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(RESEARCH ARTICLE)

To assess the incidence of vitamin D deficiency in patients receiving OHA, with comparison of metformin vs non-metformin groups

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Abstract

If gastrointestinal symptoms from metformin use can create an environment conducive to the malabsorption of vitamin B12, it Is probable that vitamin D could also be malabsorbed. This could adversely affect treatment efficacy as well as expose certain patient populations to the risk of symptoms of vitamin D deficiency. Currently, no published studies have examined the effect of metformin on vitamin D levels in a population of patients with diabetes.

Hence, this study focuses on the incidence of deficiencies of vitamin D in patients with type 2 diabetes on treatment with metformin (Biguanide) and compare with those on other OHAs.

Keywords: Buguanide; Hypovitaminosis D; Fatigue; Type 2 diabetes mellitus

1. Introduction

Type 2 diabetes mellitus currently affects 8.3% of the world's population. This disease has substantial associated morbidity and mortality, with the potential to affect adversely the cardiovascular, renal, and neurologic systems of each person with the disease (1).

Treatment of type 2 diabetes includes many options such as lifestyle changes, a variety of medications, and insulin. One medication that has proved effective in treatment of type 2 diabetes and is considered the first choice for oral management, as recommended by the American Diabetes Association, is a drug in the biguanide class, metformin. Metformin acts through multiple mechanisms including decreasing hepatic glucose output, increasing insulin-mediated glucose use in peripheral tissues, and increasing intestinal glucose utilization. Most side effects of metformin are mild and can include gastrointestinal distress, soft stools, and diarrhea (2). It is well documented that these gastrointestinal side effects can lead to malabsorption of vitamins in a dose- and time-dependent manner (3,4). Although the clinical significance of short-term treatment is variable, it has been recommended that those receiving long-term treatment undergo screening (5).

Vitamin D has a small but important role in diabetes. Investigators have suggested that an association exists between decreased vitamin D and calcium status and the risk of type 2 diabetes as well as between vitamin D deficiency and impaired glucose-mediated insulin release (6,7). Vitamin D is produced endogenously when ultraviolet rays initiate synthesis in the skin, but vitamin D is also absorbed in the intestine from various natural and fortified food sources(8). If gastrointestinal symptoms from metformin use can create an environment conducive to the malabsorption of vitamin B12, it Is probable that vitamin D could also be malabsorbed. This could adversely affect treatment efficacy as well as

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expose certain patient populations to the risk of symptoms of vitamin D deficiency. Currently, no published studies have examined the effect of metformin on vitamin D levels in a population of patients with diabetes.

Hence, this study focuses on the incidence of deficiencies of vitamin D in patients with type 2 diabetes on treatment with metformin (Biguanide) and compare with those on other OHAs.

2. Materials and methods

2.1. Source of data

The is a prospective case control study that was was carried out in a medical College affiliated to a tertiary care center for period of 2 years from October 2022 to October 2023.The study was designated as a case control study. 30 patients were on Metformin (CASES) and the other 30 were on other anti-diabetic drugs (Sufonylureas, Acarbose and Pioglitazone)(CONTROLS) with age and sex matched, fulfilling the inclusion and exclusion criteria.

2.1.1. Inclusion Criteria

- AGE > 30 years
- Type2 DM patients who are on metformin therapy for more than 6 months.

2.1.2. Exclusion criteria

- AGE < 30 years
- Type1 DM patients
- Patients who are on vitamin D supplementation
- Patients who are on vitamin B12 supplementation
- Patients who are on steroid therapy, oral contraceptive pills and diuretics
- Pregnancy
- Critically ill patients
- Patients with tuberculosis
- Patients with renal impairment

2.2. Method of collection of data

A detailed proforma was filled up for each patient,which included age,sex,IP and OP number, relevant present, past ,personal history and clinical examination was done.

Anthropometric measurements like height and weight were measured and BMI was calculated for each patient in the study group.Venous plasma glucose was measured both fasting and prandial (120 min after a 75 g glucose load). HbA1C was measured by high performance liquid chromatography method.

2.3. Measurement of serum 25-(OH) vitamin D

Serum 25-hydroxyvitamin D concentration was measured in samples stored at -20 °C collected from both cases and controls. Serum 25-(OH) vitamin D was measured by Radioimmunoassay method.

2.4. Statistical methods applied

2.4.1. Descriptive

The Descriptives procedure displays univariate summary statistics for several variables in a single table and calculates standardized values (z scores). Variables can be ordered by the size of their means (in ascending or descending order), alphabetically, or by the order in which you select the variables (the default).

2.4.2. Independent-Samples T Test

The Independent-Samples T Test procedure compares means for two groups of cases. Ideally, for this test, the subjects should be randomly assigned to two groups, so that any difference in response is due to the treatment (or lack of treatment) and not to other factors. This is not the case if you compare average income for males and females. A person is not randomly assigned to be a male or female. In such situations, you should ensure that differences in other factors

are not masking or enhancing a significant difference in means. Differences in average income may be influenced by factors such as education (and not by sex alone).

