Lower serum 25-hydroxyvitamin D3 concentration is associated with higher pain and disability in subjects with low back pain: a case-control study

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Research note

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Abstract

Objectives: Low back pain (LBP) is a common medical problem worldwide. The aim of this study is to evaluate the association between serum levels of 25-hydroxivitamin D3 and functional disability in patients suffering from LBP in a sample of Azeri middle-aged subjects, North West of Iran. Results: In this case-control study, 63 eligible patients with LBP and 55 healthy subjects enrolled in the study. Peripheral venous blood was taken for evaluating the serum Level of 25-hydroxivitamin D3. We recognized factors related with LBP by multiple regression analyses. The average plasma level of vitamin D in case group was significantly lower than that of the matched controlled group (26.25±15.95 vs. 34.20±14.92, p-value < 0.01 respectively). Subjects with vitamin D deficiency or insufficiency were more likely to exhibit LBP than subjects with normal vitamin D level [(OR= 2.388, 95% CI (1.114 to 5.119)]. According to the partial correlation analysis, there was a reverse correlation between plasma level of vitamin D with functional disability measured by Modified Oswestry Questionnaire (r = -.307, p = .017) and also with pain intensity according to Visual analogue Scale (VAS) score (r = -.268, p = .040) whilst controlling for age, sex and body mass index (BMI).

Introduction

Low back pain (LBP) is a common medical problem worldwide (1). According to research, 65-80% of people have experienced LBP at least once in their life (2). LBP is associated with difficulty in daily living activities, reduced social function, and diminished lifestyle quality (3).

Recently, Vitamin D deficiency and insufficiency have been pinpointed to be involved in many chronic disorders (4, 5) as well as chronic painful conditions (6, 7). In some cases, patients may develop general musculoskeletal pain and sensitivity depending on the severity of deficiency (8). Meanwhile, the evidence concerning serum 25 hydroxyvitamin D levels in subjects with and without LBP, and how 25 hydroxyvitamin D levels affect pain severity in subjects with LBP seems to be inconsistent. There have been reports on a relationship between vitamin D deficiency and LBP incidence in literature. However, there has not been sufficient convicting evidence regarding the ideal level of vitamin D plasma level in this situation (9, 10).

In our country, the Vitamin D deficiency or insufficiency has become increasingly evident in the current years. It is assumed that approximately 29% of normal population in Iran have vitamin D deficiency (11). Since the effect of vitamin D deficiency and vitamin D supplement vary among different populations (12-14) and considering the rising concern in vitamin D supplementation in LBP management, a broader understanding about the correlation between serum 25 hydroxyvitamin D levels and LBP is desirable. Accordingly, this study aims to evaluate vitamin D plasma level in patients suffering from LBP in a sample of Iranian population, northwest of Iran.

Methods

Patients

In this case-control study, 60 eligible patients with chronic LBP persistent in more than three months enrolled in the case group from the reference outpatient clinics of Tabriz University of Medical Sciences for further evaluation during a period of 6 months from March to August 2018. Initially, for each case with LBP, one control was selected from the same outpatient clinics without LBP who were matched based on age and body mass index (BMI). Inclusion criteria were as follows: age older than 20; BMI greater than 18.5. On the other hand, the patients were excluded based on these criteria: LBP duration less than 3 months; lumbosacral deformities; intervertebral disc herniation; osteoporosis; rheumatoid arthritis; uncompensated renal, and liver diseases. The eligible individuals were categorized in 3 subgroups based on age (18-40, 40-60, more than 60 years old) and weight (normal, overweight, obese).

A simple random sampling method was applied. Based on observations in a similar study (10), 6.2 and 6.9 were considered as the standard deviation of the case and control groups respectively and 3.6 for the effect size. With a significant level of 0.05, the power of 0.8 and using a two-way test, the sample size was estimated as 53 individuals in each group. Considering 15% chance of loss, the sample size was estimated to be 60 in each group and 120 in total.

Physical activity

Physical activity of the participants was assessed by the short-form IPAQ (International Physical Activity Questionnaire) (15). Three categories of physical activity were suggested: low, moderate, and high (16).

Vitamin D measurement

Fasting peripheral venous blood (3 ml) was collected from participants in both groups. The level of 25-hydroxyvitamin D3 was measured by ELISA. All the steps were performed exactingly according to the instructions of the kits (Euroimmun, Germany).

Anthropometric measurements

The weight was measured by a Seca 813 digital scale. BMI was calculated via dividing the weight (kg) by the square of height (m2).

