Original Article

Impacts of dietary fat changes on pregnant women with gestational diabetes mellitus: a randomized controlled study

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Objective: This study aims to determine the impact of increasing polyunsaturated fatty acid intake on blood glucose, lipid metabolism, and pregnancy outcomes of pregnant women with gestational diabetes mellitus. **Methods:** Under constant total energy and protein intake, 84 pregnant women with gestational diabetes mellitus were randomly divided into the experimental and control groups, which were given oil-rich and conventional low-oil meals, respectively. **Results:** After the dietary intervention, the intake and energy supply of fat and the three fatty acids were significantly higher in the experimental group than the control group (p<0.001). The intake and energy supply of polyunsaturated fatty acids increased significantly post-intervention in the experimental group but did not change in the control group. In both the intervention and the control group, fasting blood glucose, 2 h postprandial plasma glucose, and the insulin resistance index decreased significantly post-intervention (p<0.05); the lipid changes were consistent between groups. Pregnancy outcomes did not differ significantly between the two groups (p>0.05). **Conclusions:** An appropriate increase in polyunsaturated fatty acid intake benefits pregnant women with gestational diabetes mellitus as well as fetuses, as long as the diet therapy follows basic recommendations and total energy intake is strictly controlled.

Key Words: gestational diabetes mellitus, diet structure, vegetable oil, fatty acids, blood lipid

INTRODUCTION

Gestational diabetes mellitus (GDM) refers to diabetes in women who exhibit normal pre-pregnancy glucose metabolism that only appears during pregnancy.[1] The prevalence of GDM in pregnant women in China is 1%-5% and is currently increasing.[2,3] GDM can substantially harm both mothers and infants; more than half of pregnant women with GDM develop overt diabetes within the next 20 years, and their offspring are also at risk for obesity and diabetes.[1] Research in the latest decade shows that an inappropriate diet during pregnancy, such as high fat intake, low carbohydrate and fiber intake, and high glucose load diet, increases the risk of GDM.[4,5] In addition, reduced dietary intake of polyunsaturated fatty acids (PUFA) is an independent risk factor for GDM.[6] Meanwhile, improvements in the living standards of Chinese people have resulted in the dietary structure changing from mainly vegetables to mainly animal food products, which contain high fat and protein contents. Moreover, high fat, high saturated fatty acid (SFA), and low PUFA intake are also risk factors for GDM.[7] Dietary nutrition intervention is the most basic treatment for GDM. In clinical practice, approximately 80%-90% of GDM patients only require control of nutrition and can maintain blood sugar within the normal range and obtain good pregnancy outcomes.[8] However, it remains challenging to prepare appropriate individualized dietary interventions for pregnant women with GDM that consider the dietary habits of pregnant women as well as the limitations of traditional dietary habits for better compliance. A diet rich in n-3 PUFA could significantly improve the insulin resistance induced by SFA intake.[9] In this study, in accordance with the principle of individualization and a cultural preference for fried foods, dietary fat intake and composition were adjusted while maintaining total energy and protein intake in order to examine the effects of increased PUFA intake on postprandial glucose, lipid metabolism, insulin resistance, and pregnancy outcomes of pregnant women

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with GDM.

MATERIALS AND METHODS

Subjects

Pregnant women with GDM diagnosed in the obstetric clinics of Changzhou MCH Hospital from January 2011 to January 2013 were enrolled. The patients were aged 22-38 years and 24-28 weeks pregnant. They were not associated with pregnancy-related complications and had no history of diabetes, hypertension or GDM. Finally, the women were residents of Changzhou and only performed light physical activity (such as typewriting, 6 h/day). After considering factors such as willingness to accept dietary intervention, cook, and dine out, a total of 84 women were included. They were randomly divided into 2 groups: 41 and 43 patients were included in the experimental and control groups, respectively. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Nanjing Medical University. Written informed consent was obtained from all participants.

