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Study of Vitamin D Level in Children with Non-specific Musculoskeletal Pain

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Abstract

Background

Vitamin D deficiency is known as a one of the underlying causes of Idiopathic musculoskeletal pain (IMSP). This study aimed to evaluate the correlation between serum vitamin D (Cholecalciferol) status in patient with Non-specific Musculoskeletal Pain and healthy children.

Materials and Methods

Seventy-seven children (aged 3–14 years), with IMSP were included as cases and 90 healthy subjects were selected for control group. Demographic characteristics and biochemical levels of vitamin D and Parathyroid hormone (PTH), were obtained. Data were analysis using SPSS version 17.0 software.

Results

Results showed that vitamin D means levels of patients and healthy children were significantly different (19.5 $\pm$ 8.84 ng/mL versus 12.7 $\pm$ 11.89 ng/mL), respectively ($P<0.05$). Also, there was a significant difference between PTH level in both healthy and patient subjects ($P<0.001$). Mean levels of vitamin D in both groups were below the normal range, but lower in control group ($P<0.001$).

Conclusion

Deficiency of vitamin D was suggested as the probable identified risk factors for IMSP in children. The results of our study did not reveal clear correlation between vitamin D deficiencies in children which suffer IMSP compared the healthy children.

Key Words: Children, IMSP, Iran, Pain, Vitamin D.

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1- INTRODUCTION

Idiopathic musculoskeletal pain (IMSP), is a condition that defined as the chronic pain in different parts of musculoskeletal which occurs at least once per week and continues for six or more weeks without detectable cause. Yet our understanding of these conditions, risk factors and underlying etiology is limited. Female gender, psychological factors, deficiency of vitamin D and hyper mobility were mentioned as the probable identified risk factors for IMSP (1).

Vitamin D is a fat-soluble steroid hormone that could be obtained from sterols including vitamin D2 (Ergocalcifero), or vitamin D3 (cholecalciferol) (2). Vitamin D3 or Cholecalciferol, changes into 25-hydroxycholecalciferol (25 [OH]D), in liver and later transforms into 1,25-dihydroxycholecalciferol the renal tubules (3, 4). The serum level of 25-hydroxycholecalciferol is the most indicative index of the level of vitamin D in human body with its half-life of 2 to 3 weeks inside the body (5-9). Parathyroid hormone compensates the reduction of serum calcium via changes in the bone, absorbing the bone calcium and releasing it in the blood. This could be done through activating osteoblasts. Too much activation of osteoclasts or the increase in the level of parathyroid hormone, may end osteoporosis, rise serum calcium and or metastatic calcification (6).

Although the main role of vitamin D is the calcium homeostasis, vitamin D can also take the role of a hormone. Like other steroid hormones, it has the potential to enter the cell and synthesize a specific protein (10-12). This vitamin plays a crucial role in the central and peripheral nervous system. The discovery of receptors of this vitamin in various regions of the brain and specially the spinal cord may evidently approve the passage of this vitamin through the blood-brain barrier (13), and its connection with musculoskeletal pain (14). Vitamin D deficiency is worldwide problem (15), and according several studies reports indicate high prevalence in Asian countries including China, India, Saudi Arabia and Iran, and estimated its prevalence between 30 to 93 percent (16-22).

The clinical symptoms of vitamin D deficiency may present as a musculoskeletal pain. However, precise diagnosis of them is not quite possible based on symptoms, hence many people are unaware of their deficiency (23). Various studies have found high frequency of vitamin D deficiency in patients suffering musculoskeletal pains with unidentified origin showing a significant connection between unidentified chronic bone pain and vitamin D deficiency, independent of the age (23-26).

Considering the number of the children suffering non-specific musculoskeletal pain, finding a proper treatment for this pain like vitamin D supplement and elevating the quality of their life, are of utmost importance. The aim of the present study was to evaluate vitamin D levels in children with non-specific musculoskeletal Pain compared the healthy children.

