographic information including age, sex, weight, body mass index, obesity, body covering, and education were collected through interviews and questionnaires. Obesity was confirmed by BMI>30 kg/m² (28). Diagnostic tests and radiographies were performed for all patients to determine the cause of pain and only patients with shin pain or patients with nonspecific tibial bone pain were included in the study. In statistical analysis, patients (those with shin pain)

were compared with control subjects (those without shin pain) in terms of 25OHD concentration and the frequency of 25OHD deficiency. All control subjects were selected from the same hospital and at the same period. The control subjects were selected from among patients who referred to the hospital because of upper respiratory tract infection, dyspepsia or checkup tests with history of disease less than 6 weeks.

All the exclusion criteria were applied to the control subjects. The sample size was estimated based on at least 10 ng/ml difference in vitamin D level between patients and control subjects with 80% power and 95% confidence interval. Considering standard deviation of 20 ng/ml (1) the minimum number of patients in each group was estimated to be 64 patients. Student's t-test was used to compare the quantitative data and chi square test was used to investigate the relationship between vitamin D deficiency and bone pain (considering odds ratio), while $p < 0.05$ was considered significant.

Results

This study was conducted among 80 patients with mean age of 61 ± 8.2 years and 59 control subjects with mean age of 62.3 ± 9 years. The two groups were identical in terms of demographic and biochemical characteristics except for BMI (table 1). 65% of patients and 52.5% of control subjects were women ($p = 0.030$). BMI in patients was significantly higher than control subjects ($p = 0.001$). The prevalence of obesity in patients and control subjects was 48.7% and 23.7%, respectively ($p = 0.8$).

Obesity in men was significantly less than women (16.7% and 47.8%, respectively, $p = 0.001$). In terms of other biochemical variables, the two groups were almost identical. Vitamin D level in patients was significantly lower than control subjects ($p = 0.001$). The prevalence of vitamin D deficiency was 66.3% in patients and 12.1% in control subjects ($p = 0.001$) indicating a significant relationship between vitamin D deficiency and shin pain ($p = 0.001$, CI 95% = 2.5 – 35, OR=14.3). There was a stronger association between vitamin D deficiency and shin pain in men (table 2). After excluding the effect of other variables in regression analysis, there was an independent and significant relationship between vitamin D deficiency and pain ($p = 0.001$, CI-95%=8.5–40, OR=15.3). The prevalence of vitamin D deficiency in men was less than women (31% and 49%, respectively, $p = 0.037$).

Table 1. Demographic and biochemical characteristics of the elderly patients with shin pain and control subjects

Variable	Group	Patients(80) N(%)	Control(59) N(%)	P-value
Age (Mean $\pm$ SD)		61 $\pm$ 8.3	62.3 $\pm$ 9	0.38
Sex, Woman		65(81.3)	31(52.5)	0.003
Frequency of 25OHD deficiency		53(66.3)	7(12.1)	0.001
Obesity		37(46.2)	14(23.7)	0.11
Education				
Illiterate		38(47.5)	27(45.8)	0.89
Literate		42(52.5)	32(54.2)	0.56
		Mean$\pm$SD	Mean$\pm$SD	
25OHD level ng/ml		21 $\pm$ 16	37.4 $\pm$ 21.6	0.001
Body mass index kg/m ²		30 $\pm$ 5.5	27.1 $\pm$ 4.6	0.001
Calcium mg/dL		9.3 $\pm$ 0.76	9.2 $\pm$ 4.9	0.6
Phosphates mg/dL		3.8 $\pm$ 0.64	3.7 $\pm$ 0.47	0.47
Alkaline phosphatase IU		189 $\pm$ 63	196 $\pm$ 9.6	0.480
Erythrocyte sedimentation rate, mm/h		19.5 $\pm$ 11.8	17.4 $\pm$ 11.2	0.270
C-reactive protein (CRP)		6.3 $\pm$ 9.9	61 $\pm$ 6.6	0.920

Table 2. The relationship between vitamin D deficiency and shin pain in the elderly men and women with calculation of odds ratio with CI 95% and after modification of the effects of demographic and biochemical variables using regression analysis

*25OHD Deficiency	Women	Men	Total
Odds ratio	CI-95%	CI-95%	CI-95%
Crude odds ratio &	4.5(2.3–28)	34.7(4.5–216)	14.3(2.5–35)
Adjusted odds ratio #	10(2.3–31)	36(4.5–239)	15.3(8.5–40)
p-value	0.001	0.001	0.001

