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Beneficial effects of oral vitamin D supplementation in diabetes mellitus type II patients – a clinical study in Karachi

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Abstract: Vitamins are an essential component of the human body for growth and maintaining health. All vitamins have a significant role in metabolism, as a prophylactic in preventing various diseases, and maintaining health. Literature studies have predicted the positive impact of vitamin D on sugar level in blood of type 2 diabetes. Vitamin D plays a significant role in treating diabetes mellitus because it helps produce insulin and helps in the growth of beta cells of the pancreas. The present study was conducted for evaluating the impact of oral vitamin D in reducing the hyperglycemic conditions in patients after treatment of 1-6 months duration. 52 type 2 diabetes patients were enrolled in the study. The results showed that Vitamin D supplementation of 16 weeks reduced fasting blood glucose and HbA1C significantly in Vitamin D deficient Type 2 diabetes.

Keywords: Diabetes, fasting blood glucose, HbA1C, oral route, vitamin.

INTRODUCTION

Vitamins are organic chemical molecules that are an essential food component that humans require in small amounts for metabolic functions such as tissue growth and healing. Because the body does not manufacture these compounds, they must be acquired through food. Higher vitamins should be administered if the patient is pregnant, or suffering from a debilitating condition (Zempleni *et al*., 2013). Patients who do not eat a well-balanced diet (such as the elderly, alcoholics, youngsters, and those who follow a high-fat diet) are also at risk of developing vitamin deficiencies. Patients with such diseases need to take vitamin supplements to ensure enough vitamins to sustain their metabolism (Iddir *et al*., 2020).

Although their supplementation is necessary for treating some health disorders, there is little evidence that they provide nutritional benefits to otherwise healthy persons. One of the necessary vitamins is vitamin D. Vitamin D (D2, D3, or both) is a secosterol that can be biochemically generated in the skin or acquired from foods that contain natural vitamin D. (Fletcher *et al*., 2022; Kift *et al*., 2018).

In the skin vitamin D_3 is synthesised through 7-dehydrocholesterol (7-DHC) when exposed to UV radiation. 7-DHC is converted to cholesterol by DHCR7 (7-dehydrocholesterol reductase enzyme) because of which, 7-DHC acts as a precursor to cholesterol. (Sakaki *et al*., 2005).

Vitamin D is found in abundance in sea food such as mackerel, salmon and sardines. Vitamin D has been added to fortified cereals and milk products. D_3 Vitamin is appended to almost all regular milk (Lu *et al*., 2007). Ongoing researches have postulated that vitamin D has vibrant function in diabetes mellitus.

Hyperglycaemia is one of the signs of diabetes mellitus, which is triggered by irrational insulin synthesis, fault in insulin action, or both. Diabetes in long term may cause multiple organs damage, dysfunction, or complete failure such as of eyes, nerves, kidney, heart and blood vessels. The conditions indicating severe hyperglycaemia may be weight loss, polyphagia, polyuria, polydipsia and occasionally blurred vison (Lee *et al*., 2018). If the diabetes remains untreated, the hyperglycemia may cause two life threatening complications which are ketoacidosis and non ketotic hyperosmolar syndrome (American Diabetes Association, 2021).

Diabetes can be categorized into major two types founded on their etiologic reasons. Type 1 diabetes is caused by complete absence of insulin production whereas type 2 diabetes is caused by insulin resistance and an insufficient compensatory insulin secretory response, and this type is far more common than type 1(Chatterjee *et al*., 2017). The risk of developing diabetes can be typically identified by serological evidences of pathological process of autoimmune pancreatic islets and genetic markers (Carracedo *et al*., 2019). Hyperglycaemia can lead to various functional and pathological alterations in different tissues which might not trigger clinical symptoms and this may happen for an extensive period before diabetes is diagnosed. It is easy to determine carbohydrate malfunctioning in asymptomatic phase through testing of glucose fasting or after glucose load challenge by oral route (De Carvalho *et al*., 2022).

