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Evaluation the Response to Treatment of Vitamin D Deficiency in Iranian Overweight/obese Children

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Abstract

Background
Recently the prevalence of obesity and its comorbidities has increased in children, in the worldwide. Some evidences show that there is a reverse relation between the serum level of 25-hydroxyvitamin D[25(OH)D] and Body mass index (BMI). The purpose of this study was scrutiny response to treatment vitamin D deficiency in obese/overweight children.

Materials and Methods
In a randomized clinical trial, cross sectional study 60 children aged 5 -15 year- old with BMI≥85% were entered. After obtaining of informed consent the calcium, phosphorous, alkaline phosphatase, 25(OH) D and parathyroid hormone (PTH) levels were measured after 8 hours of fasting. According to intensity of vitamin D deficiency, intra muscularly vitamin D3, 300,000 to 600,000 unit was prescribed. All parameters were rechecked after 1 month. Data were analyzed with SPSS- 20 software.

Results
Among total 60 subjects, 49 children (81.7%) were overweight and 11 children (18.3%) were obese. Also, all of subjects had vitamin D deficiency. After intervention only 35% got normal level of vitamin D. Mean level of vitamin D in girls were lower than boys. Average level of vitamin D rose significantly after intervention in both overweight and obese groups ($P<0.05$). The mean PTH level was reduced significantly after intervention in overweight children ($P<0.05$). Mean levels of calcium and phosphoruswere increased in two groups after intervention, but this is not significant ($P>0.05$).

Discussion
With considering high prevalence of vitamin D deficiency in overweight/obese children, low response to treatment and multiple after math complications, we suggest more attention to vitamin D deficiency and renewal and early intervention in these children.

Key Words: BMI, Children, Obesity, Treatment, Vitamin D deficiency.

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1-INTRODUCTION

Over the past decade, multiple studies indicate that the prevalence of vitamin D deficiency was more elevated in obese subjects(1). Obesity has proven to be a gate way to many disorders(2) and its prevalence has significantly increased in many countries in recent years (3-5). Obesity increases the risk of numerous co-morbidities including metabolic syndrome, cardiovascular disease and cancer as well as increases risk of mortality (6). Obesity is a chronic disease with multifactorial origin (7). In the recent years, vitamin D deficiency was frequently reported both in children and adults (8) and there might be an association between the high prevalence of the vitamin D deficiency and obesity (9).

The nutritional status of vitamin D is also associated with other health problems(10) and the vitamin D deficiency was considered as risk factor for many disorders such as obesity(11), diabetes(12-14), cardiovascular diseases(15, 16), metabolic syndrome(17), hyperlipidemia(18), fatty liver(19), cancer(20-22), multiple sclerosis(23, 24) and fracture(25, 26). There are evidences indicating a reverse relationship between 25-hydroxy serum level of vitamin D and Body mass index (BMI)(27); however, there are contradictory information about the prevalence of vitamin D deficiency in obese children. More than 85.3% of non-diabetic children in the Bener et al.'s study in Qatar(28), all children in the Al-Musharaf et al.'s study in Saudi Arabia(29) and 91% and 100% of obese boys and girls had vitamin D deficiency in Zee Harel's study(27) were vitamin D deficient. In the study conducted by Aypak in Turkey, 98.2% of children had the vitamin D deficiency while there was no significant association between vitamin D deficiency and BMI(30). Vitamin D deficiency is also high in Iranian teenagers; however, its association with BMI has not been so far evaluated (31).

Response to treatment with contradictory results, have been reported in obese children with vitamin D deficiency. In the study by Zee Harel, after the administration of vitamin D to obese children, the level of vitamin D did not reach to normal amount(27). In a study by Thomas Reinehr et al., through the administration of prescribing diet and exercise in obese children with the vitamin D deficiency after losing weight without giving vitamin D, the vitamin D deficiency was compensated, its level increased, the level of parathyroid hormone (PTH) was decreased and reached to normal amount(27). There is a dearth of research on children in this regard. This study aimed to evaluate the prevalence of vitamin D deficiency and response to treatment in overweight/obese children in North West of Iran.

