Investigation of Serum Levels of Vitamin D in Patients with intractable Carpal Tunnel Syndrome Referred to Physical Medicine and Rehabilitation Clinics of Shiraz University of Medical Sciences in 2015

Seyed Mohammad Saghanezhad (1)
Sharareh Roshanzamir (2)
Marzieh Mohtashamkia (1)

(1) Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran
(2) Department of Physical Medicine & Rehabilitation, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding Author:
Sharareh Roshanzamir
Telephone: +989177111359
Email: Sharareh.roshanzamir@gmail.com

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Abstract

Introduction: One of the factors which can influence Carpal Tunnel Syndrome (CTS) is vitamin D. Vitamin D is an essential and fat-soluble vitamin which acts like a steroid hormone, is produced in the body and targets certain tissues.

Objective: This study investigated serum levels of vitamin D in patients with intractable CTS referred to the Physical Medicine and Rehabilitation Clinics of Shiraz University of Medical Sciences in 2015.
Method: This observational, cross sectional analysis evaluated 85 patients with intractable CTS referred to the Physical Medicine and Rehabilitation Clinics of Shiraz University of Medical Sciences in 2015, determined their serum level of vitamin D and compared results with 85 healthy controls.

Results: Mean age and BMI of case and control groups were identical (P>0.05). There was a significant difference (P=0.0001) in mean serum level of vitamin D between case group (23.2 ± 9.2 nm/l) and control group (41.3 ± 16.8 nm/l).

Discussion and Conclusion: It is concluded that serum level of vitamin D is lower in patients with intractable CTS compared to the general population.

Key words: carpal tunnel syndrome, vitamin D, treatment-resistant

Introduction

Carpal tunnel syndrome (CTS) is the most common peripheral neuropathy of hand and arm caused by pinched or pressed nerves in the wrist (as a result of compression of median nerve in the carpal tunnel) (1).The tunnel is a narrow path for nine tendons and one nerve (Median nerve), to pass from the forearm to the hand. This path lies on the carpal bones and is roofed by a strong ligament, flexor retinaculum. In the case of CTS there is a group of symptoms which are called a syndrome and any cause which narrows space of the tunnel, increases pressure or size of the tissues inside the tunnel and leads to these symptoms (1, 2). This pressure will lead to motor and sensory dysfunction in the affected hand and areas supplied by the median nerve and its branches such as structures on the lateral side of the hand that include the thumb, index, middle finger and the outer half of the ring finger. The pain is mainly referred to the forearm and beyond the wrist.

Prevalence of this syndrome ranges as high as 15% in the industrial population whereas the annual incidence of CTS is 1 to 3.46 per 1000 persons in the general population.

It is most common in middle-aged housewives, and caused by overuse of the wrist such as when typing on a keyboard, driving, doing carpentry, illustrating, and in butchers, automobile mechanics and workers who work with their hands all day long. (3, 4).

Causes of CTS are divided into: 1) anatomic causes such as fractures, dislocations, osteophytes of wrist bones, tumors, cysts, thickened synovium and arthritis;

2) inflammatory or neuropathic causes such as diabetes mellitus, alcoholism, pregnancy and thyroid diseases; 3) mechanical causes such as repetitive movements of the wrist and fingers and vibration, particularly in labourerss and computer users (5, 6).

CTS patients are usually diagnosed by numbness, pain and paresthesia in the median nerve distribution (thumb, index and middle finger). These symptoms significantly reduce quality of life of patients; thus, treatment of this disease is highly important (6, 7).

The patients usually complain about numbness, pain, and paresthesia in the median nerve innervation. These symptoms are often worsened during nights and with repetitive and strong movements of hands. In some cases, straightening or waving the hand will improve symptoms. Occasionally, inability in precise movements of the fingers (such as needlework) and motor weakness are reported. Thenar atrophy is one of the objective symptoms of this disorder [4, 8].

Conservative treatments such as splinting, rest, physiotherapy, exercise and nonsteroidal anti-inflammatory drugs and finally surgical release of the carpal tunnel is are usually used for treatment of CTS; however, this surgery is essential for those patients for whom other conservative therapy has not worked. In this operation the retinaculum is divided to create more space for the nerve. (9).

When medical and supportive treatments fail to reduce symptoms (less than half of the patients), surgery is prescribed for removing pressure on the nerves. The surgery tends to widen the carpal tunnel by releasing transverse carpal ligament and its extensor fascia. Surgery is successful in 90% of cases ; however, full recovery takes several months. Recently, endoscopic surgery has been used [4, 8].

If left untreated and not done in a timely manner, the patient will have irreversible nerve damage leading to intractable pain, numbness and muscle weakness in the areas innervated by the median nerve.

