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Original article

Effects of probiotic supplementation on glycaemic control and lipid profiles in gestational diabetes: A randomized, double-blind, placebo-controlled trial

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Abstract

Background. – To our knowledge, data on the effects of probiotic supplementation on glycaemic control and lipid concentrations in patients with gestational diabetes mellitus (GDM) are scarce.

Aim. – The aim of the present study was to determine the effects of probiotic supplementation on glycaemic control and lipid profiles in GDM patients.

Methods. – Sixty pregnant women with GDM, primigravida and aged 18–40 years, were divided into two groups to receive either probiotic capsules ($n=30$) or a matching placebo ($n=30$) in this randomized double-blind, placebo-controlled trial. The patients in the probiotic group took a daily capsule that contained three viable freeze-dried strains: *Lactobacillus acidophilus* (2×10^9 CFU/g), *L. casei* (2×10^9 CFU/g) and *Bifidobacterium bifidum* (2×10^9 CFU/g) for 6 weeks. The placebo group took capsules filled with cellulose for the same time period. Fasting blood samples were taken at the beginning and end of the study to quantify the relevant markers.

Results. – After 6 weeks of intervention, probiotic supplementation vs a placebo resulted in significant decreases in fasting plasma glucose (-9.2 ± 9.2 mg/dL vs $+1.1\pm12.2$ mg/dL, $P<0.001$), serum insulin levels (-0.8 ± 3.1 μIU/mL vs $+4.5\pm10.6$ μIU/mL, $P=0.01$), homoeostasis model assessment (HOMA) for insulin resistance (-0.4 ± 0.9 vs $+1.1\pm2.5$, $P=0.003$) and HOMA for β-cell function ($+1.1\pm9.8$ vs $+18.0\pm42.5$, $P=0.03$), and a significant increase in the quantitative insulin sensitivity check index ($+0.007\pm0.01$ vs -0.01 ± 0.02, $P=0.007$). In addition, significant decreases in serum triglycerides (-1.6 ± 59.4 mg/dL vs $+27.1\pm37.9$ mg/dL, $P=0.03$) and VLDL cholesterol concentrations (-0.3 ± 11.9 mg/dL vs $+5.4\pm7.6$ mg/dL, $P=0.03$) were seen following supplementation with the probiotics compared with the placebo. However, no significant changes in other lipid profiles were seen with the intervention.

Conclusion. – Overall, the results of our study have demonstrated that taking probiotic supplements for 6 weeks in patients with GDM had beneficial effects on glycaemic control, triglycerides and VLDL cholesterol concentrations, although there was no effect on other lipid profiles.

Keywords: Gestational diabetes mellitus; Insulin resistance; Lipid profiles; Probiotic supplementation

1. Introduction

Gestational diabetes mellitus (GDM), carbohydrate intolerance and insulin resistance resulting in hyperglycaemia with onset or first recognition during pregnancy is a growing problem worldwide [1]. The prevalence of GDM varies from 1.4 to 12.3% of pregnancies, depending on the diagnostic criteria, gestational

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age and characteristics of the study population [2]. However, few studies have reported that changes in the human gut microbiome are associated with metabolic diseases, including type 2 diabetes mellitus (T2DM), insulin resistance [3], inflammation and weight gain [4]. GDM women are at increased risk of adverse long-term health outcomes, including the development of T2DM, cardiovascular disease and the metabolic syndrome [5].

The potential role of intestinal microflora in decreasing insulin resistance and lipid profiles has resulted in an interest in using probiotic bacteria as both preventative and therapeutic interventions. There is emerging evidence regarding the use of probiotics in the prevention of GDM [6]. Probiotics are living microorganisms that, when administered in adequate amounts, confer health benefits to the host [7]. Luoto et al. [8] demonstrated that probiotic supplementation (with *Lactobacillus rhamnosus* GG and *Bifidobacterium lactis* Bb12 at a dose of 10^{10} colony-forming units [CFU]/day each) in normal-weight women during pregnancy resulted in a decline in the rate of GDM from 34 to 13%. In addition, a systematic review showed that probiotic use during pregnancy could significantly reduce maternal fasting glucose levels and the incidence of GDM [9]. Nevertheless, only a few studies have assessed the effects of probiotic supplementation on insulin resistance and lipid profiles during pregnancy, and their results were conflicting. Laitinen et al. [10] demonstrated that probiotic use (*L. rhamnosus* GG and *B. lactis* Bb12 at a dose of 10^{10} CFU/day each) combined with a dietary intervention in healthy pregnant women resulted in improved glycaemic control. Furthermore, our own previous study found that probiotic yoghurt consumption in healthy pregnant women without GDM for 9 weeks led to a significant reduction in all lipid levels, although these reductions were not significant compared with conventional yoghurt [11]. Some studies have even shown that *L. rhamnosus* and *B. lactis* both have antihyperglycaemic and antidiabetic effects [12,13]. The different dosages and types of probiotic bacteria used may explain any discrepant findings.