LBP assessment

Modified Oswestry Questionnaire was used for functional evaluation of LBP in individuals of the case group. This questionnaire included 10 questions regarding pain severity, LBP during self-care activities, lifting objects, walking, sitting, standing, sleeping, social life, and leisure time. Each question had 6 items, based on Likert scoring system, where 0 reflected "No Problem" while 5 represented "Severe Problem" (17, 18). LBP severity was also recorded by Visual Analog Scale (VAS) in which zero referred to "No Pain" and 10 denoted "Very Severe Pain" (19).

Statistical measurement

Measurement data were introduced as a mean±standard deviation. The two study groups were compared using Student's t-test or the Chi-square test. Logistic regression analyses were used to determine whether 25 hydroxyvitamin D level was significant factors associated with the presence of LBP. Finally, Partial correlation analyses were employed for analyzing correlation. Age, sex and BMI served as control variables. Values of P<.05 were considered as statistically significant. Statistical analysis was conducted using SPSS 17.0 software (SPSS Inc., Chicago, IL).

Results

Patients

Totally 118 (73 female and 45 male) individuals were enrolled in this study, in which 63 had LBP (case group) and 55 were without LBP (control group). Five subjects were in the control were excluded in the analysis stage because of incomplete data and missed information. Details of demographic and anthropometric characteristics of participants are presented in Table 1. All the studied variables have normal distribution.

There were no significant differences between case and control groups in anthropometric measures except weight that was significantly higher in subjects with LBP than subjects in control group (79.923±12.30 vs. 75.274±10.28 Kg, p-value=0.028 respectively). Normal waist circumference was observed in 3.6% of patients with LBP and 11 % of matched healthy controls. Based on Pearson-correlation test results, there were significant inverse correlation between weight and plasma level of 25 hydroxyvitamin D and also BMI and plasma level of 25 hydroxyvitamin D in individuals with LBP (r=-0.288, p-value=0.022 and r=-0.257, p-value=0.042, respectively).

Vitamin D measurements

Average plasma level of 25 hydroxyvitamin D in case group was significantly lower than matched control group (26.25± 15.95 ng/ml and 34.20±14.92 ng/ml, p-value < 0.01 respectively). In fact 42.85% and 22.22% of individuals with LBP and 14.54% and 27.27% of healthy controls had vitamin D deficiency and insufficiency, respectively.

The variables which were considerably associated with LBP in simple analysis at significance level of 0.25 (i.e. vitamin D deficiency or insufficiency and physical activity) included in the multiple logistic regression method with backward procedure to explore the factors influencing LBP. Vitamin D deficiency or insufficiency and physical activity were found to be the important risk factors for LBP. To determine the odds ratio (OR) of LBP in patients with vitamin D deficiency or insufficiency, multiple logistic regression was used compared to subjects with vitamin D sufficiency. The values of crude OR and Adjusted OR are shown in Table 2. Subjects with vitamin D deficiency or insufficiency were 2.39 times more likely to exhibit LBP than subjects with vitamin D sufficiency (OR= 2.388, 95% CI (1.114 to 5.119)).

LBP characteristics: Pain and disability

The average score of the Modified Oswestry score for patients suffering from LBP was 31.12± 18.48 which is equal to "moderate disability". Also the average pain severity score based on Visual Analog Scale was 5.48±2.12. A partial correlation was carried out to determine the relationship between 25 hydroxyvitamin D level and functional disability of subjects with LBP whilst controlling for age, sex and BMI. There was a moderate, negative partial significant correlation between plasma level of 25 hydroxyvitamin D and Modified Oswestry score ($r(58) = -.307$, $n = 63$, $p = .017$) whilst controlling for age, sex and BMI. However, zero-order correlations showed that there was a statistically significant, moderate, negative correlation between Vitamin D plasma level and functional disability of LBP ($r(61) = -.336$, $n = 63$, $p = .007$), indicating that for age, sex and BMI had very little influence in controlling for the relationship between Vitamin D plasma level and functional disability of LBP. There was also a negative partial significant correlation between plasma level of 25 hydroxyvitamin D and VAS ($r(57) = -.268$, $n = 63$, $p = .040$) whilst controlling for age, sex and BMI. The zero-order correlations showed that there was a statistically significant, negative correlation between Vitamin D plasma level and VAS ($r(60) = -.336$, $n = 63$, $p = .015$), indicating that for age, sex and BMI had very little impact in controlling for the relationship between Vitamin D plasma level and pain intensity in patients with LBP.