2- MATERIALS AND METHODS

This case-control study was conducted from spring to winter of 2014 on the children with unidentified chronic bone pains at the department of Pediatrician Shahid Moteheri Hospital, Urmia Iran. During the study total of 167 children (72-boy and 95- girl), were invited to study that 77 of them were selected IMSP and included in case group and 90 subjects, apparently healthy, with no complaints of IMSP were chosen for control group. Exclusion criteria were having a history of vitamin D deficiency like rickets, renal insufficiency, nephritis, epilepsy taking medications which interfere with the absorption of this vitamin D like steroids or anticonvulsant steroids, calcium and

vitamin supplement since the past 6 months. Children with history and signs of trauma, arthritis, myositis and fibromyalgia as well as children with clinical evidence of chronic systemic disease like tuberculosis, heart disease, kidney disease and malabsorption, were excluded from the study (1). Then, 5 ml blood sampling of the patients after history-taking and recording the clinical evidences along with the questionnaire asking their general and specific information on the present condition was taken by experience nurse and laboratory stuff. A letter of informed consent from parents was obtained. The samples were centrifuged for 15 minutes and frozen at -18° c in the hospital laboratory to measure the serum level of (25[(OH] D), and parathyroid hormone (PTH) by one of the experienced staff. Measurement of 25-hydroxycholecalciferol was conducted through IDS kits made in England through radioimmunoassay method. Other parameters under study including Parathyroid hormone were also measured using this method via Diasorin kits, made in USA. Anthropometric characteristic as well as length and weight measured by an experience nurse in laboratory sampling section that prepared for this study. Also, Detecto-Medic, Brooklyn. USA devices used to measure length and weight. Data between the two groups were analyzed using Chi-squared test. Pearson correlation test was used to assess the relationship between vitamin D and PTH levels, and anthropometric indices in patients and control groups.

Pearson correlation test, was used to assess the relationship between vitamin D and PTH levels; for all statistical tests P- value < 0.05 were considered to be statistically significant. Statistical analysis was performed by the SPSS version 17.0 software (SPSS, Chicago, Illinois). Although, there is no consensus about normal range of vitamin D, but most researchers estimate 30 to 70 ng/mL as a normal level of this vitamin. Based on the American Academy of Pediatrics (AAP), and the Institute of Medicine (IOM), both define vitamin D insufficiency as calcidiol (25[OH] D) concentrations < 20 ng/mL in children. In contrast, the Endocrine Society and the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines both classify insufficiency as calcidiol concentrations < 30 ng/mL (27).

3- RESULTS

During the study a total of 167 children (72- boy and 95- girl), were sampled. Seventy seven of them were selected in case group with IMSP and 90 healthy subjects were chosen in control group. Both groups' ages were 3 to 14 years. Also, 66% of cases and 62.5% of controls lived in urban areas that using Chi-square test was not significant difference between the two groups (P=0.692).

The mean ages of patient's were 7.01 ± 2.42 and 7.22 ± 2.62 years in the healthy group, respectively. The mean weight of patient group was 22.54 ± 7.04 kg and for the healthy group, it was 24.48 ± 10.18 kg. Results showed that the mean of height in patient and healthy groups were 119.04 ± 12.41 cm and 113.75 ± 17.60 cm, respectively. Although, height in case group was higher than the control group; but these difference, were not statistically significant (P>0.05).

Average vitamin D levels in both groups (patients and healthy groups) of residents in rural was greater than urban, but this difference was not statistically significant (P=0.437). The Mean vitamin D levels in patients and healthy groups being (19.48 ± 8.84 vs. 12.73±11.88), respectively and these means were statistically significant (P< 0.001). The mean PTH level in patients group (15.73 ± 2.53) was lower than the healthy group (19.09 ± 4.38), and these means were statistically significant

(P< 0.001) (**Table.1**). Results showed that the average of vitamin D levels in the patients group had a significant inverse correlation with weight (P=0.014 and r= -0.329); while the healthy group was not statistically significant (**Table.2**). Also, average of PTH levels in the patients group had a significant inverse correlation with weight (P=0.031 and r= -0.312), and length (P=0.042 and r= -0.323); while the healthy group had a significant correlation with weight (P=0.029 and r= 0.270), and length (P=0.006 and r= 0.376) (**Table.2**).

Table-1: Comparison of mean of Vitamin D, PTH, Weight, and Length among case and control groups

Groups variables		Weight	Length	Vitamin D	PTH
Patients group	Mean	22.54	119.04	19.48	25.24
	Number	55	45	77	69
	SD	7.05	12.42	8.84	9.48
Healthy group	Mean	24.48	113.75	12.73	16.08
	Number	67	55	90	87
	SD	10.19	17.61	11.89	9.72
t-test for Equality of Means		P=0.234	P= 0.092	P<0.001	P<0.001

PTH**:** Parathyroid Hormone; SD: Standard deviation.