3. Results

In this study, 25(OH)- Vitamin- D and B12 levels were done in 60 type 2 diabetic patients of which 30 patients were on Metformin(CASES) and 30 patients were on anti-diabetic drugs other than Metformin(Sulfonylureas, Acarbose, Pioglitazone)(CONTROLS).Age and sex were matched in the above groups.

In this study, the study group constituted cases between the ages 32-90 years. Majority of the cases and controls were less than 65 years of age which constituted to 66.6% of the total group.

In this study, 53.3% were males and 46.7% were females in both the groups.

In this study, the mean age of the cases was 57.8±16.15 (SD) years and of the controls was 58.7±10.47(SD) years.

Table 1 BMI correlation between the groups

			GROUP		Total
			Case	Ctrl	
BMI	**<25**	**Count**	15	12	27
		% of GROUP	50.0%	40.0%	45.0%
	>25	**Count**	15	18	33
		% of GROUP	50.0%	60.0%	55.0%
Total		**Count**	30	30	60
		% of GROUP	100.0%	100.0%	100.0%

In this study, mean FBS among the cases was 120.63±34.62(SD) mg/dl whereas that of controls was 149.9±42.47(SD)mg/dl. In this study, the mean PPBS among the cases was 184.2±56.09(SD) mg/dl,whereas among the controls was 215.33±67.35 (SD)mg/dl.

In this study, the mean HbA1C among the cases was 6.76±1.3 (SD)%, whereas among the controls was 7.15±1.32 (SD) %.

In this study, the mean S. Creatinine among the cases was 0.89±0.14 (SD) mg/dl, whereas among the controls was 1.03±0.19 (SD) mg/dl

Table 2 Vitamin-D levels among cases and controls

	Group	N	Mean	Std. Deviation	Std. Error Mean
Vit-D	Case	30	15.1497	4.73958	0.86533
	Control	30	17.8077	7.05819	1.28864

p-value 0.092

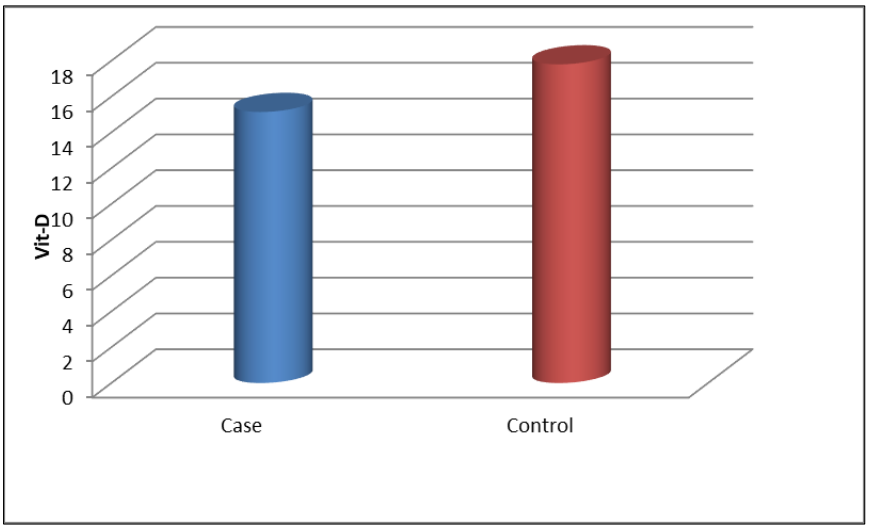

Figure 1 Vitamin-D levels among cases and controls

In this study, the mean vitamin-D levels among the cases was 15.14±4.73 (SD) ng/ml, whereas among the controls was 17.8±7.05 (SD) ng/ml.

Table 3 Classification of cases and controls in terms of Vit-D levels

Vitamin-D (ng/ml)	Cases	Controls	Total
<20 (deficient)	25 (41.66)	20 (33.33)	45 (75)
20-29.9 (Insufficient)	5 (8.33)	8 (13.3)	13 (21.66)
>30 (Sufficient)	0 (0)	2 (3.33)	2 (3.33)
Total	30	30	60

*number in bracket indicates %

In this study, among the cases 83.32% were Vitamin-D deficient, 16.66% were insufficient and 0% were sufficient. Among the controls, 66.66% were deficient, 26.6% were insufficient and 6.66% were sufficient.

Also, as a whole, 75% were Vitamin-D deficient, 21.66% were insufficient and 3.33% were sufficient

4. Discussion

In the present study, serum 25(OH)-Vitamin D and B12 levels were estimated in type 2 diabetic patients of which 30 patients were on Metformin (CASES) and the other 30 were on other anti-diabetic drugs(Sufonylureas, Acarbose and Pioglitazone)(CONTROLS) with age and sex matched, fulfilling the inclusion and exclusion criteria.