Discussion

There was a significant difference in plasma level of 25 hydroxyvitamin D in patients with LBP in comparison to subjects without LBP. The level of vitamin D was significantly lower in patients with LBP where 42.85% and 22.22% of them had vitamin D deficiency and insufficiency, respectively. However, those without LBP showed 14.54% and 27.27% in subjects without LBP. According to the findings, subjects with lower level of plasma 25 hydroxyvitamin D (vitamin D deficiency or insufficiency) were 2.39 times more likely to exhibit LBP than subjects with normal vitamin D. In a similar study in women with LBP, Hypovitaminosis D (25 hydroxyvitamin D < 40 ng/ml) was found in 49/60 patients with LBP (81%) and 12/20 (60%) of subjects without LBP, with an odds ratio of 2.97 (10). However, Thorneby *et al.*, in a cross-sectional study on individuals with chronic LBP, could not find any significant relationship between plasma level of vitamin D and LBP (20). The reason for this variety of findings in studies regarding vitamin D level and LBP could be due to population variations across different societies. In the scientific literature, the Vitamin D status varies in various countries, even in various areas of the same country, in response to diversity in exposure to the sunlight and dietary habits.

There were significant inverse correlations between weight as well as BMI and plasma level of 25 hydroxyvitamin D in individuals with LBP. That means higher weight and BMI were associated with lower vitamin D plasma level. Along with this, there are interesting findings in various studies where the vitamin D deficiency is associated with obesity (21, 22).

In the current study, lower levels of vitamin D were associated with higher scores of disability questionnaire. The same pattern of relationship was also found for pain severity. Lower levels of vitamin D in plasma were associated with higher scores of LBP in VAS. Observational studies have suggested that vitamin D deficiency is correlated with a broad range of chronic pain conditions (23). In favor of

findings in the current study, in a retrospective observational study in Turkey by Gokcek et.al. (24) there was an inverse correlation between level of 25 hydroxyvitamin D and VAS score in patients with LBP (r = -0.594, P < 0.001). In contrast, in a nested case-control study by Heuch et.al (9), no association was found between 25 hydroxyvitamin D status and risk of chronic LBP (OR per 10 nmol/L 25(OH)D=1.01, 95% CI 0.97 to 1.06). What matters is that the interpretation of the findings of these studies will not be bias-free, regardless of the characteristics of the population studied. The prevalence and severity of vitamin D deficiency is very important in determining the association between the level of 25 hydroxyvitamin D and LBP. In this regard, in the study of Brady et al. (25) on those with 25 hydroxyvitamin D <30 nmol/L, cholecalciferol supplementation led to a significant reduction in back pain disability according to Chronic Pain Grade Questionnaire.

The exact mechanism linking vitamin D to pain is not completely clarified physiologically. It has been shown that vitamin D is associated with pain feelings through regulation of inflammatory cytokines (26) and modulation of sensory nerves (27). Since there are some receptors of vitamin D available in the central nervous system, there have been theories proposed on relationship between vitamin D and fibromyalgia in literature (28). Vitamin D may also reduce the production of Prostaglandin E2 (PGE2) in fibroblasts which is a crucial factor for pain perception (29).

Limitation

This study had some limitations, however. Firstly, finding representative control participants in the case-control design is not easy. Secondly, we did not determine the dietary intake of vitamin D in the participants. Nevertheless, a smaller quantity vitamin D is acquired from food than from sun exposure. Also, the sample size was relatively small. Finally, causality cannot be confirmed because of retrospective design, and prospective and interventional studies are required to verify these findings.

Abbreviations

BMI: body mass index; IPAQ: International Physical Activity Questionnaire; LBP: Low back pain; OR: odds ratio; VAS: Visual analogue Scale

Declarations

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conduct and results of the study.

Authors' contributions

AP, ND and SKS designed the study, and prepared the first draft, and supervised the conduct data collection and analyses. MH refined the research questions and helped to draft the manuscript. FJ participated in the design of the study and will perform the statistical analysis. AM and MDR conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

All patients will be provided written informed consent and approval has been received from the Ethics Committee of the Research Vice-Chancellor of Tabriz University of Medical Sciences (IR.TBZMED.REC.1396.63). Personal information about patients will be preserved in a database to protect patients' security.

Consent for publication

Not applicable.

Availability of supporting data

The datasets generated during the current study are available from the corresponding author on reasonable request.

Competing interests

All authors declare that they have no competing interests.

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Tables

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