Agata Bronisz, Małgorzata Sobiś-Żmudzińska, Małgorzata Pujanek, Roman Junik ORIGINAL

Chair and Clinic of Endocrinology and Diabetology with the Nuclear Medicine Laboratory, Medical College in Bydgoszcz, Nicolaus Copernicus University in Toruń, Poland

An evaluation of selected lipid parameters in pregnancy complicated by gestational diabetes mellitus (Part 2): differences resulting from the method of treatment

Abstract

Background. The aim of the study was to compare selected lipoproteins [total cholesterol (TC), LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C) and triglycerides (TG)] in gestational diabetes mellitus (GDM) in relation to the method of antidiabetic treatment.

Material and methods. The study included 121 patients with GDM. A total of 85 patients were managed by diet alone (G1) and 36 were managed by diet and insulin (G2). The study parameters were determined at the time of GDM diagnosis (baseline) and at the end of the 3rd trimester of pregnancy (T3).

Results. An improvement of glycaemic control was observed in both groups, which was reflected by a significant reduction in both fasting blood glucose (FBG), mean blood glucose (MBG) and fructosamine in G2 (4.5 ± 0.8 *vs*. 4.1 ± 0.4, P < 0.001; 5.5 ± 0.9 *vs*. 5.1 ± 0.4, P < 0.001; 1.9 ± 0.2 *vs*. 1.8 ± 0.2, NS [mmol/L], respectively in G1, and 5.5 ± 1.3 *vs*. 4.6 ± 0.4, P < 0.001; 6.9 ± 1.4 *vs*. 5.6 ± 0.4, P < 0.001; 2.1 ± 0.3 *vs*. 1.9 ± 0.1, P < 0.001 [mmol/L], respectively in G2). No significant changes in HbA_{1c} were observed. Baseline values of TC, LDL-C and HDL-C were significantly higher in G1 *vs*. G2 (6.4 ± 1.2 *vs*. 5.7 ± 1.1, P < 0.01; 3.6 ± 1.0 *vs*. 3.1 ± 1.0, P < 0.05; 1.7 ± 0.4 *vs*. 1.5 ± 0.4, P < 0.05 [mmol/L], respectively). TG did not differ significantly between the groups. At T3, TG increase from baseline was significant in both groups (from 2.8 ± 1.0 to 3.3 ± 0.9 [mmol/L], P < 0.01, in G1 and from 2.7 ± 1.0 to 3.3 ± 1.1 [mmol/L], P < 0.05, in G2). TC and LDL-C did not change significantly and HDL-C increased significantly in G2. The lipoprotein levels at T3 in both groups did not differ significantly.

Conclusion. A significant increase in TG irrespective of the method of antidiabetic treatment is observed in GDM. The only change in cholesterol fractions consisted in a significant increase of HDL-C at the end of pregnancy in the group managed by insulin.

key words: lipids, management of gestational diabetes mellitus

Introduction

The set of carbohydrate metabolism abnormalities during pregnancy, referred to as gestational diabetes mellitus (GDM), is a heterogenous disorder. Depending on the method of treatment adopted, patients with GDM may fall into two classes: class G1 (patients managed with diet only) and class G2 (patients in whom the achievement of glycaemic control requires insulin therapy in addition to diet). GDM alters the metabolism of lipoproteins characteristic of uncomplicated pregnancy. As described in Part 1 of this paper, patients with gestational diabetes have higher triglyceride (TC) levels than healthy pregnant women. Treatment has reduced TG and significantly decreased cholesterol levels compared to values observed during normal pregnancy. Surprisingly, the group of patients with pregestational obesity presented with less pronounced abnormalities of lipid metabolism than patients who were overweight before pregnancy or whose body mass was normal before pregnancy. We therefore decided to evaluate whether our findings could have been affected by the method of antidiabetic treatment during pregnancy.

