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The comparative assessment of vitamin D supplement on glycemic indices in autoimmune diseases

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ABSTRACT

Vitamin D deficiency is common among diabetes mellitus and type 2 and multiple sclerosis patients. Type 2 diabetes is recognized by both insulin resistance and β-cell dysfunction. Vitamin D may treat diabetes according to recommended possible effect of vitamin D on glucose homeostasis. Existing evidence implies a possible connection between disturbed glucose metabolism and MS pathogenesis. The aim of the present study was to compare the effect of complementary vitamin D supplementation on glycemic indices between MS and diabetes type 2 patients. Method: MS and diabetes type 2 patients were divided into 2 groups (group1=40 patients with MS, group 2=40 patients with type 2 diabetes mellitus). Both groups were treated by vitamin D injection (300,000 units every 2 weeks for a period of 8 weeks). Glycemic Indies and serum levels of vitamin D were measured and compared before and after the treatment.

Results: significant increase in vitamin D levels was seen in both groups particularly in diabetic patients. Significant relationship was found between serum levels of vitamin D and HbA1C in patients with diabetes. There was no relationship between serum levels of vitamin D and lipid profile. Conclusion: vitamin D supplements, is more effective on glycemic indices and serum levels of vitamin .D in patients with Type 2 Diabetes than in MS patients.

Keywords: *multiple sclerosis, vitamin D, glycemic indices, Type 2 diabetes*.

1. INTRODUCTION

Vitamin D is a fat-soluble vitamin[1, 5], which its deficiency is widespread[2, 20]. in recent years, due to the discovery of additional biological actions of vitamin D beside its traditional role in bone and mineral metabolism it became a research topic of interest [3, 4] observational studies have revealed an inverse association between vitamin D status and the risk of cancer, diabetes, and certain autoimmune diseases[4, 6]. Diabetes is the most common metabolic disease worldwide. Globally, as of 2010, an estimated 285 million people had diabetes, with type 2 making up about 90% of the cases [1]. About six people approximately die every minute because of type 2 diabetes mellitus worldwide [5, 10] Type 2 diabetes mellitus is a progressive chronic disease recognized by both insulin resistance and β-cell dysfunction [6, 21]. beta-cells in the pancreas are vitamin D receptor-containing cells in type 2 diabetes mellitus which implies the possible effect of vitamin D on glucose homeostasis [7, 33]. Low vitamin D levels are common in patients with type 2 diabetes [8, 7].studies have identified relationship of vitamin D deficiency with changes in blood glucose and insulin levels, and insulin sensitivity of target tissues. Vitamin D may also treat diabetes by increasing insulin sensitivity and secretion [8-10]. several cross-sectional studies have shown an inverse relationship between serum vitamin D 25(OH)D and glycemic status measures, such as oral glucose tolerance tests, hemoglobin A1c [HbA1c], fasting plasma glucose, and insulin resistance [11-18]. Moreover, vitamin D deficiency is commonly linked to a status of hypocalcaemia that can cause a decrease in glucose-stimulated insulin secretion in β-cell[19]. Data on the effects of vitamin D supplementation in patients with type 2 diabetes are unclear. A number of studies failed to show any improvement in glycemic control or indices of insulin sensitivity during supplementation [20-24].

Multiple sclerosis [MS] is the most common demyelinating disease of the central nervous system [23, 2]. It affects about 2.5 million people worldwide and is the most common cause of neurologic disability in young and middle-aged adults[24, 3]. Vitamin D deficiency is currently one of the most studied risk factors for multiple sclerosis [25]. oligodendrocytes in the brain in MS are vitamin D receptor-containing cells[26, 34].One of the mentioned additional biological actions of vitamin D is modulatory effects on neurotrophins, and neurotransmitters in the CNS of mammals. In general, 1,25-(OH)2D seems to be neuroprotective and anti-inflammatory [27, 35]. As, Some studies support a protective role for vitamin D in MS development [28] [26]. It has been shown that administration of the biologically active hormone 1, 25-dihydroxyvitamin D prevents EAE onset and progression in mice [29, 27]. Patients with MS are often exposed to corticosteroid treatment and conflicting reports exist regarding complications of corticosteroid [30, 48] .A common side-effect of these drugs is their propensity to cause hyperglycemia [31, 47]. Existing evidence hints to a possible connection between disturbed glucose metabolism and MS pathogenesis [32, 41]. an inhibitory

effect of a low glucose level on myelin protein production has been reported [33, 54]. Glucose hemostasis in MS patients and the effect of vitamin D therapies on it, needs to be more investigated.

