Original Article

# The effect of combined supplementation with vitamin D and omega-3 fatty acids on blood glucose and blood lipid levels in patients with gestational diabetes

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**Background:** To investigate the effects of vitamin D and omega-3 fatty acids on glucose and blood lipid metabolism in gestational diabetes (GDM) women.

**Methods:** A total of 150 patients with GDM aged 18–40 who were admitted to our hospital from May 2019 to December 2020 were enrolled in this study. The subjects were divided into test and control groups according to whether they took vitamin D and omega-3 fatty acids. The test group took 40,000 IU of vitamin D and 8,000 mg of omega-3 fatty acids twice a day. Comparative analysis of the changes in blood glucose and blood lipid levels of the two groups of patients was performed after 6 weeks. The *t*-test was used to compare the differences between groups, and the chi-square test was used to assess percentage differences. Repeated measures variance was used to analyze the effects of vitamin D and omega-3 fatty acids on insulin metabolism markers and blood lipid profiles.

**Results:** After adjusting for baseline age and weight, it was found that the fasting blood glucose (FBG), fasting insulin, homeostasis model assessment of insulin resistance (HOMA-IR), triglycerides (TGs), total cholesterol, low-density lipoprotein (LDL), and very-low-density lipoprotein (VLDL) in the test group were decreased by 0.3±0.2 mmol/L, 1.0±0.6 uIU/mL, 0.2±0.1, 0.3±0.1 mmol/L, 0.5±0.2 mmol/L, 1.1±0.4 mmol/L, and 0.03±0.01 mmol/L, respectively, while homeostasis model assessment of beta cell (HOMA-β) was increased by 0.4±0.1. Compared to the placebo group, the test group's FBG, insulin, HOMA-IR, TGs, total cholesterol, LDL, and VLDL were all significantly decreased, and HOMA-β was markedly improved. However, no notable statistical difference was observed in the change of high-density lipoprotein (HDL) ($P>0.05$).

**Conclusions:** Combined supplementation with vitamin D and omega-3 fatty acids for 6 weeks in patients with GDM can effectively reduce blood sugar and blood lipids, improve HOMA-β and insulin resistance, and ultimately effectively improve the glucose and lipid metabolism of patients.

**Keywords:** Vitamin D; omega-3 fatty acids; gestational diabetes (GDM)

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## Introduction

Gestational diabetes (GDM) refers to diabetes diagnosed for the first time during pregnancy, and accompanied by any carbohydrate intolerance and impaired insulin metabolism (1). According to diagnostic criteria and pregnancy age, GDM affects 1–14% of pregnancies (2). GDM has an important impact on the health of pregnant women and their offspring, and can easily induce a series of chronic metabolic diseases, dystocia and neonatal diseases (3-5). Also, hyperinsulinemia and hyperglycemia during pregnancy may not be conducive to the growth and development of the offspring, which has an inhibitory effect on the growth of the fetal period and easily induce neonatal inflammation and diabetes (6-8).

Previous studies have shown that compared with healthy pregnant women, GDM patients have lower vitamin D and omega-3 fatty acids (9,10). However, there are currently no studies that fully analyze the effects of vitamin D supplements and omega-3 fatty acids on metabolism (11,12). Also, the effect of supplementing vitamin D or omega-3 fatty acids alone in women with GDM is uncertain. Studies have shown that vitamin D at a dose of 50,000 IU every 3 weeks for 6 weeks can improve blood glucose, total cholesterol, and low-density lipoprotein (LDL) cholesterol levels in GDM women, however it does not improve insulin resistance (13). Also, after 6 weeks of daily intake of 1,000 mg of omega-3 fatty acids, it was observed that insulin resistance in GDM subjects was significantly improved, but there was no change in blood glucose, insulin sensitivity, and blood lipid levels (14). Another study by Baidal *et al.* showed that high-dose omega-3 fatty acids and high-dose vitamin D3 treatment improved homeostasis model assessment of beta cell (HOMA-β) in patients with type 1 new-onset diabetes (15).

Therefore, this study aimed to investigate the effects of vitamin D and omega-3 fatty acids on glucose and blood lipid metabolism in GDM women.

We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/apm-21-1018).

## Methods

### Research object

One hundred and fifty patients with GDM between 18 and 40 years old who were admitted to our hospital from May 2019 to December 2020 were included. According to the guidelines of the American Diabetes Association (16), GDM is defined as no previous history of diabetes, and any of the following criteria is met during pregnancy: (I) fasting blood glucose (FBG) ≥5.1 mmol/L; (II) oral glucose tolerance test (OGTT)-1 h blood glucose ≥10.0 mmol/L; (III) OGTT-2 h blood glucose ≥8.5 mmol/L. The exclusion criteria were as follows: (I) patients who were using insulin; (II) those with placental abruption; (III) patients with pre-eclampsia; (IV) patients with eclampsia; (V) those with hypothyroidism or hyperthyroidism; (VI) smokers; and (VII) patients with kidney or liver disease. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Haikou Hospital of the Maternal and Child Health (No. 2018281) and informed consent was taken from all the patients.

