Glucose Tolerance and Plasma Insulin Levels During the Last Trimester of Pregnancy

TEIJI HAMADA, KIYOTAKA YOSHIMATSU, TOSHIYUKI OOSHIMA,
NORIO KUBO, JUNJI ISHIMATSU AND TOSHI KATO

*Department of Obstetrics and Gynecology, Kurume University School of Medicine,
Kurume, 830 Japan*

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Summary: Plasma glucose and plasma immunoreactive insulin (IRI) levels were measured during the 75 g glucose tolerance test (GTT) in healthy pregnant women, to clarify the changes of glucose metabolism during the last trimester of pregnancy. The glucose tolerance decreased with gestational time. After 33 weeks of gestation, the peak levels of the post-glucose loading occurred at 60 minutes instead of 30 minutes after glucose ingestion. The parameter that best reflected the decrease in glucose tolerance was the level 60 minutes after glucose ingestion, which at the 33rd gestational week was significantly higher than the level at the 28th gestational week. The IRI reaction accompanying the rise in plasma glucose appeared to increase gradually during gestation, even in the last trimester. The largest increases of plasma IRI levels after glucose loading were seen at or after the 36th week of gestation.

Key words: glucose tolerance—75 g glucose load—last trimester of pregnancy—plasma glucose—plasma IRI

Introduction

Glucose tolerance decreases during pregnancy, especially in the last trimester, as compared to non-pregnant subjects. Few reports, however, give detailed data on the changes during the last trimester. In this study on normal pregnant females, the changes in glucose tolerance and plasma insulin (immunoreactive insulin, IRI) were measured after ingestion of glucose.

Subjects and Methods

The subjects in this study were outpatients in the Department of Obstetrics and Gynecology who had no family history of diabetes, no history of previous heavy-for-date births, stillbirths or neonatal

deaths of unknown causes, no history of hydramnious or severe toxicosis of pregnancy, no obesity of 20 % or more above standard body weight, and who had neither hydramnious or severe toxicosis pregnancy nor complications of the fetus or neonate during the course of the present pregnancy. Complications of the fetus or neonate would include: heavy-for-date baby, asphyxia, respiratory distress syndrome, hypoglycemia, hyperbilirubinemia, polycythemia, and congenital anomaly. The pregnant women who had none of these complications were considered normal and given the 75 g glucose tolerance test (GTT). The principal subjects were those who took the test during the period from the 28th to the 38th week of gestation. The values for this group were compared with those for the group that

had not yet reached the 28th week.

Blood samples were taken from the cubital vein and plasma glucose levels were determined by the glucose oxidase method using an autoanalyzer. Plasma immunoreactive insulin (IRI) was measured by radioimmunoassay. Statistical analysis of the data was performed primarily by using the Student's t-test.

Results

1. Plasma glucose levels before and after ingestion of 75g glucose by normal pregnant women at various gestational times.

The results of the 75g GTT in 243 normal pregnant females were compared according to the week of gestation. Table 1 shows the number of cases and the average plasma glucose level for each group. Fig. 1. is a three-dimensional pattern obtained by plotting the plasma glucose levels against time after glucose loading and the gestational week at which the GTT was performed. Fig. 2. shows the one-dimensional regression equation for the correlation between the gestational week and the glucose levels at fasting, and 30, 60

and 120 minutes after ingestion of glucose. The data demonstrate that fasting plasma glucose levels decrease with increasing gestational time after the 28th week. In contrast, the post-glucose loading plasma glucose levels increase at each time of measurement (30, 60, and 120 minutes). The most striking increase occurred 60 minutes after glucose ingestion.

2. Plasma IRI levels before and after ingestion of 75g glucose by normal pregnant women at various gestational times.

Plasma IRI levels after ingestion of glucose by 234 normal pregnant females at various gestational times were compared. Table 2 shows the number of cases and the average plasma IRI level for each gestational week at which the measurements were made. Fig. 3 and 4 show the plasma IRI data illustrated by the same methods used in Fig. 1 and 2. The fasting plasma IRI levels did not vary during the last trimester. The plasma IRI levels, 30, 60 and 120 minutes after ingestion of glucose, all showed marked rises with increasing gestational time. The rise at 60 minutes was especially pronounced.