Probiotic intake may improve markers of insulin resistance and lipid profiles in GDM patients through its anti-inflammatory effects (both locally in the gut and systemically) [14,15], increased production of bacteriocins [16] and short-chain fatty acids (SCFAs) such as butyric acid [17], and by downregulating inflammation and blocking suppression of glucose transporter type 4 (GLUT4) [18]. However, to our knowledge, data thus far on the effects of probiotic supplementation on markers of insulin resistance and lipid concentrations in patients with GDM are scarce. Thus, the objective of the present study was to assess the effects of probiotic supplementation on glycaemic status and lipid profiles in pregnant women with GDM.

2. Methods

In the present prospective randomized double-blind, placebo-controlled clinical trial, 60 pregnant primigravida women, aged 18–40 years and without previous diabetes, who had all been diagnosed with GDM by a 'one-step' 2-h 75-g oral glucose tolerance test (OGTT) at 24–28 weeks of gestation and referred to Kosar Clinic in Arak, Iran, between November 2015 and January 2016, were selected as our study participants. They were diagnosed as GDM based on American Diabetes Association guidelines [19]. Women whose plasma glucose levels met any of the following criteria were considered to have GDM: fasting plasma glucose (FPG) $\geq$ 92 mg/dL; 1-h OGTT $\geq$ 180 mg/dL; or 2-h OGTT $\geq$ 153 mg/dL [19]. Before the intervention, women with preterm premature rupture of membranes, placental abruption, preeclampsia, eclampsia, hypo- or hyperthyroidism, a history of T2DM, a family history of GDM, smokers, and those with kidney or liver disease, or taking probiotics, antibiotics or glucocorticoids, or requiring insulin therapy, were excluded.

The current study was conducted according to the principles of the Declaration of Helsinki, and the study protocol was approved by the ethics committee of the Arak University of Medical Sciences (AUMS; reference number IR.ARAKMU.REC.1394.256). The study protocol was carefully explained to all participants before obtaining their informed consent. The study was registered on the Iranian website (http://www.irct.ir) for registration of clinical trials (http://www.irct.ir: IRCT201601035623N63).

2.1. Study design

At the beginning of the study and after stratification of participants based on their baseline body mass index (BMI; < 25 and $\geq$ 25 kg/m^2) and age (< 30 and $\geq$ 30 years), the recruited women were randomized into two groups to receive either probiotic supplements ($n = 30$) or a placebo ($n = 30$) for 6 weeks. As the participants in our study were all primigravida, their stratification was based on age 30 years. On starting the study, the women were requested not to change their routine physical activity or usual dietary intakes throughout the study, and not to consume any supplements other than the one provided to them by the investigators and also not to take any medications that might affect any findings during the 6-week intervention. All participants had to complete 3-day food diaries and physical activity records at weeks 0, 3 and 6 of the intervention. Dietary intakes were quantified by a trained nutritionist and evaluated by the Nutritionist IV software programme (First DataBank, San Bruno, CA, USA), modified for Iranian foods for total energy, carbohydrates, fats, proteins and micronutrients. In the present study, physical activity was described as metabolic equivalents (METs) in h/day. To determine the METs for each patient, the times (as h/day) reported for each physical activity was multiplied by its related MET coefficient, using the standard tables [20].

The probiotic capsules contained *L. acidophilus* (2×10^9 CFU/g), *L. casei* (2×10^9 CFU/g) and *B. bifidum* (2×10^9 CFU/g) strains. Participants in the placebo group received capsules containing starch and no probiotic bacteria. These placebo capsules were indistinguishable in colour, shape, size and packaging, as well as in smell and taste, from the probiotic capsules. All capsules were produced by the Tak Gen