



TYPE 2 DIABETES;

EFFICACY OF VITAMIN D SUPPLEMENTATION ON GLYCEMIC CONTROL IN TYPE 2 DIABETIC PATIENTS.

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Article received on:
17/01/2017

Accepted for publication:
30/04/2017

Received after proof reading:
05/06/2017

ABSTRACT... Background: The data among vitamin D supplementation on glycemic control is variable and contradictory in various clinical studies. **Objectives:** To determine the efficacy of vit D supplementation on glycemic control in type 2 diabetic patients. **Study Design:** Case control study. **Setting:** Private Clinical Set up of District, Rahim Yar Khan. **Period:** August to October 2016. **Patients and methods:** 100 cases of type 2 diabetes were randomly divided into group A and group B each contained 50 patients. The cases in group A were treated with vitamin D3 at the dose of 50,000 units per week orally while cases in group B were treated with placebo along with the standard doses of anti-diabetic drugs. The value of HbA1c and Vit D were assayed pre and post treatment by high performance liquid chromatography. **Results:** There was significant post treatment changes observed in vitamin D level in group A vs group B in males 20.46 ± 2.45 vs 15.16 ± 1.47 ($p = 0.001$) and females 18.32 ± 1.44 vs 13.95 ± 2.48 ($p = 0.09$). There was significant post treatment changes in HbA1c in males 6.65 ± 0.12 vs 8.34 ± 0.71 ($p = 0.01$) and in females 6.81 ± 0.43 vs 8.04 ± 0.71 ($p = 0.03$) in group A and group B respectively. Similarly better improvement in vitamin D and HbA1c level was seen with respect to aged group 30-50 years and duration of diabetes less than 5 years. **Conclusion:** Vitamin D is deficient in our population and its supplementation not only improves its own level but also glycemic control in type 2 diabetic patients.

Key words: Type II Diabetes mellitus, Vitamin D, HbA1c.

Article Citation: Babar MZM, Hussian M, Manzur A. Type 2 Diabetes; Efficacy of vitamin d supplementation on glycemic control in type 2 diabetic patients. Professional Med J 2017;24(6):899-903. DOI: 10.17957/TPMJ/17.3929

INTRODUCTION

Diabetes Miletus (DM) is among the most prevalent metabolic syndromes globally. According to an estimate more than 150 million people are labeled with this disease and their number is on the rise day by day and is expected to cross 300 million by the year 2025.¹ A strong relationship exists between diabetes and vitamin D. Its low level has a significant contributing role in the initiation, progression as well as complications in the form of myocardial infarction, stroke, retinopathy, neuropathy and nephropathy in diabetic patients in various clinical studies. Therefore multifaceted approach is required to identify diabetes associated vitamin D deficient cases and treat them accordingly in order to reduce disease burden.²⁻³

Vitamin D is amongst the fat-soluble vitamins in the body and is more than 90% activated in skin

due to sun exposure. Vitamin D acts through vitamin D receptors VDRs which are nuclear receptor and have diverse location in the body that plays a key role in calcium and phosphate metabolism. On the other its adequate level has a protective effects against musculoskeletal disorders, infectious diseases, autoimmune diseases, malignant diseases, cardiovascular diseases, metabolic syndromes, type 1 and type 2 diabetes mellitus, infertility, various respiratory and CNS disorders.⁴⁻⁵

Studies showed that polymorphism of the VDRs gene leads to decrease insulin sensitivity, increase insulin resistance and development of type 2 diabetes that leads to increase cardiovascular risk.⁶⁻⁷ On the contrary a meta-analysis of 57 case control study concluded that out of the four polymorphism in the VDR gene only Bslm polymorphism have been associated with type 1

diabetes especially in Asians. Similarly in another meta-analysis there was increased risk of type 2 diabetes mellitus in Asians in Fokl polymorphism of the VDR gene.⁸⁻⁹

In spite of satisfactory evidence from genetic studies data about clinical studies is contradicted and controversial. A meta-analysis of seventeen randomized control trials and seven longitudinal studies showed that vitamin D supplementation cannot improve glycemic control in type 2 diabetic patients over a follow up period of one month.¹⁰ However sunny trial showed that vitamin D supplementation improves glycemic control and quality of life in type 2 diabetic patients over a period of 6 months.¹¹ In another systemic review and meta-analysis a favorable effect of vitamin D supplementation on fasting blood sugar in poorly controlled diabetic patients have been identified.¹² Similarly data from the 21 observational prospective studies and meta-analysis of 12 studies reveals that low level of vitamin is a predisposing factor for development of type 1 and type 2 diabetes and other metabolic diseases.¹³⁻¹⁴

There is need to investigate this doubt as there was no studies conducted in Pakistan up till now to investigate the effect of vitamin D supplementation on glycemic control. So this study was designed to determine the effect of vitamin D effect on glycemic control in type 2 diabetic patients.