One of the factors which can improve symptoms of CTS is vitamin D. Vitamin D is an essential and fat-soluble vitamin which acts like a steroid hormone produced in the body and certain target tissues. Vitamin D is naturally present in very few foods, is added to others and available as a dietary supplement; however, it can be absorbed along with other fats (50% absorption efficiency)(10,11).Vitamin D is also synthesized endogenously by ultraviolet rays from sunlight striking the skin. Serum levels less than 18 nmol/l are considered as severe deficiency, 18 to 23 nmol/l are considered as average deficiency, 23 to 36 nmol/l are considered as mild deficiency and over 36 nmol/l are considered as a sufficient amount of vitamin D (12).

Vitamin D promotes calcium absorption in the gut and maintains adequate serum calcium and phosphate concentrations to enable normal mineralization of the bone and prevent hypocalcemia (10, 11).

Calcitriol increases tubular reabsorption of calcium and phosphate in kidneys. Calcitriol is also involved in cell differentiation, proliferation and growth of many tissues such as skin, muscles, pancreas, nerves, parathyroid gland and immune system (10, 11) .

It is also needed for bone growth and bone remodeling by osteoblasts and osteoclasts. Without sufficient vitamin D, bones can become thin, brittle, or misshapen. Vitamin D sufficiency prevents rickets in children and osteomalacia. Together with calcium, vitamin D also protects older adults from osteoporosis. Serum level of vitamin D is closely regulated by parathyroid hormone, calcium and phosphate (10, 11).

The main function of calcitriol is similar to steroid hormones, that is, reacting with membrane and nuclear receptors and influences on gene transcription in many tissues. Binding of calcitriol to nuclear receptor proteins increases affinity of these proteins to specific precursor regions of the genes or vitamin D response elements (VDRE), leading to their binding. Then, specific mRNA transcription begins in order to induce production of specific proteins or prevent their production. There are over 50 known genes including the gene related to Calbindin of which activity is regulated by vitamin D (10, 11).

Risk factors of vitamin D deficiency include preterm birth, skin pigmentation, lack of light exposure, obesity, malnutrition and aging. Serum level of 25-hydroxyvitamin D is higher in northern European countries than in southern European countries(11,12).

Involvement of vitamin D in the immune system (immunomodulatory effect) and increase in levels of inflammatory markers such as 6-IL/10-IL ratio and CRP are associated with decrease in serum levels of vitamin D. An optimal serum level of vitamin D is required to increase function of immune system, particularly in the elderly (13, 14).

The role of vitamin D has been noted in the development of many musculoskeletal disorders (11, 12). However, no study has been conducted on serum level of vitamin D in patients with CTS compared to the general population.

Accordingly, this study evaluates serum level of vitamin D in patients with intractable CTS referred to the Physical Medicine and Rehabilitation Clinics of Shiraz University of Medical Sciences in 2015.

The developed hypothesis is that serum level of vitamin D in patients with treatment-resistant CTS is different from the normal population.

Materials and Methods

This is an observational, cross-sectional analysis. With Assumption of Confidence: 95%, D:0.1, P:70% , estimated Sample size was 85, estimated Control Group was 85 and Sample selection pattern was Simple.

Population and Sample

The studied population included 170 patients with treatment-resistant CTS. The patients were assigned to two groups of 85 with and without treatment-resistant CTS by using convenient sampling. Inclusion criteria included treatment-resistant CTS (6 months of treatment with NSAIDs (Non steroidal Anti-inflammatory Drugs), splint and physiotherapy), consent to participate, 18 to 24 BMI and age 20 to 50 years. Exclusion criteria included treatment-responding CTS, known history of trauma to the wrist and hand, diabetes, hypothyroidism, radiculopathy, peripheral neuropathy, known chronic liver and renal disorder, pregnancy, lactation and metabolic diseases.

Methods

This observational, cross-sectional analysis evaluated 85 patients with treatment-resistant CTS referred to the Physical Medicine and Rehabilitation Clinics of Shiraz University of Medical Sciences in 2013-2014. Serum level of vitamin D was determined by high-performance liquid chromatography (HPLC) and compared with 85 healthy controls who were selected from people accompanying the patients. A questionnaire was designed to collect data including age, gender, BMI, past medical history, drug history, exclusion and inclusion criteria and serum level of vitamin D.

Inclusion and Exclusion Criteria

Inclusion criteria included treatment-resistant CTS (6 months of treatment with NSAID, splint and physiotherapy and dissatisfaction with treatment), consent to participate, 18 to 24 BMI and age 20 to 50 years. Exclusion criteria included severe CTS, known history of trauma and tumor in the wrist and hand, diabetes, hypothyroidism, radiculopathy, peripheral neuropathy, known chronic liver and renal disorder, pregnancy, lactation, and metabolic diseases.

Ethical considerations

This study was approved by the Ethics committee of Shiraz University of Medical Sciences at 2015-08-19 with the reference number of IR.SUMS.REC.1394.S290
Personal information was not disclosed. Nobody was forced to participate in the study. Written informed consent was obtained from all participants before any test.

