Original Article
A study on serum IGF-1, VEGF, MCP-1 levels in patients with GDM and its clinical significance

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Abstract: Objective: This study aimed to discuss the relevance between the serum levels of insulin-like growth factor-1 (IGF-1), vascular endothelial growth factor (VEGF) and monocyte chemoattractant protein-1 (MCP-1), blood glucose and lipids in gestational diabetes mellitus (GDM) patients and neonatal weight index. Methods: In total, 120 pregnant women admitted to our hospital from June 2016 to June 2019 were included as the study subjects, of whom, 65 patients with diabetes were set up as the experiment group, and 55 without diabetes as the control group. Both groups were tested for serum levels of IGF-1, VEGF and MCP-1 by enzyme linked immunosorbent assay (ELISA) test kits, and carbohydrate and lipid metabolism indexes in a fasting status with automatic biochemistry analyzers. Changes in serum IGF-1, VEGF and MCP-1 levels, and carbohydrate and lipid metabolism indexes, as well as neonatal weights were compared. Relevance was analyzed by the Pearson method. Results: As compared with the control group, the experimental group demonstrated higher BMI index, serum IGF-1, VEGF and MCP-1 levels, fasting plasma glucose (FPG), fasting insulin (FINS), and glycosylated hemoglobin (HbA1c) levels as carbohydrate metabolism indexes, total cholesterol (TC), triacylglycerol (TG), apolipoprotein B (Apo-B) and low density lipoprotein cholesterol (LDL-C) levels as lipid metabolism indexes, neonatal weight and body length parameters, and lower fasting glucagon (FGC), apolipoprotein A1 (Apo-A1) and high density lipoprotein cholesterol (HDL-C) levels ($P<0.05$). According to Pearson relevance analysis results, in the experiment group, the serum IGF-1, VEGF and MCP-1 levels interacted positively with the body mass index (BMI), carbohydrate metabolism indexes (FPG, FINS and HbA1c) and lipid metabolism indexes (TC, TG, Apo-B and LDL-C) of the pregnant women, and the neonatal weight (r between 0 and 1, $P<0.05$), and negatively with carbohydrate metabolism index (FGC) and lipid metabolism indexes (Apo-A1 and HDL-C). Conclusions: The serum IGF-1, VEGF and MCP-1 levels and carbohydrate and lipid metabolism indexes in pregnant women with GDM are closely associated with the neonatal weight.

Keywords: Gestational diabetes mellitus, IGF-1, VEGF, MCP-1, carbohydrate metabolism indexes, lipid metabolism indexes, neonatal weight

Introduction

Gestational diabetes mellitus (GDM) refers to elevated carbohydrate metabolism or potential symptoms of impaired glucose tolerance in patients before pregnancy, or the first sign of abnormal carbohydrate metabolism in various degrees during pregnancy [1, 2]. As one of the most common complications in duration of pregnancy, GDM involves complicated factors and may lead to adverse pregnancy results [3-6]. According to most of the studies, it is believed that GDM is associated with factors such as obesity, heredity, less exercise, older age, and excess food intake [7, 8], and has potential to cause injury to both the mother and baby, including abortion and premature delivery, or even ketoacidosis and increased risks of fetal growth retardation or giant babies [9-13]. Some studies have revealed that the blood glucose level in pregnant women may have a close association with the growth and development of fetuses. Insulin-like growth factor-1 (IGF-1) is a blood substance related to insulin and carbohydrate and lipid metabolism [14-16]. Vascular endothelial growth factors (VEGF) participate in

the processes of vascularization, vasoconstriction, and proliferation and division of vascular endothelial cells, which may affect the development of blood vessels in the placenta [17, 18]. Monocyte chemoattractant protein-1 (MCP-1) is an important inflammatory mediator produced by various cells in the human body, which plays a chemotactic role in monocytes and causes inflammatory reactions [19, 20]. So far, clinically it is observed that the three indexes of IGF-1, VEGF and MCP-1 may change significantly during the duration of pregnancy, accompanied by changes in carbohydrate and lipid metabolism indexes if the mother has GDM. However, few studies have been carried out for the relevance between the three indexes, carbohydrate and lipid metabolism indexes, and neonatal weight; while the role of the three indexes in carbohydrate and lipid metabolism of GDM patients correlated to the growth process of neonates is unclear. This paper mainly reports the relevance between the IGF-1, VEGF and MCP-1 levels, blood glucose and lipids in GDM patients and neonatal weight.

