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Original Article (Pages: 987-994)

Effect of Vitamin D supplementation on Lipid Profile in Children Aged 10-14 Years Old

Kokab Namakin [1], *Fatemeh Tavakoli [1], Mahmoud Zardast [2]

[1]Department of Pediatric, Faculty of Medicince, Birjand University of Medical Sciences, Birjand, Iran.
[2]Department of Pathology, Faculty of Medicince, Birjand University of Medical Sciences, Birjand, Iran.

Abstract

Introduction

Considering the high prevalence of vitamin D deficiency in our country and the importance of blood lipid profile as a protective factor, aim of this study was to investigate the effect of vitamin D supplementation on lipid profile in children 10 to 14 years.

Materials and Methods

In this controlled clinical trial study, 40 children who were studying on 2014 in Birjand elementary schools were selected and randomly divided into two groups containing 20 participants. Children in both group examined for level of lipid profile and serum vitamin D after and before consumption of drugs (vitamin D supplement and placebo). Questionnaire was used in order to record demographic information. Data was analyzed using SPSS-16 statistical software and statistical tests of Chi-square, Fisher exact test, t-paired, independent-t, and Pearson correlation at significance level of $P< 0.05$.

Results

The results showed that in children of intervention group the average of High-density lipoprotein (HDL) serum level and vitamin D was significantly higher after intervention before it ($P<0.05$); the average of Low-density lipoprotein (LDL) serum level was significantly increased ($P<0.05$), but there was no significant difference in LDL/HDL ratio, cholesterol and Triglyceride before and after intervention. In control group there was no significant difference between the average of vitamin D and blood lipid profile before and after intervention.

Conclusion

According to the results of this study there is a significant increase in HDL and LDL after using vitamin D supplement, and suggested more studies with larger sample sizes to be done in this area.

Key Words: Children, Lipid profile, Vitamin D.

Corresponding Author:

Fatemeh Tavakoli, MD, Department of Pediatric, Facultyof Medicince, Birjand University of Medical Sciences, Birjand, Iran .

Email: tavakolihzb3@yahoo.com

Received date: Aug 5, 2015 Accepted date: Aug 22, 2015

Introduction

Currently cardiovascular diseases are the most common causes of mortality in most regions of the world and Iran, and include 40% of all deaths (1). Twenty-five percent of people with this disease died without previous symptoms as sudden death or acute myocardial infarction (2).

In 1998, about 30.9 percent of death caused by cardiovascular disease and expected in 2020 will occur 12 million deaths of cardiovascular disease (3). Researches show that the rate of cardiovascular disease in recent years is between 20 and 45 percent (4).

Atherosclerosis or hardening of the arteries is one of the cardiovascular diseases, that causes thickening and hardening of the walls of arteries and reduces their elasticity which contributes to plaque build-up in one or more coronary arteries and restricts blood flow (5). Pathological changes of atherosclerosis begin in childhood and present in several stages in the old age. In fact we can say that changes in progresses of atherosclerosis increasing with age and eventually lead to disability and death in the elderly (6). Factors such as hypertension and hyperlipidemia, as well as blood sugar disorders can increase the risk of atherosclerosis in several times (7-8). Scherr and Magalh^{a}es in their study in 2007 concluded that lipid disorders, cholesterol, triglycerides, LDL and low HDL are the most important risk factor for coronary artery disease such as atherosclerosis (9). The results of different studies showed that low level of HDL was associated with higher risk of cardiovascular disease (9-10).

In addition there is an increasing evidence to suggest that vitamin D deficiency may be an important factor in the development of cardiovascular disease (11). Vitamin D is a fat-soluble vitamin with hormonal activity in homeostasis of calcium, phosphorus and bone metabolism and has an important role in regulation of immune system, proliferation and cell survival (12).

Vitamin D receptor is present in many organs such as bone, heart, kidneys, nervous system, skin, teeth and thyroid gland. Therefore deficiency Leave very bad effects on all parts of the body. So that vitamin D deficiency has correlation with risk of diabetes, metabolic syndrome, insulin resistance, hypertension, hyperlipidemia and cardiovascular disease (13). New researches and clinical epidemiology studies confirm that the lack of vitamin D is associated with hypertension (14), hyperlipidemia and cardiovascular diseases (15). The results of some studies suggest that there is a correlation between blood levels of vitamin D with lower levels of HDL cholesterol (HDL-C), triglycerides and apolipoprotein in blood (16-17). In this regard, John and Associates study results show that there is a significant relationship between total cholesterol, LDL and apolipoprotein A and B with vitamin D (18). According the high prevalence of vitamin D deficiency in our country (19) and the importance of blood lipid profiles as a protective factor, the aim of this study was to investigate the effect of vitamin D supplementation on serum levels of vitamin D and blood lipid profile in children aged 10 and 14 years old in Birjand primary school.

Materials and Methods

This study was a clinical trial study which conducted in 2014 on children (10-14 years old). Confirmation invitations by education experts on how to explain the work was distributed in selected schools. 40 children were selected by cluster random sampling method and randomly divided in two groups (case and control). This means after receiving permission from the Medical Ethics and Clinical Trials Registry System

(1N2014050717608) and after explaining the aims of the study and obtaining informed consent from patients eligible children were studied and referred to the laboratory. 20 girls and 20 boys who had the inclusion criteria were willing to participate in this study were evaluated.