In this study, we attempted to compare the effect of vitamin D supplement on glycemic indices changes among Type 2 Diabetes Mellitus patients and Multiple Sclerosis Patients.

2. EXPERIMENTAL SECTION

2.1. Study Population. We performed a double-blind randomized clinical trial study. 40 patients with type 2 diabetes mellitus, referred to Al-Zahra hospital, and 40 patients, referred to MS clinic of Kashani hospital, with Relapsing-Remitting Multiple Sclerosis(All aged 25-50). Patients which their vitamin D levels were less than 20 ng /ml, and their HbA1C was between 7% to 8%, definitively diagnosed with type 2 diabetes or multiple sclerosis patients based on standard criteria were included in the study. Patients were excluded if they had a history of taking vitamin D supplements for 6 months or taking insulin. Also patients with any thyroid, kidney or liver diseases were excluded.

Written informed consent was obtained from all participants. Patients were divided in two groups according to their disease (group1=40 patients with multiple sclerosis, group 2=40 pateints with type 2 diabetes mellitus).

2.2. Measurments and interventions. Serum 25(OH)D levels were measured in all patients. Then both groups were treated by vitamin D injection 300,000 units every 2 weeks for a period of 8 weeks. Fasting blood sugar, 2 hour postprandial blood sugar, lipid profile (total cholesterol, triglycerides, HDL) as well as HbA1C in all patients were measured before and after 8 weeks of treatment with vitamin D.

We attempted that in all subjects, diabetes control, diet and activity levels stay almost in an identical range.

Stat fax 2100 (made in the United States of America) , was used for measuring the serum levels of vitamin D 25(OH). HbA1C was measured using column chromatography. Erba – XL 300 was used to measure Fasting blood sugar and 2 hour postprandial blood sugar. Serum lipids were measured by Pars diagnostic test kits made in Germany.

2.3. Data analysis. The collected data was analyzed by the SPSS (18). To compare serum levels of vitamin D and glycemic indices between MS and diabetes patients, Tukey test was used. Pearson correlation study with qualitative variables were analyzed by chi-square.

3. RESULTS SECTION

In this study 80 patients with type II diabetes and MS were divided into two groups. There were no significant differences between the groups in terms of age, sex and body mass. Prior to intervention, the mean serum levels of vitamin D in MS patients were significantly lower than in patients with type 2 diabetes (6/3 ± 5/12 comparing to 03/4 ±3/21)($p<0.01$).After eight weeks of treatment with vitamin D significant increase in vitamin D levels was seen in both groups particularly in diabetic patients.(8/10± 6/75 comparing to 03/8 ±8/45) ($p<0.01$) (Table 1).

Significant relationship was found between serum levels of vitamin D and HbA1C in patients with diabetes. There was no relationship between serum levels of vitamin D and lipid profiles.

Table 1. Laboratory parameters of both groups before and after intervention.

Measuring stage	baseline	baseline		After intervention	After intervention		P value (before and after)	P value (before and after)
group	MS	diabetes		MS	diabetes		MS	diabetes
Statistical Indicators	Mean ± SD	Mean ± SD	P value (between 2 groups)	Mean ± SD	Mean ± SD	P value (between 2 groups)		
25OHD (ng/ml)	12.5±3.6	21.38±4.03	0.01	45.8±8.30	75.6±10.8	0.03	0.04	0.035
HbA1C (mmol/l)	6.75±0.28	10.02±0.32	0.65	6.05±0.85	7.51±1.15	0.39	0.06	0.05
TG (mg/dL)	152.10±70.96	198.33±101.21	0.278	155.93±65.16	207.6±111.36	0.25	0.92	0.50
Total Cholesterol(mg/dL)	152.43±37.34	157.40±26.82	0.59	157.72±19.88	161.46±28.12	0.71	0.562	0.55
LDL(mg/dL)	78.46±31.52	77.54±35.13	0.344	81.96±35.31	87.50±35.17	0.65	0.78	0.60
HDL(mg/dL)	41.92±20.12	42.97±9.35	0.544	43.32±13.05	45.53±16.15	0.41	0.86	0.068