Materials and methods

General materials

In total, 120 pregnant women admitted to our hospital from June 2016 to June 2019 were included and grouped according to whether they had diabetes or not of the 120 pregnant women, 65 of them with diabetes were included as the experimental group, with mean age of (30.75±6.92) years and mean gestational of (36.13±1.99) weeks; while 55 pregnant women without diabetes were included as the control group, with mean age of (29.46±7.74) years, and mean gestational of (36.61±1.75) weeks. Inclusion criteria: the subjects included complied with the GDM diagnosis criterion [21, 22] of elevated glucose level after oral administration of 75 g glucose following fasting for 12 h on the baselines of 5.0 mmol/L in fasting status, 10.0 mmol/L 1 h after dinner, and 8.5 mmol/L 2 h after dinner. Only women aged between 20 and 40 years with a single birth through natural process and without any other history of disease were included. Exclusion criteria: patients who had functional injuries in the heart, liver and kidney, concurrent infection and anemia in the duration of pregnancy or multiple births, or who failed to provide com-

plete clinical data were exclude from the study. This study was approved by the Ethics Committee of Liaocheng People's Hospital. All pregnant women and their family members have been informed of the study, and provided written informed consent.

Experimental methods

Detection of serum IGF-1, VEGF and MCP-1 levels by ELISA: Five mL blood was collected from both groups in the morning in a fasted status, and was placed at room temperature for 2 h. When the serum was isolated, the blood sample was put into a centrifuge for centrifugation for 10 min at 500 r/min to seperate the supernatant serum which was then stored in a freezer at -80°C. Enzyme-linked immunosorbent assay (ELISA) method was adopted to detect the serum IGF-1, VEGF and MCP-1 levels in both groups in strict accordance with the instrucions on the test kits (purchased from Ray-Biotech, the United States).

Detection of carbohydrate and lipid metabolism indexes by automatic biochemistry analyzers: Five mL blood was taken from both groups in the morning of in a fasted state after food prohibition for 12 h and water prohibition for 8 h, and was analyzed by an automatic biochemistry analyzer (ADVIA2400, purchased from Sys-mex, Japan) for carbohydrate metabolism indexes [23, 24] of fasting plasma glucose (FPG), fasting insulin (FINS), fasting glucagon (FGC), glycosylated hemoglobin (HbA1c), and lipid metabolism indexes [25, 26] of total cholesterol (TC), triacylglycerol (TG), apolipoprotein A1 (Apo-A1), apolipoprotein B (Apo-B), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C) in strict accordance with the instructions for the instrument.

Measurement of body mass index (BMI) of the pregnant women and the growth parameters of the neonates: By measurements of the pregnant women's height and weight, BMI was calculated as weight (kg)/height (m^2) [27-29]. After delivery, professionals measured and recorded the neonates' weight, length, chest circumference and head circumference, etc.

Statistical analysis

Statistical analysis was performed with SPSS 22.0. In the case of numerical data it was ex-

Table 1. Comparison between the pregnant women of the two groups for serum IGF-1, VEGF and MCP-1 levels (Mean ± SD)

	Experiment group (n=65)	Control group (n=55)	T	P
IGF-1 (ng/L)	31.02±6.79	16.73±5.39	7.923	<0.05
VEGF (pg/mL)	189.37±37.42	142.71±40.11	8.134	<0.05
MCP-1 (µg/L)	71.33±18.09	40.25±11.43	11.253	<0.05

IGF-1: insulin-like growth factor-1; VEGF: vascular endothelial growth factor; MCP-1: monocyte chemoattractant protein-1.

Table 2. Changes in carbohydrate metabolism indexes in the pregnant women of the two groups (Mean ± SD)

Carbohydrate metabolism indexes	Experiment group (n=65)	Control group (n=55)	t	P
FPG (mmol/L)	6.14±0.83	4.28±0.23	6.125	<0.05
FINS (mIU/L)	21.37±2.51	8.17±1.27	3.164	<0.05
FGC (ng/L)	22.19±6.07	31.79±8.71	10.154	<0.05
HbA1c (%)	5.73±0.51	4.96±0.36	6.214	<0.05

FPG: fasting plasma glucose; FINS: fasting insulin; FGC: fasting glucagon; HbA1c: glycosylated hemoglobin.

pressed as Mean ± Standard Deviation (Mean ± SD), comparison studies were carried out through independent-samples T test; in the case of nominal data it was expressed as [n (%)], comparison studies were carried out through X^2 test for intergroup comparison. Relevance was analyzed by the Pearson method. For all statistical comparisons, $P<0.05$ is considered as a significant difference.

Results

Comparison of general data in both groups

The general data such as number of women, age, and distribution of gestational weeks of the two groups had no statistical difference ($P>0.05$), and as such the groups were comparable.

Comparison between the two groups for serum IGF-1, VEGF and MCP-1 levels in the pregnant women

Serum IGF-1, VEGF and MCP-1 levels in the pregnant women were higher in the experiment group as compared with the control group ($P<0.05$, **Table 1**).