Diagnostic criteria for GDM

A 75 g oral glucose tolerance test (OGTT) was performed at 24-28 weeks of pregnancy. Glucose levels after fasting, and 1 and 2 h after glucose administration <5.1, <10.0, and <8.5 mmol/L, respectively, were considered normal; if the glucose level exceeded the standard at any point, the patient was diagnosed as GDM.[10]

Dietary assessment

A dietary survey was performed at 24-28 weeks of pregnancy. Before the survey, food weight models were introduced to the pregnant women, and a 24 h dietary survey was subsequently performed by a special nurse. All types and amounts of daily food intake during the past 3 days were recorded, and a perinatal nutrition management system (Shanghai Zhending Computer Technology Co., Ltd., Shanghai, China) was used to analyze the intake of total energy, nutrients, proteins, fats, carbohydrates, and fatty acids. During the dietary survey, height, weight, and other information such pre-pregnancy weight were measured by a special nurse. Pre-pregnancy body mass index (BMI) and weight gain were subsequently calculated (BMI=body weight in kg/height in m^2).

Dietary interventions

After the dietary survey, a 75 g OGTT was performed. After the diagnosis of GDM, a nutritionist from the maternal nutrition clinic provided individualized dietary guidance. The total daily calories were calculated according to the patient's height, weight, gestational weeks, and physical strength. The total caloric intake of a light physical worker in late pregnancy was calculated as follows: ideal weight × 30 kcal/kg· day + 200 kcal. Protein should account for 15%-20% of the total energy (i.e., energy supply percentage) in order to maintain total energy and protein intake. The experimental group was prescribed an oil-rich diet, with carbohydrates and fat accounting for 50%-54% and 31%-35% of the total energy, respectively; sunflower oil (45-50 g daily) was used as cooking oil. Meanwhile, the control group was prescribed a low-oil diet, with carbohydrates and fat accounting for 55%-60% and 25%-30% of the total energy, respectively; sunflower oil (20 g daily) was also used as cooking oil. Breakfast, snacks, lunch, snacks, dinner, and snacks composed 20%, 5%, 35%, 5%, 30%, and 5% of total energy intake, respectively. Three days after the initiation of dietary intervention, fasting and postprandial blood glucose levels were measured. Blood lipids were retested 6-8 weeks later. The patients were subsequently tracked until childbirth; during this period, special nurses performed weekly follow-up by telephone to ascertain the patients' dietary situations as well as 24 h dietary surveys in person every 4 weeks. The patients were also asked to keep a daily food diary to ensure they adhered to the intervention. Finally, each patient was given an oil control pot to control the amount of cooking oil used.

Evaluation indicators

The pre-intervention diet analysis included the intake of total energy, macronutrients, (i.e., proteins, fats, and carbohydrates), and fatty acids; fasting blood glucose (FBG), 2 h postprandial blood glucose (2hPG), fasting insulin, serum total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C). After the intervention until to delivery, the diet analysis included FBG, 2hPG, fasting insulin, TC, TG, and HDL-C. Blood lipid and sugar levels were measured by a Hitachi 7180 automatic biochemical analyzer, and the reagents were provided by Wako (Tokyo, Japan). Pregnancy weight gain, infant birth weight, and maternal and perinatal complications were also assessed. The insulin sensitivity index (IAI) was calculated as follows: IAI=-ln (FPG × fasting insulin). Insulin was detected by enhanced chemiluminescence by using a Roche Cobas 6000 and an insulin detection kit (Roche).

Statistical analysis

Statistical analysis was performed by using SPSS version 19.0. The data are expressed as mean±standard deviation (SD). Inter- and intra-group comparisons were made by using independent sample and paired *t*-tests, respectively. The level of significance was set at $p<0.05$. Rates were compared by Fisher's exact test.

RESULTS

General characteristics

Age, pre-pregnancy BMI, gestational weeks at diagnosis, gestational weeks at intervention initiation, 75 g OGTT, FBG, 1hPG, and 2hPG did not differ significantly between the 2 groups (Table 1).

