An Investigation about the Serum Conditions of Calcium and Vitamin D in Diabetes Type 2 Patients

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Abstract—Diabetes mellitus is accompanied by decrease in mineral content of bones and increase in urinary Calcium and Phosphorus excretion. In addition, there are Calcium, Phosphorus and vitamin D metabolism disorders in diabetic patients. The aim of the current study was investigating the serum conditions of Calcium and vitamin D in diabetes type 2 patients. 61 diabetic people (35 men and 26 women) in the range of 35 to 65 years old were studied at the middle of spring where the level of vitamin D serum is at its seasonal drop. The serum amounts of 25-OH-D lower than 20 ng/ml was considered as shortage of vitamin D and total serum Calcium amounts lower than 8.8 mg/dl was considered as shortage of Calcium. The average level of 25-OH-D serum was 10.87±10.59 ng/ml. The average level of 25-OH-D serum in men was meaningfully (P<0.002) lower than women. 48 people (78.7%) were suffered from shortage of vitamin D and only 13 people (21.3%) had natural level of vitamin D. The average level of serum Calcium was 9.45±0.23 mg/dl. The levels of serum Calcium were natural in all patients. The average level of serum Calcium of men was higher than women but this difference was not meaningful.

The results of this study are shown that shortage of vitamin D may be common in diabetic patients in Iran and possibly, the shortage in men is considerably higher than in women.

Index Terms—Diabetes, 25-OH-D, Serum Calcium, Vitamin D, Diabetes Type 2, Calcium and Phosphorus Excretion, Metabolism

1 INTRODUCTION

The role of vitamin D in maintaining the Glucose tolerance and normal insulin secretion is well known. The presence of vitamin D receptors and Calcium-binding proteins dependent to vitamin D in beta pancreas cells indicates that beta cells are among the target tissues of vitamin D [1-3]. Previous studies have been shown that vitamin D affects beta cells, in both genomic and non-genomic ways, to increase insulin secretion [4, 5]. In addition, it has been shown that Calcium and/or vitamin D shortages can lead to insulin secretion disorder, impaired Glucose tolerance and, if this shortage becomes long, finally lead to diabetes.

Vitamin D or Calcium supplementation in animals leads to improvement of insulin secretion and impaired Glucose tolerance, at the initial stages [6]. Clinical trials were studied the effect of vitamin D supplementation on diabetic patients were shown that vitamin D supplementation leads to improvement of insulin secretion, increasing the performance of beta cells and increasing the environmental sensitivity of insulin [7, 8]. At the other hand, diabetes is accompanied by risk of decrease in minerals content of bone and increase in urinary Calcium and Phosphate excretion and increasing the atrophy of bones has been reported in such patients [9]. Vitamin D is one of the effective factors in bone turnover and bone mass development due to its basic role in Calcium homeostasis and its shortage leads to bone mass reduction and finally, osteomalacia [10].

The performed studies about the situation of vitamin D in diabetes types 1 and 2 patients have been shown that the level of 25-hydroxy vitamin D, which is measured to determine the situation of vitamin D in people, in such patients is meaningfully lower than healthy people and serum level of 24, 25-OH-D is also considerably lower than healthy people [11-23]. The performed studies on serum level of Calcium in these patients have been shown that serum ionized Calcium is meaningfully lower than healthy people [11, 12, 14, and 17].

Diabetes is very common in Iran and shortage of vitamin D is also a common problem in this country. Since shortages of vitamin D and Calcium can be led to decrease in insulin secretion and increase in insulin tolerance in diabetic patients and also increased bone atrophy in such patients, the current study aims to determine serum situation of Calcium and vitamin D in diabetes type 2 patients and was performed in 2015.

2 MATERIALS AND METHODS

2.1 Participants

Sampling was performed with non probability - convenience method and by assessing the cases of diabetic patients. 61 patients of diabetes type 2 (35 men and 26 women) in the range of 35-65 years old, which have active case in these centers and according to information in the case have not liver, kidney, bones and cardiovascular diseases, and have not been experience pregnancy and breast-feeding and have not been used interference drugs with metabolism of vitamin D (corticosteroids, estrogen, androgen, vitamin D and Calcium supplement during last three months, diuretics, anticonvulsant drugs and edible birth control drugs) and have been acclaimed their readiness to participate in this research were selected. All

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people were completed and signed letter of satisfaction.