Changes in carbohydrate metabolism indexes in pregnant women of the two groups

In terms of carbohydrate metabolism indexes, the experiment group demonstrated higher

FPG, FINS and HbA1c levels and lower FGC level as compared with the control group ($P<0.05$, **Table 2**).

Changes in lipid metabolism indexes in the pregnant women of the two groups

In terms of lipid metabolism indexes, the experiment group demonstrated higher TG, TC, Apo-B and LDL-C levels and lower Apo-A1 and HDL-C levels as compared with the control group ($P<0.05$, **Table 3**).

Comparison between the growth parameters for neonates delivered by the pregnant women of the two groups

Neonates delivered by the experiment group have exceeded the control group in terms of neonatal weight and body length ($P<0.05$), but no difference was observed in terms of chest and head circumferences ($P>0.05$) (**Table 4**).

Relevance analysis

Serum IGF-1, VEGF and MCP-1 levels were positively associated with the BMI, FPG, FINS and HbA1c ($P<0.05$), TC, TG, Apo-B, LDL-C of the pregnant women and neonatal weight ($P<0.05$), and negatively associated with the FGC level, Apo-A1 and HDL-C levels in the experiment group ($P<0.05$) (**Table 5**).

Discussion

GDM is a common complication during pregnancy, which imposes a great threat to the health and safety of both the mother and the baby [30]. A pregnant woman with GDM has a high risk of type 2 diabetes [31] although she can recover back to normal after delivery, while the baby may suffer from hypoglycemia, hypocalcemia, hypomagnesemia, hyperbilirubinemia, and polycythemia [32]. To this end, the timely diagnosis and treatment of GDM is of great importance to a pregnant woman. This paper mainly studied the relevance between IGF-1, VEGF and MCP-1 levels, carbohydrate and lipid metabolism indexes of the GDM patients, and the neonatal weight, to thus provide some data for the clinical prevention, diagnosis and treatment of this disease.

Table 3. Changes in lipid metabolism indexes in the pregnant women of the two groups (Mean ± SD)

Lipid metabolism indexes	Experiment group (n=65)	Control group (n=55)	t	P
TC (mmol/L)	6.93±0.72	5.12±0.44	11.125	<0.05
TG (mmol/L)	4.66±0.25	3.01±0.13	3.621	<0.05
Apo-A1 (g/L)	0.61±0.27	1.79±0.61	8.136	<0.05
Apo-B (g/L)	0.95±0.21	0.49±0.19	4.579	<0.05
HDL-C (mmol/L)	1.23±0.14	1.86±0.23	6.149	<0.05
LDL-C (mmol/L)	3.72±0.13	2.39±0.11	4.135	<0.05

TC: total cholesterol; TG: triacylgycerol; Apo-A1: apolipoprotein A1; Apo-B: apolipoprotein B; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol.

Table 4. Comparison between the neonates delivered by the two groups for growth parameters ($\overline{x}$±s)

Growth parameters	Experiment group (n=65)	Control group (n=55)	t	P
Weight (kg)	3.49±0.46	3.01±0.22	8.349	<0.05
Body length (cm)	52.11±1.93	51.02±1.80	12.468	<0.05
Chest circumference (cm)	33.23±1.96	33.19±1.93	3.246	>0.05
Head circumference (cm)	33.79±1.51	33.65±1.54	5.168	>0.05

Table 5. Relevance between serum IGF-1, VEGF and MCP-1 levels, BMI, carbohydrate and lipid metabolism indexes of the pregnant women with GDM, and the neonatal weight

Related indexes		IGF-1		VEGF		MCP-1	
		r	P	r	P	r	P
BMI		0.682	0.042	0.705	0.043	0.687	0.004
Carbohydrate metabolism indexes	FPG	0.221	0.025	0.253	0.005	0.437	0.007
	FINS	0.314	0.003	0.361	0.035	0.392	0.046
	FGC	-0.436	0.001	-0.504	0.027	-0.696	0.039
	HbA1c	0.712	0.014	0.688	0.042	0.713	0.004
Lipid metabolism indexes	TC	0.593	0.041	0.606	0.024	0.822	0.042
	TG	0.690	0.004	0.572	0.027	0.931	0.040
	Apo-A1	-0.579	0.015	-0.687	0.036	-0.713	0.006
	Apo-B	0.801	0.014	0.743	0.043	0.756	0.023
	HDL-C	-0.587	0.018	-0.654	0.044	-0.542	0.044
	LDL-C	0.612	0.045	0.643	0.036	0.869	0.047
Neonatal weight		0.537	0.035	0.640	0.007	0.799	0.022

IGF-1: insulin-like growth factor-1; VEGF: vascular endothelial growth factor; MCP-1: monocyte chemoattractant protein-1; BMI: body mass index; FPG: fasting plasma glucose; FINS: fasting insulin; FGC: fasting glucagon; HbA1c: glycosylated hemoglobin; TC: total cholesterol; TG: triacylgycerol; Apo-A1: apolipoprotein A1; Apo-B: apolipoprotein B; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol.

