ORIGINAL ARTICLE

EFFECT OF VITAMIN D SUPPLEMENTATION ON LIPID PROFILE IN PATIENTS OF ACUTE CORONARY SYNDROME

Sidra Jabeen, Humaira Fayyaz Khan*, Sana Majeed*, Mehvish Ashfaq, Hina Munir, Saira Safder*****

Department of Physiology, Rawalpindi Medical University, *Riphah International University Al-Maizan Campus, Rawalpindi, **AJK Medical College, Muzaffarabad, ***Islamabad Medical and Dental College, Islamabad, Pakistan

Background: Association studies have proposed a link between vitamin D levels and lipid profile. Deranged lipid profile is hallmark of acute coronary syndrome (ACS) patients. The present study was aimed to determine the role of vitamin D supplementation in improving the lipid profile of ACS patients. **Methods:** A total of 40 patients diagnosed with ACS were included in the study. They were divided into control (n=20) and experimental group (n=20). Experimental group received vitamin D supplementation as a single dose of 200,000 IU orally. Baseline vitamin D levels and lipid profile were done. Post sampling was done after an interval of 2 months for the same parameters. **Results:** The serum levels of cholesterol were decreased significantly in the experimental group (p=0.05) while TG levels showed trend towards a decrease (p=0.084). Serum HDL was increased (p=0.03), while serum LDL (p=0.04) and cholesterol ratio (p=0.012) were decreased significantly. **Conclusion:** Vitamin D supplementation improved lipid profile in ACS patients, and can be used as adjunct therapy in ACS patients.

Keywords: Vitamin D, Cholesterol, TG, HDL, LDL, Cholesterol ratio, Acute Coronary Syndrome

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INTRODUCTION

Coronary artery disease (CAD) is one of the leading cause of morbidity and mortality in the world. According to World Health Organization, CAD causes 17.1 million deaths per year worldwide.[1] The most significant expression of CAD is Acute Coronary Syndrome (ACS). The underlying pathophysiological mechanism for acute coronary syndrome is coronary atherosclerosis.[2] Atherosclerosis is considered as a chronic inflammatory vascular disease which causes hardening of the arteries as a result of plaque formation.[3] It can subsequently lead to erosion, fissure or rupture of the plaque leading to thrombosis. The conventional risk factors for coronary atherosclerosis include hypertension, cigarette smoking, hypercholesterolemia, diabetes, obesity and genetic predisposition.[4] Research has proved atherosclerosis as an inflammatory vascular disease that is initiated after accumulation of lipids within the arterial walls. Hypercholesterolemia and other risk factors for atherosclerosis induce changes in the endothelium that leads to increased endothelial wall permeability and allows accumulation and aggregation of LDL-cholesterol within the arterial wall.[5] Besides the more common and traditional risk factors for development of acute coronary syndrome, studies are conducted to discover new risk factors towards which future therapeutic targets can be directed. Among these, vitamin D deficiency is a new emerging risk factor for development of acute coronary syndrome. Vitamin D deficiency has been demonstrated in patients suffering from acute myocardial infarction.[6] Observational studies have proposed a link between dyslipidemia and vitamin D deficiency.[7] A study by Kim MR *et al* showed that low vitamin D levels can progress to dyslipidemia and obesity.[8] A study by Ying Wang *et al* showed that serum concentrations of vitamin D are associated with serum lipids and atherogenic index of plasma (AIP).[9]

The pathogenesis of acute coronary syndrome involves the process of atherosclerosis which accelerates because of deranged lipid levels in serum. The studies linking the vitamin D deficient state with deranged lipid profile have revealed controversial results. Vitamin D deficiency has been proved by various researches to affect lipid profile. Correction of vitamin D levels among ACS patients may reduce the incidence of future adverse cardiovascular events. Data on supplementation impact on these parameters does not provide conclusive results. The incidence of ACS is rising despite vast srudies and therapeutic advancement. The present study is aimed towards highlighting the impact of vitamin D supplementation on serum lipid profile parameters in ACS patients.

