ANALYSIS OF VITAMIN-D INTAKE ON LIPID PROFILE IN PATIENTS WITH TYPE-II DIABETES MELLITUS TAKING METFORMIN.

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ABSTRACT

Introduction: vitamin D deficiency if a global issue. **Objective:** To analyze role of vitamin-D (Vit.D) supplementation on the lipid profile of individuals having type-II diabetes mellitus, taking metformin. **Methods:** This observational and interventional study was conducted inthe Pharmacology department in cooperation with Sindh Institute of Endocrinology & Diabetes (SIED) affiliated with Liaquat University of Medical and Health Sciences, Jamshoro from 1st March to 31st August 2018.One hundred and forty diagnosed cases of diabetes type-2 were selected under strict inclusion criteria. These were alienated into 2 groups of seventy each (A & B). Group-A acted as control while group B was given Vit D supplement 800 IU per day daily for three months. Vit.D level & lipid profile were estimated at base line and after 3 months. **Results:** After 3 months of Vit. D supplementation in group B, lipid profile parameters including total cholesterol, high density lipoproteins (HDL), low density lipoproteins (LDL), and triglycerides (TG) revealed a significant decrease as compared to group A. No any major variation in HDL levels of group-B as compared to group-A was noticed. Level of Vit.D revealed a significant increase after 3 months in group-B in relation to group-A. **Conclusion:** Vitamin-D levels in blood are increased by vitamin-D supplementation. Blood Vit.Dconcentrationis enhanced by increased intake of VitD, with improvement in levels of serum total cholesterol (TC), TG and LDL with no beneficial effect on serum HDL.

Key words: Vitamin-D, Type-2 Diabetes mellitus, Lipid Profile, Metformin

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How to cite this article: Kumar G[1], Sheikh SA[2], Shahani MY[3], Ashraf S[4], Laghari MJ[5], Memon S[6]. **ANALYSIS OF VITAMIN-D INTAKE ON LIPID PROFILE IN PATIENTS WITH TYPE-II DIABETES MELLITUS TAKING METFORMIN. JPUMHS;2020;10(03)49-53.**
http://doi.org/10.46536/jpumhs/2020/10.02.225

Introduction

Diabetes mellitus is a syndrome described as increased than normal blood glucose level, decreased or absolute insulin secretion and/or decreased insulin sensitivity[1]. It is usually accompanied by impaired carbohydrates, protein and lipid metabolism[2].It has been that Worldwide diabetes mellitus affects nearly 400 million people[3].Diabetes mellitus type-II(DMT2), the most common type in adults, is mostly prevalent in developing countries. In Pakistan, approximately 5.2 million are affected with DMT2, placing it at number six among list of countries affected by this metabolic syndrome[4].

It has been reported through various research studies conducted across the globe that DMT2 not only affects carbohydrate metabolism, but decreased utilization of glucose due to deficiency or lack of insulin,also affects metabolism of proteins and lipids reflected by deranged lipid profile as increased serum cholesterol, triglycerides and low density lipoprotein (LDL) and decreased high density lipoproteins (HDL)[5]. As a result of decreased blood glucose utilization for energy, oxidation of lipids becomes the main source of energy leading to increased formation of free fatty acids in the plasma[6]. This in turn, leads to increased formation of triglycerides causing release of apolipoprotein B (Apo-B) and very low density lipoproteins (VLDL)[7]. All these consequences, resulting as a result of deranged lipid profile in patients with DMT2, put such individuals at 1.5-2.5 times increased risk of cardiovascular diseases (CVD) especially ischemic heart disease (IHD)[8]. The aim of treatment in DMT2 patients therefore is not only to control hyperglycemia but also to manage lipids parameter through various means including statins[9], commonly prescribed lipid lowering agents, although associated with adverse effects[10].

In recent years, several studies have reported the increased incidence of vitamin D insufficiency in DMT2 patients and have suggested its association with deficiency/lack of insulin secretion[11-13].Some researchers have even suggested the linkageof onset of type-2 diabetes mellitus& deficiency of Vitamin-D as the latter can lead to development of insulin resistance thus putting people at increased risk for development of type-2 diabetes mellitus[14]. In the

light of several such suggestions, manystudies were undertaken to assess the impactofVit D supplementation in individuals havingT2DM and several research reports have shown a beneficial effect of vitamin D supplementation in Type-2 diabetics on their lipid profile parameters as consequence of improved glucose metabolism[15]. Furthermore, vitamin D supplements have also shown to be effective in stimulating insulin release and increasing its sensitivity in peripheral tissues[16].