Comparative analysis of BMI and serum IGF-1, VEGF and MCP-1 levels between the pregnant women in the two groups

The experiment group reported higher BMI, and serum IGF-1, VEGF and MCP-1 levels than those of the control group, indicating that GDM is a cause of obesity, high body weight, high blood glucose and blood lipids, which triggers chronic inflammation, and damages pati- ents' bodies continuously and persistently. Fatty lipid is an internal secretion and an important premise producing pro-inflammatory factors, including MCP-1 and IGF-1. As GDM may result in vasculopathy in pregnant women and lead to vascular endothelial cells thickening and lumen narrowing, to promote the secretion of VEGFs, serum IGF-1; VEGF and MCP-1 levels in pregnant women with GDM positively interacted with their BMI.

Comparative analysis of carbohydrate metabolism indexes, and serum IGF-1, VEGF and MCP-1 levels in pregnant women of the two groups

For carbohydrate metabolism indexes, the experiment group reported higher FPG, FINS and HbAlc levels, and lower FGC level as compared with the control group. In the pregnant women with GDM, hyperglycaemia is expected and accompanied with disturbance of carbohydrate metabolism. Elevated FPG promotes the synthesis of insulin, while the rising of FINS can avoid high blood glucose to a certain degree, but the Langerhan's island hypofunction results in failure to resist elevation of blood glucose. Therefore, the blood glucose in pregnant women is maintained at a high level and FGC is reduced. HbAlc is a product of erythrocytic hemoglobin combined with serum glucide, which increases with the elevation of blood glucose, while IGF-1 is an insulin like growth factor capable of regulating blood glucose. The secretion of IGF-1 increases with the elevation of blood glucose in pregnant women with GDM. Therefore, serum IGF-1, VEGF, and MCP-1 levels are positively associated with the carbohydrate metabolism indexes of FPG, FINS and HbAlc, and negatively with FGC.

Comparative analysis between lipid metabolism indexes and serum IGF-1, VEGF and MCP-1 levels of pregnant women in the two groups

The experiment group showed significantly higher TC, TG, Apo-B and LDL-C levels, and lower Apo-A1 and HDL-C than those of the control group. In the pregnant women with GDM, disturbance of lipid metabolism is also observed, forming a vicious circle with the disturbance of carbohydrate metabolism. TC, TG and LDL-C are the most common indexes to reflect the degree of lipid metabolism disorder in the body, and their level is consistent with the degree of fat accumulation. HDL-C is a lipoprotein reversely transporting lipids. Apo-B is the corresponding apolipoprotein of LDL-C with consistent expression tendencies, and Apo-A1 is the corresponding apolipoprotein of HDL-C with consistent expression tendencies. As lipids accumulate in the body of pregnant women with GDM, lipid synthesis is accelerated, leading to elevation of TC, TG, Apo-B and LDL-C levels, and reduction of Apo-A1 and HDL-C levels.

Therefore, the serum IGF-1, VEGF and MCP-1 levels in the pregnant women with GDM are positively associated with TC, TG, Apo-B and LDL-C levels, and negatively with the Apo-A1 and HDL-C levels.

Comparative analysis between the weight of neonates delivered by the pregnant women of the two groups and their serum IGF-1, VEGF and MCP-1 levels

The neonates delivered in the experiment group were heavier than those in the control group. IGF-1 is a growth hormone that plays a significant role in fetal growth and development, while fetal blood vessel development and vascularization are related to VEGF. In GDM, the fetus may suffer from chronic hypoxia and ischemia due to the high blood glucose of the mother, and the placenta is hypervascularized, leading to changes in hormones, growth factors and inflammatory factors. Pregnant women with GDM have higher serum IGF-1, VEGF and MCP-1, which contributes a higher neonatal weight, between which, there is a positive interaction.

In conclusion, the serum IGF-1, VEGF and MCP-1 levels, carbohydrate metabolism indexes (FPG, FINS and HbAlc) and lipid metabolism indexes (TC, TG, Apo-B and LDL-C) in the pregnant women with GDM are positively associated with the neonatal weight and negatively with the FGC (carbohydrate metabolism index) and Apo-A1 and HDL-C (lipid metabolism indexes).

Disclosure of conflict of interest

None.

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