Dietary analysis

Pre-intervention, total energy, macronutrient, and fatty acid intake and energy supply percentages did not differ significantly between the 2 groups. Post-intervention, total energy and protein intake did not differ significantly between the 2 groups. Fat, SFA, monounsaturated fatty acids (MUFA), and PUFA were significantly higher in the experimental group than the control group, while the carbohydrate intake was significantly lower in the experimental group than the control group ($p<0.001$). Total energy and macronutrients intake increased significantly

Table 1. Comparison of general clinical parameters in the two groups of GDM

Index	Experiment group		Control group		p
	Cases	Mean±SD	Cases	Mean±SD	
Age (years)	41	30.3±4.17	43	29.7±4.64	0.555
Pre-pregnancy BMI (kg/m^2)	41	21.4±3.0	43	22.2±3.60	0.267
Gestational weeks when diagnosed	41	26.7±1.56	43	26.7±1.27	0.765
The intervention-started gestational weeks	41	27.4±1.52	43	27.3±1.96	0.850
75 g OGTT (mmol/L)					
FBG	41	4.73±1.04	43	4.82±0.50	0.460
1 h glucose	39	11.4±1.64	41	11.0±1.20	0.220
2 h glucose	39	9.21±1.38	41	9.34±1.45	0.694

Table 2. Diet analysis at baseline and end-of-intervention in the two groups of GDM

	Before the intervention		p	After the intervention		p^*	p^{**}	
	Experiment	Control		Experiment	Control		Experiment	Control
Cases	41	43		41	43		41	43
Energy (kcal)	2514±465	2577±319	0.474	1960±89.5	1978±107	0.410	<0.001	<0.001
Protein (g)	96.8±23.9	103±21.6	0.226	88.3±5.68	88.6±6.40	0.799	0.027	<0.001
Protein energy supply ratio (%)	15.5±2.84	16.0±2.86	0.393	18.0±0.71	17.9±0.97	0.644	<0.001	<0.001
Fat (g)	86.9±23.5	84.9±18.0	0.669	74.8±3.45	58.6±4.60	<0.001	<0.001	<0.001
Fat energy supply ratio (%)	31.1±6.36	29.7±5.75	0.292	34.3±0.21	26.7±1.27	<0.001	<0.001	<0.001
Carbohydrate (g)	336±77.6	350±63.9	0.366	234±10.6	274±17.3	<0.001	<0.001	<0.001
Carbohydrate energy supply ratio (%)	53.4±7.10	54.3±6.72	0.566	47.7±0.65	55.4±1.95	<0.001	<0.001	0.315
Carbohydrate/fat	4.13±1.41	4.41±1.67	0.420	1.39±0.02	2.09±0.17	<0.001	<0.001	<0.001
SFA(g)	15.4±8.92	14.8±5.52	0.735	14.8±0.59	12.7±0.92	<0.001	0.675	0.016
SFA energy supply ratio (%)	7.91±3.12	7.64±2.59	0.658	8.14±0.22	7.37±0.35	<0.001	0.599	0.503
MUFA (g)	24.2±8.39	23.3±6.57	0.601	15.2±0.54	12.1±0.83	<0.001	<0.001	<0.001
MUFA energy supply ratio (%)	12.9±3.01	11.9±2.52	0.089	8.38±0.10	7.00±0.26	<0.001	<0.001	<0.001
PUFA (g)	19.2±7.06	19.9±5.76	0.884	32.2±1.41	21.2±2.16	<0.001	<0.001	0.137
PUFA energy supply ratio (%)	10.3±2.84	10.2±2.39	0.884	17.8±0.34	12.3±1.02	<0.001	<0.001	<0.001

p: comparison of the 2 groups before the intervention; *p**: comparison of the 2 groups after the intervention; *p***: comparison of the same group before and after the intervention.

in the experimental group post-intervention ($p<0.001$). SFA intake did not change significantly ($p>0.05$). Meanwhile, MUFA and PUFA intake and their respective energy supply percentages decreased and increased significantly, respectively ($p<0.001$). Total energy and macronutrient intake in the control group increased significantly post-intervention ($p<0.001$). The SFA and PUFA intake did not change, however in the control group the MUFA and PUFA intakes and their respective energy supply percentages decreased and increased significantly, respectively ($p<0.001$, Table 2).