With this background, this study was designed and conducted to determine if there is any role of vitamin D supplementation in patients suffering from DMT2 on their blood glucose levels and lipid parameters keeping in view increased prevalence of diabetic patients in our population and the consequent high mortality associated with it.

Material & Methods

The approval for the study has been obtained from the Institutional Ethical review committee (ERC). The Study protocol strictly followed the ethical principles. The study was conducted in the Pharmacology department in cooperation with Sindh Institute of Endocrinology & Diabetes (SIED) affiliated with the university. After explaining the purposesofthisresearch,aninformedconsentwasobtainedfrom all affected individuals.It was an observational and interventional type of study that continued for six months from March to August 2018.Total 140 patients were enrolled for the study having age ranging from 36-60 years. Care was taken to includepatientshaving type-II diabetes mellitus with duration of more than five years and taking metformin having following lipid profile parameters:

- HbA1c equal to or more than 6.0 mg/dl
- Triglycerides level> 150 mg/dl
- Whole cholesterol level > 200 mg/dl
- Vitamin D deficiency (levels<30ng/ml)

Patients with type-1 Diabetes, any major known disease, with history of steroid intake and oral contraceptive pills for more than 6 months, those on vitamin D supplements and normal Vitamin-D levels were excluded from this study.

A history of diabetes along with the duration and treatment was recorded in detail. Blood was analyzed for biochemical parameters mentioned above initially just beforebeginningofthisresearch and then 3 months after patients were supplemented with vitamin D. The patients were divided equally (A & B) with 70 in each group. Only those individuals having diabetes mellitus were included in the group A, who were taking metformin 1gm without any supplementation of vitamin D. Group-B included individuals with diabetes mellitus, kept on metformin 1g & vitamin-D 800IU daily given as capsule sunvit 400IU (Novametpharma, B.I.D). Blood was obtained before and after three months of vitamin-D supplementation for lipid profile and VitD levels. Serum was collected carefully after centrifugation at 3,500 rpm for 10 minutes. Tests were performed using Hitachi Cobas C 311 analyzer (for lipid profile) & Architect i2000SR immunoassay analyzer (for vitamin D level).

SPSS version 22.0 was used to analyze the data. With regard to categorical variablesfor instance, age (in groups) and sex, frequency and percentage were calculated & chi square test was used to linktherelationships amongst the groups. For numerical parameters, just like age, weight, height, BMI, periodof DM, lipid Profile and serum vitamin-D level, Mean & standard deviation (SD) was computed &Student t-test was applied to relatetheaveragesb/w these two groups . P value less than 0.05 was considered to be a point of significance.

Results

140 patients with type-II diabetes were included in this study. No any substantialstatisticalalterationwas observed in the mean age, gender, and duration of diabetes in two groups. The results are summarized in tables from 1 and 2.

Table-2A shows mean cholesterol level in two groups at base line and 3 months after the start of study. There was no significant difference in mean base line cholesterol level. Cholesterol levels 3 months after Vit D supplementation showed significant decrease in group-B as relatedto group-A.

Table-2B shows mean LDL levels in two groups on base line &at 3 months. There was no majordifference in mean base line LDL level. Levels after 3 months after Vit D supplements showed significant decrease in group-B as related to group-A.

Table-2C shows mean HDL level in two groups at base line &subsequentlyat3 months. There was no major difference in mean base line LDL level. Levels after 3 months after Vit D supplements also showed no significant difference between group-B and group-A.

Table-2D shows mean triglycerides level in two groups at base line &subsequentlyat3 months. There was no major difference in mean base line LDL level. Levels after 3 months after Vit D supplements showed significant decrease between group-B and group-A.

Table-2E shows mean Vit D levels in two groups at base line &subsequentlyat3 months. There was no major difference in mean base line LDL level. Levels after 3 months ofVit D supplements showed substantial rise in Vitamin-D level in group-B as compared to group A.