4.1. Age distribution of cases and controls

In this study, the study group constituted cases between the ages 32-90 years. Majority of the cases and controls were less than 65 years of age which constituted to 66.6% of the total group. The mean age of the cases was 57.8±16.15 (SD) years and of the controls was 58.7±10.47(SD) years. This was similar to the findings of R Anil Kumar et al (9)

4.2. Sex wise distribution of the cases and controls

In this study, 53.3% were males and 46.7% were females in both the groups. The males and females were almost equally distributed with a male to female ratio of 1.14:1. This was corroborating with the findings of R Anil Kumar et al (9) and Elizabeth Kos et al (10).

4.3. Vitamin-D levels among cases and controls

In this study, among the cases 83.32% were Vitamin-D deficient, 16.66% were insufficient and 0% were sufficient. Among the controls, 66.66% were deficient, 26.6% were insufficient and 6.66% were sufficient.

Also, as a whole, 75% were Vitamin-D deficient, 21.66% were insufficient and 3.33% were sufficient

According to a south Indian study, Vitamin D deficiency was present in 83% of type 2 diabetes individuals and 82% of normal individuals. So both south Indian type2 and non type 2 diabetes individuals are equally deficient in vitamin D.[9]

However in a study by Elizabeth Kos et al, vitamin D deficiency is not a clinical concern among metformin-treated patients with type 2 diabetes and that metformin does not negatively affect treatment of vitamin D deficiency in these patients. (10)

Additionally in a study by S S Zharghani et al (11), they found that combining vitamin D with Metformin can help combat insulin resistance and diabetes mellitus in the obese diabetic patients.

Similarly, Khalid M Alkharfy and team (12), Metformin improves 25-hydroxyvitamin D levels but did not seem to confer other added cardiometabolic benefits.

5. Conclusion

This study also suggests that vitamin D deficiency is not a clinical concern among Metformin-treated patients with type 2 diabetes. Also, Vitamin D deficiency is common among Indian type 2 diabetics and general population.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

Ethical approval sougt.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] National Diabetes Information Clearinghouse (NDIC). National Diabetes Statistics, 2011. NIH publication no. 11-3892, February 2011. http://diabetes.niddk.nih.gov/dm/pubs/statistics/. Accessed for verification October 5, 2011.

[2] Nathan DM, Buse JB, Davidson MB, et al. Management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy, a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes [published correction appears in Diabetes Care. 2006, 29:2816-2818]. Diabetes Care. 2006, 29:1963-1972.

[3] Ting RZ, Szeto CC, Chan MH, Ma KK, Chow KM. Risk factors of vitamin B12 deficiency in patients receiving metformin. Arch Intern Med. 2006, 166:1975-1979.

[4] Tomkin GH, Hadden DR, Weaver JA, Montgomery DA. Vitamin B12 status of patients on long-term metformin therapy. Br Med J. 1971, 2:685-687.

[5] Mittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes: a systemic review and meta-analysis. J Clin Endocrinol Metab. 2007, 92:2017-2029.

[6] Chiu KC, Chu A, Go VL, Saad MF. Hypovitaminosis D is associated with insulin resistance and beta cell dysfunction. Am J Clin Nutr. 2004, 79:820-825.

[7] National Institutes of Health (NIH) Office of Dietary Supplements. Dietary supplement fact sheet: vitamin D. http://ods.od.nih.gov/factsheets/VitaminD_pf.asp. Accessed for verification October 5, 2011.

[8] Laurence L. Brunton, Endocrine Pancreas and Pharmacotherapy of Diabetes Mellitus and Hypoglycemia. In Goodman & Gilman's The Pharmacological Basis of Therapeutics. Twelfth Edition. The McGraw-Hill Companies, Inc

[9] R. Anil Kumar, R. Lalitha, Surekha B. Shetty. A comparative study to determine vitamin D status in type 2 diabetes and normal subjects in south India. Int J Med Res Rev 2017, 5(10): 888-893.doi:10.17511/ijmrr. 2017.i10.03.

[10] Kos, E., Liszek, M. J., Emanuele, M. A., Durazo-Arvizu, R., & Camacho, P. (2012). Effect of metformin therapy on vitamin D and vitamin B_{12} levels in patients with type 2 diabetes mellitus. Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists, 18(2), 179–184. https://doi.org/10.4158/EP11009.OR

[11] Shojaei Zarghani S, Abbaszadeh S, Alizadeh M, Rameshrad M, Garjani A, Soraya H. The Eeffect of Metformin Combined with Calcium-Vitamin D3 Against Diet-Induced Nonalcoholic Fatty Liver Disease. Adv Pharm Bull. 2018 Mar, 8(1):97-105. Doi: 10.15171/apb.2018.012. Epub 2018 Mar 18. Erratum in: Adv Pharm Bull. 2021 Jan, 11(1):205. PMID: 29670844, PMCID: PMC5896400.

[12] Alkharfy, K.M., Al-Daghri, N.M., Sabico, S.B. et al. Vitamin D supplementation in patients with diabetes mellitus type 2 on different therapeutic regimens: a one-year prospective study. Cardiovasc Diabetol 12, 113 (2013). https://doi.org/10.1186/1475-2840-12-113