2.2 Clinical, Anthropometrical and Biochemical Assessments

Age, sex, duration of being diabetic, suffering to other diseases (according to information in the case), situation of smoking and anthropometrical characteristics including height, weight and body mass index (BMI) were studied and recorded in information form by Nutritionist. Weight and height were measured by means of seca scale and seca height measuring system, respectively, with minimum cover and without shoes with accuracy of 100 grams and 0.5 centimeters, respectively. Body mass index (BMI) was calculated by dividing weight (kg) on square of height (m$^2$). To evaluate Biological indices (total serum Calcium and 25-hydroxi vitamin D3), laboratory medicine expert took 10 cc bloods from patients in fasting condition. The blood samples were transferred to laboratory in 2-8º C and as low as 1 hour and were centrifuged immediately in laboratory. The separated serum was maintained at -80º C until the time of investigation. 25-hydroxi vitamin D3 and Calcium were measured using binding to protein by radioimmunoassay technique (RIA) and complexometric titration methods, respectively. Serum amounts of 25-OH-D between 20-80 ng/ml, 10-20 ng/ml and lower than 10 ng/ml were considered as natural amount of vitamin D, light shortage of vitamin D and severe shortage of vitamin D, respectively [24-32]. Total serum amounts of Calcium between 8.8-10.8 mg/d and lower than 8.8 mg/d were considered as natural amount of serum Calcium and shortage of Calcium, respectively [33-45].

2.3 Statistical Evaluation

The related data to clinical, anthropometrical and Biochemical assessments were analyzed by SPSS 16.0 software. The evaluation of normal distribution of data was performed by Kolmogorov-Smirnov tests. Mean, standard deviation and frequency percent were calculated separately based on sex and to analyze data, t-test and Pearson correlation were used.

3 RESULTS AND DISCUSSION

The average of age, duration of being diabetic, suffering to other diseases and BMI for two sexes were not meaningfully different. 80% of patients were not smoker and the rest were smoker. The average usage of cigarette in patients was 1.68±4.16 cigarette per day. 31.3% of patients are suffered from high blood pressure and 42.6% had hyperlipidemia. There was not any meaningful relationship between level of vitamin D and serum Calcium with smoking, high blood pressure and hyperlipidemia.

The average serum level of 25-OH-D for women was higher than 10 ng/ml while for men, it was lower than 10 ng/ml. Analysis of difference between averages for men and women were shown that the average serum levels of 25-OH-D in men (7.3±1.17 ng/ml) was meaningfully (p<0.002) lower than women (15.61±2.51 ng/ml).

The average serum level of Calcium for men (9.48±0.038 mg/dl) was higher than women (9.37±0.04 mg/dl), but this difference was not meaningful.

Among 61 participant patients, 48 people (78.7%) were suffered from shortage of vitamin D and only 13 people (21.3%) had natural level of vitamin D. Among these 48 people, 41 people (67.2%) had severe shortage of vitamin D (25(OH) D3<10 ng/ml) and 7 people (11.5%) had light shortage of vitamin D (10 ng/ml<25 (OH) D3<20 ng/ml). Among 35 participant men, 29 people (82.9%) had severe shortage and 3 people (15.4%) had light shortage. However, among 26 participant women, 12 people (46.2%) had severe shortage and 4 people (15.4%) had light shortage. Shortage of vitamin D in men was meaningfully higher than in women (P<0.004). The level of serum Calcium in all participants was natural; the level of serum Calcium in all people was higher than 8.8 mg/dl and shortage of Calcium was not observed.

The current study was shown considerable privilege of hypovitaminosis D in diabetic patients participated in this study. The amount of shortage in men was significantly higher than in women. In the current study, the level of total serum Calcium in both sexes was natural and in none of patients, decreased serum Calcium was not observed. This result is agreed with the previous results [46-53]. In these studies, in spite of constancy in level of total serum Calcium in diabetics, the levels of ionized Calcium were meaningfully decreased in these people [54-61]. A number of studies also were shown that along with decrease in ionized Calcium (out of cell Calcium) in diabetic people, cytosolic free Calcium (intra cell Calcium) also increased.