Address for correspondence: Agata Bronisz, MD
Chair and Clinic of Endocrinology and Diabetology
Ludwik Rydygier Medical College in Bydgoszcz
ul. Skłodowskiej-Curie 9, 85–094 Bydgoszcz
Tel (+48 52) 585 40 20, tel/fax (+48 52) 585 40 41
e-mail: agabrr@poczta.onet.pl

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Table 1. Characteristics of the study groups (mean ± standard deviation)

Parameter [U]	G1	G2	P value
Age (years)	29.6 ± 5.7	32.5 ± 5.3	0.01
Gestational age at the diagnosis of diabetes (weeks of gestation)	30.5 ± 3.7	27.5 ± 6.0	0.05
Pregestational body mass index [kg/m^2]	24.2 ± 5.0	28.4 ± 7.5	0.01
Weight gain during pregnancy [kg]	12.5 ± 5.2	10.2 ± 4.9	0.05
Due date (weeks of gestation)	39.8 ± 1.8	39.4 ± 2.1	NS

G1 — gestational diabetes mellitus managed with diet only; G2 — gestational diabetes mellitus managed with diet and insulin; NS — not signifficant

Material and methods

The study included 121 women with GDM. Duration of pregnancy was estimated from the Naegele's rule, based on the first day of last menstrual period, and verified by ultrasound. Hypertensive patients, current smokers and patients taking pharmacologic agents which might affect lipid metabolism were excluded from the study.

The study group characteristics are summarised in Table 1.

In all the subjects, total cholesterol (TC), LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C) and triglyceride (TG) levels were obtained at two time points: at presentation due to a referral for GDM and at the end of pregnancy (between 36 and 39 weeks of gestation). Glycaemic control was evaluated on the basis of glucose values obtained by the patients themselves every day: after an overnight fast (FBG, fasting blood glucose) and 1 hour after main meals. The correctness of the measurements was verified every 2 weeks by determinations performed at the laboratory using glucose oxidase and by determination of fructosamine and glycated haemoglobin (HbA_{1c}). The methods have been described in Part 1.

The distribution of data was verified by the Kolmogorov-Smirnov test. Data with a near-normal distribution were analysed by the t-Student test, data for samples significantly different from the normal distribution were analysed by the rank sum test (Mann-Whitney U test) and data for matched pairs were analysed by the Wilcoxon test. Differences with a P value of < 0.05 were considered statistically significant.

Results

The results are summarised in Table 1 and in Figures 1 and 2.

Compared to patients in class G1, patients in class G2 were significantly older and their pregestational body mass was significantly higher, although the percentage of patients with pregestational obesity was similar in both groups. GDM was diagnosed in G2 significantly earlier than in G1, and the weight gain in patients managed with diet only was significantly higher than in the group managed with diet and insulin. In both groups, the women gave birth at term and there were no differences in the mean due date (Table 1).

The parameters of glycaemic control: FBG, mean blood glucose (MBG) and fructosamine levels are summarised in Figure 1. G1 patients were characterised by significantly better values of short-term glycaemic control in the course of the entire pregnancy versus G2 patients. FBG and MBG were significantly lower both at the time of diagnosis (FBG: 4.5 ± 0.8 *vs*. 5.5 ± 1.3; MBG: 5.5 ± 0,9 *vs*. 6.9 ± 1.4 [mmol/L], respectively) and by the end of pregnancy (FBG: 4.1 ± 0.4 *vs*. 4.6 ± 0.4; MBG: 5.1 ± 0.4 *vs*. 5.6 ± 0.4 [mmol/L], respectively), and a significant reduction of these parameters were observed in both groups with the advancement of pregnancy. No significant differences in fructosamine levels were observed between the groups. While this parameter significantly decreased by the end of pregnancy in G2 only (2.1 ± 0.3 *vs*. 1.9 ± 0.1 [mmol/L]), no improvement was observed in G1 (Figure 1). HbA_{1c} at both time points did not differ between the groups and there was also no significant change from baseline in either group (G1: 4.78 ± 0.7 *vs*. 4.82 ± 0.7 [%], NS; G2: 5.01 ± 1.1 *vs*. 4.95 ± 0.9 [%], NS).

