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Effect of Calcium-D Supplementation on Glucose Control of Patients with Gestational Diabetes

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Abstract

Background: *Gestational diabetes (GDM) is a complication of pregnancy that is characterized by intolerance to carbohydrates and metabolic diseases. Gestational diabetes has many maternal and fetal complications that need to be carefully controlled. Therefore, the aim of the present study was to investigate the effect of calcium-D supplementation on glucose control of patients with gestational diabetes.*

Methods: *This randomized clinical trial study was performed on 84 pregnant women with GDM. Some inclusion criteria included a positive one-step test during the 24th-28th week of pregnancy and definitive diagnosis of GDM and some exclusion criteria including patients with a previous history of diabetes who required insulin therapy during the intervention. The intervention group were given routine treatment and calcium supplements plus vitamin D and the control group were given routine treatment only. Fasting blood glucose was measured monthly in both groups until the end of pregnancy. All analyses were performed using SPSS software version 16 and related tests like mean±SD, chi-square test and multivariate logistic regression. Significant level was set at 0.05.*

Results: *Of the 84 patients examined, the mean age was 29.4 ± 5.2 years old and there were no significant differences between the two groups (Pvalue=0.189). The mean BMI of all patients was 25.31 ± 2.72 kg/m2 and there was no significant difference between the two groups (Pvalue=0.312). The mean of the FBS level at the end of the study in the case group was 91.5 ± 12.9 mg/dl and in the control group it was 98.9 ± 15.8 mg/dl, which was significantly lower in the case group (P=0.014). GDM variables were significantly associated with a positive history of diabetes mellitus (Pvalue<0.033), previous history of GDM (Pvalue<0.013) and FBS (Pvalue<0.001) and there was no significant relationship with other variables.*

Conclusions: *The results of this study showed that calcium-D supplementation has a significant effect on glucose control in patients with GDM and its use is recommended in these patients.*

Keywords: Gestational diabetes, Calcium, Vitamin D, Glucose.
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Introduction

Gestational diabetes mellitus (GDM) is a complication of pregnancy which is defined as intolerance of carbohydrates and metabolic disorders.[1] Approximately 7% of all pregnant women in America are GDM, but its prevalence is between 1% and 4% of all pregnancies in the world which depends on the population studied and the criteria for diagnosis.[2] Generally, 4.7% of pregnant women in Iran have this condition.[3] Various factors for this condition include higher age at the time of the first pregnancy, stressful living conditions and sedentary lifestyles with little or no physical activity, inappropriate diet and high intake of food have been reported which leads to increased risk.[4] GDM is related to insulin resistance and vascular inefficiency, vascular disease, macrosomia, neonatal hypoglycemia, increased bilirubinemia, cesarean section, pregnancy blood pressure, and early delivery.[5-6] Current GDM treatments include a diet with a low glycemic index, for carbohydrate restriction, the use of some glycemic control agents and insulin therapy.[7] A number of recent studies have shown that supplements of calcium and vitamin D for patients with GDM may affect pregnancy outcomes.[8] It has been observed in several studies that 25 hydroxy vitamin D levels are significantly lower in diabetic patients than in healthy subjects. Although the complementary effect of calcium plus vitamin D supplementation on glucose homeostasis and oxidative stress biomarkers have not been tested in GDM patients, some studies have reported their separate supplemental effects on metabolic profile and oxidative stress in these patients.[9-10] Our previous study on GDM patients showed that 6 weeks of vitamin D supplementation resulted in improved insulin function and decreased total cholesterol and LDL.[11-12] It is assumed that calcium and vitamin D do not function independently and work together. Previous reports have shown that their complementary supplementation is much more effective than a separate supplement of calcium or vitamin D on the metabolic profile.[13-14] The most important known role of vitamin D is that it helps calcium balance and absorption, but recently, studies have shown that it plays a role in the development of the brain and the immune system of the fetus and in the prevention of many autoimmune diseases, such as type I diabetes and multiple sclerosis.[15] Furthermore, given the need for vitamin D and calcium during pregnancy, the lack of proper nutrition during this important period of life may increase the risk of GDM.[16] Several mechanisms have been proposed for linking vitamin D and type II diabetes. These mechanisms relate to diabetes and vitamin D in three ways and affect insulin secretion, the resistance of environmental tissues to insulin and inflammation.[17-18] The benefits of supplementing with calcium and vitamin D may be due to their effect on cell cycle regulation, the activation of antioxidant enzymes and parathyroid hormone (PTH) suppression, and their role in metabolic profiles and oxidative stress.[18] The effect of simultaneous supplementation of calcium plus vitamin D on

insulin function, lipid profile, inflammatory factors, and oxidative stress biomarkers in GDM are not yet clear. Therefore, the present study was designed to investigate the effect of Calcium-D supplementation on control of glycemic control in patients with gestational diabetes who referred to Shahroud Bahar Hospital during 2018.