MATERIAL AND METHODS

This non-randomized experimental study was conducted in the Department of Physiology and Multidisciplinary Laboratory, Islamic International Medical College, Rawalpindi in collaboration with Armed Forces Institute of Cardiology (AFIC). The study was approved by the Ethical Review Committee of Islamic International Medical College, Riphah International University, Islamabad along with approval from the Ethical Review Board of AFIC.

All patients were recruited from AFIC. They were approached from PCI units, wards, and CCU of the respective hospital. Informed written consent was obtained from patients who were willing to participate in the study. Complete history was recorded including complete personal profile along with present history of presenting complaints, history of the percutaneous coronary intervention procedure, past history, family history, assessments of risk factors for myocardial infarction and vitamin D deficiency. General physical examination was done including blood pressure, pulse rate, temperature and respiratory rate.

A total of 50 patients were interviewed for the study out of which 40 consented for the study. All these patients were diagnosed with ACS and had undergone percutaneous coronary intervention procedure. All patients below 70 years of age, not on any vitamin supplementation for the last 6 months and not having any renal impairment were included in the study. These patients were divided into control group (n=20) and experimental group (n=20).

Overnight fasting blood samples were taken from cubital fossa, and 4 ml blood was withdrawn using aseptic techniques. Samples were collected in serum vials with proper numbering and precautions keeping it upright and storage under cool temperature. Samples were centrifuged at 1,500 rpm for 5 minutes. The supernatant serum was collected through micropipettes in ependorf tubes with proper numbering on caps and were kept at -80 °C till analysis.

The experimental group (n=20) received vitamin D as single oral dose of 200,000 IU. Nothing was administered to the control group. The patients were reassessed on their follow up visits. After 4 months blood sampling was performed for same parameters. Pre and post sampling was done for serum lipid profile including total cholesterol, TG, HDL, LDL and TC/HDL ratio. The parameters including total cholesterol, TG, HDL were analysed in the laboratory using Microlab 300 analyser (ELITech Group). The concentration of LDL was determined by using a formula:

LDL= Total cholesterol-HDL-TG/5

The cholesterol ratio was calculated by dividing total cholesterol and HDL levels of the patients.

Cholesterol ratio= Total cholesterol/ HDL[10]

Statistical analysis of the data was done on SPSS-21. Results of data were expressed as Mean±SD and percentages. Independent sample *t*-test was used to compare effect of vitamin D intervention between control group and intervention group, and $p \leq 0.05$ was considered statistically significant.

RESULTS

The baseline characteristics are presented in Table-1 which shows no significant differences between the two groups.

Table-1: Baseline characteristics of study participants

Variable	Control group (n=20)	Experimental group (n=20)	*p*
Age (Yrs) (Mean±SD)	53.70±11.50	54.10±8.03	0.799
Weight (Kg) (Mean±SD)	79.90±15.57	85.50±14.32	0.345
Smoking status			
Smoker	8 (40%)	12 (60%)	0.224
Non-smoker	12 (60%)	8 (40%)	
Diabetes			
Diabetic	7 (35%)	7 (35%)	1.000
Non-diabetic	13 (65%)	13 (65%)	
Hypertension			
Hypertensive	9 (45%)	11 (55%)	0.602
Normotensive	11 (55%)	9 (45%)	
Family history			
Positive	14 (70%)	13 (65%)	1.000
Negative	6 (30%)	7 (35%)	