Comparison of blood sugar, IAI, and lipids

There were no significant differences in IAI, TC, TQ or HDL-C between the 2 groups pre-intervention. Meanwhile, FBG, 2hPG, IAI, TC, TG, and HDL-C did not differ significantly between groups post-intervention ($p>0.05$). FBG and 2hPG decreased significantly while IAI increased significantly post-intervention in both ($p<0.05$). In the experimental group, TC levels did not change, and TG levels increased significantly ($p<0.05$) and HDL-C levels decreased significantly ($p<0.01$). The lipid changes were consistent between groups (Table 3).

Comparison of pregnancy outcomes

Gestational weeks at delivery, infant birth weight, the incidence of macrosomia, and pregnancy weight gain did not differ significantly between groups (Table 4).

DISCUSSION

The American Diabetes Association (ADA) guidelines for nutrition[11] recommend that all pregnant women with GDM consult a nutritionist upon diagnosis. Thus, food intake, metabolic status, and lifestyle can be assessed, and the nutritionist can develop an individualized program according to the patient's height, weight, and gestational weeks. In China, it is recommended that after the second trimester of pregnancy (i.e., after the fourth month), energy intake should increase by 200 kcal/day compared to pre-pregnancy intake; daily carbohydrate intake should be at least 175 g, and its energy supply percentage should be 40%-60%; protein and fat energy supply percentages should be 15%-20% and 20%-30%, respectively.[12]

As the type of dietary fat and fatty acid intake are closely related with the occurrence of diabetes, they have received substantial attention in recent years. Excessive SFA intake might increase insulin resistance and reduce glucose transporters in fat cells. Meanwhile, PUFA intake

Table 3. Blood glucose, IAI and blood fat at baseline and end-of-intervention in the two groups of GDM (mean±SD, mmol/L)

	Before the intervention		p	After the intervention		p^*	p^{**}	
	Experiment	Control		Experiment	Control		Experiment	Control
FBG	4.69±1.04	4.82±0.50	0.460	4.33±0.93	4.15±0.69	0.346	0.02	<0.001
2hPG	8.42±1.03	8.02±1.47	0.161	6.79±0.58	6.81±0.67	0.877	<0.001	<0.001
IAI	-4.47±0.52	-4.33±0.43	0.156	-4.11±0.81	-4.15±0.69	0.210	0.011	<0.001
TC	6.2±1.62	6.64±1.21	0.194	5.92±1.48	6.44±1.31	0.093	0.325	0.466
TG	2.96±1.23	3.22±0.96	0.252	3.41±1.33	3.91±1.79	0.153	0.031	0.021
HDL-C	2.02±0.59	2.21±0.59	0.143	1.71±0.45	1.79±0.49	0.453	0.004	0.010

Table 4. Comparison of pregnancy outcomes in the two groups of GDM

	Experiment	Control	p
Gestational weeks when delivery (weeks)	39.8±6.05	38.8±1.05	0.293
Premature delivery (cases)	0	0	-
Polyhydramnios (cases)	0	0	-
Insulin application (cases)	0	0	-
Infant birth weight (g)	3342±335	3502±437	0.064
Macrosomia (%)	2.4%	6.0%	0.360
Pregnancy weight gain (kg)	12.9±5.09	14.9±5.84	0.104

may enhance glucose transporter mRNA expression and enhance the hypoglycemic effect of insulin.[13-15] Regarding fatty acid intake, the ADA recommends that in diabetes patients, daily SFA intake should not exceed 7% of the total energy and fish should be consumed more than twice weekly to provide n-3 PUFA;[11] however, there are no specific recommendations for GDM. The 1998 ADA recommendations have been adopted more widely in China; these recommendations state that SFA and PUFA should not exceed 10% of the total fat energy supply each and the rest is to be provided by MUFA.[16]

The pre-intervention dietary survey showed that local Changzhou women with GDM generally misunderstood what constitutes an appropriate diet; vegetable oil intake was excessive, and energy and macronutrient intake were above requirements. GDM patients should consume low-oil meals such that fat energy supply percentage does not exceed 30%. In addition to limiting the meat intake, especially red meat, vegetable oil intake should also be restricted, usually to no more than 25 g per day; thus, low-oil meals limit not only SFA intake, but unsaturated fatty acid intake as well. Such meals conflict with the cooking habits of local residents; therefore, they could not be accepted by all GDM patients.