Table 1: Age, gender and duration distribution in both groups with diabetes mellitus.

Age Distribution (in years) of subjects in both groups.				
Age (in Groups)	Group A (Without Supplementation) n=70	Group B (With Supplementation) n=70		P Value
Mean ± SD	48.60 ± 7.26 (35-60)	48.77± 7.13 (35-60)		0.88
Age Distribution (in groups) of subjects in both groups				
Age in groups	Group A (Without Supplementation) n=70	Group B (With Supplementation) n=70	Total	P value
35-45 46-55 >55 years	29 (41.4%) 29 (41.4%) 12(17.1%)	25 (35.7%) 31 (44.3%) 14 (20.0%)	54 (38.6%) 60 (42.9%) 26 (18.6%)	0.77
Gender Distribution in both groups				
Gender	Group A (Without Supplementation) n=70	Group B (With Supplementation) n=70	Total	P value
Male Female	30 (42.9%) 40 (57.1%)	45 (64.3%) 25 (35.7%)	75 (53.6%) 65 (46.4%)	0.01
Distribution of subject according to duration of diabetes mellitus (in years) in both groups				
Duration of DM (years)	Group A (Without Supplementation) n=70	Group B (With Supplementation) n=70		
Mean ± SD Range	10.34±4.10 (5.0 to 20 years)	12.07±5.25 (5.0 to 25 years)		0.03

Table 2: Cholesterol, LDL, Triglycerides, HDL and Vitamin D distribution in both groups with diabetes mellitus at baseline and 3 months after taking vitamin D supplements.

A-Distribution of subjects according to Total cholesterol levels at baseline and after 3 months intervention in both groups.				
Total Cholesterol mg/dl	Group A (Without Supplementation) n=70	Group B (With Supplementation) n=70	Difference	P value
At baseline	245.61±30.03 (200 to 335)	250.80±26.97 (201 to 298)	-5.19	0.28
After 3 months	240.61±30.03 (195 to 330)	231.01±27.20 (181 to 278)	9.6	0.04
B-Low Density Lipoproteins (LDL) levels at baseline and after 3 months intervention in both groups				
Low Density Lipoproteins (mg/dl)	Group A (Without Supplementation) n=70	Group B (With Supplementation) n=70	Difference	P value
At baseline	146.57±14.31 (126 to 189)	146.47±11.06 (119 to 167)	0.1	0.96
At 3 months	142.82±14.40 (123 to 184)	137.48±11.05 (110 to 158)	5.34	0.01
C-Distribution of subjects according to High Density Lipoproteins levels (HDL) at baseline and after 3 months intervention in both groups.				
High Density Lipoproteins (mg/dl)	Group A (Without Supplementation) n=70	Group B (With Supplementation) n=70	Difference	P value
At baseline	39.65±10.41 (19 to 78)	41.72± 6.63 (24 to 58)	-2.07	0.16
At 3 months	41.20± 10.34 (21 to 79)	43.72±6.63 (26 to 60)	-2.52	0.08
D-Triglycerides levels at baseline and after 3 months intervention in both groups				
Triglycerides (mg/dl)	Group A (Without Supplementation) n=70	Group B (With Supplementation) n=70	Difference	P value
At baseline	242.57±50.31 (177 to 506)	231.72±24.30 (178 to 294)	10.85	0.10
At 3 months	242.15±50.88 (179 to 508)	219.72±24.30 (166 to 282)	22.43	0.001
E-Vitamin D levels at baseline and after 3 months intervention in both groups				
Vitamin D (ng/ml)	Group A (Without Supplementation) n=70	Group B (With Supplementation) n=70	Difference	P value
At baseline	16.23±3.45 (6.3 to 19.4)	15.60± 3.13 (7.7 to 19.4)	0.63	0.26
After 3 Months	16.40±3.63 (6.3 to 22.4)	28.96± 5.25 (20.5 to 40.1)	-12.56	0.0001