Materials and Methods

This study was a parallel randomized clinical trial study that was performed on 84 pregnant women with gestational diabetes who were referred to Bahar hospital in Shahroud (Northeastern Iran) between January and December 2018 (figure 1). Patients were randomly divided into two groups of 42 cases (taking calcium supplements plus vitamin D) and 42 in the control group (routine only). Since the prevalence of vitamin D deficiency is about 50% in Iranian pregnant women, the selection of patients was done in the two groups of intervention and control randomly without measuring vitamin D levels.

Inclusion criteria: pregnant women aged 18 and 40 years old, positive one-step test (75 grams of pure glucose and 2 hours later glucose measurement) during the 24th-28th week of pregnancy and definitive diagnosis of GDM.

Pregnant women with no previous diagnosis of glucose intolerance were screened and GDM was diagnosed using ADA criteria. Thus, the women whose plasma glucose had one of the fasting blood glucose levels≥95 mg/dl, one hour≥180 mg/dl and two hours≥155 mg/dl, as people with GDM were considered suitable for the study.[19]

Exclusion criteria: patients with a previous history of diabetes, premature rupture of the membrane, sudden discontinuation of placenta, gestational hypertension, pregnancy congestion, chronic hypertension, hypothyroidism, or of those requiring insulin therapy during the intervention (Plasma Glucose Fasting 5.8 mmol/L, and 2 hours post-fasting blood glucose greater than 6.7 mmol/L) and also, those who did not give written consent to enter the study or requested to leave the study at some point.