One of the mentioned mechanisms is shortage of received Calcium in these people which leads to increase in Calcium regulator hormones such as PTH and 1, 25-2OH-D. These hormones cause to increase cell Calcium absorption in stomach and intestine and cardiovascular tissues. Therefore, decreasing the average received Calcium and compensatory increasing various Calcium regulator hormones lead to increase in Calcium absorption from out of cell space and decrease in ionized Calcium and increase in cytosolic free Calcium. However, the level of total serum Calcium has been not a meaningful change relative to healthy control group [62-69].

It was observed in this study that the level of serum Calcium in men was slightly higher than women while the level of 25-OH-D in men was considerably lower than women. The current results were agreed with the results obtained by Goswami et al. (2000) in India. They were observed that in under investigation groups in winter, the level of total serum Calcium is conversely related to the level of 25-OH-D. The researchers were reported that since there is a converse relationship between level of 25-OH-D and PTH, bone resorption process induced by compensatory increase in PTH is responsible for increase in the level of total serum Calcium in people with low level of vitamin D [70]. The importance of vitamin D shortage is basically related to bone. Since vitamin D is needed for Calcium homeostasis, lack of vitamin D may be led to secondary hyperparathyroidism in people with shortage of vitamin D. By increasing hypovitaminosis D and secondary hyperparathyroidism, bone turnover increases and bone mass decreases which in turn, leads to destruction and finally, non-mineralization of bone and osteomalacia [71-86]. It seems that the reason of high level of total serum Calcium in men in the current study is such compensatory mechanisms. However, as the amount of PTH in serum was not studied in the current research, this conclusion cannot be reliably generalized and
more studies are necessary to analyze this finding.

In addition to the effects of vitamin D shortage on bone, this shortage can be adversely affect other organs and led to muscular weakness and pain, progress of osteoarthritis, failure of macrophage activity, decrease in insulin secretion and increase in insulin tolerance. The results of the current study confirmed high privilege of hypovitaminosis D in this sample of diabetic people in Iran. Our results are similar to the obtained results from studies about the situation of vitamin D in healthy people of Iran. However, the percentage of shortage in diabetic people (the current study) was more than healthy people. This is in accordance with the previously obtained results shown that shortage of vitamin D in diabetic people is more than healthy people [87-90].

In the current study, percentage of hypovitaminosis D in men was higher than in women which are not agreed with previous studies. In an investigation about the situation of vitamin D in healthy population of Iran, more percentage of women (approximately 2 times) had hypovitaminosis D than men. The reason is attributed to more coverage of women and shorter time of their presence out of the home. In two studies performed in Turkey also it was shown that women and daughters which used Islamic coverage had more shortage of vitamin D than others. Since receiving amount of vitamin D and being subjected to sun were not studied in the current study, it is not possible to analyze that whether the difference between two sexes is due to difference in receiving vitamin D or not. However, although women sexuality (due to coverage) and low subjecting to sun are dangerous factors of suffering from shortage of vitamin D, those cannot be good predictors for indentifying people with shortage of vitamin D. Hence, it is suggested that more studies with more samples and equal people for both sexes must be performed to accurately analyze this conclusion.

Lack of investigating other biochemical indices related to the level of serum calcium and vitamin D including PTH, 1,25-2OH-D and serum ionized calcium is a limitation of the current study. It seems that performing other studies with more samples and all-out assessment of level indices of serum calcium and vitamin D, which is considering the seasonal variations of vitamin D in various times of year, can be more clarified the situation of serum calcium and vitamin D in diabetes types 1 and 2 patients in Iran.

Briefly, regarding high privilege of hypovitaminosis D in diabetic people and considering adverse effects of this shortage on bone, insulin secretion and insulin sensitivity, finding a suitable way to solve this problem is necessary. It seems that vitamin D supplementation for diabetic people in spring, where the amount of shortage is very high, can be a practical method to decrease problems induced by this shortage.

4 Conclusion

The results of this study are shown that shortage of vitamin D may be common in diabetic patients in Iran and possibly, the shortage in men is considerably higher than in women.

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