### Data collection

The patients were divided into test and control groups according to whether they took vitamin D and omega-3 fatty acids. The test group took 40,000 IU of vitamin D and 8,000 mg of omega-3 fatty acids twice a day. Comparative analysis of the changes in blood glucose and blood lipid levels of the two groups of patients was performed after 6 weeks. The clinical and laboratory data of the research subjects were collected, including gender, age, body mass index (BMI), FBG, fasting insulin, triglyceride (TG), high-density lipoprotein (HDL), LDL, very-low-density lipoprotein (VLDL), and total cholesterol. Also, the homeostasis model assessment of insulin resistance (HOMA-IR) and HOMA-β were calculated.

### Statistical methods

Continuous variables were expressed as mean ± standard deviation, and categorical variables are expressed as the number of cases (percentage). The differences between groups were compared using the *t*-test, and the chi-square test was used to assess percentage differences. Repeated measures variance was used to analyze the effects of vitamin D and omega-3 fatty acids on insulin metabolism markers and blood lipid profiles. The mother's age and baseline BMI were adjusted to avoid potential confounding effects. SAS software (version 9.4, North Carolina State University, USA) was used to analyze the data, and the difference was considered statistically significant when P<0.05.

**Table 1** Clinical data of study subjects

| Variables | Test group (n=80) | Control group (n=70) | P value |
|---|---|---|---|
| Age (year) | 31.5±4.1 | 31.3±4.7 | 0.09 |
| Height (cm) | 163.7±3.8 | 163.4±3.0 | 0.17 |
| Baseline weight (kg) | 73.8±3.8 | 75.9±4.0 | 0.28 |
| Weight after 6 weeks (kg) | 75.8±3.6 | 77.8±3.9 | 0.31 |
| Weight change (kg) | 2.0±0.9 | 1.9±0.6 | 0.47 |
| Baseline BMI (kg/$m^2$) | 28.9±3.2 | 29.1±0.8 | 0.51 |
| BMI after 6 weeks (kg/$m^2$) | 29.3±3.5 | 30.1±3.8 | 0.29 |
| BMI changes (kg/$m^2$) | 0.4±0.1 | 0.8±0.2 | 0.67 |

BMI, body mass index.

## Results

### *Clinical data of study subjects*

Among the 150 patients with GDM included in the study, 80 patients took vitamin D and omega-3 fatty acids. The average age of these 80 patients was 31.5±4.1 years, the height was 163.7±3.8 cm, and the baseline weight was 73.8±3.8 kg. After taking vitamin D and omega-3 fatty acids for 6 weeks, the body weight was 75.8±3.6 kg, the body weight change was 2.0±0.9 kg, and the baseline BMI, BMI, and BMI change after 6 weeks were 28.9±3.2 kg/$m^2$, 29.3±3.5 kg/$m^2$, and 0.4±0.1 kg/$m^2$, respectively (*Table 1*). There were no statistical differences (P>0.05) in the clinical data between the test and control groups.

### *Baseline glucose and lipid metabolism of the study subjects*

The subjects' baseline glucose and lipid metabolism data showed that the average FBG, fasting insulin, HOMA-IR, and HOMA-β of the experimental group were 5.6±0.9 mmol/L, 13.5±4.6 uIU/mL, 3.2±1.1, and 47.8±16.3, respectively. The average levels of TGs, total cholesterol, LDL, HDL, and VLDL were 2.7±1.2 mmol/L, 6.3±2.1 mmol/L, 4.2±1.8 mmol/L, 1.3±0.9 mmol/L, and 0.92±0.11 mmol/L, respectively (*Table 2*). No significant statistical differences were observed between the baseline levels of glucose and lipid metabolism between the test and control groups (all P>0.05).

### *Changes in glucose and lipid metabolism after using vitamin D and omega-3 fatty acids for 6 weeks*

After using vitamin D and omega-3 fatty acids for 6 weeks, the FBG (–0.5±0.2 *vs.* 0.8±0.1 mmol/L), fasting insulin (–1.9±1.1 *vs.* 2.3±1.2 uIU/ mL), HOMA-IR (–0.4±0.2 *vs.* 0.9±0.5), TGs (–0.5±0.2 *vs.* 0.4±0.1), total cholesterol (–0.8±0.6 *vs.* 2.8±0.9), LDL (–1.4±0.6 *vs.* 1.8±0.4), and VLDL (–0.05±0.02 *vs.* 0.08±0.03) of the test group were markedly decreased compared to the control group (all P<0.05). As shown in *Table 3*, HOMA-β (0.5±0.2 *vs.* –0.1±0.3) was significantly improved (P<0.05). However, there were no notable differences in the changes of HDL between the test and control groups (P>0.05).

