Original Article

Response of blood sugar fasting to vitamin D3 in individuals with pre-diabetes

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Objective: To ascertain the outcome of vitamin D3 supplementation on blood sugar fasting (BSF) of individuals with pre-diabetes and co-existing hypovitaminosis D3.

Methodology: This quasi experimental study was carried out in the Department of Pharmacology and Therapeutics, Army Medical College, Rawalpindi from January to December 2019. Non-probability convenience sampling was done, and 140 individuals with pre-diabetes (BSF: 5.7 – 6.9 mmol/L) and co-existing hypovitaminosis D_3 (< 50 nmol/L) were included in the study. Age wasbetween 21 to 60 years of either gender. They were randomly selected to receive 200,000 IU of cholecalciferol (vitamin D_3 n = 70) or placebo (n = 70), in one dose at the commencement of study, and after one month. The outcome between BSF and vitamin D_3 were comparedand analysed after 12 weeks by SPSS version 23.

Results: The median of blood sugar fasting in the vitamin D3 group decreased from 5.4 to 5.1 and the interquartile range (IQR) decreased from 5.7 – 5.1 to 5.6 – 5.0 versus placebo (p = 0.001). Thus, there was a significant reduction in BSF in Vit. D3 group versus placebo.

Conclusion: Vitamin D_3 supplementation in individuals with pre-diabetes and co-existing hypovitaminosis D_3 resulted in decrease in BSF and thus lowered the risk of progression to type 2 diabetes mellitus.

Key words: Cholecalciferol, hypovitaminosis, placebo, pre-diabetes, supplementation.

INTRODUCTION

Worldwide prevalence of type 2 diabetes mellitus (T2DM) and vitamin D3 (cholecalciferol) deficiency is increasing.[1] Individuals who develop diabetes mellitus have a higher risk of developing a number of severe negative health complications, which may result in increased morbidity and mortality.[2]

Vitamin D3, a fat-soluble vitamin, is either synthesized in the skin, or ingested as part of the diet. The chief natural source of vitamin D3 comes from the skin. Diet plays only a minor role.[3] Most important function of vitamin D3 is bone mineralization.[4] However, it is becoming obvious that vitamin D3 has a number of non-skeletal functions too. Its deficiency has a risk of not only skeletal, but also non-skeletal disorders, which include T2DM, immune disorders and cardiovascular diseases.[5] Vitamin D3's role in glucose regulation is well established and it is claimed that insufficient level of vitamin D3 has an inverse relationship with pre-diabetes and T2DM.[6] Furthermore, increase in plasma vitamin D_3 concentration is related with reduced risk of diabetes.[7]

"Pre-diabetes" is defined as a condition in which individuals have glucose levels which do not fall in the criteria for diabetes, but are very high to be considered as normal values. These individuals have impaired blood glucose tolerance, impaired fasting blood glucose (BSF: 5.7-6.9) and slightly elevated glycosylated hemoglobin (HbA1c: 5.7 – 6.8%).[8] Pancreatic β cells and the immune system express a lot of vitamin D-binding protein and vitamin D receptors (VDR).[6] VDR are abundantly expressed in β cells of the pancreas and in the immune system.

Several studies have shown the binding of the circulating active form of vitamin D_3, 1,25-dihydroxy vitamin D_3, (1,25 $(OH)2D_3$) to the vitamin D receptor, which are expressed in pancreatic β cells.[9] Thereupon, it is not surprising to appreciate pancreatic stimulation of insulin production in response to vitamin D_3. Hence, this could be another mechanism in preventing T^2DM and impeding conversion from pre-diabetes to full blown diabetes mellitus.[6] If preventive measures are carried out while the patient is in the pre-diabetic stage, it will be useful in preventing or delaying the start of fully developed diabetes mellitus.[10] The principal objective of this study was to evaluate the role of vitamin D_3 on BSF of individuals with pre-diabetes.

METHODOLOGY

It was a twelve-week, quasi experimental study conducted in Pharmacology Department, Army Medical College, Rawalpindi in cooperation with Chemical

Pathology Department and Armed Forces Institute of Pathology (AFIP), Rawalpindi, Pakistan. G*Power version 3 Calculator was used for sample size estimation. The study was approved by ethical review committee of Centre for Research in Experimental and Applied Medicine, of Army Medical College. A written informed consent was taken from all subjects.

Keeping in view population prevalence proportion of 26.3%1, level of significance at 5% and power of test as 80%, sample size was 70 patients in each group. 140 individuals with pre-diabetes with coexisting hypovitaminosis D3 between the ages of 21 to 60 years of age were included in the study. They were all in pre-diabetic category (BSF: 5.7 – 6.9 mmol/L) and vitamin D3 deficient patients (< 20 ng/mL) or vitamin D3 insufficient patients (20 – 30 ng/mL).[8] Exclusion criteria were patients having vitamin D^3 in sufficient range, suffering from full blown T^2DM and diagnosed kidney or liver ailments, any mental illness or patients on anti-epileptic drugs, pregnant or lactating females and those suffering from hemoglobinopathies.

Individuals were randomly split by lottery method into two groups. Group I (Controls n = 70) were assigned to receive placebo orally, one stat at the beginning of study and after one month and group 2 (Cases n = 70) received vitamin D^3 200,000 IU at the beginning of study and after one month. Sample for vitamin D^3 and blood sugar fasting were taken at the beginning of the study and at 12 weeks after first dose. BSF was measured on ADVIA 1800 Siemens by hexokinase method and Vitamin D3 was measured on ADVIA Centaur by chemiluminescence.

Statistical Analysis: All data were analysed using SPSS 23. Data was not normally distributed, consequently, Kruskal-Wallis-H test was applied which is a nonparametric test. The quantitative variables, vitamin D^3 and blood sugar fasting were presented as median {interquartile range (IQR). $p < 0.05$ was taken to indicate statistical significance.