2- MATERIALS AND METHODS

In a cross sectional clinical trial study (Trial Registration Number: IRCT201602071580N6) from October 2014 to September 2015, all children and adolescence aged between 5 and 15 years old who referring to pediatric Gastroenterology clinic of Maternal and Childhood Obesity Research Center of Shahid Motahari Hospital of Urmia University of Medical Sciences, Iran, due to high BMI (BMI percentile greater than 85%), were enrolled in the study.

Height and weight were measured and BMI and its percentile for age and gender was calculated and recorded. After obtaining a written consent from parents, a questionnaire including demographic characteristics including age, gender, and habitat in the past five years, ethnicity, birth order, birth weight, birth date and past medical history was filled out. Exclusion criteria were: any chronic diseases such as hepatic, renal,

gastrointestinal and metabolic disease, hypothyroidism, diabetes, and history of taking corticosteroid or vitamin D in the last 6 months. Calcium, phosphorous, alkaline phosphatase, 25(OH) D and parathyroid hormone levels were measured after 8 hours of fasting. Serum 25(OH) D3 was determined using a chemiluminescence immunoassay. Serum vitamin D3 levels of children was ranking to 4 dignity; sufficient (normal), insufficient, deficient and severe deficient and definedas 25(OH) D3 level was more than 30 ng/ml, 20-29.9 ng/ml, 10-19.9 ng/ml and <10 ng/ml, respectively (32).

300,000 IU and 600,000 IU of vitamin D were prescribed intramuscularly for vitamin D insufficiency and deficiency, respectively. One month after treatment all variables were measured for all children with the vitamin D deficiency again.

2-1. Data analysis

Data were processed and analyzed by using SPSS version 20 software. We used descriptive statistical methods for mean, frequency and percentage. Paired and independent t-test were applied to determine the relationship among quantitative data, as well as, Mc. Nemar test, chi-square test and log-linear were used to investigate the relationship among qualitative data.

3- RESULTS

A total of 60 children (34 girls and 26 boys) with BMI percentile more than 85% for age and gender were recruited in the research. Children divided into two overweight and obese groups. BMI percentile between 85% and 95% for age and gender was defined overweight and BMI percentile more than 95% was considered as obese. 49 children (81.7%) were overweight and 11 subjects (18.3) were obese. The mean age of overweight and obese groups were 9.63±2.90 (the age range of 5 to 15 years) and 8.64±2.01 (the age range of 5 to 10 years), respectively. The mean level of serum vitamin D was 14.39±6.05 ng/ml in overweight and 11.11±8.37 ng/ml in obese subjects.

Results shown, there was no statistically significant correlation between the serum levels of vitamin D and BMI (P =0.07). In this study, we assessed the serum levels of calcium, phosphorous, alkaline phosphatase (ALP), 25(OH) D and parathyroid hormone (PTH), before and after treatment in vitamin D deficient children. Serum vitamin D level of patients was ranking to 4 dignity; sufficient, insufficient, deficient and severe deficient and definedas 25(OH) D level was: more than 30 ng/ml; 20-29.9 ng/ml; 10-19.9 ng/ml and <10 ng/ml, respectively.

We prescribed 300,000 IU vitamin D3 to patients with vitamin D insufficiency and 600,000 IU to patients with vitamin D deficiency. Findings from patients were shown in (Table.1).

All of participates in the study have had lower level of vitamin D. The mean level of vitamin D was 15.3 ± 6.69 ng/ml in males and 12.6 ± 6.23 ng/ml in females, and there was no statically significant difference between level of vitamin D and gender (P=0.115).

Given to the number of patients in each groups frequency of insufficient serum vitamin D levels in overweight [3/11(27.3%)] and obese [10/49 (20.4%)] children was almost similar and the vitamin D deficiency in children with overweight [26/49 (53.06%)] was more than that in obese [4/11 (36%)] children. While the severe vitamin D deficiency was more common in obese [4/11 (36%)] children than overweight [13/49 (26.5%)] ones, but no relationship was found between serum levels of vitamin D with BMI and gender (P =0.22). As shown in the (Table.2), only 34% of overweight and 36% of obese children (entirely 35% of

patients) had normal level of vitamin D after the intervention while in 65% of children, there were some degrees of the vitamin D deficiency. The relationship between serum 25-hydroxy vitamin D after treatment and BMI was not statistically significant (P =0.48).

