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Effect of Atorvastatin on Vitamin D Levels in Type 2 Diabetic Patients with Hypercholesterolemia

Huda Jaber [1*], Kassim Mohmmed [1], Azhar Abed Flayyih[2] , Amal Rasheed[3]

[1]College of pharmacy, Mustansiriyah University, Baghdad.
[2]Safeer Alimam Al-Hussain (A.S) Surgical Hospital,Karbala.
[3]Institute of medical Technology, Baghdad, Iraq.
[*]Corresponding author .Email: hudaiq84@yahoo.com

Abstract

Objective: The decrement of 25-hydroxy-vitamin D [25-OH-D] concentrations has been increase the severity of cardiovascular disease especially in diabetic patients. The aim of the present study was to assess the effect of atorvastatin on 25-OH-D concentration in diabetic patients with hypercholesterolemia. **Methods and patients:** Forty diabetic patients with hypercholesterolemia were participated in this work. For comparison, thirty healthy subjects were inserted in the present study. Serum vitamin D levels and lipid profile (total cholesterol, triglyceride, HDL, LDL and VLDL) were measured. **Results:** Vitamin D levels significantly decrease ($p<0.05$) in diabetic patients group (22.4±5.1 ng/ml) when compared to healthy group (32.44±4.12 ng/ml) .After 8 weeks from taking atorvastatin (20 mg/day) the mean of serum vitamin D were a slightly increase(26.4± 5.6) but not significant. Total cholesterol significantly decreases after therapy. **Conclusion:** Vitamin D levels significantly decrease in diabetic patients when compared to healthy subjects. There was no significant difference in vitamin D patients before and after lipid lowering therapy.

Key words: T2DM, hypercholesterolemia, vitamin D, atorvastatin.

1. Introduction:

Type 2 diabetic patients are more prone to dyslipidemia and cardiovascular complications. Patients with type 2 diabetes are at high risk for cardiovascular diseases (Benjamin M Leon & Thomas M Maddox, 2015). Previous medical studies recorded that atorvastatin, an inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A reductase, which decreased the Probability of occurrence of cardiovascular complications in diabetic patients (Ahmed Abbas, et al., 2012; Kayama Y, et al., 2015). The advantage of statin using to decrease the incidence of cardiovascular complications in diabetic patients and also noted that the effect of atorvastatin and pravastatin on glycemic control (Manjunath G. Raju, et al., 2013).

Vitamin D is a steroid vitamin, has an important role in several biological functions. Its deficiency consider as a risk factor for osteoporosis and other chronic diseases such as diabetes, thyroid disorders, hypertension and other cardiovascular diseases, metabolic syndrome and ischemic heart disease (Daria M. Adamczak, 2017). Vitamin D is synthesized by exposing the skin to the sun that works on 7-dehydrocolesterol which hydroxylate carbon number 25 by the action of 25-hydroxyvitamin D-1 hydroxylase or CYP27B1,which is enzyme found in the mitochondria of the liver cells. The resulting molecule (25-hydroxyvitamin D) is the best formula to determine vitamin D levels (Matthias Wacker & Michael F. Holick, 2013). Both cholesterol and vitamin D together share by the 7-dehydrocolesterol conversion pathway. Statin is a treatment used for patients with high cholesterol, which inhibits the manufacture of cholesterol inside the body by inhibit 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase (catalyze the rate limiting step in cholesterol synthesis) (Ahmed Abbas, et al., 2012). Statins have significant benefits effect in reducing acute ischemic heart disease degradation (Rose Gilbertab, et al., 2017). These patients often have a vitamin D deficiency and they will undergo statin treatment as secondary prevention (Ulrich Laufs, et al., 2015). This calls attention to the importance of studying the effect of this treatment on the levels of vitamin D, which are often critical in these patients. The aim of the present study was to assess the effect of atorvastatin on 25-OH-D concentration in diabetic patients with hypercholesterolemia.

2. Material and Methods:

Forty T2DM patients with hypercholesterolemia were collected from National Diabetic Center/Al- Al-Mustansiriyah University, Baghdad. Venous blood was drown from fasting diabetic patients and left for 30 min. then centrifuged to separate serum. For comparison, thirty healthy subjects were inserted in the present study. Serum vitamin D levels was measured by Cobas C111, Germany. Lipid profile (total cholesterol, triglyceride, HDL, LDL and VLDL) were measured by reflatron (Roch, Germany) and glycemic status parameters include FPG measured by reflatron(Roch, Germany), insulin hormone measured by ELISA (Diagnostic Automation Company/USA) and variant hemoglobin A_{1c} measured pack for HbA_{1c} mesurment (Bio-Rad Variant, Italy).