RESULTS

The study included 140 individuals. Baseline characteristics are shown in the Table 1, which shows no statistically significant difference in the age, gender and smoking history. Gender wise distribution is shown in Fig. 1. Several were current or ex-smokers (Fig. 2).

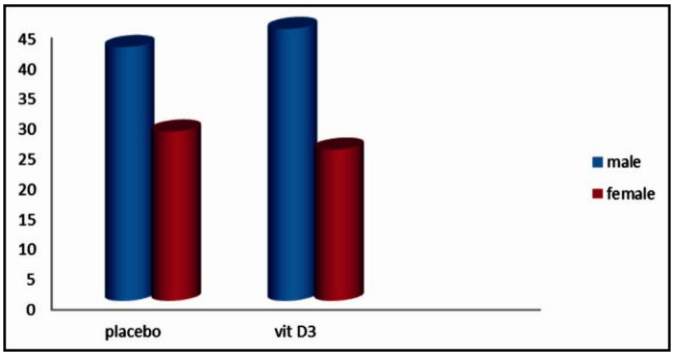

Fig. 1: Gender wise distribution between 2 groups.

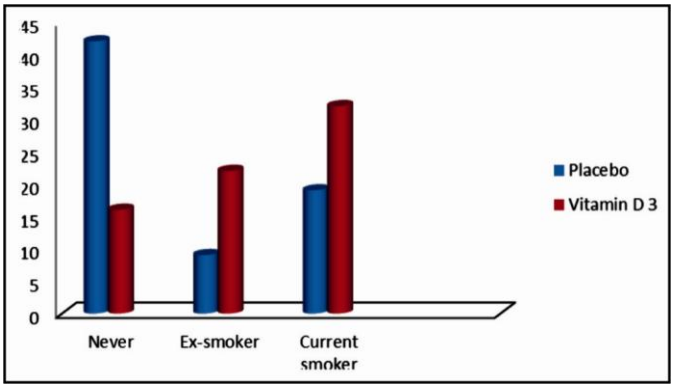

Fig. 2: Smoking status of two groups.

A statistically significant and inverse association was found between the serum level of vitamin D_3 and BSF in pre-diabetic subjects as compared to placebo at the end of the study. In group 1, there was no significant change in the level of BSF, when compared to baseline (Table). Nevertheless, BSF decreased quite significantly in patients treated with D3 than in the placebo group (mean: 5.4 interquartile range: 5.6 – 5.0) significant p = 0.01).

Table 1: Comparison of change in serum blood sugar fasting between the groups by Kruskal-Wallis Test.

BSF (mmol/L)		Group 1 (Placebo)	Group – 2 (Vit D_3)	p-value
Before treatment with vitamin D_3	Median	5.5	5.4	.190^{NS}
	IQR	5.8 – 5.2	5.7 – 5.1	
12 Weeks Post-treatment with vitaminD_3	Median	5.8	5.1	.001*
	IQR	5.9 – 5.5	5.6 – 5.0	

DISCUSSION

Diabetes mellitus (DM) is a serious metabolic disorder. Approximately one in eleven adults worldwide have DM, ninety percent of whom have T2DM.[2] Pakistani people have a high prevalence of T2DM and vitamin D_3 deficiency. Medical science has advanced both in the diagnostic and treatment strategies of diabetes, but accomplishing optimum blood sugar level is still very challenging.

The management of T2DM requires life style modifications, multiple oral anti-diabetic drugs and sometimes, insulin.[11] Accumulating evidence has shown an association between low vitamin D_3 levels with impaired glucose tolerance and diabetes mellitus. In the past few years, various studies have indicated that higher vitamin D_3 intake is associated with a lower risk of T2DM.[6] Pancreatic β cells and the immune system express a lot of vitamin D-binding protein and vitamin d receptors (VDR). Binding of the circulating active form, 1, 25$(OH)^2D_3$ to the vitamin D receptor expressed in pancreatic β cells.[12] Taking into consideration the increased prevalence of T2DM and vitamin D_3 deficiency, it becomes compelling to analyze this relationship. In our twelve week study, vitamin D3 therapy in pre-diabetic individuals who had D_3 hypovitaminosis displayed a sensational response.

In this study, statistical analysis showed that vitamin D_3 supplementation improved BSF in the pre-diabetic individuals. Similar findings were reported by Prakash et al, who found that vitamin D_3 supplements in pre-diabetes subjects helped in lowering BSF and thus, helped in preventing risk of T2DM.[13] Mathieu in 2015 performed a pilot study by administrating two doses of vitamin D_3 and found that Vitamin D_3 deficient participants demonstrated significant improvements in BSF in overweight and obese Australians.[14]

The results of our study are consistent with those of Tang et al which revealed that Vitamin D_3 supplementation significantly lowered BSF.[15] A cross-sectional study on 797 women having pre-diabetes (aged 20 – 60 years) concluded that low vitamin D_3 status was connected with increased blood glucose levels.[8] Likewise, a study was conducted by Prasad in 2016 on vitamin D_3 deficient type 2 diabetic patients with near-normal HbA1c and well controlled T^2DM,after three months of vitamin D_3 supplementation, there was reduction of BSF.[16] Another literature review accomplished by Goldenberg and Punthakeefound beneficial effect of vitamin D_3 therapy in ameliorating BSF.[17]

CONCLUSION

We found that there is a relationship between low vitamin D_3 levels and individuals who were pre-diabetics. Extrapolation from the results in the current study proposes that vitamin D_3 therapy has an encouraging effect on blood sugar fasting in patients who are pre-diabetics.

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