Results showed the mean parathyroid hormone was significantly reduced in patients after the intervention in the overweight group (P=0.01), while it had no statistically significant change in the obese group (P=0.319). As seen in the (Table.3) the mean value of calcium, phosphorous, and vitamin D were increased after intervention, but increasing was not statically significant among overweight and obese children (P>0.05).

The mean value of ALP and PTH were decreased after the intervention, while this decrease was not significant between two overweight and obese groups (P>0.05).

Table 1: Seroprevalence of basic vitamin D level in overweight and obese groups

Status of vitamin D	Overweight group n (%)		Obese group n (%)		Total
	girls	boys	girls	boys	
Normal	0	0	0	0	0
Insufficient	5 (8.33%)	5 (8.33%)	2 (3.33%)	1 (1.7%)	13 (21.7%)
Deficient	17 (28.33%)	9 (15%)	2 (3.33%)	2 (3.33%)	30 (50%)
Severe deficient	7 (11.7%)	6 (10%)	1 (1.7%)	3 (5%)	17 (28.33%)
Total	29 (48.33%)	20 (33.33%)	5 (8.33)	6 (10%)	60 (100%)

Table 2: Seroprevalence of vitamin D after treatment in overweight and obese groups

Status of vitamin D	Overweight group n (%)		Obese group n (%)		Total
	girls	boys	girls	boys	
Normal	10 (17%)	7 (11.7%)	2 (3.33%)	2(3.33%)	21 (35%)
Insufficient	11 (18.3%)	8(13.3%)	1 (1.7%)	2(3.33%)	22 (37%)
Deficient	8 (13.3%)	4 (6.7%)	2 (3.33%)	2 (3.33%)	16(26.7%)
Severe deficient	0	1 (1.7%)	0	0	1 (1.7%)
Total	29 (48.33%)	20 (33.33%)	5 (8.33)	6 (10%)	60 (100%)

Table 3: The comparison of mean Ca, P, ALP, PTH and 25(OH)D levels before and after treatment in overweight/obese children

BMI	Overweight group (mean ±SD)			Obese group (mean ±SD)		
Variables	Before	After	P- value	Before	After	P- value
Ca	9.69±0.37	9.83±0.32	0.35	9.57±0.46	9.79±0.44	0.75
P	5.43±0.88	5.45±0.73	0.46	5.20±1.04	5.22±0.89	0.12
ALP	432.86±152.27	358±192.20	0.39	411.06±130.80	350.10±167.21	0.2
Vitamin D	14.39±6.05	28.55±11.42	0.001	11.11±8.37	27.44±17.2	0.02
PTH	31.9±10.8	29.03±10.01	0.01	32.63±12.35	30.76±14.63	0.31

Ca: calcium; P: phosphorous; ALP:alkaline phosphatase; PTH: parathormon; 25(OH)D:25-hydroxyvitamin D

4-DISCUSSION

Recent evidences show that obese individuals have lower levels of 25-hydroxy vitamin D compared to normal people (1, 33). Obesity is a serious chronic disease that increases the risk of numerous co-morbidities including metabolic syndrome, cardiovascular disease and cancer as well as risk of mortality (6). The vitamin D deficiency also was considered as risk factor for many disorders such as obesity(11), diabetes(13), cardiovascular diseases(15), metabolic syndrome(17), hyperlipidemia(18), fatty liver(19), cancer(22), multiple sclerosis(24) and fracture (25). Conversely, weight excess interferes in the response to vitamin D supplementation, leading to a lower increase in 25(OH)D level(29, 34). Vitamin d storage in adipose tissue in obese individuals, thus increased vitamin D doses are needed for obese adolescents possibly (35, 36). We aimed to evaluate the response to treating the vitamin D deficiency in overweight/obese children. Our findings support researches with low response to traditional dose of vitamin D in overweight/obese subjects(36). In Musharaf et al. study that was done on 331 healthy urban children and adolescents in Saudi Arabia, results showed that vitamin D deficiency was noted in all subjects, and vitamin D deficiency was in girls were significantly lower than boys (29). In the cross-sectional descriptive analytical study by Ebrahimi et al on 1,047 junior high and high school students of both gender from urban and rural areas of Shahroud-Iran(2011), 100% of studied adolescents had the vitamin D deficiency and mean vitamin D levels were 14.7 $\pm$ 9.4 ng/mL(37). In our study, the average vitamin D in girls (12.6±6.25) was lower than boys (15.3±6.69), but it was not statistically significant. This finding is similar to multiple other findings such as Harel et al.(35), Al-Musharaf (29), Ebrahimi et al. (36). In the study by Harel et al. (2011) conducted on 68 obese adolescents, 100% of girls and 91% of boys had the vitamin D deficiency and after the treatment with vitamin D supplementation, 28% of individuals achieved the normal level of vitamin D and about 72% had still the vitamin D deficiency(35). In our study, after the therapeutic intervention, only 35% of children got normal amount of vitamin D and 65% had still the vitamin D deficiency despite receiving it.