At the time of GDM diagnosis, TC, LDL-C and HDL-C were significantly higher in G1 versus G2. At this time point no differences were found between the groups with respect to TG. With the advancement of pregnancy, a significant increase of TG in both groups was observed, although the levels of cholesterol fractions did not change significantly. Only HDL-C significantly increased in G2 at T3. By the end of pregnancy, lipoprotein values did not differ between the groups (Figure 2).

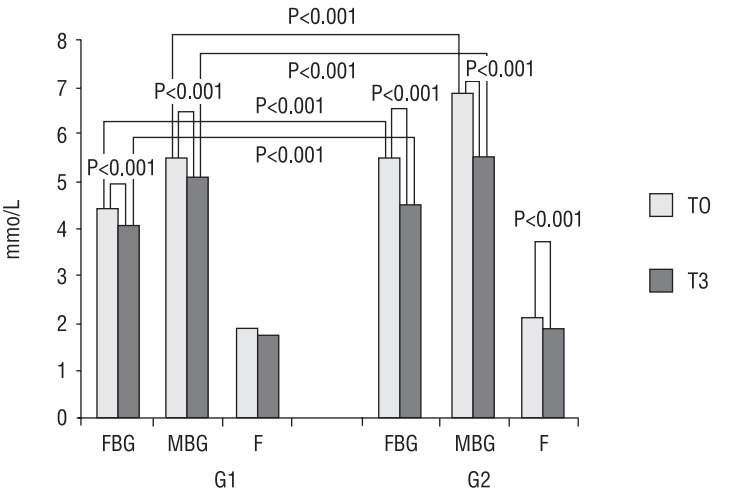

Figure 1. Parameters of glycaemic control in pregnant women with gestational diabetes mellitus relative to the method of antidiabetic treatment (all the significant differences marked in the figure are at the significance level $P < 0.001$); G1 — pregnant patients managed with diet; G2 — pregnant patients managed with diet and insulin; T0 — diagnosis of gestational diabetes mellitus; T3 — end of third trimester; FBG — fasting blood glucose; MBG — mean blood glucose; F — fructosamine

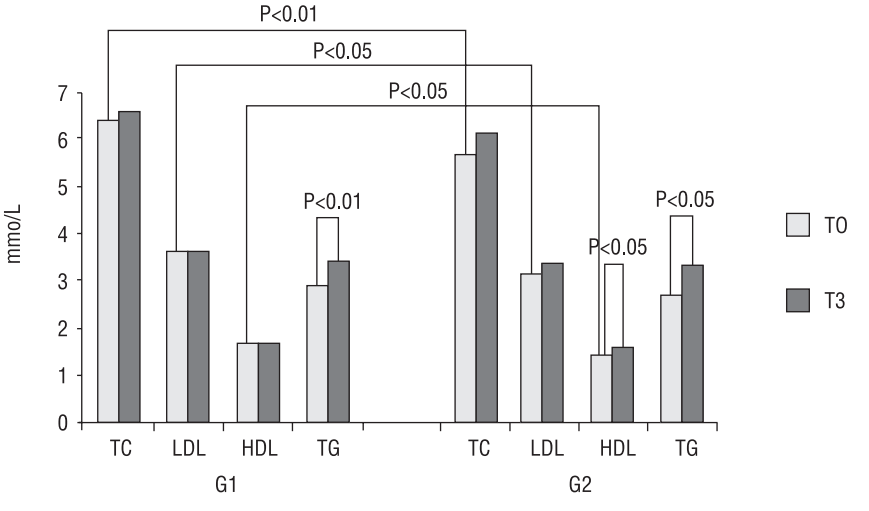

Figure 2. A comparison of selected parameters of lipid metabolism in pregnant women with gestational diabetes mellitus relative to the method of antidiabetic treatment; G1 — pregnant patients managed with diet, G2 — pregnant patients managed with diet and insulin; T0 — diagnosis of gestational diabetes mellitus, T3 — end of third trimester; TC — total cholesterol, LDL — LDL-cholesterol, HDL — HDL-cholesterol; TG — triglycerides