Discussion

Results of the study demonstrated that there was a significant relationship between 25OHD decline and pain and sensitivity of shin. The pain was mostly felt on the anterior surface of shin and a little pressure intensified the pain in the patients of this study. The results of this study are consistent with the results of previous studies dedicated to the relationship between vitamin D deficiency and skeletal pains (4, 5, 7, 8, 11, 22). However, no relationship was found between vitamin D deficiency and skeletal pains in some studies, or treatment with vitamin D was not effective (12, 28–30). These different results may be due to differences in method of patient selection, location of bone pain, definition of pain or characteristics of patients. Patients of the present study constitute one

homogeneous group in terms of quality and location of the pain, which is not consistent with other studies, since most studies are conducted among patients with different musculoskeletal pains (8, 9, 12, 19–21, 30). Localized pain in tibia was the cause of referring to the hospital in the patients of this study and may be early signs of subclinical osteomalacia. Some patients with shin pain and vitamin D deficiency responded to vitamin D replacement therapy (19–21, 31). Vitamin D deficiency may cause pain in patients with knee osteoarthritis by weakening quadriceps strength and can be modified by replacement therapy (17, 18, 34). Vitamin D deficiency in these patients increases the sensitivity of nerve fibers in addition to increasing the pain (25). Other studies demonstrated the relationship between vitamin D deficiency and chronic unexplained shin pain and found improvements using vitamin D therapy (23, 24, 33).

Identifying the treatable causes of lower extremity pain in the elderly is of great importance, since one can prevent the incidence of disability by modifying this problem (2, 18, 21, 22,27). Modification of vitamin D deficiency, particularly in the elderly women, is also effective in the treatment of osteoporosis (34), because osteoporosis is caused by several factors in the elderly

women (35,36) and vitamin D deficiency intensifies osteoporosis. To interpret the results of this study, we need to consider the limitations such as the type of study and the inadequate number of male patients. This is a case –control study and the patients were not studied in terms of treatment with vitamin D, so that the cause of pain is attributed to vitamin D deficiency. The reduced number of male patients compared to female ones may justify the observed difference in the relationship.

Results of the study demonstrated that localized pain and localized unexplained sensitivity in the shin in the elderly is associated with vitamin D deficiency. This effect might be due to the sensitivity of nerve fibers in regard with vitamin D deficiency or weakened lower extremity muscle strength.

Acknowledgments

Hereby, we express our deepest sense of gratitude and indebtedness to Deputy of Research and Technology of Babol University of Medical Sciences for their financial support as well as our colleagues in Clinical Research Development Unit of Ayatollah Rouhani Hospital in Babol.

References

1. Heidari B, Haj Mirghassemi M. Seasonal variations in serum vitamin D according to age and sex. *Caspian J Intern Med*. 2012;3(4):535-40.
2. Holick MF. The influence of vitamin D on bone health across the life cycle. The vitamin D epidemic and its health consequences. *Am J Clin Nutr*. 2004;80:1678S-88S-review
3. Hilger J, Friedel A, Herr R, Rausch T, Roos F, Wahl DA3, et al. A systematic review of vitamin D status in populations worldwide. *Br J Nutr*. 2014;111(1):23-45.
4. Heidari B, Javadian Y, Heidari P. Vitamin D deficiency is associated with nonspecific low back pain in young women. *Br J Med Med Res*. 2014;4:5053-61.
5. Heidari B, Heidari P, Samari E, RamzanianJalali M. Prevalence of vitamin D deficiency in common musculoskeletal conditions. *J Babol Uni Sci*. 2014;16:7-15.[in Persian]
6. Heidari B, Heidari P, HajianTilaki K. Association between serum vitamin D deficiency and knee osteoarthritis. *Int Orthop*. 2011;35(11):1627-31.
7. Ghadimi R, Esmailzadeh S, Firoozpour M, Ahmadi A. Does vitamin D status correlate with clinical and biochemical features of polycystic ovary syndrome in high school girls?. *Caspian J Intern Med* 2014, 5(4): 202-8.
8. Heidari B, Heidari P, Tilaki KH. Relationship between unexplained arthralgia and vitamin D deficiency: a case control study. *Acta Med Iran*. 2014;52(5):400-5
9. Heidari B, Shirvani JS, Firouzjahi A, Heidari P, Hajian-Tilaki KO. Association between nonspecific skeletal pain and vitamin D deficiency. *Int J Rheum Dis*. 2010;13(4):340-6.
10. Plotnikoff GA, Quigley JM. Prevalence of severe hypovitaminosis D in patients with persistent, nonspecific musculoskeletal pain. *MayoClin Proc*. 2003;78(12):1463-70.
11. Lotfi A, Abdel-Nasser AM, Hamdy A, Omran AA, El-RehanyMA. Hypovitaminosis D in female patients with chronic low back pain. *Clin Rheumstol*. 2007;26(11):1895-901.
12. Erkal MZ, Wilde J, Bilgin Y, Akinci A, Demir E, Bödeker RH, et al. High prevalence of vitamin D deficiency, secondary hyperparathyroidism and generalized bone pain in Turkish immigrants in Germany: identification of risk factors. *Osteoporos Int*. 2006;17(8):1133-40.
13. McBeth J, Pye SR, O'Neill TW, Macfarlane GJ, Tajar A, Bartfai G, et al. Musculoskeletal pain is associated with very low levels of vitamin D in men: results from the European Male Ageing Study. *Ann Rheum Dis*. 2010;69(8):1448-52.
14. Heidari B, Javadian Y, Monadi M, Dankob Y, FirouzjahiA. Vitamin D status and distribution in patients with chronic obstructive pulmonary disease versus healthy controls. *Caspian J Intern Med*. 2015;6(2):93-7.
15. Bayani MA, Ghadimi R, Akbari R, Saeedi F, Banasaz B. Status of Vitamin-D in diabetic patients. *Caspian J Intern Med*. 2014; 5(1):40-2.
16. Monadi M, Heidari B, Asgharpour M, Firouzjahi A, Monadi M, Ghazi Mirsaied MA. Relationship between serum vitamin D and forced expiratory volume in patients with chronic obstructive pulmonary disease (COPD). *Caspian J Intern Med*. 2012;3(3):451-5.
17. HeidariB. Knee osteoarthritis diagnosis, treatment and associated factors of progression: part II. *Caspian J Intern Med*. 2011;2(3):249-55.
18. Heidari B. Knee osteoarthritis prevalence, risk factors, pathogenesis and features: Part I. *Caspian J Intern Med*. 2011;2(2):205-12.
19. Javadian Y, Adabi M, Heidari B, Babaei M, Firouzjahi A, Ghahhari BY, Hajian-Tilaki K. Quadriceps Muscle Strength Correlates With Serum Vitamin D and Knee Pain in Knee Osteoarthritis. *Clin J Pain*. 2017;33(1):67-70.