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Another common type of diabetes that develops in women during pregnancy is Gestational diabetes mellitus which is a functional taxonomy relatively than a pathophysiologic disorder. In most women, GDM occurs in the third trimester of pregnancy. (McIntyre *et al*., 2019). The present study was conducted to assess the effects of oral vitamin D in Type II diabetes.

MATERIALS AND METHODS

Design and settings of study

The current study was a prospective study of 06months period, conducted to measure the result of Vitamin D supplementation on FBS and HbA1C in patients of Type 2 Diabetes Mellitus with Vitamin D insufficiency and deficit.

The patients were taken from the OPD of a Tertiary care Government Hospital in Karachi whereas all the Baseline and follow up investigations were conducted at Dr. Essa's Laboratory and Diagnostic Centre, Karachi. The patients were assorted according to the below mentioned criterias.

Number of patients

The sample size of the study was 52 patients.

Gender

Both male and female patients were included.

Inclusion criteria

Patients who were diagnosed with type 2 diabetes and were on oral medication having high FBS and HBA1C were included in the study. Besides that, the patients also had Vitamin D levels <30 ng/ml.

Whereas,

The deficiency values of vitamin D were considered as <20 ng/mL and

The insufficiency values of vitamin D were considered as 20- 29.9 ng/ml.

Exclusion criteria

The exclusion criteria included all those patients with diabetes who had any acute medical emergencies, any metabolic disorder, cardiovascular diseases, gastrointestinal problems, any kidney issues or liver disorders. Patients who were already on calcium or vitamin supplementation and had any history of surgeries or undergoing any surgery during the study time were not included. Patients who had vitamin D hypersensitivity, history of any drug abuse and the women who were lactating or pregnant were all excluded from the current study.

Intervention

In addition to oral antidiabetic medicines, 52 patients who met the inclusion and exclusion standards were given 50,000 IU of Vitamin D_3 through oral route once a week for six months. The baseline values of FBG, HbA1C, calcium, phosphate, prothrombin and serum 25(OH) D were recorded during the preliminary study after a thorough patient history and clinical investigation, and these patients were traced up every 02months up to 06months subsequently starting the administration of vitamin supplements in them.

Throughout this research, signs, indications and adverse effects of patients were noted. FBG levels, HbA1C, serum 25(OH) D, serum calcium, serum phosphate, serum prothrombin levels were recorded after every 2 months up to 06months. It was also restricted not to change their oral antidiabetic medicine and diet during the study.

Ethical approval

The study was approved by the institutional board of studies and assigned number BASR/No/02532/Pharm.

STATISTICAL ANALYSIS

The data of the study was calculated through descriptive testing. Shapiro-Wilks test was used to conclude the normality of variables, which were displayed in mean and standard deviation. To examine the effect of vitamin D supplementation, Paired Student's t-test was applied. The P value was obtained to determine the level of significance, with $p>0.05$ denoting no significance, $p<0.05$ denoting significance at the 5% level (*), $p<0.01$ denoting significance at the 1% level (**), and $p<0.001$ (***) denoting extremely significant result. All the data was evaluated with the help of software SPSS version 26.0.

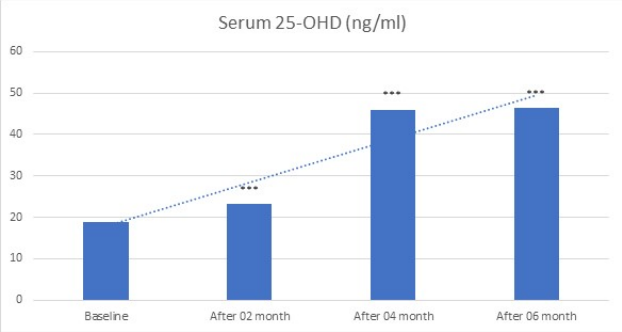
RESULTS

The study included a total of 52 patients. Out of which there were 38 males and 14 females. These patients were followed up after every 02 months up to 06 months after starting the administration of vitamin supplement in them.