PATIENTS AND METHODS

This case control study was conducted on type 2 diabetic patients aged 30-70 years at a private clinic of district Rahim Yar Khan, Punjab Pakistan from September to November 2016. Initially 150 patients were recruited out of which 100 patients were enrolled in the study based upon history of diabetes which was confirmed by standard ADA criteria. The patients were excluded if they had neuropathy, nephropathy, retinopathy and hepatic complication associated with diabetes. In addition patients who were taking vitamin D, calcium and any other drugs which effect calcium and vitamin D metabolism such as thiazide & loop diuretics, bisphosphonates, HRT, calcitonin, and

various steroids were excluded from the study.

All the cases which were on oral anti-diabetic drugs were then asked to choose a shield opaque envelope marked as A or B The cases in group A were treated with oral cap vitamin D3 at the dose of 50,000 units weekly for a period of 12 weeks while group B was given cap placebo in a similar manner but it contained microcrystalline cellulose as an active ingredient. BMI was calculated by dividing the weight (kg)/height (m²) without shoes and wearing light clothes. A 5ml blood sample was calculated from the median cubital vein after an overnight fasting of 12 hours. The samples were used for analyzing HbA1c and vitamin D level which were estimated in the laboratory by high performance liquid chromatography.

STATISTICAL ANALYSIS

Data was analyzed by using statistical package for social sciences SPSS-16. Chi square test was used to compare nominal data and independent sample t test was used to compare the ordinal data. Post stratification independent sample t test was applied to compare the two groups to look for reduction in HbA1c, taking p value of ≤ 0.05 as significant.

RESULTS

No significant major adverse effects were noted during the study and all patients completed the study with nice cooperation. Ten patients in the vitamin D group complaints of minor abdominal bloating during first 2 weeks of therapy which settle down itself without any intervention. There were 50 cases in each group. Group A contained 28 (56%) males and 22 (44%) females while Group B had 30 (60%) males and 20 (40%) females (Table-I) with $p= 0.95$. The mean age of group A was 47.38 ± 5.40 years while of group B was 45.34 ± 6.17 years. Table-II reveals that there was no significant difference in terms of mean age, BMI, duration of DM, pre-treatment vit D and HbA1c level in both groups. On comparison of group A vs B after treatment with vit D, the mean Vit D level in males was 20.46 ± 2.45 vs 15.16 ± 1.47 ($p= 0.001$) while in females it was 18.32 ± 1.44 vs 13.95 ± 2.48 with ($p= 0.09$) while post treatment HbA1c in

males was 6.65 ± 0.12 vs 8.34 ± 0.71 ($p = 0.01$) and in females it was 6.81 ± 0.43 vs 8.04 ± 0.71 ($p = 0.03$) respectively in group A and B as in Table-III. There was also significant improvement in treatment group A where there was significant

improvement in terms of Vit D level and HbA1c level in both the groups regarding different age groups and duration of DM and it was better seen in cases with age group 30- 50 years and in cases with DM less than 5 years (table-IV & V).

Variables	Group A (N=50)	Group B (N=50)	p value
Male/Female ratio	30/20	28/22	0.95
Age (years)	45.34 ± 6.17	47.38 ± 5.40	0.65
BMI (kg/m ²)	28.41 ± 2.72	26.34 ± 4.11	0.22
Duration of DM (years)	9.76 ± 2.43	11.45 ± 3.30	0.09
Pre treatment vit D (ng/ml)	14.15 ± 3.22	13.26 ± 2.70	0.97
Pre treatment HbA1c (%)	7.96 ± 1.02	8.15 ± 0.65	0.14

Table-I. Baseline demographic characteristic of two groups.

