

Original Contribution

The effects of vitamin D and omega-3 fatty acid co-supplementation on glycemic control and lipid concentrations in patients with gestational diabetes

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KEYWORDS:

Vitamin D;
Omega-3 fatty acid;
Supplementation;
Glycemic control;
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OBJECTIVE: This study was performed to evaluate the effects of vitamin D and omega-3 fatty acids co-supplementation on glucose metabolism and lipid concentrations in gestational diabetes (GDM) patients.

METHODS: This randomized double-blind placebo-controlled clinical trial was done among 140 GDM patients. Participants were randomly divided into 4 groups to receive: (1) 1000 mg omega-3 fatty acids containing 360 mg eicosapentaenoic acid and 240 mg docosahexaenoic acid (DHA) twice a day + vitamin D placebo ($n = 35$); (2) 50,000 IU vitamin D every 2 weeks + omega-3 fatty acids placebo ($n = 35$); (3) 50,000 IU vitamin D every 2 weeks + 1000 mg omega-3 fatty acids twice a day ($n = 35$), and (4) vitamin D placebo + omega-3 fatty acids placebo ($n = 35$) for 6 weeks.

RESULTS: After 6 weeks of intervention, patients who received combined vitamin D and omega-3 fatty acids supplements compared with vitamin D, omega-3 fatty acids, and placebo had significantly decreased fasting plasma glucose (-7.3 ± 7.8 , -6.9 ± 6.6 , -4.0 ± 2.5 , and $+1.0 \pm 11.4$ mg/dL, respectively, $P < .001$), serum insulin levels (-1.9 ± 1.9 , -1.3 ± 6.3 , -0.4 ± 6.3 , and $+2.6 \pm 6.5$ μ IU/mL, respectively, $P = .005$), homeostatic model of assessment for insulin resistance (-0.7 ± 0.6 , -0.5 ± 1.4 , -0.2 ± 1.5 , and $+0.6 \pm 1.5$, respectively, $P < .001$) and increased quantitative insulin sensitivity check index ($+0.01 \pm 0.01$, $+0.008 \pm 0.02$, $+0.002 \pm 0.02$, and -0.005 ± 0.02 , respectively, $P = .001$). In addition, changes in serum triglycerides (-8.2 ± 41.0 , $+7.6 \pm 31.5$, $+3.6 \pm 29.9$, and $+20.1 \pm 29.6$ mg/dL, respectively, $P = .006$) and

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very low-density lipoprotein cholesterol (-1.6 ± 8.2 , $+1.5 \pm 6.3$, $+0.8 \pm 6.0$, and $+4.0 \pm 5.9$ mg/dL, respectively, $P = .006$) in the vitamin D plus omega-3 fatty acids group were significantly different from the changes in these indicators in the vitamin D, omega-3 fatty acids, and placebo groups.

CONCLUSION: Overall, vitamin D and omega-3 fatty acids co-supplementation for 6 weeks among GDM patients had beneficial effects on fasting plasma glucose, serum insulin levels, homeostatic model of assessment for insulin resistance, quantitative insulin sensitivity check index, serum triglycerides, and very low-density lipoprotein cholesterol levels.

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Introduction

Gestational diabetes (GDM) is defined as any carbohydrate intolerance and impaired insulin metabolism with the onset or first recognition during pregnancy.¹ GDM affects 1% to 14% of pregnancies depending on the diagnostic criteria, gestational age, and characteristics of the study population.² GDM is associated with a marked effect on the future health of both mother and offspring including pre-eclampsia,³ shoulder dystocia, higher rates of cesarean section,⁴ macrosomia, neonatal hypoglycemia, and respiratory distress syndrome.⁵ In addition, hyperinsulinemia and hyperglycemia during pregnancy have the potential to be detrimental to growth and metabolism in the offspring.⁶ Dyslipidemia is associated with type II diabetes mellitus,⁷ endothelial dysfunction, atherosclerosis, and intrauterine growth retardation.⁸

Prior studies have suggested that circulating levels of vitamin D⁹ and omega-3 fatty acids¹⁰ were low in GDM subjects than those healthy pregnant women. In addition, data on the effect of vitamin D or omega-3 fatty acids supplementation alone on metabolic profiles are conflicting. Nowadays, there is a growing interest to use vitamin D and omega-3 fatty acids during pregnancy. The basis of this interest is because of both vitamin D deficiency during pregnancy¹¹ and the results of epidemiologic observations exhibiting the significant inverse association between vitamin D or omega-3 fatty acids and pregnancy complications.^{12,13} Furthermore, few studies have reported the beneficial effects of vitamin D or omega-3 fatty acids supplementation alone among GDM women. We have previously shown that vitamin D treatment at dosage of 50,000 IU every 3 weeks for 6 weeks in women with GDM improved glycemia, total cholesterol, and LDL cholesterol concentrations but did not influence other lipid profiles.¹⁴ Improved insulin resistance was also observed after the intake of 1000 mg omega-3 fatty acids per day for 6 weeks in GDM subjects, but unchanged plasma glucose, insulin sensitivity, and lipid profiles.¹⁵ In another study by Baidal et al.¹⁶ was seen that combined high-dose omega-3 fatty acids and high-dose vitamin D3 therapy improved beta-cell function in patients with new onset type I diabetes mellitus.

There are speculations that vitamin D and omega-3 fatty acids may improve metabolic status because of their shared functions and each nutrient-specific role that complements the other nutrient's functions.^{17,18} This trial was, therefore,

conducted to investigate the effects of vitamin D and omega-3 fatty acids co-supplementation on parameters of glucose homeostasis and lipid concentrations in GDM women.

Methods

Trial design

The present study was a 6-week prospective randomized double-blind placebo controlled clinical trial.

Participants

This study was done among 140 GDM subjects aged 18-40 years without prior diabetes that have been diagnosed with GDM by "one-step" 2-h 75-g oral glucose tolerance test (OGTT) at 24-28 weeks' gestation referred to Kosar Clinic in Arak, Iran from March 2016 to July 2016. We diagnosed GDM based on the American Diabetes Association guidelines¹⁹: those whose plasma glucose met 1 of the following criteria were considered as having GDM: fasting plasma glucose (FPG) ≥ 92 mg/dL, 1-hour OGTT ≥ 180 mg/dL, and 2-hour OGTT ≥ 153 mg/dL.¹⁹ Exclusion criteria were taking vitamin D and/or omega-3 fatty acids supplements, taking insulin, placenta abruption, pre-eclampsia, eclampsia, hypothyroidism and hyperthyroidism, smokers, those with kidney or liver diseases.

Ethics statements

This research was conducted according to the principles of the Declaration of Helsinki, and the study protocol was approved by the ethics committee of Arak University of Medical Sciences (reference number IR.ARAK-MU.REC.1394.373). The study protocol was carefully explained to all subjects before obtaining informed consent form. This trial was registered in the Iranian Web site (www.irct.ir) for registration of clinical trials (<http://www.irct.ir: IRCT201605135623N78>).

Study design

Patients were initially randomized to "intervention vs Placebo," and then divided into the 4 groups to intake omega-3 fatty acids ($n = 35$), vitamin D ($n = 35$), vitamin

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