ROLE OF VITAMIN D ON HbA1c LEVEL, AS AN ADJUVANT TO ORAL HYPOGLYCAEMIC DRUGS IN TYPE 2 DIABETIC PATIENTS

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ABSTRACT

BACKGROUND
The incidence of type 2 diabetes mellitus is increasing at an alarming rate both nationally and internationally with more than 1 million new cases diagnosed every year. Diabetes warrants intense lifestyle adaptations, polypharmacy and insulin centred regimens. Conventional oral antidiabetic medications are associated with hypoglycaemias. Besides insulin, treatment has been linked to poor compliance, weight gain and possibly adverse cardiovascular outcomes. The role of vitamin D in the pathogenesis and prevention of diabetes has sparked widespread interest. Vitamin D receptors are present in both pancreatic beta-cells and immune cells. Besides its classical role as the major regulator for calcium absorption, vitamin D mediates the activity of β-cell calcium-dependent endopeptidases, promotes conversion of pro-insulin to insulin and increases insulin output.

Objective of this study is to see the effect of vit D on HbA1c level, as an adjuvant to oral hypoglycaemic drugs (of any class) in type 2 diabetic patients.

MATERIALS AND METHODS
Sixty patients (previously known cases of type 2 DM) aged above 18 years, attending Medicine OPD of Rama Medical College Hospital & Research Centre, Kanpur, over a period of one year were included in the study. The eligible patients (N=60) based on inclusion and exclusion criteria were divided in two groups of 30 patients in each group: group A (control group) on oral hypoglycaemic drugs without vit D supplementation & group B (study group) on oral hypoglycaemic drugs with vit D supplementation. The patients were randomly selected and the vit D supplementation was given on the basis of physician’s direction and the dose of vit D (2000 IU orally) was fixed at the time of the inclusion in the study. Patients were then followed up for a period of 3 months.

RESULTS
On day 0, mean of fasting blood sugar levels in control group and in study group was 155.17 mg/dL ± 9.07 mg/dL and 152.13 mg/dL ± 3.45 mg/dL and mean of postprandial blood sugar levels in control group and in study group was 200.07 mg/dL ± 12.69 mg/dL and 197.37 mg/dL ± 5.40 mg/dL respectively (Table No. 1A) and on day 90, mean of fasting blood sugar levels in control group and in study group was 159.47 mg/dL ± 8.90 mg/dL and 120.10 mg/dL ± 21.99 mg/dL and mean of postprandial blood sugar levels in control group and in study group was 205.00 mg/dL ± 12.09 mg/dL and 160.17 mg/dL ± 22.43 mg/dL respectively (Table No. 1B) respectively. Mean HbA1c in control group on day 0 was 6.457 mg/dL ± 0.778 mg/dL and on day 90 was 6.873 mg/dL ± 0.699 mg/dL and in study group on day 0 was 6.403 mg/dL ± 0.65 mg/dL and on day 90 was 5.61 mg/dL ± 0.533 mg/dL (Table No. 2). The difference in mean of HbA1c level in both the groups was p <.001 which is highly significant, means that vitamin D therapy has had beneficial effect on the control of blood sugar in diabetic patients.

CONCLUSION
HbA1c level in patients included in the study was significantly better on day 90 as compared to day 0 & the blood sugar levels (both fasting and postprandial) were improved in the study group significantly.

KEYWORDS
Type 2 diabetes mellitus, Vitamin D.


BACKGROUND
The incidence of type 2 diabetes mellitus is increasing at an alarming rate both nationally and internationally with more than 1 million new cases diagnosed every year. Despite the advancements in the diagnosis and management of diabetes, achieving normoglycaemia or optimal glycaemic control is still considered challenging. This is because care of type 2 diabetes warrants intense lifestyle adaptations, polypharmacy and insulin centred regimens. Conventional oral antidiabetic medications are associated with hypoglycaemias. Besides insulin, treatment has been linked...
to poor compliance, weight gain and possibly adverse cardiovascular outcomes. The role of vitamin D in the pathogenesis and prevention of diabetes has sparked widespread interest. Vitamin D receptors are present in both pancreatic beta-cells and immune cells. Beside its classical role as the major regulator for calcium absorption, vitamin D mediates the activity of β-cell calcium-dependent endopeptidases, promotes conversion of proinsulin to insulin and increases insulin output. In peripheral insulin target tissues, vitamin D enhances insulin action via regulation of the calcium pool. The effect of vitamin D on insulin secretion may be mediated by changes in intracellular calcium concentration in β-cells.