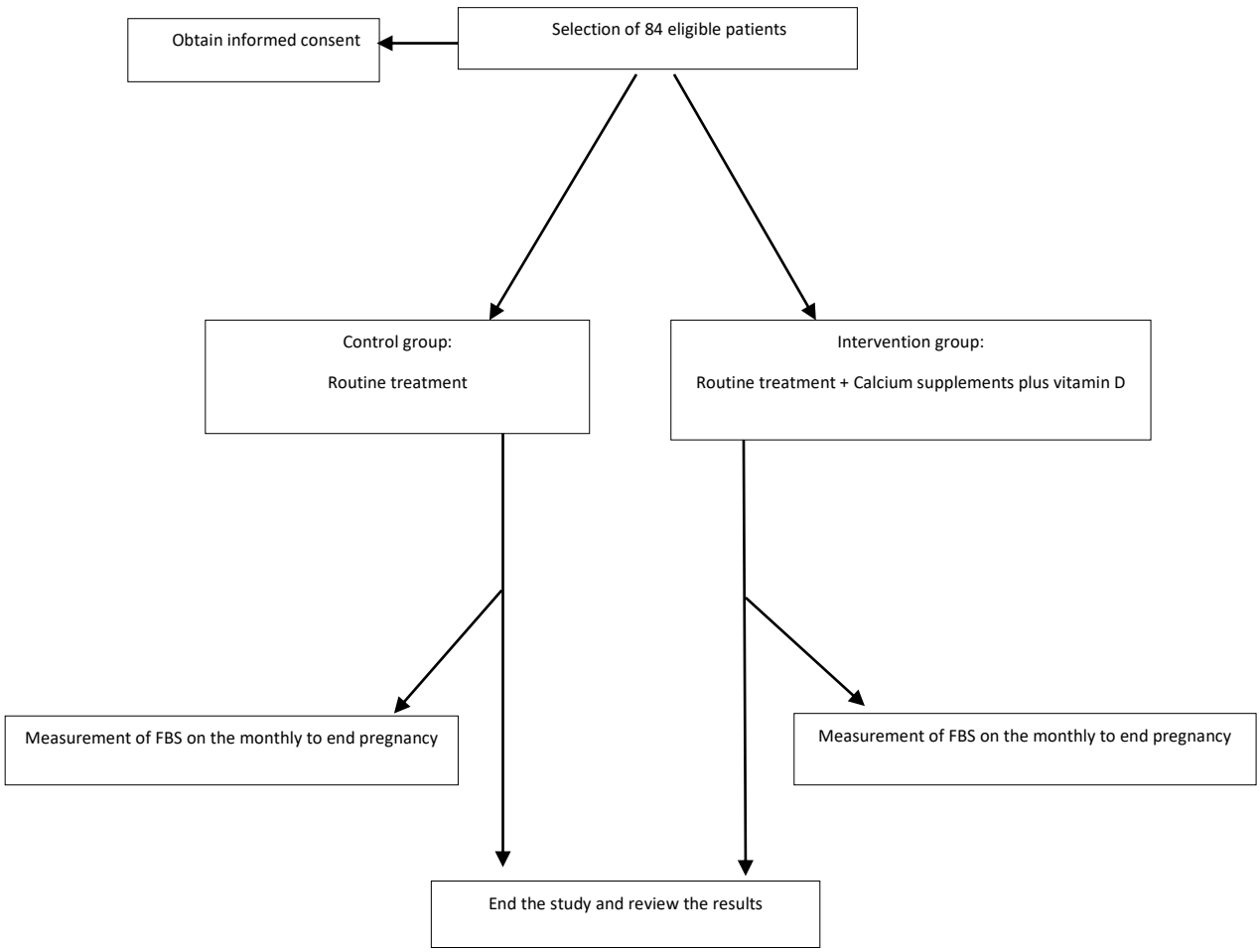

Figure 1. Consort diagram of study

For patients in the intervention group, 500 mg of calcium carbonate per day plus 1000 units of vitamin D was administered once daily in subjects with routine gestational diabetes mellitus during the study and in the control group, no case group drugs were administered and only routine gestational diabetes mellitus therapy was prescribed. **********EDITOR'S NOTE; PLEASE CHECK PREVIOUS SENTENCE********** The duration of the intervention continued until the end of pregnancy. It should be noted that routine gestational diabetes therapy continued for both groups during this period. Participants were also asked not to change their physical activity or dietary intake during the study, and not add any other supplements apart from the supplement provided by the researchers. Fasting blood glucose was measured monthly in both groups until the end of pregnancy.

Descriptive statistics including mean and standard deviation, as well as relative frequency were used to describe the data. To examine the relationships and comparisons between the two groups the chi-square test and multivariate logistic regression were used to evaluate the odds of each of the variables. All analyses were performed using SPSS software version 16 and a significant level (Pvalue<0.05). Sample size using Epi info 7.2 at a significant level of 5% and a power of 80% was determined, and was equal to 42 people in each group and a total of 84 people.

This study with the code of ethics number (IR.SHMU.REC.1396.41) from the research deputy of Shahroud university of medical sciences and with code IRCT20100102002954N11 has been registered in the Iranian clinical trials system. The essential information and the objectives of the study were explained to the patients, and written consent was obtained for participation in the research.

Results

In this study, the mean age of all patients was 29.4 ± 5.2 years and there was no significant difference between the two groups (Pvalue=0.189). The mean BMI of all patients was 25.31 ± 2.72 kg/m2 and there was no significant difference between the two groups (Pvalue=0.312). The mean of the FBS level at the end of the study in the case group was 91.5 ± 12.9 mg/dl and in the control group was 98.9 ± 15.8 mg/dl, showing it was significantly lower in the case group (Pvalue=0.014). The results of the biochemical tests of patients in the two groups are shown in table 1. In this study, independent variables with GDM were investigated in a multivariate regression model. As shown in table 2, GDM variables were significantly associated with a positive history of diabetes mellitus (Pvalue<0.033), the previous history of GDM (Pvalue<0.013) and FBS (Pvalue<0.001) and there was no significant relationship with other variables. The results of the multivariate logistic regression model are presented in table 2.

This study with the code of ethics number (IR.SHMU.REC. 1396.41) was obtained from the research deputy of Shahroud university of medical sciences. Informed consent was obtained from all individual participants included in the study

Table 1. Results of biochemical tests in two groups

Lab test	Case group Mean±SD	Control group Mean±SD	Total Mean±SD	Pvalue
FBS at the beginning of the study (mg/dl)	103.7 ± 12.5	101.5 ± 15.5	102.2 ± 14.5	0.142
FBS at the end of the study (mg/dl)	91.5 ± 12.9	98.9 ± 15.8	95.7 ± 13.5	0.014
BS of 2hpp at the beginning of the study (mg/dl)	156.7 ± 18.6	154.2 ± 16.3	135.5 ± 16.8	0.103
BS of 2hpp at the end of the study (mg/dl)	132.3 ± 11.7	140.4 ± 15.6	115.5 ± 13.8	0.011
HbA1c at the beginning of the study (%)	5.2 ± 1.3	5.1 ± 1.1	5.1 ± 1.7	0.127
HbA1c at the end of the study (%)	4.8 ± 2.1	5.0 ± 1.8	4.9 ± 1.8	0.079

Table 2. Relationship between independent variables with fatty liver in multivariate logistic regression model