20. Heidari B, Javadian Y, Babaie M, Yousef-Ghahari B. Restorative effect of vitamin d deficiency on knee pain and quadriceps in knee osteoarthritis. *Acta Med Iran*. 2015;53(8):466-70
21. Reginato AJ, Falasca GF, Puppu R, McNight B, Agha A. Musculoskeletal manifestations of osteomalacia: report of 26 cases and literature review. *Semin Arthritis Rheum*. 1999;28(5):287-304.
22. Hicks GE, Shardell M, Miller RR, Bandinelli S, Guralnik J, Cherubini A, Lauretani F, Ferrucci L. Associations between vitamin D status and pain in older adults: the Invecchiare in Chianti study. *J Am Geriatr Soc*. 2008;56(5):785-91.
23. Whitehurst JL, Reid CM. Vitamin D deficiency as a cause of chronic pain in the palliative medicine clinic: two case reports. *Palliat Med*. 2014;28(1):87-9.
24. Kessenich CR. Vitamin D deficiency and leg pain in the elderly. *Nurse Pract*. 2010;35(3):12-3.
25. Glover TL, Horgas AL, Fillingim RB, Goodin BR. Vitamin D status and pain sensitization in knee osteoarthritis: a critical review of the literature. *Pain Manag*. 2015;5(6):447-53.
26. Laslett LL, Quinn S, Burgess JR, Parameswaran V, Winzenberg TM, Jones G, et al. Moderate vitamin d deficiency is associated with changes in knee and hip pain in older adults: a 5-year longitudinal study. *Ann Rheum Dis*. 2014;73(4):697-703.
27. Al-Said YA, Al-Rached HS, Al-Qahtani HA, Jan MM. Severe proximal myopathy with remarkable recovery after vitamin D treatment. *Can J Neurol Sci*. 2009;36(3):336-9.
28. Bjorkman M, Sorva A, Tilvis R. Vitamin D supplementation has no major effect on pain or pain behavior in bedridden geriatric patients with advanced dementia. *Age Ageing*. 2008;37(4):315-321.
29. Shipton EE, Shipton EA. Vitamin D deficiency and Pain: clinical evidence of low levels of vitamin D and supplementation in chronic pain states. *Pain Ther*. 2015;4(1):67-87.
30. Helliwell PS, Ibrahim GH, Karim Z, Sokoll K, Johnson H. Unexplained musculoskeletal pain in people of South Asian ethnic group referred to a rheumatology clinic: relationship to biochemical osteomalacia, persistence over time and response to treatment with calcium and vitamin D. *Clin Exp Rheumatol*. 2006;24(4):424-7.
31. Bhan A, Rao AD, Rao DS. Osteomalacia as a result of vitamin D deficiency. *Endocrinol Metab Clin North Am*. 2010;39(2):321-31.
32. Heidari B, Hajian-Tilaki K, Babaie M. Determinants of pain in patients with symptomatic knee osteoarthritis. *Caspian J Intern Med*. 2016;7(3):153-161.
33. Gloth FM, Lindsay JM, Zelesnick LB, Greenough WB. Can vitamin D deficiency produce an unusual pain syndrome? *Arch Intern Med*. 1991;151(8):1662-4.
34. Malabanan AO, Turner AK, Holich MF. Case study severe generalized bone pain and osteoporosis in a premenopausal black female: effect of vitamin D replacement. *J Clin Densitom*. 1998;1(2):201-204.
35. Heidari B, Hosseini R, Javadian Y, Bijani A, Sateri MH, Nouroddini HG. Factors affecting bone mineral density in postmenopausal women. *Arch Osteoporos*. 2015;10:15.
36. Heidari B, Heidari P, Nouroddini HG, Hajian-Tilaki KO. Relationship between parity and bone mass in postmenopausal women according to number of parities and age. *J Reprod Med*. 2013;58(9-10):389-94.