Statistical analysis:

Statistical analysis was done by computer program (SPSS-21). Unpaired t test was applied to find the significant difference between studied parameters. $P \leq 0.05$ considered significant.

3. Results:

In the current study, Patients and control group were similar in both age and BMI and there was no significant difference between them [P value >0.05], as shown in table (3.1)

Table (3.1): The characteristics of T2DM patients and control groups

Parameters (mean ± SD)	Controls (n = 30)	Patients (n = 40)	P.value
Age	42.63±5.27	44.47±5.56	0.85
BMI	30.24±1.96	30.83±2.38	0.18
Duration of disease (year)		5.42±3.43	-

Table (3.2) illustrate the mean± **SD** for each studied parameters which include vitamin D, total cholesterol, trigluceride, HDL , insulin hormone , FPG and Hba1c.

Table 2 : the biochemical parameters in studied groups.

Parameters (mean ± SD)	Control (n=30)	Patients (n=40)	
		Baseline	After 8 weeks
Vit D ng/ml	32.44±4.12a	22.4±5.1 b	26.4± 5.6b
Total Cholesterol mg/dl	166±44a	212±43c	186±37b
Triglyceride mg/dl	123±30a	173±41c	142±21b
HDL mg/dl	47±8.6a	36±6.2b	44±9.3a
Insulin hormone IJU/mL	12.4±7.4a	24.1± 5.9b	23.45±6.3b
FPG mg/dl	87.50 ± 1.62a	181.50 ± 9.37b	172.8±8.68b
Hba1c	5.7±0.6a	8.4±0.7b	8.2±0.6b

Means with different subscript letters refer to significant difference (P<0.05)

There is a significant decrement in the levels of vitamin D in diabetic patients when compare to control group (p<0.001), but there was no significant difference in vitamin D levels after treatment (P>0.05), as shown in table 2.

Total cholesterol significantly elevated in patients group when compare to control (P>0.05), as well as there was a significant difference after treatment.

Table 2 also show that there was a significant difference in HDL levels when compare between patients and control groups (P>0.05), also there was a significant difference when compared in patients before and after treatment.

There were a significant difference in all glycemic status parameters (FPG,serum insulin and Hba1c) in patients when compare to healthy subjects but there was no significant differences were found in serum insulin, FPG and Hba1c before and after treatment (P>0.05), as shown in table 2.

4.Discussion:

The current study confirms that vitamin D levels are low in Iraqi society and this means that living in a sunny country such as Iraq does not necessarily lead to adjustment of vitamin D levels.

In agreement with previous studies (Akio Nakashimam et al., 2016; Alvarez JA, et al. 2010) vitamin D levels were significantly lower in diabetic patients when compared to healthy people. Recent study suggests that there is an inverse relationship between levels of vitamin D and blood glucose level. In other words, high blood glucose levels lead to lower vitamin D concentrations (Mattila Mannisto, 2018).

Low vitamin D levels lead to decrease the secretion of insulin secretion (Bourlon PM, et al., 1999). Other study suggest that the indirect effects of vitamin D on the secretion of insulin may be due to the effect of calcium on the secretion of insulin. vitamin D levels maintain on the calcium level outside the cell depending on the permeability characteristic of cell membrane to cross the calcium ion out of the cell (Teresa Martin,2011) . In fact the role of vitamin D in regulation insulin sensitivity and secretion not clear until now. Diabetic patients after 8 weeks of statin treatment also measured vitamin D levels and found there was no significant change on the levels of vitamin D.

Current study recorded that dyslipidemia associated with T2DM and the levels of lipid profile improve after using atorvastatin. Cholesterol improves cell response to insulin and work to amplify GLUT4 / glucose that regulates secretion of insulin. statin-induced PM effect which accurs in skeletal muscle, a site which responsible for approximately 80% from glucose consume and is considered as a major tissue for insulin resistance (Floriana Elvira Ionică, et al., 2010).

In conclusion. Current study found that the vitamin D deficiency association with T2DM . After 8 weeks from atorvastatin the vitamin D levels slightly increase but not significant.

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