Discussion

In women with GDM, alterations in the metabolism of lipids as well as in the metabolism of carbohydrate are observed. The main changes in untreated GDM include significantly higher TG and LDL-C values and, according to some authors, reduced HDL-C values [1–3]. The main reason for these changes is insulin resistance, which increases with pregnancy and whose aim is to ensure appropriate supply of glucose to the foetus and increased utilisation of fats by the mother [4]. Insulin resistance leads to increased production of maternal insulin, although in some women the amount of insulin secreted is insufficient for the maintenance normal glucose tolerance. Studies of patients with a history of GDM demonstrated persistently reduced insulin secretion also after labour, more pronounced in women who had required insulin therapy during pregnancy. This may suggest an insulin secretion defect that existed before pregnancy [5, 6].

In our group of patients with GDM we found differences in glycaemic control between patients managed with diet only (G1) and patients requiring insulin therapy (G2). In G2, a significantly better glycaemic control was observed at the time of diagnosis, which persisted throughout pregnancy. This may be associated with a more pronounced impairment of insulin secretion in G2. In both groups, FBG and MBG tended to decrease significantly with the advancement of pregnancy as a result of the treatment. The parameter of glycaemic control which failed to improve significantly was HbA_{1c}, which is associated with a long period of reduced glucose levels necessary for the value of this parameter to change.

At the time of GDM diagnosis all cholesterol fractions were significantly higher in G1 versus G2. One cannot rule out that this may be associated with significantly more delayed diagnosis of GDM in this group of women, as a gradual increase in lipoprotein levels is observed in normal pregnancy. We did not observe this increase of the cholesterol fractions (with the exception of HDL-C) in either group. We did observe, however, a significant increase of TG, but by the end of pregnancy the values of lipoproteins did not differ between the groups.

The lack of differences between G1 and G2 in lipoprotein levels by the end of pregnancy may be associated with the method of treatment. Exogenous insulin supply modifies lipid metabolism and the changes that are typical of GDM may disappear [7]. Insulin inhibits lipolysis, increases the uptake of lipoproteins by the peripheral tissues and reduces their synthesis in the liver, resulting in reduced blood levels [8]. In patients with very well controlled type 1 diabetes mellitus, with an ample supply of exogenous insulin, lower levels of TC, TG, LDL-C and VLDL and higher levels of HDL-C are often observed compared to the population without abnormalities of carbohydrate metabolism [9–11]. We observed these lipoprotein changes in pregnant women managed with insulin and we believe that the lack of the physiological increase of TC and LDL-C by the end of pregnancy and the significant increase of HDL-C have been a result of insulin treatment.

Diet is one of the main factors affecting lipid levels. G2 patients showed a significantly lower weight gain during pregnancy, which was most probably a result of better compliance with the dietary recommendations. This behaviour could have stemmed from the fear of insulin treatment or its modification (increased frequency of insulin injections or doses). On the other hand, in G2 patients, excessive pregestational body mass was more prevalent and, as we demonstrated in Part 1, pregnant women with GDM who had been obese before pregnancy presented with lower lipoprotein values than patients who were overweight or whose body mass was normal (Part 1 — Table 3).

Conclusions

1. Intensive treatment of gestational diabetes significantly improves current blood glucose values. In the group managed with insulin, we observed a higher improvement of medium-term glycaemic control, as measured by fructosamine levels.
2. In gestational diabetes there is a significant increase of triglyceride levels, irrespective of the method of antidiabetic treatment. The only change in the cholesterol fractions was the significant increase of HDL-cholesterol by the end of pregnancy in the group of patients managed with insulin. Total and LDL-cholesterol levels did not change with the advancement of pregnancy in the group managed with insulin and in the group managed with diet only.

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