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Original Article

The study of the prevalence of vitamin D3 deficiency and its relationship with blood glucose level after coronary artery bypass graft operation among patients with diabetes

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Abstract

Objectives: Nowadays, vitamin D3 (VitD3) deficiency is among the most common dietary deficiencies around the world. Researchers have paid more attention to VitD3 because it is a vital element of the body and has a plausible relationship with various diseases such as diabetes mellitus type II. This study was conducted to examine the prevalence of vitamin D3 deficiency and its relationship with blood sugar levels in people with diabetes undergoing coronary artery bypass grafting (CABG).

Methods: An observational study was conducted in 2017 in Shahid Madani Hospital, Tabriz, Iran, for 8 months. Due to the use of census sampling, only 115 patients with diabetes and open-heart surgery were enrolled in the study. A questionnaire collected information on the participants' demographics, medical history, VitD3 levels and blood glucose levels. Data were analyzed using SPSS ver. 25. Independent t-test was used to compare quantitative data, and chi-square test was used to compare categorical variables.

Results: One hundred and fifteen out of 348 patients who had CABG surgery were diabetic. Moreover, 24.7% of patients with diabetes had VitD3 deficiency. The results of the coefficient-correlation test indicated that there was a significant relationship between the mean blood glucose level and VitD3 level ($p < 0.05$).

Conclusions: The results of this study suggest that patients with diabetes can improve their blood glucose control after CABG surgery by taking sufficient VitD3. Therefore, it should be considered as a principle of the hospital operation to prescribe VitD3 prior to surgery for these patients.

Keywords: Blood glucose level; Cholecalciferol; Coronary artery bypass; Diabetes mellitus

Introduction

There is a common nutritional deficiency in developed countries known as vitamin D3 deficiency (VitD3), which occurs both in children and adults. Because of this problem food supplements and food are enriched with VitD3.

In spite of this, VitD3 shortages are still observed in countries without enrichment; this is the case even when sun exposure is limited (1, 2). In America and Europe, more than 40% of adults over 50 have vitamin D3 deficiency. The human skin can produce VitD3 when exposed to sunlight; however, in areas where the sun is high in the sky, there is a deficiency of VitD3. In most countries of the world, VitD3 deficiency is a significant problem. For many years, enriched foods containing VitD3 have been produced in low latitudes with plenty of sunlight and industrialized countries to prevent the deficiency (4). In general, this is done to compensate for a vitamin deficiency. VitD3 levels low in the obese people and those with type II diabetes (DM II) have been linked. Vitamin D3 is a steroid hormone that plays an essential role in skeletal and non-skeletal tissues (5). Due to poor lifestyle choices, diabetes, especially DM II, has skyrocketed in recent years (6). Obesity and diabetes mellitus type II are diseases of human health. However, it is unclear what the molecular mechanisms are underlying this relationship. VitD3 has also been found to play a pivotal role in the development of DM II (3). VitD3 also prevents lipid accumulation, increases insulin synthesis, reduces insulin resistance, and decreases hunger, thereby possibly treating obesity and diabetes type II (7).

In recent clinical studies, it's been found that patients with susceptible blood glucose levels should pay more attention to their blood glucose levels. These studies show that patients who have their blood glucose controlled adequately have a lower mortality rate. The reduction of wound infection risks is one of the benefits of post-surgical glucose control (8) ischemic heart disease and recurrent episodes (9). Furthermore, the study found that an increase in blood glucose following sternum regeneration may increase the risk of infection in the bone marrow (10, 11).

Cardiovascular disease is one of the most life-threatening diseases in diabetic patients. Diabetes patients are particularly at risk from blood glucose control problems because uncontrolled blood sugar levels cause metabolic diseases, wound healing issues, exacerbation of ischemic brain damage during surgery, and more extended hospital stays and costs involved in hospitalization (2, 12). There is increasing evidence that adjusting blood glucose level in the physiologic range in patients undergoing cardiac surgery, particularly coronary artery bypass graft (CABG) surgery, reduces infections, hospital stay time and possibly improves the results of patients' treatments (13, 14). After surgery, especially cardiac surgery, blood glucose levels in diabetic patients are a therapeutic challenge, and despite intensive insulin control, this issue remains (7, 15). Thus, the blood glucose level of diabetic patients undergoing cardiac surgery is fundamental in preventing hypoglycemia and hyperglycemia and, consequently, the majority of perioperative complications for these patients (8, 14, 16, 17).