	Gender	Group A	Group B	P value
Post Treatment vit D	Male	20.46 ± 2.45	15.16 ± 1.47	$p = 0.001$
	Female	18.32 ± 1.44	13.95 ± 2.48	$p = 0.09$
Post Treatment HbA1c	Male	6.65 ± 0.12	8.34 ± 0.71	$p = 0.01$
	Female	6.81 ± 0.43	8.04 ± 0.71	$p = 0.03$

Table-II. Glycemic control with respect to Gender

	Age groups	Group A	Group B	P value
Post Treatment vit D	30-50 years	21.35 ± 2.92	14.23 ± 2.56	$p = 0.001$
	> 50 years	16.33 ± 2.41	13.55 ± 2.65	$p = 0.03$
Post Treatment HbA1c	30-50 years	6.25 ± 0.45	8.04 ± 0.49	$p = 0.0001$
	> 50 years	7.06 ± 0.95	8.06 ± 0.33	$p = 0.04$

Table-III. Glycemic control with respect to age groups.

	Duration of DM	Group A	Group B	Significance
Post Treatment vit D	< 5 years	19.31 ± 2.47	13.44 ± 2.48	$p = 0.002$
	> 5 years	16.22 ± 2.42	14.22 ± 1.75	$p = 0.03$
Post Treatment HbA1c	< 5 years	6.35 ± 1.04	8.02 ± 0.45	$p = 0.001$
	> 5 years	7.12 ± 0.94	8.12 ± 0.55	$p = 0.04$

Table-IV. Glycemic control with respect to Duration of DM

DISCUSSION

In this study there was better improvement in terms of HbA1c in experimental group as compared to control group. This was also seen by different studies in the past that the cases that were treated with vit D had better DM control and had decrease in HbA1c.15-17 The study conducted by Kostoglou-Athanassiou I et al¹⁵ found an inverse relationship between the HbA1c and the vitamin D level that the higher the vit D level and lower is the HbA1c. According to study done by Ochs-Balcom, H et al and Holick M et

al, the vit D is thought to act on adipose tissue and also increases the sensitivity of insulin in various ways and hence its deficiency can lead to diabetes and vice versa.¹⁸⁻¹⁹ The studies have documented that the low vit D level is associated with increased risk of DM in pre diabetic cases and also the risk of gestational DM and its supplementation can decrease their incidence.²⁰⁻²¹ However, in other studies done by Liu et al and Pittas et al, the reverse was seen that the cases that took vitamin D had more incidence of metabolic syndromes like Type II DM.²²⁻²³

The reason of it in their study is unexplainable. There was also better control in treatment group B where there was significant improvement in terms of Vit D level and HbA1c in both the groups regarding age group 30- 50 years as compared to older age group. This was also seen by the other studies with higher improvement in younger age groups.^{17,23} However, they did not use the cut off values like our study. The reason of higher control in younger age groups can be due to their active life, so that they are more exposed to sun and the activation of vit D via sunlight can be a factor. Secondly, the social factors of earning and to live with the disease can be another boosting factor to show better compliance towards the treatment. Moreover, physical activity also leads to better glycemetic control.

In the present study one more thing was found that the cases with duration of DM less than 5 years had better control. This was also observed by the other studies.²⁴⁻²⁵ This can be explained by the above mentioned factors as the earlier stage of disease is commoner in young groups. The other factors influencing this, along with the early stage of the disease can be relatively lesser degree of vit deficiencies and enthusiastic approach to manage this complication.

Limitation of Study

We are unable check markers of insulin sensitivity and resistance such as HOMA-IR and serum insulin level and compare them with HbA1c and vitamin D. This will give some clearer picture about the action of vitamin D either it increase insulin sensitivity or not. Moreover we cannot rule out confounding environmental factors that strongly effect vitamin D level such as dietary habits, physical activity, seasonal variation and sun exposure.

Future Directions

A large sample size and long duration studies will be recommended in future

CONCLUSION

Diabetic patients who are deficient in vitamin D, its supplementation have a strong impact on

glycemetic control in type 2 diabetic patients.



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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. M. Zafar Majeed Babar	Conceived the idea plagiarism, manuscript review and statistical analysis.	
2	Dr. Mazhar Hussain	Designed the study, preparing the manuscript and data analysis.	
3	Dr. Asma Manzur	Search the literature, collected the clinical data, manuscript editing and drafting of the manuscript.	