Less fat intake is not necessarily better. A meta-analysis shows that compared to a high-fat/low-carbohydrate diet (carbohydrates/fats: 0.6~1.56), a low-fat/high-carbohydrate diet (carbohydrates/fats>3) can significantly increase FBG and TC, and decrease HDL-C. In other words, substituting fats with carbohydrates can increase insulin resistance.[17] Therefore, some authors also recommend carbohydrate and fat energy supply percentages of 40%-50% and 35%-40%, respectively, for GDM patients.[12] Some studies revealed that in normal individuals, a high-MUFA diet can significantly improve insulin sensitivity; however, this protective effect disappears when the fat energy supply ratio exceeds 38%.[18] This was taken into account in the present study by increasing vegetable oil intake in oil-rich meals to increase the fat energy supply percentage; daily intake of 45-50 g oil could maintain the fat energy supply percentage at approximately 35% while increasing PUFA intake and maintaining energy intake. Compared with the low-oil meals in the control group, total energy and protein intake were maintained, the carbohydrates energy supply percentage decreased (50%-54% of total energy intake), fat energy supply percentage increased (~35% of total energy intake), carbohydrate/fat percentage decreased, and SFA intake increased slightly. Furthermore, PUFA and MUFA intake increased significantly. Like the low-oil meals, the SFA energy supply percentage did not exceed 33% of the fat energy supply in the experimental group; meanwhile, the energy supply percentage of PUFA was greater than that of MUFA and accounted for more than 33% of fat energy supply. The composition of fatty acids of the 2 meals was mainly a result of sunflower oil, which is rich in PUFA. Although olive oil contains the lowest and highest SFA and MUFA contents among all oils, respectively, it is much more expensive than sunflower oil, which is moderately priced. As the study grouping was randomized, sunflower oil was selected to facilitate acceptance by GDM patients. Unsaturated fatty acids are the main ingredient of sunflower oil; the SFA contents are slightly higher than those of olive oil. Sunflower oil contains 13.4, 18.4, and 65.2 g SFA, MUFA, and PUFA per 100 g, respectively. Among PUFA, n-3 (i.e., a-linolenic acid) and n-6 (i.e., linoleic acid) account for 4.5% and 63.2% of the total fatty acids, respectively.[19]

In the present study, changes in lipids were evaluated on the basis of TG, TC, and HDL-C. The post-intervention lipid changes in both groups were consistent: TC levels did not change, TG levels increased, and HDL-C levels decreased. Pregnant women normally present with physiological hyperlipidemia during late pregnancy; TG and TC levels decrease before delivery. On the other hand, GDM patients exhibit significant lipid metabolism abnormalities; in particular, TG is abnormally elevated during late pregnancy.[20] Therefore, lipid regulation could not be compared pre- and post-intervention in pregnant women with GDM. Post-intervention, both groups exhibited trends in TC, TG, and HDL-C consistent with those in normal pregnant women. The TC, TG, and HDL-C levels did not differ significantly between the 2 groups, suggesting that the experimental and control meals have the same effects on lipid regulation. The oil-rich meals resulting in increased intake unsaturated fatty acid intake, especially PUFA. However, the effects of lipid regulation were no better than those observed in the low-oil group; this may be related to the short intervention time and when the intervention was performed. Because the intervention was performed close to the 28th week of pregnancy, the pregnant women with GDM had already developed dyslipidemia and were affected by the interference of several placental hormones and insulin resistance. Thus, dietary intervention starting from the 10th week of pregnancy might improve lipid metabolism while not significantly reducing hyperlipidemia.