According to recent research, VitD3 deficiency increases the risk of chronic diseases such as cancer, autoimmune diseases, DM II, heart disease, increased blood pressure, and infectious diseases. Vitamin D3 deficiency has been associated with these diseases, as it is with osteoarthritis (5, 16, 17). Since blood glucose needs to be controlled after surgery and VitD3 plays a crucial role in diabetes patients' health, this study investigated the prevalence of VitD3 deficiency and its relationship with blood glucose levels in diabetic patients who were undergone CABG surgery.

Materials and Methods

This observational study was conducted on diabetic patients underwent CABG in Shahid Madani Hospital Tabriz-Iran during a period of 8-months (April- November) 2017. All patients were operated by on pump method. It attempted to examine the patients' VitD3 level and blood glucose level according to their medical records. The day before surgery, vitamin D3 levels were measured, and blood glucose levels were measured 6 hours after surgery and then every six hours for four consecutive days. All qualified patients were examined and the level of VitD3 in plasma and blood glucose level were evaluated and recorded. In cases of no control, the parameters involved in this disproportion were investigated. The primary outcome of the study was the VitD3 level of diabetic patients undergone cardiac arrhythmias to investigate the prevalence of VitD3 deficiency. The secondary outcome variable was the level of VitD3 in the blood of the patients before the surgery and the blood glucose level of the patients every 6 hours for 4 consecutive days after the operation. This was carried out to compare blood glucose and VitD3 level and evaluate the effect of VitD3 on the blood glucose level.

Accordingly, 348 patients who were undergone an open-heart surgery were enrolled in the study, the number of participants was based on the census method. There were 115 diagnosed diabetics in the total sample, but the remaining subjects were excluded. The study was open to the ICU patients undergone the CABG surgery, diabetic patients more than three months before surgery, patients between the ages of 18 and 80, and patients who

completed the consent form. Exclusion criteria were as followed: non-diabetic hyperglycemia, liver disease symptoms, renal dysfunction, pregnancy or lactation, difficulty in understanding the consent form, autoimmune diseases, and illiterate and blind people lacking consent. A questionnaire containing five sections designed and prepared by the researcher, was used. The questionnaire was found to be content valid in terms of the experts' theories in the field. The reliability of the questionnaire was investigated by conducting a pilot study and calculating the Cronbach's alpha coefficient (r=84%). The first part of the questionnaire contained demographic information including the patients' age, sex, height, weight, body mass index (BMI), case number, and hospitalization histories. The second part, required the medical background records. The third section of the questionnaire focused on smoking habits and addiction. Among the fourth section's components there were the previous sections' histories, fast blood sugar results (FBS), vitamin D level 3 (VITD3), type of surgery (CABG), and complications. In the fifth section, researchers assessed the patients' routine blood tests, such as Blood Urea Nitrogen (BUN), Platelets (Plt), Hemoglobin (Hb), Red Blood Cells (RBC), Hct, and Creatinine (Cr).

Analysis of the data was performed via SPSS 25 software. Means and standard deviations were calculated for parametric data. Furthermore, repeated measures and post hoc tests were used to examine the relationship between continuous data. Correlation analysis of continuous data was conducted. P <0.05 showed a significant difference in the mean scores of the groups. In addition, Mauchly (sphericity) tests were performed within groups, and related tests were computed using P-values. Likewise, P <0.05 showed the significance of the tests. The researchers obtained informed consent from the subjects; in addition, for those with difficulty reading the consent form, a close relative was consulted to obtain the consent. The study protocol was approved by the Ethics Committee of Tabriz University of Medical Sciences under the ethical code of IR.TBZMED.REC.1396.247.

Results

In this study, 75 out of 115 patients were males (65%) and 40 were females (35%). The mean age of the patients was 62.4 ± 7.5 years. In this study, hypertension was the most common risk factor associated with 101 patients (87.8%), while alcohol consumption was the least frequent (20%). 112 of the participants 108(97.3% had cardiovascular drugs, 88 (76.5%) anti-lipid drugs, 72 (62.6%) diabetic drugs and 56 (48.6%) used another drug. According to the obtained information, the prevalence of VitD3 deficiency was 73.2%. Based on the collected data and the findings of the study, there were 3 different groups in terms of VitD3:

1-VitD3deficiency (<20ng / ml)

2. Insufficient amount of vitD3 (20-30ng / ml)

3. Sufficient VitD3 (> 30ng / ml) (Table 1)

Blood glucose levels of each patient were recorded every six hours for four consecutive days following the operation (based on mg/dl) (Table 2). In spite of the fact that the operation of the patients started at 8 o'clock in the morning and took 4 hours for each patient, the researcher started a blood glucose record at noon (12:00 p.m./18:00 /24:00 /6:00 a.m.). All diabetic patients were tested for blood glucose after surgery based on insulin protocol.