Scales

Questionnaire was used to collect data.

Data Analysis

Data was compiled on the Excel 2013 software. Independent-Samples T Test with P value of 0.05 in SPSS20 were used to analyze data.

Results

Table 1 reports distribution of age, BMI and level of vitamin D in the two groups studied.

Table 1: distribution of age, BMI and level of vitamin D in the two groups studied

		Mean	Std. Deviation	Std. Error	P Value
Age year	Case	42.0706	10.44121	1.13251	> 0.05
	Control	40.8353	7.95351	.86268	
	Total	41.4529	9.27430	.71131	
BMI	Case	21.1353	1.20482	.13068	> 0.05
	Control	21.1471	1.17985	.12797	
	Total	21.1412	1.18888	.09118	
Vit. D nm/l	Case	23.1882	9.16709	.99431	0.0001
	Control	41.2941	16.83804	1.82634	
	Total	32.2412	16.28284	1.24884	

Total sample size was set at 170 cases who were assigned to control group (85) and experiment group (85). In the experiment group, lower bound of age was 39.81 and upper bound of age was 42.07 (42.07±10.44; p-value>0.05). In the control group, lower bound of age was 39.11 and upper bound of age was 42.55 (40.83±7.95; p-value>0.05). In total (control group + experiment group), lower bound of age was 40.04 and upper bound of age was 42.85 (41.45±9.27; p-value>0.05). In the experiment group, lower bound of BMI was 20.87 and upper bound of BMI was 21.39 (21.13±1.20; p-value>0.05). In the control group, lower bound of BMI was 20.89 and upper bound of BMI was 21.40 (21.14±1.17; p-value>0.05). In total (control group + experiment group), lower bound of BMI was 20.96 and upper bound of BMI was 21.32 (21.14±1.18; p-value>0.05). In the experiment group, lower bound of serum vitamin D was 21.21 nm/l and upper bound of serum vitamin D was 25.16 nm/l (23.18±9.16; p-value=0.0001). In the control group, lower bound of serum vitamin D was 37.66 nm/l and upper bound of serum vitamin D was 44.92 nm/l (41.29±16.83; p-value=0.0001). In total (control group + experiment group), lower bound of serum vitamin D was 29.77 nm/l and upper bound of serum vitamin D was 34.70 nm/l (32.44±16.28; p-value=0.0001). Mean age was identical in both groups (P>0.05). Moreover, mean BMI was identical in both groups (P>0.05). There was a significant difference (p=0.0001) in mean serum level of vitamin D between the case group (23.2 ± 9.2 nm/l) and control group (41.3 ± 16.8 nm/l).

Discussion and Conclusion

Some CTS patients do not respond well to the treatments which are currently used. It will be helpful to identify effective factors on lack of response. It is essential to provide solutions for promoting health and increasing quality of life of these people.

Vitamin D is a fat-soluble element that seems to have some anti-inflammatory and immune-modulating properties. In addition, recent epidemiologic studies have observed relationships between low vitamin D levels and increased overall and cardiovascular mortality, cancer incidence and mortality, and autoimmune diseases such as multiple sclerosis.(13)

A cross-sectional descriptive study in a multi-ethnic general practice in Norway in 2010 showed a high prevalence of hypovitaminosis D in patients with non-specific musculoskeletal pain, headache, or fatigue for whom the GP had suspected a low vitamin D level. These results indicate that GPs should maintain awareness of hypovitaminosis D and refer such patients with minimal sun exposure and a low dietary vitamin D intake for more evaluation.(9)

According to a study conducted in 2014, a strong relationship can be found between low level of vitamin D concurrent with the increased level of inflammatory markers such as IL-6/IL-10 ratio and CRP in the elderly; an optimal serum level of vitamin D is required to increase function of immune system, particularly in the elderly (14).

Moreover, practitioners should be aware of non-calciotropic effects of vitamin D, such as differentiation control, meiosis and its involvement in immune system (immunomodulatory effects) (15).

One potential cause of CTS is the role of vitamin D. Accordingly, this study evaluated serum level of vitamin D in patients with intractable CTS referred to the Physical Medicine and Rehabilitation Clinics of Shiraz University of Medical Sciences in 2015.

No study has been conducted in this regard; most of the studies conducted focused on vitamin B6. However, Oh et al (2013) evaluated six CTS patients and compared them with six controls. They reported down regulation of vitamin-D binding protein (VDBP) in CTS patients compared to controls. This is consistent with the current study.

In this study, mean age and BMI were identical in both groups (P>0.05). There was a significant difference (p=0.0001) in mean serum level of vitamin D between the case group (23.2 ± 9.2 nm/l) and control group (41.3 ± 16.8 nm/l).

In conclusion, serum level of vitamin D is lower in patients with intractable CTS compared to the general population. Finally, it is recommended to conduct further studies with larger samples in order to confirm current findings.

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