In the control group the serum vitamin D levels were decreased significantly from 16.10±5.90 ng/dl to 10.20±3.99 ng/dl. In the experimental group, the serum vitamin D levels were increased significantly from 18.27±8.98 ng/dl to 30.74±18.40 ng/dl. The total cholesterol levels were increased in the post group from 163.65±52.9 mg/dl to 177.88±48.6 mg/dl. The experimental group showed a trend towards decrease from mean value of 214.95±60.61 mg/dl to a value of 174.05±44.75 mg/dl. The independent *t*-test comparing the effect of intervention among the post values of both the groups showed $p=0.05$ which was statistically significant. The mean serum TG levels in the control group was increased from 152.9±74.76 mg/dl to 157.75±67.07 mg/dl. The mean value in the experimental group showed a trend towards decease from mean value of 124.6±55.73 mg/dl to mean value of 94.6±54.34 mg/dl. The independent *t*-test comparing the post values of both groups showed insignificant results ($p=0.084$). The mean values of HDL changed from 37.95±20.6 mg/dl in the control group to the mean of 40.95±26.3 mg/dl. In the experimental group the mean value was increased to 66.6±21.25 mg/dl from mean value of 49.45±16.73 mg/dl. The independent *t*-test showed significant results ($p=0.03$). The mean of pre-control group for LDL came out to be 125.12±61.83 mg/dl which was increased to 135.42±55.54 mg/dl in the post-control group. The mean value of the pre-vitamin D group showed a trend towards decrease from 144.5±55.71 mg/dl to mean value of 88.53±45.43 mg/dl in the post-vitamin D group. The impact of intervention was compared by independent *t*-test. The two groups showed significant differences ($p=0.04$).

The calculated ratio was 6.06±5.21 in the control group initially which was high. On the other hand, the experimental group showed a pre-mean of

5.5±5.13 which was also high. In the control group the ratio increased to a mean value of 7.02±3.2 while the experimental group showed a significant decrease (p=0.012) with a mean value of 2.91±2.1. (Table-2).

Table-2: Serum levels of Vitamin D, Total Cholesterol, TG, HDL, LDL and Cholesterol ratio among control and experimental groups

Parameters	Control group		Experimental group		*p*
	Pre-levels	Post-levels	Pre-levels	Post levels	
Vitamin D (ng/ml)	16.10±5.9	10.20±3.99	18.27±8.98	30.74±18.40	0.000
Total Cholesterol (mg/dl)	163.65±52.9	177.88±48.6	214.95±60.61	174.05±44.75	0.05
TG (mg/dl)	152.9±74.76	157.75±67.07	124.6±55.73	94.6±54.34	0.084
HDL (mg/dl)	37.95±20.6	40.95±26.3	46.45±16.73	66.6±21.25	0.03
LDL (mg/dl)	95.12±61.83	135.42±55.54	141.5±50.71	88.53±45.43	0.04
Total Cholesterol/HDL ratio	6.06±5.21	7.02±3.2	5.51±5.13	2.91±2.1	0.012

TG= triglycerides, HDL= high density lipoproteins, LDL= low density lipoproteins

DISCUSSION

The present study has shown improvement in serum lipid profile after supplementation with vitamin D, with the exception of TG. Serum total cholesterol was decreased significantly in the experimental group. This finding is in accordance with a study in which type 2 diabetic patients were treated with a weekly dose of 16,000 IU vitamin D for 8 weeks and this correction significantly decreased total cholesterol levels and also produced a statistically non-significant reduction in LDL and TG.[11] Our results are in contradiction to some other studies which have reported that correction for deficiency of vitamin D levels may not be able to translate into meaningful alterations in the lipid profiles.[12] The possible explanation for these null results may be that vitamin D levels more than 28–32 ng/ml are needed for extra-skeletal benefit of supplementation.[13]

The randomized control trials presenting impact of vitamin D intervention on serum lipid profile have revealed controversial results.[14,15] These studies are divergent in terms of dose of supplementation used, duration of study, disease state of the body, and increment of vitamin D levels after supplementation. Vitamin D may have direct effects on lipid metabolism or it may affect the lipid profile indirectly. Direct effects according to some studies, involve maintaining adequate levels of apolipoprotein A-I which is an important component of HDL cholesterol.[16] HDL cholesterol has also been positively correlated with vitamin D levels. The indirect effects of vitamin D on lipid metabolism can be attributed to its effects on calcium and phosphate metabolism. Vitamin D can enhance insulin sensitivity and its release affecting lipid metabolism through hormonal regulation.[16]