### *The effect of using vitamin D and omega-3 fatty acids for 6 weeks on glucose and lipid metabolism*

After adjusting for baseline age and weight, we found that the test group's FBG, fasting insulin, HOMA-IR, TGs, total cholesterol, LDL, and VLDL were decreased by 0.3±0.2 mmol/L, 1.0±0.6 uIU/mL, 0.2±0.1, 0.3±0.1 mmol/L, 0.5±0.2 mmol/L, 1.1±0.4 mmol/L, and 0.03±0.01 mmol/L, respectively, however HOMA-β was improved by 0.4±0.1. Compared with the placebo group, the test group's FBG, insulin, HOMA-IR, TGs, total cholesterol, LDL, and VLDL all decreased significantly and HOMA-β was markedly improved, however there was no statistically significant difference in the change of HDL (P>0.05) (*Table 4*).

**Table 2** Baseline glucose and lipid metabolism of subjects

| Variables | Test group (n=80) | Control group (n=70) | P value |
|---|---|---|---|
| FBG (mmol/L) | 5.6±0.9 | 5.8±0.7 | 0.42 |
| Fasting insulin (uIU/mL) | 13.5±4.6 | 13.8±2.8 | 0.32 |
| HOMA-IR | 3.2±1.1 | 3.2±1.5 | 0.19 |
| HOMA-β | 47.8±16.3 | 49.2±9.3 | 0.12 |
| TGs (mmol/L) | 2.7±1.2 | 2.6±0.9 | 0.43 |
| Total cholesterol (mmol/L) | 6.3±2.1 | 6.5±3.7 | 0.56 |
| LDL (mmol/L) | 4.2±1.8 | 4.4±2.0 | 0.72 |
| HDL (mmol/L) | 1.3±0.9 | 1.2±0.6 | 0.86 |
| VLDL (mmol/L) | 0.92±0.11 | 0.91±0.12 | 0.91 |

FBG, fasting blood glucose; HOMA-IR, homeostasis model assessment of insulin resistance; HOMA-β, homeostasis model assessment of beta cell; TG, triglyceride; LDL, low-density lipoprotein; HDL, high-density lipoprotein; VLDL, very low-density lipoprotein.

**Table 3** Changes in glucose and lipid metabolism after using vitamin D and omega-3 fatty acids for 6 weeks (uncorrected)

| Glucolipid metabolic variables | Change from baseline to week 6 | | |
|---|---|---|---|
| | Control group (n=70) | Test group (n=80) | P value |
| FBG (mmol/L) | 0.8±0.1 | –0.5±0.2 | <0.001 |
| Fasting insulin (uIU/mL) | 2.3±1.2 | –1.9±1.1 | <0.001 |
| HOMA-IR | 0.9±0.5 | –0.4±0.2 | <0.001 |
| HOMA-β | –0.1±0.3 | 0.5±0.2 | <0.001 |
| TGs (mmol/L) | 0.4±0.1 | –0.5±0.2 | <0.001 |
| Total cholesterol (mmol/L) | 2.8±0.9 | –0.8±0.6 | <0.001 |
| LDL (mmol/L) | 1.8±0.4 | –1.4±0.6 | <0.001 |
| HDL (mmol/L) | 0.3±0.5 | 0.4±0.5 | 0.89 |
| VLDL (mmol/L) | 0.08±0.03 | –0.05±0.02 | 0.008 |

FBG, fasting blood glucose; HOMA-IR, homeostasis model assessment of insulin resistance; HOMA-β, homeostasis model assessment of beta cell; TG, triglyceride; LDL, low-density lipoprotein; HDL, high-density lipoprotein; VLDL, very low-density lipoprotein.

## Discussion

Vitamin D is an essential vitamin for the human body. It is involved in regulating calcium and phosphorus metabolism, as well as maintaining healthy bone mineralization (17). Experimental studies have shown that 1,25-dihydroxy vitamin D [1,25(OH)$_2$D], the active form of vitamin D, plays an important role in the stability of the innate and adaptive immune systems, as well as the stability of endothelial cell membranes. The relationship between low serum 25-hydroxyvitamin D levels and increased risk of various immune-related diseases and disorders has been observed, including psoriasis, type 1 diabetes, multiple sclerosis, rheumatoid arthritis, tuberculosis, sepsis, and respiratory tract infections, etc. (18-22). Omega-3 fatty acids are an important component of cell membranes and have antioxidant effects (23,24). Previous studies have found that patients with GDM are often prone to vitamin D and omega-3 fatty acid deficiencies, which may be related to the increased demand during pregnancy and the development of diabetes (25). During pregnancy, hyperglycemia and hyperinsulinemia may lead to permanent diabetes and neonatal complications, including macrosomia and hyperbilirubinemia (26).