Inclusion criteria were: lack of disease symptoms, such as chronic pain, fatigue and failure to thrive, without the use of vitamin D supplementation and lipid-lowering drugs and Antiepileptic drugs, no diabetes, no genetic disorders and congenital absence of cardiovascular disease, cancer, hypothyroidism or hyperthyroidism, known history of thyroid or kidney disease and hepatic history.

Based on the results of the study of Hirschler et al. (20) sample size (based on the formula) (mean ± SD blood HDL cholesterol levels before and after the intervention of Vitamin D, $n = \frac{(u+v)^2(S_1^2+S_2^2)}{(m_1-m_2)^2}$, the α error= 0.05 and test power of 90%) were estimated 20 patients in each group. We were collected demographic and medical history and medication through a questionnaire that confirmed validity by 5 professionals.

Questionnaires included demographic characteristics, weight, history of drugs and congenital cardiovascular disease, cancer, hypothyroidism or hyperthyroidism, known history of thyroid, kidney and liver disease and other diseases. Again children randomly divided in 2 groups and in both groups evaluated tests (serum lipid profile levels and vitamin D).

Blood sampling performed after 12 to 14 hours fasting, from radial vein by using a 10 cc syringe and collected in 5 ml vial, and poured by BD activator gel and cot activator. The samples were centrifuged and serum samples were isolated immediately (divided in two micro-tubes that the volume is 1.5 cm2 ependorf (tube). One micro-tube frized in -20 tempreture and defrost after collecting all samples and measured vitamin D. The second micro-tubes were used to measure the level of blood lipid profiles. Then, given 30 tablets of 1,000 IU of vitamin D for case group for daily use for a month and given 30 tablets of placebo for control group for daily use for a period of one month (In cases empty capsules, Was filled with 1,000 IU of vitamin D tablets from the Galinus company. Empty capsules wa given for consumption for the control group.)

Package that given to both group, contain 30 capsules in the same plastic package provided by partner assessment project (the investigator). Evaluator and two groups did not know the drug information they were used. After a month, the children were examined in the same laboratory using the same test kits and the process was repeated with the conditions listed above. To assess serum HDL-LDL-CHOLESTROL and TRIGLYCERID use enzyme method by biochemical device and for 25-hydroxy vitamin D use automatic device, Close company Roche E411 Series kits made in Germany in 2013 and Electro-Chemi-Luminsence (ECL) was used from the same company.

The data were analyzed by SPSS version 16. Data have a normal distribution as well as the Kolmogorov-Smirnov. Given a normal distribution from t-test and paired t-test and Pearson's correlation coefficient was used $P<0.05$ was considered as significant level.

Results

From 40 children studied, 20 children were in experimental group (case group) and 20 children were in control group. 13 children (65%) in the experimental group and 7 child (35%) from control group were female (p=0.06). The average age of

children in the experimental group and control group was 11.55 ±1.36 and 11.45 ± 0.99 year-old respectively (Table. 1).

The results showed there was no significant correlation between the average of vitamin D and HDL, LDL, ratio of LDL to HDL and cholesterol in case and control group (P>0.05), but average level of triglyceride in experimental group was significantly higher than the control group, in before and after intervention (P <0.05). (Table.2). Paired t- test results showed that, children in the cases group significantly increased mean HDL and vitamin D levels after the intervention than before (P=0.007). Also mean LDL was significantly higher after study (P=0.003).

Results showed the average ratio of LDL to HDL, cholesterol and triglycerides in case group was not significantly different before and after the intervention (Table. 2). Also independent t- test results showed that in case group, the mean change in scores HDL, LDL, cholesterol was significantly higher than the control group (P<0.05), but were not significantly different in the mean change of ratio of LDL to HDL cholesterol and triglycerides in both groups (P=0.58) (Table 2).

Results of Pearson correlation showed that there was no significant relationship in mean change of vitamin D with mean changes of lipid profiles in children, in cases and control group (P>0.05).

Table 1: Demographic characteristics of children in the case and control group

Variable		Case	Control	P-value
		Number(percent)	Number(percent)	
Gender	male	7 (35)	13 (65)	0.06
	female	13 (65)	7 (35)	
Age	10-11 years	9 (45)	8 (40)	0.15
	12 year	5 (25)	10 (50)	
	13-14 years	6 (30)	2 (10)	

Table 2: Comparison of changes in serum levels of vitamin D and lipid profiles (HDL, LDL, LDL/ HDL ratio, cholesterol, triglyceride) in both groups before and after intervention