Vitamin D is not only essential for maintaining bone health, but it also plays a role in several other biochemical mechanisms within the human body. The mechanism of action of the active form of vitamin D is similar to that of other steroid hormones and is mediated by its binding to vitamin D receptor (VDR). VDRs are found in most tissues, not just in those that participate in the classic actions of vitamin D such as bones, intestines and kidneys. The enzyme responsible for converting 25 (OH) D to 1, 25 (OH) 2D is also expressed in a variety of extrarenal sites, such as endothelial cells, beta cells and immune cells.

Studies suggest an inverse association between vitamin D status and glucose intolerance/type 2 diabetes. Accumulating evidences suggest that vitamin D deficiency is associated with increased risk for diabetes. Hypovitaminosis D is a risk factor for glucose intolerance and diabetes. Vitamin D deficiency appears to be related to the development of type 2 diabetes mellitus. Mild-to-moderate vitamin D insufficiency has been proposed as a risk factor for type 2 diabetes. Higher plasma vitamin D has been shown to be related with a lower risk for the development of diabetes mellitus in high risk patients.

So, with this background the present study is being undertaken to see the effect of vitamin D in glycaemic control in type 2 diabetic patients on oral hypoglycaemic drugs.

MATERIAL AND METHODS

Study Setting
This study was conducted in the Department of Pharmacology and General Medicine, Rama Medical College Hospital and Research centre – Mandhana, Kanpur.

Study Design
Descriptive Study
This study is a prospective, open label, randomised control trial done in the Department of Pharmacology and General Medicine, Rama Medical College Hospital and Research Centre Kanpur, over a period of twelve months. 60 subjects of type 2 diabetes mellitus were recruited from Medicine OPD after taking informed consent.

Study Population
Study was conducted over a period of twelve months. 60 subjects of type 2 diabetes mellitus were recruited from the Department of Medicine OPD at Rama Medical College Hospital.

Inclusion Criteria
1. Patients of both sexes aged between 30 years to 60 years.
2. Established diagnosis of Type 2 DM, without complications.
3. Patients without any concurrent illness.

Exclusion Criteria
1. Patients diagnosed as Type 1 DM.
2. Patients on vitamin D supplementation for last 12 weeks.
3. Patients with any acute or long term comorbidity.
4. Pregnant or lactating women.

Collections
Blood sample was collected from the patients followed for both fasting and postprandial blood sugar levels every fortnightly.

Study Duration
Study was conducted over a period of twelve months.

Sampling and Sample size
Statistical Analysis- The treatment groups were compared and the results were analysed by using Unpaired t test on SPSS 21 trial version.

\[
\begin{align*}
\text{n} & \geq \frac{(s.d_1^2 + s.d_2^2) (z_\alpha + z_\beta)^2}{(S.E \text{ of difference})^2} \\
& = \frac{(4^2 + 1.2^2) (2.8)^2}{(1.1)^2} \\
& = 29.58 \approx 30 \text{ for each group}
\end{align*}
\]

n = no. of sample in study for each group
\(z_\alpha = .84\)
\(z_\beta = 1.9\)
d = 1.1


Sampling and Sample Size
60 type 2 diabetic patients attending medicine OPD were randomly divided into two groups by card system and 30 cards per group.
- Group A- (Control group)- 30 Type 2 diabetic patients on oral hypoglycaemic drugs without vitamin D supplementation.
- Group B- (Study group)- 30 Type 2 diabetic patients on oral hypoglycaemic drugs with vitamin D supplementation.

Estimation of HbA1c
Various methods for detection of glycosylated Hb:
2. Column chromatography technique. This method is very slow.
3. High performance liquid chromatography method (HPLC) for HbA1c level. The method has been used in this study.

Method of Collection of Data
All the eligible patients underwent both routine and specific investigations (HbA1c level) on the first visit. The study group (group B) were prescribed Vitamin D 2000 IU orally daily for twelve weeks (as prescribed by the physician). Patients were followed for both Fasting and postprandial blood sugar levels every four weeks. At the end of the therapy (After 12 weeks) again patients underwent both routine and specific investigations and were compared from the baseline (day 0). The cases were followed for compliance with the therapy and adverse drug reactions if any on each follow up visit.

Ethical Issues
The study was started after approval from the institutional ethical committee.

RESULTS
On day 0, mean of fasting blood sugar levels in control group and in study group was 155.17 mg/dL ± 9.07 mg/dL and 152.13 mg/dL ± 3.45 mg/dL and mean of postprandial blood sugar levels in control group and in study group was 200.07 mg/dL ± 12.69 mg/dL and 197.37 mg/dL ± 5.40 mg/dL respectively (Table No. 1A) and on day 90, mean of fasting blood sugar levels in control group and in study group was 159.47 mg/dL ± 8.90 mg/dL and 120.10 mg/dL ± 21.99 mg/dL and mean of postprandial blood sugar levels in control group and in study group was 205.00 mg/dL ± 12.09 mg/dL and 160.17 mg/dL ± 22.43 mg/dL respectively (Table No. 1B).