The baseline studies indicated the average age of the patients was 48.6±4.8 years. The minimum age of the patients was 40 years whereas the maximum age of the patients was 60 years. The mean height and weight of patients were 5.2±0.34 f/inch and 68.4±3.4 kg respectively. The mean value of serum 25-OHD at baseline was 18.75±6.2ng/ml. The mean value of FBS was 172.95±3.6 mg / dl. The mean HbA1c level was 9.3± 0.35 % with 8.5% and 9.9% lowest and highest serum levels respectively. The mean values of other biochemical parameters including serum calcium, serum PO4 and Serum PTH were 8.9±0.28, 3.6±3.3 and 27.9±9.5 respectively and all were in normal range. (table 1).

After 2 months of starting the vitamin D orally, the mean value of serum 25-OHD was 23.19±4.5ng/ml as

compared to 18.75±6.2ng/ml at baseline. It can be observed that although the concentration of serum 25-OHD had increased after the supplementation of vitamin D for 2 months with a substantial P value i.e P = 0.000 but it did not reach the normal levels. The mean value of serum FBS was 172.62±3.2 mg / dl i.e. insignificant with P value P= 0.107. The mean Serum HbA1c level was 9.2 ±0.32% i.e. insignificant with P value P= 0.531. The mean values of other biochemical parameters including serum calcium, serum PO4 and Serum PTH were 8.9± 0.22 with insignificant P=0.599, 3.2±0.5 with insignificant P=0.324 and 27.8±9.1with P=0.367 respectively. (table 2).

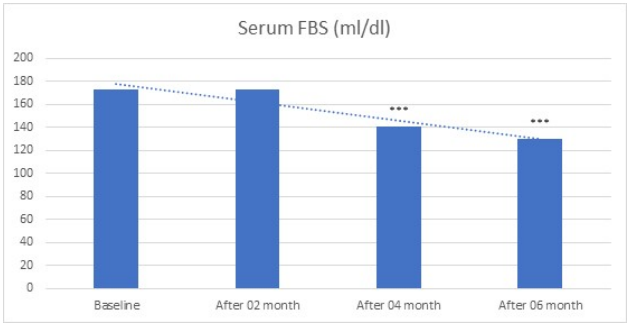


*** p<0.001 when compared with baseline readings

Fig. 1: effect of oral vitamin d supplementation on serum 25-OHD in type 2 diabetics

After 4 months of starting the vitamin D orally, the mean value of serum 25-OHD was 46±4.1ng/ml that is significantly higher within normal limits with P=0.000 (i.e. highly significant) as compared to 18.75±6.2ng/ml at baseline and 23.19±4.5ng/ml after 02 months of starting the vitamin supplements. It is also noted the momentous reduction in the mean value of serum FBS that had diminished to 130.7±4.1mg/dl with a extremely significant P value i.e P=0.000. The mean HbA1c level had also significantly decreased to 6.8±0.28% with an extremely significant P value i.e P=0.000. The mean values of other biochemical parameters including serum calcium, serum PO4 and Serum PTH were almost the same i.e. 8.9 ±0.25 with insignificant P=0.921 , 3.2±0.54 with insignificant P=0.0397 and 28.9±9.5 with insignificant P=0.493 respectively (table 3)

After 6 months of starting the supplementation of vitamin D orally, the mean value of 25-OHD was 46.4 ± 3.9 ng/ml that was also significantly higher, with P=0.000 (i.e. highly significant) within normal limits and was consonant to the mean level of serum 25-OHD i.e. 46± 4.1 ng/ml observed after 4 months of starting the vitamin D supplements. The mean value of serum FBS was 130± 4.0 mg /dl with a exceedingly significant P value i.e P = 0.000 that was almost consonant to the mean levels of serum FBS levels that were observed that were observed after 4 months of vitamin D supplementation i.e. 130.7± 4.1 mg / dl. The mean HbA1c level had also significantly decreased to 6.7±0.2% with a extremely significant P value i.e P =0.000 that was also consonant to the mean levels of serum HbA1c that had been observed after 4 months of starting the vitamin D supplements i.e. 6.8± 0.28 %. The mean values of other biochemical parameters including serum calcium, serum PO4 and Serum PTH were almost the same i.e.8.9±0.23 with insignificant P=0.880, 3.2±0.49 with insignificant P=0.394 and 28.8± 9.3 with insignificant P=0.501 respectively. (table 4).