As the cruel blood glucose level in female subjects was 220 mg/dl and the cruel blood glucose level of male patients was 212 mg/dl, there was no critical distinction in blood glucose based on the sex of the subjects (p= 0.3).

A repeated measure design statistical test showed that the mean blood glucose levels were statistically significant (p = 0.004) across the different VitD3 groups. There was a substantial difference between three groups with respect to VitD3, particularly among the group with low VitD3 levels (p = 0.0013). Mauchly's test with an index value of P=0.4 revealed that the Sphere's requirements were not met; therefore, it is necessary to correct the degree of freedom and use other tests that do not rely on the Sphere's condition. As a result, further tests were carried out to compare the blood glucose levels at different times. All three tests indicated that blood glucose level was significantly different at various times based on the VitD3 groups (p = 0.003) (Table 3).

According to the results of statistical tests, it can be concluded that VitD3 deficiency has the most significant role in controlling the total blood glucose of the patients in the study. Moreover, Table 4 showed that with the increase of VitD3 levels, the mean of fast blood glucose level was also reduced (p = 0.045).

Table 1. Patients' VitD3 Range

VitD3 Range	No. of patients	Percent of patients
Deficient (<20ng/ml)	84	73.2
Insufficient (20-30ng/ml)	10	8.6
Sufficient (30-100ng/ml)	21	18.2
Poisoning (>100ng/ml)	0	0

Table 2. Mean of Patients' Blood Glucose during the First 4-days after CABG Operation

Day & time of blood glucose report	MD± SD	Day & time of blood glucose report	MD± SD
First day (12:00 pm)	56.3±172.5	Third day (12:00 pm)	79.5±242
First day (18:00 pm)	77.4±206.7	Third day (18:00 pm)	15.4±243.6
First day (24:00 am)	50.1±194.3	Third day (24:00 am)	64±224.3
First day (6:00 am)	96.1±199.9	Third day (6:00 am)	84±183.4
Second day (12:00 pm)	81.7±217.1	Fourth day (12:00 pm)	91.2±261.1
Second day (18:00 pm)	76.1±224.7	Fourth day (18:00 pm)	93.1±237.2
Second day (24:00 am)	62.1±208.4	Fourth day (24:00 am)	103.2±256.5
Second day (6:00 am)	52.6±181.6	Fourth day (6:00 am)	58.3±177.8

Table 3. Within-group Tests for Different Blood Glucoses Records (16 Consecutive Periods)

Test	F	Mean square	df	Type III sum of squares
Sphericity assumed	5.709	38150.227	15	572253.404
Greenhouse-geisser	5.709	86715.701	6.599	572253.404
Huynh-feldt	5.709	79687.442	7.181	572253.404
Lower-bound	5.709	572253.404	1.000	572253.404

Table 4. Comparing the Patients' Mean of Fast Blood Sugar with VitD3 Level

Mean of fast blood sugar of patients	No. of patients	VitD3 level of patients
215.5	84	>20
210.9	10	30-20
153.9	21	100-30

Discussion

The results of this study showed that the patients with VitD3 deficiency had a higher blood glucose level compared to those with normal VitD3 levels or insufficient levels of VitD3 ($p = 0.001$). In the patients with VitD3 deficiency, frequent blood glucose control had only normal glucose levels at one time; though in the patients with adequate levels of VitD3 or lacking VitD3 level, this value was higher and about 4.6 times over the 4 days of measurement of blood sugar level. The results of the analysis of the fast blood glucose level of patients with sufficient VitD3 levels indicated that their fast blood glucose level was significantly low and close to normal level ($p = 0.045$) (mean FBS = 153.9 mg / dl).

The results of this study are consistent with the findings of other studies on the effect of VitD3 on post-surgical glucose levels (5, 16). VitD3 plays an essential role in diabetes mellitus metabolism in diabetics. Evidence indicates that VitD3 deficiency increases the risk of many chronic diseases, including cancer, autoimmune diseases, diabetes type II, heart disease, high blood pressure, and infectious diseases (18-20). VitD3 deficiency was only considered as an effective ingredient in bone metabolism (3), but it has recently been recognized as a risk factor for DM II (3), but it has recently been recognized as a risk factor for DM II (21, 22). Studies have also found that infants who have received 2,000 units of VitD3 daily in their first year of life had a lower risk of type 1 diabetes for 31 years in 78 percent (23). The present study also showed a significant relationship between VitD3 levels and blood glucose levels in certain diabetic patients.