Mean HbA1c in control group on day 0 was 6.457 mg/dL ± 0.778 mg/dL and on day 90 was 6.873 mg/dL ± 0.699 mg/dL and in study group on day 0 was 6.403 mg/dL ± 0.65 mg/dL and on day 90 was 5.61 mg/dL ± 0.533 mg/dL (Table No. 2).

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Table 1A. Relationship between Fasting and Postprandial Levels in Control and Study Group (day-0)

The difference in mean HbA1c level was p < 0.001 which is highly significant.

DISCUSSION
Hypovitaminosis D is a risk factor for glucose intolerance and diabetes. Mild-to-moderate vitamin D insufficiency has been proposed as a risk factor for type 2 diabetes. Higher plasma vitamin D level has been shown to be related with a lower risk of the development of diabetes mellitus in high risk patients. Vitamin D improves insulin sensitivity by its anti-inflammatory activity. Currently vitamin D is called as “Sunshine Hormone”. Major amount of vitamin D is synthesised by the skin on exposure to UVB rays. There is...
a growing global concern about the deficiency of vitamin D. The best marker for vitamin D status is 25 hydroxyvitamin D [25 (OH)D]. Vitamin D receptors are present in both pancreatic beta-cells and immune cells. From a biological perspective, the presence of the vitamin D receptor in many cell types and organs, and the local production of 1, 25 (OH)2D in several extrarenal organs, including β-pancreatic cells, supports potential broad-ranging effects of vitamin D outside of skeletal health, including type 2 diabetes. Vitamin D is thought to have both direct (by the activation of the vitamin D receptor) and indirect (by the regulation of calcium homeostasis) effects on various mechanisms related to the pathophysiology of type 2 diabetes, including impaired pancreatic-β cell function and insulin resistance. Found an inverse relation between 25 (OH) vitamin D concentration and FPG, but a direct relation with insulin sensitivity. As to these studies, our study shows that mean FPG and mean HbA1c was significantly reduced after increased vitamin D intake. The main purpose of this study was to investigate the effects of vitamin D supplementation on glucose homeostasis. The results showed that vitamin D supplementation significantly decreased serum FPG, insulin in patients with T2DM. Thus, showing an inverse relation between final FPG and basal 25 (OH) D concentration. In other words, higher serum basal 25 (OH) D led to lower final FPG. This showed that patients who had a higher serum basal 25 (OH) D concentration benefited more of vitamin D intake to lowering final FPG. This may be because of non-skeletal effects of vitamin D which appears in higher vitamin D concentration and the effects of lower vitamin D concentration are limited to the bone and muscles. The rationale of addition of vit D in the present study was based on inadequate glycemic control with oral hypoglycaemic drugs. The dose of vit D was fixed (2000 IU/Day) throughout the study period after the selection of patients as per their clinical presentation at the time of start of study. Mean HbA1C in control group on day 0 was 6.457 mg/dL ± 0.778 mg/dL and on day 90 was 6.873 mg/dL ± 0.699 mg/dL and in study group on day 0 was 6.403 mg/dL ± 0.65 mg/dL and on day 90 was 5.61 mg/dL ± 0.533 mg/dL(Table No. 2). The difference in mean HbA1C level was p <0.01 which is highly significant. The findings of this study indicate that the metabolic profile of T2DM subjects is significantly improved after the onset of vitamin D supplementation. To conclude, the add on therapy was seen to be effective in lowering the blood glucose level (both fasting and postprandial) along with reduction in HbA1c when used in combination therapy with vitamin D over a period of three months in type 2 diabetic subjects. The benefit seen in blood glucose control was highly significant in both the groups. In view of the positive effects seen in all parameters with the use of combination therapy, it can be assumed that if the therapy had been continued for a longer duration, even better results would have been seen. Moreover, this combination therapy was safe and no serious adverse events were reported in the study.

CONCLUSION

HbA1c level in patients included in the study was significantly better on day 90 as compared to day 0 and the blood sugar levels (both fasting & postprandial) were also improved significantly in the study group. There was no intergroup difference in the level of HbA1c. No serious adverse events were reported in the study. This indicates the potential of this supplementation in the treatment of type 2 diabetes and may halt the progression of disease-related complication because of controlling the blood glucose levels at optimal levels.

REFERENCES