*** p<0.001 when compared with baseline readings

Fig. 2: effect of oral vitamin d supplementation on serum FBS in type 2 diabetics

DISCUSSION

During the research, the efficacy of vitamin D was evaluated when it was used as a supportive therapy with oral antidiabetic medicines for diabetes mellitus type 2. The study comprised of 52 patients with diabetes Type 2 who had Vitamin D insufficiency and their diabetes was not controlled with various oral diabetes medications. They were administered 50,000 IU weekly Vitamin D3 supplement orally for 16 weeks and their glycemic status was compared to baseline values.

It was noted that Vitamin D treatment for 16 weeks significantly lowers HbA1C and FBG in Vitamin D deficient Type 2 diabetics, according to the findings. A large number of research have looked into the effects of vitamin D supplementation on levels of blood sugar in people with diabetes mellitus type 2.

Resistance of insulin is the catalyst towards the onset of diabetes. Vitamin D's involvement ensures that pancreatic beta cells continue to release insulin typically. The beta-cells can overcome this resistance and prevent hyperglycemia by releasing more insulin. However, as the -cells' hyperactivity rises, they encounter a rise in Ca2+ and reactive oxygen species (ROS) signaling, it is also noted that deficiency of vitamin D may also leads to development of diabetes because of the beta cell death and may also cause resistance of insulin. Vitamin D helps in reducing the inflammation, which is a vital step in developing resistance of insulin thus it is concluded that vitamin D helps in the levels of normal resting of Ca2+ and ROS in the -cells, which are raised during diabetes (Berridge, 2017).

Table 1: Effect of oral supplementation of vitamin D in type 2 diabetes at baseline

Parameter	Min	Max	Mean	Std. Deviation
Age (years)	40	60	48.60	4.888
Height (Feet, Inch)	4.60	5.90	5.2923	0.34914
Weight (kg)	60.0	78.0	68.404	3.4769
Baseline Serum 25- OHD (ng / ml)	7.00	29.00	18.7519	6.21300
Baseline Serum FBS (mg/dl)	166	181	172.95	3.673
Baseline Serum HbA1C (%)	8.50	9.90	9.3154	0.35886
Baseline Serum Ca++ (mg/dL)	8.60	9.90	8.9558	0.28035
Baseline Serum PO4 (mg/dL)	2.50	27.00	3.6923	3.33930
Baseline Serum PTH (pg/mL)	15	51	27.96	9.596

Table 2: Effect of vitamin D supplementation in type 2 diabetes patients at baseline and 2 months

Parameters	(Baseline) Values			(After 2 months) Values			P value
	Minimum	Maximum	Mean value	Minimum	Maximum	Mean value	
Serum 25-OHD (ng/ml)	7.0	29	18.751±6.21	15	31	23.19±4.529	0.000
Serum FBS (mg/dL)	166	181	172.96±3.67	167	181	172.62±3.243	0.107
Serum HbA1C (%)	8.5	9.9	9.315±0.358	8.7	9.9	9.298±0.328	0.531
Serum Ca++ (mg/dL)	8.6	9.9	8.955±0.280	8.6	9.9	8.940±0.226	0.599
Serum PO4 (mg/dL)	2.5	27	3.692±3.33	2.5	4.3	3.226±0.507	0.324
Serum PTH (pg/ml)	15	51	27.96±9.59	15	51	27.83±9.158	0.367

Table 3: Effect of oral vitamin D supplementation in type 2 diabetes patients at baseline and 4 months