The prevalence of macrosomia in the Chinese population is 7%.[2] The BMI of both groups were within the normal range (i.e., 18.5-24.9 kg/m^2). Pregnancy weight gain should be controlled within 11.5-16 kg;[1] in this study, the pregnancy weight gains of the experimental and control groups were 12.93±5.09 and 14.91±5.84 kg, respectively. In addition, there was no incidence of polyhydramnios or premature birth, and no patients required insulin to control blood sugar. The pregnancy outcomes of both groups were good, which were related to the good results of blood glucose control after the dietary intervention; FBG and 2hPG were controlled at 4-5 and 6-7 mmol/L, respectively. Maternal hyperglycemia can lead to fetal hyperglycemia and hyperinsulinemia. This would promote fetal uptake of amino acids, accelerating tissue protein synthesis and reducing lipolysis; fat and glycogen would consequently be deposited within tissues, resulting in macrosomia and polyhydramnios. Meanwhile, fetal oxygen consumption would increase, predisposing the fetus to hypoxia. In the last 4-8 weeks of pregnancy, a FBG level exceeding 5.8 mmol/L increases the risk of fetal death.[21] Interventions should be performed to reduce postprandial blood glucose in order to reduce the risk of large-for-gestational-age infant and subsequent obesity.[22] Good blood glucose control might be attributable to energy control. Many studies show that for women with GDM, it is unimportant whether a diet is high-fat/low-carbohydrate, low-fat/high-carbohydrate, or low- or moderate-glycemic-index carbohydrates as long as energy intake is controlled. This would result in positive efficacy towards weight control. Furthermore, when total energy intake is controlled, its impacts on lipids, IAI, and pregnancy outcomes will be consistent.[17,23]

In summary, women with GDM received an interventional diet with oil-rich meals, with a fat energy supply percentage of approximately 35%. Despite the increased fat intake, the PUFA inside sunflower oil was responsible for the majority of the increase, while SFA intake was controlled at approximately 8%-10%. Meanwhile, energy and protein intake were consistent with those in the low-oil meals. The pregnancy outcomes as well as improvements in blood glucose control, lipid metabolism, and insulin resistance were the same between groups. The results show that as long as dietary treatment for GDM follows basic recommendations and total energy intake is strictly controlled, an appropriate increase in PUFA intake positively affects both the woman and fetus. Furthermore, the kinds of meals described herein are more consistent with local dietary habits in Changzhou, making such interventions more acceptable by pregnant women and their families. Thus, the intervention described herein is feasible and could be used as a dietary treatment for GDM in China.

AUTHOR DISCLOSURES

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Original Article

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一项随机对照研究：饮食中的脂肪变化对孕妇妊娠期糖尿病的影响

目的：观察增加植物油中多不饱和脂肪酸的摄入对妊娠期糖尿病孕妇血糖、脂质代谢以及妊娠结局的影响。**方法**：84 例 GDM 孕妇，孕 24~28 周，不伴有其他妊娠合并症和并发症，随机分为实验组 41 例，对照组 43 例，在总能量和蛋白质摄入量相同情况下，给予实验组多油配餐，对照组为传统少油配餐。**结果**：饮食干预后，实验组脂肪和三种脂肪酸摄入量和供能比均高于对照组（$p<0.001$），实验组多不饱和脂肪酸摄入量和供能比较干预前增加，对照组多不饱和脂肪酸摄入量无改变。两组空腹血糖、餐后 2h 血糖、胰岛素抵抗指数均较干预前显著降低（$p<0.05$），两组的血脂变化一致；两组妊娠结局差异无统计学意义。**结论**：GDM 的饮食治疗只要遵照基本规则，严格控制总能量的摄入，适当增加植物油中多不饱和脂肪酸的摄入对孕妇和胎儿是有益的。

关键词：妊娠期糖尿病、膳食结构、植物油、脂肪酸、血脂