In study of Aguirre et al. 18 obese adolescents (aged 12-18 years) and the same number of age, gender and season-matched non-obese adolescents received vitamin D3 (2,000 IU/day) orally for 12 weeks. The increment in 25(OH)D levels following vitamin D supplementation was significantly lower in the obese adolescents (mean change 5.8 vs. 9.8 ng/ml; P >0.05). The researchers concluded that higher doses of vitamin D are required to treat vitamin D deficiency in obese adolescents compared to their non-obese peers(38). Because of the need for stronger bonesto support body weight, obese people require higher vitamin D, while the bio availability of this vitamin is lower in them and does not meet their needs. On the other hand, those who have low level of serum vitamin D, often suffer from secondary hyperparathyroidism and high elevated levels of PTH. This hormone inhibits lipolysis through boosting the risk of insulin resistance and causes an accumulation of fat in the body as a result, obesity (27).

In our study, the amount of PTH before the intervention was high in both groups; the mean parathyroid hormone after intervention reduced significantly in overweight group (P=0.01), while there was no significant change in the obese group (P=0.319). In a study by Thomas Reiner et al. (2007) in Germany, obese children significantly had low vitamin D and higher PTH in comparison with

normal children (27, 39). The main sources of vitamin D in human are sunlight to skin, lesser extent of diet and using dairy products containing vitamin D; although, the vitamin D deficiency is not theoretically expected in areas with high sun lights.The high incidence of vitamin D deficiency has also been reported in countries with high sunlight (40-46).

The status of vitamin D is somewhat diverse among different communities, because of the kind of geographic location of race and skin pigmentation (31). In current study, the average vitamin D level was lower in urban children than rural children while it was no statistically significant. Also, the average of vitamin D was lower in Turkish race than that in Kord race, while it was no statistically significant. In general, the vitamin D deficiency has become a worldwide unknown epidemic (47) and Iran is also among countries with high prevalence of vitamin D deficiency (37, 48). West Azerbaijan of Iran has high prevalence of the vitamin D deficiencydue to the high altitude geographical location. The current study indicated that the vitamin D deficiency is a major problem in obese children. That is why intervention strategies are required to improve the status of vitamin D and reduce obesity among children and adolescents in order to prevent chronic diseases over future years of their lives.

Low sample size and no randomization of this study are its limitations. We suggest that a clinical trial with randomization and large sample size could be done for determination of exact prevalence of vitamin D deficiency among overweight/obese children and their need to vitamin D for full recovery. It seems to be need to high dose of vitamin D per kilogram or body surface of overweight/obese children than normal weight ones.

5-CONCLUSION

Finding of this study revealed that vitamin D deficiency is prevalentin overweight/obese childrenand adolescence of North West of Iran. On the other hand, low responsible to traditional dose of vitamin D require renewal of the vitamin D management in these subjects. Thus for estimating a sufficient adjusted dose of vitamin D for obese people with vitamin D deficiency, a large multi-centric randomized controlled clinical trial should be done.

6-CONFLICT OF INTEREST: None.

7-ACKNOWLEDGMENTS

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