Discussion

Worldwide, type 2 diabetes mellitus is a major health problem. It is predicted that, till the year 2030, number of DM patients will reach to 366 million. Nowadays, deficiency in vitamin-D in T2DM affected individuals is also considered as possible hazard[17] Regarding endocrinology, DM is very common condition in which constant rise in blood glucose level leads to formation of free radicals or reactive oxygen species (ROS). Vitamin-D is very effective anti-oxidant so it can prevent the tissues from damaging effects of free radicals by inhibiting non-enzymatic glycosylation of proteins. Due to anti-inflammatory properties of vitamin D, it can protect the lipids of cell membranes from oxygen free radicals[18,19]. Purpose of current research was to assess role of vitamin-D on the lipid profile in patients of T2DM. This study observed the response of vitamin D supplementation for 3 months in patients of T2DM. According to the study criteria, one hundred and forty individuals having type-2 diabetes were selected. A number of research studies revealed Vit D levels' association with lipid profile[20]. In the current study, Vitamin D as an adjuvant therapy significantly reduced TG levels, total cholesterol, and LDL level after 3 months of intervention while change in serum HDL was not significant. In a comparable study, Ramiro-Lazano et al (2015) perceived a significant reduction in total cholesterol but no major alteration in LDL[15], HDL and triglycerides. Mohammad M et al established no noteworthy variation in lipid profile status after vitamin D supplementation[17]. Another study of 92 subjects with T2DM with an average plasma level of vit D as 25 ng/ml showed that total cholesterol & LDL levels were extensivelyreduced by prescribing 2000 IU of vitamin-D every day up to 18 months. Cholesterol, triglycerides and HDL cholesterol levels were only increased at an average of 8 ng / ml was achieved at plasma levels of TG and twenty five (OH) D without change[21]. LDL cholesterol and HDL cholesterol triglyceride in patients with Type-2DM with anaverageserum concentration of vitamin-D with 11.8ng/ml were managed with cholecalciferol at 1,000 U / day for 12 months. The average plasma Concentration of Vitamin-D post-treatment was only 17.6 ng / ml[22]. Only 24% of participants, compared with other studies on 100 type 2 diabetics with vitamin D deficiency, administered cholecalciferol at 50,000 U / week for 8 weeks resulted in serum total cholesterol, Low Density Lipoprotein, High Density Lipoprotein and triglyceride[23]. In 87 diabetics with type-II diabetes having vitamin D insufficiency, 6,000 U of cholecalciferolper day up to 3 months and 3,000 U per dayup to 3 months, did not affect lipid factors[24]. This unique analysis accompanied to investigate effect of VitD therapy on lipid profiles in twelve research reports & 1,346 affected individuals revealed a statistically momentous rise in Low Density Lipoprotein cholesterol and rise in total cholesterol, decreased HDL cholesterol and triglyceride levels. This analysis, however, comprises heterogeneous findingsoftwenty five (OH) D, Vit-D doses, baseline for managementperiod& patient features and serum levels after treatment[25]. There is significant increase in vitamin D concentration after 3 months of supplementation in this study. In this study, 68 subjects (97.1%, n = 70) with diabetes had vitamin D levels under 20 ng/ml before therapy whereas 47(69.1%, n = 70) of patients with diabetes had 21 to 30 (Insufficient) and 21(30.9%, n = 70) of subjects with diabetes had vitamin D > 30(sufficient). When compared with controls, results showed significant decrease in the mean level of serum vitamin D. Significantrise in 25(OH) D concentrations with Vit D therapy after 12 weeks of intervention was noticed. Similarly, previous research has mentioned that vitamin D insufficiency were found to be prevalent among type-2 diabetic patients[26-28]. This means that deficiency in vitamin D levels are linked to type-2 diabetes. Such outcome is in agreement with that demonstrated by Subramanian et al (2011). In addition, Talaie and Nasri et al., (2014) established that vitamin D therapy is related with a lower risk of type-2 diabetes[29-30].

Conclusion

To conclude, the present study demonstrated that patients with T2DM on metoformin have decreased Vit.D levels. Supplemenation with Vit.D therefore not only improve plasma vitamin D levels but also certain parameters of lipid profile such as TC, TG and LDL leading to decreased risk of cardiovascular event in future.

Recommendation

In the light of the current study, it is recommended that all T2DM patients on metformin should be screened for plasma Vit.D levels and if decreased should be supplemented with the same in order to decrease the risk of any cardiovascular incidence in such patients.

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