Variabel	Group	Before intervention	After intervention	P-value	Mean change score before and after intervention
		mean± standard deviation	mean± standard deviation		mean± standard deviation
Vitamin D	case	7.55±4.96	11.50±5.84	0.001	3.95±2.15
	control	9.71±5.48	9.26±4.97	0.27	-0.45±1.74
P-value (Related to comparing two groups)		0.20	0.20	-	<0.001
HDL	case	45.55±12.28	49.65±11.53	0.007	4.10±6.10
	control	45.30±10.38	43.65±11.47	0.27	-1.65±6.44
p-value (Related to comparing two groups)		0.95	0.11	-	0.006
LDL	case	78.70±16.26	88.25±18.23	0.003	9.55±12.54
	control	81.55±15.27	83.40±14.16	0.37	1.85±8.95
P-value (Related to comparing two groups)		0.57	0.35	-	0.03
Ratio LDL /HDL	case	1.85±0.60	1.89±0.67	0.46	0.05±0.29
	control	1.92±0.64	2.04±0.62	0.14	0.11±0.33
P-value (Related to comparing two groups)		0.70	0.49	-	0.52
Cholostrol	case	144.80±22.09	152.25±23.82	0.06	7.45±16.58
	control	152.75±15.94	150.35±19.77	0.38	-2.40±12.03

P-value (Related to comparing two groups)		0.20	0.79	-	0.04
triglyceride	case	71.50±28.02	68.30±22.01	0.53	-3.20±22.42
	control	90.30±30.40	92.10±40.45	0.81	1.80±33.37
P-value (Related to comparing two groups)		0.05	0.03	-	0.58

Discussion

The results showed significantly increased in mean serum levels of HDL in experimental group after intervention compared with before intervention. In experimental group significantly increased average serum levels of LDL after treatment, but the mean ratio of LDL to HDL, cholesterol and triglycerides were not significantly different before and after the intervention.

In a study by Maki et al. (21) were found direct relationship between HDL cholesterol and vitamin D supplements. In this regard, the study results done by Smotkin-Tangorra et al. (22) showed that obese children and adolescents with vitamin D deficiency had lower levels of HDL cholesterol. Maki et al. (23) concluded that vitamin D supplement significantly increased the mean serum levels of HDL and significantly reduced in the TC / HDL; the results of this study are consistent to increase serum levels of HDL in the results of this study and are controversial to cholesterol.

A study by kashi and colleagues (24) on two groups of people with low vitamin D levels (less than or equal 20 ng/ml) and normal vitamin D levels (above 20 ng/ml) in more than 40 years old show that there is no significant difference on average of cholesterol, triglycerides and LDL in two group. As the mentioned above, results matched with results of this study on the effect of vitamin D supplementation on serum levels of HDL. In support of our Theory, liver cells have shown that vitamin D metabolites potentially have inhibitory effect on the production of Apolipoprotein AI (Apo A-I) deficiency (25). In animal studies also found that the HDL and Apo A-I mRNA of liver secretion in rats that received vitamin D was significantly higher than the control mice (26).

The results showed that the mean serum levels of vitamin D significantly increased in children of the case group after than before, but there was no significant difference in the control group before and after the treatment. Several studies showed daily intake of vitamin D, increase the mean serum 25-hydroxy vitamin D (27-28). In this context, Maki and Associates study results showed that concentrations of vitamin D in groups receiving vitamin D supplementation was significantly higher than those in the control group (21).

Exposure to sunlight has a decisive role in serum 25(OH) vitamin D. Vitamin D is fat soluble and separated from fat tissue. Therefore the large storage capacity for vitamin D in obese and overweight persons may reduce the serum vitamin D (21). Level of vitamin D was significantly higher among those who received statins. Statins prevent HMG-COA r reductase activities (29). This enzymes involved in the synthesis of cholesterol and lead to the synthesis of 7-Dehydrocholesterol (7-DHC). 7-DHC can be converted to cholesterol (at the same time through 7-DHC reductase to precursor of vitamin D through exposure to sunlight) (30).

Based on the results of this study, there was no significant association between the mean changes of vitamin D, with the mean changes of blood lipid profiles in case and control groups. The results of Carbone et

al. (31) on healthy adolescents showed a significant inverse relationship between 25- (OH) vitamin D and the LDL and HDL cholesterol (31). In the same study, Rodríguez-Rodríguez et al. (32) showed a significant negative relationship between vitamin D levels and triglycerides. In study by Nwosu and colleagues (33) on 45 children to demonstrate the relationship between vitamin D as early markers of cardiovascular disease, results showed that vitamin D levels are inversely associated with HDL level. The results of these studies inconsistent with our results.

In a study by Jorde and colleagues (34) found different results with our study. During this study, the 8018 case of non-smokers were studied, and significant relationship between 25- (OH) vitamin D, Total cholesterol (TC), HDL and LDL were observed, but after adjustment for age, sex, month sampling and Body mass index (BMI) they were observed significant reverse correlation between 25-(OH) vitamin D levels and HDL and LDL (34). Among the reasons for the difference in results may be due to this fact that in our study, we examined children with normal body mass index. Also, the main limitation of this study was the small sample size.

Conclusion

This research could be the source of importance of dietary supplements, with the low cost to achieve the desired result. Vitamin D supplementation can be prescribe longer period of time without fearing of reaching toxic level. Base on the results of this study, administration of vitamin D not only increases blood levels of vitamin D, but also can increases blood levels of HDL and may be effective in reducing the risk of cardiovascular disease.

Conflict of Interest: None.

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