Independent variables		Odds ratio	95% Confidence	Pvalue
Age category	18 to 35 years	1.000		
	Less than 18 years	0.812	1.082-0.0672	0.088
	More than 35 years	1.091	1.251-0.0912	0.063
Gravity	1 Pregnancy	1.000		
	2-3 Pregnancy	1.109	1.313-0.915	0.069
	More than 3 Pregnancy	1.188	1.388-0.952	
Body mass index (kg/m^2)	18-25	1.000		
	<18	0.823	0.985-0.756	0.075
	>25	1.275	1.435-0.962	0.053
Positive history of diabetes mellitus	Negative	1.000		
	Positive	1.405	1.748-1.011	0.033
Previous history of GDM	Negative	1.000		
	Positive	1.511	1.823-1.271	0.013
Previous history of stillborn	Negative	1.000		
	Positive	1.026	1.142-0.909	0.079
Fasting blood sugar (mg/dl)	<92	1.000		
	92-125	1.451	1.754-1.256	0.012
	>126	2.885	3.213-2.615	0.001
BS of 2hpp (mg/dl)	<135	1.000		
	135-153	1.121	1.354-0.856	0.059
	>153	1.172	1.413-0.815	0.053
HbA1c (%)	<5.6	1.000		
	5.6-6.5	1.028	1.182-0.957	0.079
	>6.5	1.049	1.213-0.915	0.065

Discussion

The results of this study showed that vitamin D is effective in reducing glycemic gestational diabetes, in such a way that the fasting and glucose levels of 2 hours in the intervention group were less than the control group. Holick et al., in their study on a new approach to the pathogenesis of GDM and insulin resistance, concluded that there is a correlation between vitamin D deficiency and gestational diabetes mellitus. Therefore, it has been suggested that administering vitamin D supplementation in pregnancy is necessary to control many conditions, especially GDM. This finding is in agreement with the results of the present study.[19] The most important known role of vitamin D is in helping calcium balance and absorption, but recently, studies have shown vitamin D plays a role in the development of the brain and the immune system of the fetus and prevention of many autoimmune diseases, such as diabetes and multiple sclerosis in later years.

Lau et al., in a clinical study of hyperglycemia and its complications in pregnancy have shown that vitamin D levels which indirectly correlate with poor blood glucose control, and with correct vitamin D levels, can reduce the incidence of gestational diabetes and its complications.[20] This finding is largely aligned with the results of our study.

Maghbooli et al., in their study, investigated the effect of supplementation of calcium and vitamin D on insulin function, lipid parameters, inflammatory factors and oxidative stress biomarkers in 56 pregnant women with GDM and found that following a prescription of calcium supplements with vitamin D, significantly decreased levels of fasting blood glucose compared with those of the control group; it is consistent with the findings of our research.[21]

Baker et al., found that calcium supplementation with vitamin D in women with GDM has beneficial effects on metabolic parameters and can reduce fasting glucose levels, but it does not have a significant effect on random sugars.[22] This finding is partly consistent with the results of our study but contrasts with non-fasting sugar and perhaps the reason for this is the timing of the non-fasting study of the present study or the type of diet.

Poel et al., reviewed the effect of supplementation and vitamin D in controlling abnormalities of beta cells in pregnant women and showed that prescribing this supplement with vitamin D can greatly increase the levels of natural blood sugar in these women.[23] This finding is similar to that of our research.

In a study by Akhlaghi et al., it was found that many maternal and fetal complications are a risk during gestational diabetes and it is necessary to control diabetes as soon as possible and one of the most important ways is to correct the nutritional status and use of appropriate supplements, including calcium- D.[24] The discovery of the importance of using calcium plus vitamin D in the Pal study is similar to the findings of this study.

As has been seen, the present study showed a strong relationship between the history of diabetes mellitus, previous history of GDM and fasting blood sugar with the incidence of GDM. Considering the pathogenesis of diabetes and progressive degeneration of pancreatic beta cells in diabetic patients and insulin deficiency or in decreasing the sensitivity of cells to insulin, these factors seem to significantly predispose pregnant women to gestational diabetes, therefore it is necessary to carefully observe the history of maternal diabetes in pregnancy and even before pregnancy.[25-27]

The results of this study showed that calcium -D supplementation can significantly reduce the level of glucose and control the condition of women with GDM, so it is recommended that Calcium-D supplementation be prescribed for this group of women.

The limitations of this research include the lack of precise control over the diet of pregnant women during pregnancy and inevitably, one has to rely on what the subjects say about their amount of carbohydrate intake. Therefore, it is of upmost importance that the subjects be educated and persuaded to pay attention to the maximum dietary intake allowed.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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