Fast blood glucose levels in the VitD3 group are 153, which are almost near-normal levels; in the other two groups, however, fast blood glucose levels are over 200. After surgery, uncontrolled blood glucose has a significant impact on patients, which can be attributed to a disorder in skin repair following surgery. In addition, the patients with uncontrolled blood glucose after surgery were hospitalized for longer periods (24).

During general anesthesia and surgery, anti-regulatory hormones such as cortisol, epinephrine, glucagon, and inflammatory cytokines such as tumor-alpha necrosis factor have been increased. The result of these neurohormonal changes is metabolic abnormalities such as insulin resistance, impaired insulin secretion, increased lipolysis, and elevated catabolism, which are all associated with hyperglycemia. Vitamin D3 has anti-inflammatory effects and its deficiency affects postoperative inflammation control, eventually leading to high blood glucose levels.

According to the study, blood glucose levels in the patients admitted in the past two decades have been very flexible, and it is well known that there is a strong relationship between diabetes and blood glucose levels, as well as life expectancy, mortality, and the length of stay in the hospital (25). Lack of glycemic control in diabetic patients undergoing CABG surgery is very serious and dangerous, as it can cause metabolic disorders, impaired wound healing, aggravate cerebral ischemia lesions during surgery, and increase mortality and the length of hospital stay (14, 26). A study conducted by Mcalister et al reviewed 291 diabetic patients and concluded that controlling blood glucose could significantly influence the recovery after an operation, length of hospital stay, and the risk of experiencing side effects (12). In contrast with the present study, another study showed that controlling blood sugar after surgery could aid cardiac procedures in the patients who did not have diabetes; however, no tangible results were found for diabetic patients (27). Greg and his colleagues have examined the cost, duration of hospitalization, breathing problems, and heart problems of diabetics and non-diabetics in addition to infections and death caused by a lack of glycemic control. According to the literature, controlling blood glucose levels below 180 mg/dl reduces the length of hospitalization by 1.6 days, 12.5% in respiratory issues, 1.4% in infection risks, and a significant reduction in the cost of hospitalization for diabetics who are already taking insulin (28). Grec et al's study was in agreement with the findings of the present study. Researchers concluded that VitD3 in the hypothalamus controls blood glucose and energy homeostasis in a study on VitD3 receptors in the brain (29). Our study reported similar findings. In another study, the role of VitD3 supplementation in moderating insulin sensitivity was examined among the people with VitD3 deficiency. This study, which was conducted in the Netherlands, showed no improvements in insulin sensitivity among pre-diabetic subjects or in the beta cell function and metabolic syndrome. The insulin production performance in pancreatic beta cells improved in diabetics with VitD3 levels higher than 60 nmol/L (30), this is also confirmed in the present study. In another study which was conducted in Iran, the results indicate that the addition of VitD3 improved insulin sensitivity, decreased hemoglobin A1C, decreased fast glucose, and also, homeostasis of glucose in blood (31) were observed. The results of our study support this conclusion since an increase in VitD3 was significantly associated with postoperative blood glucose levels and fasting blood glucose levels. In a study on diabetic subjects, the concentration of fast glucose and blood glucose two hours after eating and HbA1c decreased significantly after 12 months of taking the VitD3 supplement in the experimental group, compared to the control group that did not take this supplement (32). This is also consistent with the results of the present study.

Additionally, in another study, the researcher looked at how VitD3 affected insulin and leptin, which affect diabetes homeostasis. The active group receiving VitD3 for over a year was compared with a placebo group. VitD3 increased both leptin and adiponectin in DM II3, which is an essential factor in the pathogenesis of the disease. In this way, the findings of the present studyare further supported.

This study was conducted on diabetic patients admitted to one of Tabriz hospitals. Therefore, the results from this study are unlikely to apply to the patients outside of this range. The findings should be studied on a broad population to ensure that the results can be generalized. Furthermore, it is suggested that future studies compare the effects of VitD3 intake with and without it among CABG patients.

Conclusion

In summary, the results of this study indicate that VitD3 deficiency is prevalent in diabetic patients having CABG surgery. The postoperative blood sugar levels of diabetics increase more if Vitamin D3 is deficient. As a result, according to this study, VitD3, together with other factors, may

play an important role in controlling blood glucose levels during postoperative periods.

Conflicts of Interest

The authors have no conflict of interest.

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