 

**Table 4** Changes in glucose and lipid metabolism of vitamin D and omega-3 fatty acids for 6 weeks (after correction)

| Glucolipid metabolic variables | Change from baseline to week 6 | | |
|---|---|---|---|
| | Control group (n=70) | Test group (n=80) | P value |
| FBG (mmol/L) | 0.6±0.1 | –0.3±0.2 | 0.007 |
| Fasting insulin (uIU/mL) | 1.8±0.7 | –1.0±0.6 | 0.004 |
| HOMA-IR | 0.3±0.1 | –0.2±0.1 | 0.03 |
| HOMA-β | –0.1±0.1 | 0.4±0.1 | 0.005 |
| TGs (mmol/L) | 0.3±0.1 | –0.3±0.1 | 0.02 |
| Total cholesterol (mmol/L) | 1.8±0.6 | –0.5±0.2 | 0.002 |
| LDL (mmol/L) | 1.2±0.3 | –1.1±0.4 | 0.001 |
| HDL (mmol/L) | 0.3±0.1 | 0.3±0.1 | 0.71 |
| VLDL (mmol/L) | 0.04±0.01 | –0.03±0.01 | 0.02 |

FBG, fasting blood glucose; HOMA-IR, homeostasis model assessment of insulin resistance; HOMA-β, homeostasis model assessment of beta cell; TG, triglyceride; LDL, low-density lipoprotein; HDL, high-density lipoprotein; VLDL, very low-density lipoprotein.

This study reported, for the first time, the effect of combined vitamin D and omega-3 fatty acid supplementation on blood sugar. After 6 weeks of supplementation with vitamin D and omega-3 fatty acids in GDM patients, FBG, insulin, HOMA-IR, TGs, total cholesterol, LDL, and VLDL were all significantly decreased, while HOMA-β was dramatically improved. Studies have shown that improving insulin resistance may help to reduce maternal mortality and neonatal complications (27). Consistent with previous studies, this study found that supplementation with vitamin D and omega-3 fatty acids can considerably reduce blood sugar levels (28). Vitamin D is closely related to calcium and phosphorus metabolism. It can affect blood sugar by up-regulating insulin receptor gene expression and transcription (29).

Vitamin D and omega-3 fatty acids may be more effective in treating patients with GDM than a single supplement. In affecting islet blood sugar, omega-3 fatty acids and vitamin D may have a synergistic effect (30). Also, supplementing with omega-3 fatty acids may lead to increased vitamin D content. An *et al.* observed that, compared with the control group, the vitamin D 1,25$(OH)_2$D levels of dialysis patients who took omega-3 fatty acids without vitamin D increased significantly after 3 months compared with the baseline examination (31). Studies have found that vitamin D deficiency and inflammation alleviation could reduce insulin resistance (32).

This study shows that supplementation with vitamin D and omega-3 fatty acids in GDM patients for 6 weeks can significantly reduce serum TGs, LDL, and VLDL cholesterol, which is consistent with the findings of Davis *et al.*, which indicated the total cholesterol and LDL cholesterol were decreased in healthy people who supplemented with vitamin D and omega-3 fatty acids for 18 months (33). Furthermore, a previous study showed that the increase in maternal lipids was related to complications such as macrosomia, with 36 cases of preeclampsia and 37 cases of preterm delivery (34). However, this study lacked consideration of baseline levels and the specific effects of the subjects themselves. Vitamin D intake may improve lipid distribution and improve insulin sensitivity by increasing calcium absorption (35). Moreover, the intake of omega-3 fatty acids may eliminate chylomicrons and reduce liver production to reduce TGs and VLDL cholesterol levels (36).

This study has certain limitations that should be noted. Firstly, the average age of GDM patients included in this study was >30 years old. Although these patients belong to the high incidence of GDM age group, they are not within the general age of normal pregnancy. Thus, the included population is relatively limited, and further research is needed to confirm our conclusions. Secondly, polycystic ovary syndrome is an important risk factor for the progression of GDM itself, but because the collected clinical data was very limited, it was impossible to analyze the confounding influence of polycystic ovary syndrome on blood glucose changes.

 

In summary, combined supplementation with vitamin D and omega-3 fatty acids for 6 weeks in patients with GDM can effectively reduce fasting blood sugar, TGs, HDL, LDL, and total cholesterol, improve HOMA-β and insulin resistance, and ultimately effectively improve the glucose and lipid metabolism of patients.

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## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist Available at http://dx.doi.org/10.21037/apm-21-1018

*Data Sharing Statement:* Available at http://dx.doi.org/10.21037/apm-21-1018

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/apm-21-1018). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Haikou Hospital of the Maternal and Child Health (No. 2018281) and informed consent was taken from all the patients.



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