Vitamin D has been involved in reducing expression of adipocyte uncoupling protein-2 and regulates lipid metabolism by inhibiting lipogenesis and inducing lipolysis. The reduction of proliferation of T-helper cells also reduces generation of important cytokines involved in regulation of fat metabolism.[11]

The present study showed insignificant reductions in levels of TG in experimental group. In some of the previous studies vitamin D supplementation had proved beneficial effects on serum lipid profile parameters including total cholesterol and TG.[14] Vitamin D was able to reduce the serum levels in patients with hypercholesterolemia. The insignificant results of serum triglycerides are similar to study conducted by Ponda MP *et al*[12] which was highly attractive cost-effective approach. These results showed an unfavourable lipid profile with vitamin D deficient state. On improving vitamin D levels non-significant changes in the LDL and TG levels have been reported.[17]

Serum HDL in the present study showed significantly increased level in Experimental Group (p=0.03). The intervention of vitamin D was able to raise sufficiently the HDL levels to 66.6 mg/dl. Previous studies have demonstrated a positive association between serum vitamin D levels and HDL in which improved vitamin D levels were linked with sufficient HDL level.[18] HDL-C was also found to be significantly high in vitamin D sufficient group while reduced in vitamin D deficient group in a study performed by Alkhatatbeh *et al*[19]. On the other hand some studies also have revealed controversial results. A randomized control trial by Ponda MP *et al*[20] showed that short term repletion of vitamin D may not be able to improve serum lipid levels including HDL levels.

Serum LDL levels in our study were reduced significantly. In a study performed on children suffering from non-alcoholic fatty liver (NAFL), the association of vitamin D deficiency with LDL was found to be negative and significant.[21] These results are contrary to the results of previous trials which proved an increase in the LDL level on supplementation with vitamin D.[14,22] Association of vitamin D levels with the serum lipid profile discussed in the observational studies do not show a causal relationship. A study by Kane L *et al*[23] has explained that the vitamin D if given along with atorvastatin, a lipid lowering drug, in vitamin D insufficient subjects, can lead to significant reductions of total cholesterol and LDL levels. This might be the case in the present study that patients were on statin drugs, and vitamin D might have augmented the lipid lowering effect.

Serum lipids can be influenced by various factors like diet, and exercise etc. The randomized control trials have revealed controversial results.[14,15] All these were heterogeneous in terms of vitamin D dose

used, duration of treatment, baseline vitamin D and lipid profile, and characteristics of study population. Many studies were not able to indicate baseline vitamin D levels and percentage increment of vitamin D with supplementation. The form of vitamin D used whether D_2 or D_3 is also important. Vitamin D_2 biologically has reduced activity as compared to the more active form, vitamin D_3. These factors can influence the results.

The present study showed significant results in improving the cholesterol ratio. The cholesterol ratio was decreased significantly from 7.02±5.99 to 2.91±1.33. According to American Heart Association the ideal ratio is 3.5, while the cardiovascular risk increases with increase in ratio of >5. TC/HDL ratio seems to be a strong indicator and powerful predictor of acute coronary events.[10] Vitamin D may be involved by multiple mechanisms improving lipid profile. It may serve as lipid lowering agent in patients of ACS specially who are on statin drugs. Its use as an adjunctive therapy may be considered in future research.

CONCLUSION

Vitamin D supplementation showed promising results in improving the lipid profile parameters resulting in significant reductions in total cholesterol, low density lipoproteins and cholesterol ratio while significant rise in high density lipoproteins levels when given along with statin drugs. Triglyceride levels were non-significantly reduced. Giving vitamin D as an adjunct therapy in the form of single high dose can help improve these parameters in patients of ACS.

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Address for Correspondence:

Dr. Sidra Jabeen, Department of Physiology, Rawalpindi Medical University, Rawalpindi, Pakistan. **Cell:** +92-332-5255719

Email: drsidraasad2011@gmail.com

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SJ: Conception and design of project, analysis and interpretation
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