Table-2: The correlation between Vitamin D, PTH, Weight, Length and BMI among case and control groups

Group	Variables	Statistics	Weight	Length	Vitamin D	PTH
Case	Weight	Pearson Correlation		0.842	-0.329	-0.312
		P-value		<0.001	0.014	0.031
	Length	Pearson Correlation	0.842		-0.266	-0.323
		P-value	< 0.001		0.078	0.045
	Vitamin D	Pearson Correlation	-0.329	-0.266		-0.193
		P-value	0.014	0.078		0.111
	PTH	Pearson Correlation	-0.323	-0.266	-0.193	
		P-value	0.031	0.045	0.111	
	BMI	Pearson Correlation	0.718	0.243	-0.222	-0.233
		P-value	<0.001	0.107	0.142	0.154
Control	Weight	Pearson Correlation		0.772	-0.154	0.270
		P-value		<0.001	0.212	0.029
	Length	Pearson Correlation	0.772		-0.037	0.376
		P-value	<0.001		0.789	0.006
	Vitamin D	Pearson Correlation	-0.154	-0.037		0.073
		P-value	0.212	0.789		0.502
	PTH	Pearson Correlation	0.270	0.376	0.073	
		P-value	0.029	0.006	0.502	

PTH**:** Parathyroid Hormone; BMI: Body mass index.

4- DISCUSSION

Vitamin D deficiency is a common problem in many countries (28-31). In Asian countries and countries with rich sunshine, this deficiency was emphasized (32-36). In line with the findings of this investigation and in accordance with the

findings of other researchers in our country (and the world) (37-39), can be deduced that in general, the level of vitamin D in children considerably lower than the accepted standard worldwide. Although, there is no consensus about normal range of vitamin D, but most researchers estimate 30 to70 ng / ml as a normal level of this vitamin (40). Our hypothesis was expected that the levels of vitamin D deficiency in patients, who suffer from IMSP, be more severe than in healthy group. The obtained results in this study showed contrary to our hypothesis. In a pilot study by Dresser et al., there was not a strong relationship between serum 25-hydroxycholecalciferol (25[OH] D), and pressure-pain thresholds (41).

Nasirinezhad et al. showed the existence of this relation between muscles aches and skeletal pain with vitamin D deficiency in adults (13). High prevalence of vitamin D deficiency in healthy teenagers was reported in outpatient clinic by other studies (42). The relationship between vitamin D and pain was already remarked, which shows itself as a pain exacerbation in chronic diseases; in this study patients who had higher levels of vitamin D, were taller (**Table.1**), than the healthy group. It may be due to that faster growth in stature and bone that may be a reason for stimulation of receptors on nerve and cause pain. High prevalence of vitamin D deficiency in healthy teenagers was reported in outpatient clinic by other studies (43). In this study, patients who had higher levels of vitamin D, were taller than the healthy group. It may be due to that faster growth in stature and bone that may be a reason for stimulation of receptors on nerve and cause pain.

Another aimed in this study was assessment of PTH levels. Generally it is believed that vitamin D deficiency increases level of PTH in the blood (16, 44-46). According to this fact, the level of PTH in our patient group must be lower compared the control group. In this study in healthy group with more vitamin D deficiency, PTH level was lower than the patient group, and there was a significant difference between the two groups ($P<0.05$). We do not have a specific explanation for this inconsistency in our study. It is possible that PTH and its effects on bone have been more active in group which suffers bone pain and seems that correlation among vitamin D deficiency and its stimulatory effect on the PTH secretion is different among child with bone pain in comparison with child without bone pain. Harkness et al. study showed that there was a stronger correlation between 25-hydroxyvitamin D concentrations and parathyroid hormone concentrations in non-black girls than in black girls (43). So, correlation between 25-hydroxyvitamin D concentrations and parathyroid hormone concentrations may be affected by race and ethnicity

4-1. Limitations of the study

Study limitations include the unmeasured all variables, such as nutrition and diet, alkaline phosphatase, food supplements and other factors, and also recommended that future studies be performed with large sample sizes.

5- CONCLUSION

The results of this study did not reveal a clear correlation between vitamin D deficiencies in children that suffer from nonspecific bone pain in comparison with healthy children. In this research the level of vitamin D in both groups (healthy and patient children) was considerably lower than the accepted standard reported worldwide. Also In our study in healthy group with more vitamin D deficiency, PTH level was lower than the patient group. It is suggested in addition to check vitamin D levels in children with IMSP, other probable causes and risk factors (such as sun light, nutritional status, etc.) should be considered.

6- CONFLICT OF INTEREST: None.

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