In this study, sugar and lipid profile of patients with multiple sclerosis and type II diabetic patients were measured before and after treatment with vitamin D and the changes was assessed. Patients of both groups had inadequate levels of serum vitamin D prior to intervention. Our findings showed a significant decrease in HbA1C levels, after treatment with vitamin D, especially in patients with diabetes. There are several studies supporting that vitamin D is an important nutrient in control of glucose homeostasis [34, 49, 50]. Yousefirad *et al*. [35, 51] reported beneficial effect of vitamin D supplementation in decreasing HbA1c in diabetic type 2 patients. Conversely, A RCT by Mitri *et al*. [36, 55] examining the effect of vitamin D supplementation in adults at high risk of diabetes concluded that short-term supplementation with cholecalciferol did not have a

significant effect on HbA1c. A meta-analysis in 2012 reported a small improvement on fasting glucose and insulin resistance but no beneficial effect was seen on HbA1c [37, 52]. Lower 25-hydroxy vitamin D levels are associated with poorer glycemic control [38, 28]. An inverse relationship between vitamin D levels and fasting blood glucose and postprandial blood sugar, was shown in nonobese nondiabetic patients by Champe *et al*. [45]. In addition to the cross-sectional studies, many studies have examined the effect of vitamin D and calcium supplementation on glycemic indices and they had conflicting results according to the study design, type, duration and form of intervention [39, 29]. Kamilia T *et al*. [40, 43] studied the effect of treatment with vitamin D on blood glucose and plasma insulin in nondiabetic patients with vitamin deficiency and reported no relationship between short time correction of vitamin D and glucose, insulin, or insulin sensitivity during oral glucose tolerance test.

Many studies have been conducted to study the hypothesis that vitamin D has a possible effect on glycemic indices control in diabetic patients but there is no study considering this possible effect in multiple sclerosis patients. Vitamin D is potentially the most promising in terms of new clinical therapeutic implications for MS. However, little is known about the role of perturbed glucose metabolism in MS pathology[32, 41]. A study indicates increased activity of extra-mitochondrial pathways of CNS glucose metabolism in individuals with MS [41, 42]. In the study of Ionescu *et al*. [42, 53] the integrated concentration of plasma glucose over long-term (the last 6-8 weeks) was established by measurement of the percent of the HbA1c and it was concluded that clinical activation in definite MS is not associated with disturbances of glucose metabolism. In the study of Richeh *et al*. a longitudinal relationship between the levels of glucose and progression of disability in patients with MS have been reported.

Our findings showed a lack of significant effect of vitamin D on lipid profiles. Similarly, results from systematic reviews of RCTs of vitamin D on lipids reported that viatmin D has no effect on total cholesterol, LDL-cholesterol, and HDL-cholesterol which was clearly consistent with our study [43, 44, 56, 57]. Conversely, study of Jorde *et al*. [45, 58] reported highly significant positive associations between serum 25(OH) D and serum TC, HDL-C and LDL-C which implies that high serum 25(OH)D concentration is associated with a desirable lipid profile.

Despite the very extensive studies on the impact of vitamin D on the control of hyperglycemia in diabetic patients, randomized double-blinded cohort studies that are well designed and detailed, mostly indicate ineffectiveness of vitamin D on hyperglycemia in diabetes [30] however, most of the evidences reflecting the positive impact of vitamin D on Hyperglycemia in diabetes control are derived from animal studies [31]. Most of the researches that reported a negative correlation between serum levels of vitamin D and blood sugar levels and insulin resistance have been epidemiological or animals-based studies, or have been conducted in nondiabetic patients.

In target cells of insulin, the active form of vitamin D promotes insulin sensitivity is several ways. Including an increase in expression of genes which are related to insulin receptors or factors that play a role in glucose homeostasis, or indirectly through its effect on calcium (calcium intake has effect on glucose metabolism) [46].

4. CONCLUSIONS

We concluded that vitamin D supplements, injection of 300,000 units every fortnight for 8 week, is more effective on glycemic indices in patients with Type 2 Diabetes Mellitus rather than in multiple sclerosis patients. The same intervention is more effective in multiple sclerosis patients to improve vitamin D deficiency, rather than in diabetic patients.

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