Parameter	(Baseline) Values			(After 4 months) Values			P value
	Minimum	Maximum	Mean value	Minimum	Maximum	Mean value	
Serum 25-OHD (ng/ml)	7.0	29	18.751±6.21	39	52	46.00 ± 4.159	0.000
Serum FBS (mg/dL)	166	181	172.96±3.67	129	150	140.73±4.907	0.000
Serum HbA1C (%)	8.5	9.9	9.315±0.358	6.7	8.0	7.260±0.286	0.000
Serum Ca++ (mg/dL)	8.6	9.9	8.955±0.280	8.60	9.80	8.959±0.253	0.921
Serum PO4 (mg/dL)	2.5	27	3.692 ± 3.33	2.50	4.50	3.286±0.548	0.397
Serum PTH (pg/ml)	15	51	27.96 ± 9.59	16	52	28.9± 9.572	0.493

Table 4: Effect of oral vitamin D in type 2 diabetes patients at baseline and 6 months

Parameter	(Baseline) Values			(After 6 months) Values			P value
	Minimum	Maximum	Mean value	Minimum	Maximum	Mean value	
Serum 25-OHD (ng/ml)	7.0	29	18.751±6.21	40	52	46.40±3.996	0.000
Serum FBS (mg/dL)	166	181	172.96±3.67	132	149	130±4.0	0.000
Serum HbA1C (%)	8.5	9.9	9.315±0.358	6.9	7.7	6.7±0.2	0.000
Serum Ca++ (mg/dL)	8.6	9.9	8.955±0.280	8.60	9.70	8.950±0.235	0.880
Serum PO4 (mg/dL)	2.5	27	3.692±3.33	2.60	4.40	3.284±0.497	0.394
Serum PTH (pg/ml)	15	51	27.96±9.59	17	51	28.87±9.326	0.501

In this context, the outcomes of the current study were consonant with plenty of other studies in which there was a momentous progress in both fasting blood glucose and HbA1C levels in a patient with diabetes mellitus type 2. However, no such study was previously reported for population in Karachi in this respect.

Previous literature studies on hundred patients of diabetes mellitus type 2 have reported that after the supplementation with fifty thousand (50000) IU (international units) of vitamin D in these patients, there was a considerable reduction in levels of fasting blood sugar (Talaei *et al*., 2013).

Another study conducted in India showed a significant reduction in HbA1C values compared to those not on vitamin D supplementations in all the patients who were previously either severely, moderately, or mildly deficient in vitamin D (Sripathi *et al*., 2011).

A study concluded that there is no direct relation of vitamin D and HbA1C before the vitamin D supplementation (i.e.50000 units/week for 12 weeks). However, after 12 weeks of supplementation, it was found that it had a significant beneficial effect on lowering HbA1C levels in diabetes mellitus type 2 (Nasri *et al*., 2014).

One of the meta-analysis of vitamin D also discovered that vitamin D can improve metabolic parameters such as resistance of insulin and beta-cell functions and glycemic controls (Haroon *et al*., 2015).

The calcium levels during the study were evaluated to rule out the possibility of hypercalcemia may be attributable to hyperparathyroidism or toxicity after administration of vitamin D. During the current study, the total calcium levels remained between the usual range at the baseline and the end of the research. These results were consonant to those obtained after a study (Gouda *et al*., 2019).

A momentous fall in HbA1C levels was detected in diabetes mellitus type 2 patients having vitamin D<15 mg/ml in the literature studied (Krul-Poel *et al*., 2015). It was also noted that vitamin D levels were highly improved after 16 weeks of administration of vitamin D orally. Overall, 100% of patients showed an increased levels of 25 (OH) D which are upto 30mg/ml.

In the context of safety and toxicity of vitamin D, there were no unwanted side effects or any symptom of toxicity during the period of research and even after the research. This might be because of inclusion of only vitamin D deficit patients who remained on vitamin D supplementation for only 6 months of period.

CONCLUSION

The above study confirms the role of oral vitamin D effect in type 2 diabetes patients. This can be very beneficial for those patients who are vitamin D deficient and suffering from diabetes too. As majority of our population is suffering from both these disorders so the study results can provide a great treatment regime for these patients. Furthermore the Type II diabetes patients can be tested for Vitamin D deficiency too as one of the risk factors which can lead to better prognosis.

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