TABLE 1
Plasma glucose levels before and after 75g glucose loading in normal pregnant women at the 28th to the 38th gestational week

Gestational week	No. of cases	75g GTT (M $\pm$ SD mg/dl)			
		fast	30 min	60 min	120min
28	13	85 $\pm$ 8	126 $\pm$ 18	108 $\pm$ 30	103 $\pm$ 18
29	25	84 $\pm$ 7	127 $\pm$ 21	119 $\pm$ 28	107 $\pm$ 22
30	43	84 $\pm$ 7	126 $\pm$ 16	118 $\pm$ 25	109 $\pm$ 15
31	36	84 $\pm$ 6	127 $\pm$ 17	125 $\pm$ 31	104 $\pm$ 17
32	30	86 $\pm$ 8	128 $\pm$ 19	125 $\pm$ 29	108 $\pm$ 21
33	27	83 $\pm$ 6	129 $\pm$ 16	132 $\pm$ 26	107 $\pm$ 14
34	17	84 $\pm$ 8	134 $\pm$ 16	141 $\pm$ 21	115 $\pm$ 13
35	18	82 $\pm$ 12	131 $\pm$ 19	137 $\pm$ 29	118 $\pm$ 21
36	14	83 $\pm$ 6	128 $\pm$ 15	129 $\pm$ 22	103 $\pm$ 15
37	13	83 $\pm$ 8	132 $\pm$ 14	143 $\pm$ 28	108 $\pm$ 20
38	7	83 $\pm$ 10	131 $\pm$ 24	129 $\pm$ 39	107 $\pm$ 16

Fig. 1. Plasma glucose levels before and after 75g glucose loading in normal pregnant women at the 28th to the 38th gestational week (N=243)

Fig. 2. Plasma glucose levels before and after 75g glucose loading in normal pregnant women at the 28th to the 38th gestational week (N=243)

TABLE 2
Plasma IRI levels before and after glucose loading in normal pregnant women at the 28th to the 38th gestational week

Gestational week	No. of cases	75 g GTT (M±SD μ U/ml)			
		fast	30 min	60 min	120min
28	12	5± 3	48±18	44±31	33±18
29	23	7± 7	49±30	45±27	35±27
30	40	7± 7	52±34	48±29	41±28
31	34	9±10	56±32	63±40	40±32
32	29	6± 4	57±27	55±30	50±33
33	27	10± 9	60±39	65±37	46±34
34	17	7± 6	52±41	63±40	42±32
35	18	9±14	51±30	63±39	55±35
36	14	6± 6	58±23	61±34	40±33
37	13	6± 4	62±35	69±34	33±12
38	7	8± 9	64±31	78±46	78±50

Fig. 3. Plasma IRI levels before and after 75g glucose loading in normal pregnant women at the 28th to the 38th gestational week (N=234)

Fig. 4. Plasma insulin levels before and after 75g glucose loading in normal pregnant women at the 28th to the 38th gestational week (N=234)

Fig. 5. Insulinogenic index (IRI/PG, 30 min.) after 75g glucose loading in normal pregnant women at the 28th to the 39th gestational week (N=447)

3. Insulinogenic index in normal pregnant women given the 75g GTT.

The insulinogenic index (I.I.) is the ratio between the increase of plasma IRI and the increase of plasma glucose (PG), 30 minutes after the ingestion of 75g glucose ($\Delta\text{IRI}/\Delta\text{PG}$). The insulinogenic indices of normal pregnant females at different gestational times were compared and were found to be higher during the last trimester than during the second trimester of pregnancy. From the 28th to the 35th week, the index did not change, but at the 36th and later weeks, the index again rose sharply (Fig. 5).

Discussion

Changes in glucose tolerance during pregnancy have been the subject of many reports. The current view is that fasting plasma glucose levels are lower during pregnancy than at other times and the reduction becomes larger during the later stages of pregnancy (Bleicher et al. 1964; Lind 1980; Victor 1974). It is also thought

that post-glucose-loading glucose tolerance also gradually decreases during the pregnancy (Daniel et al. 1974; Fisher et al. 1974; Kalkhoff et al. 1970; Kühl 1975; O'Sullivan et al. 1970; Silverstone et al. 1961). These changes in glucose tolerance have been studied when glucose loading is performed either by oral ingestion (Daniel et al. 1974; Kalkhoff et al. 1970; Kühl 1975; Silverstone et al. 1961) or intravenous injection (Benjamin and Casper 1966; Fisher et al. 1974; O'Sullivan et al. 1970). In almost all studies using oral ingestion methods, 50 g (Kühl 1975; Lind et al. 1973) or 100 g (Daniel et al. 1974; Hansen and Kallner 1984; Kalkhoff et al. 1970; Silverstone et al. 1961) of glucose is given. In the present study of glucose tolerance, an intermediate dose of 75 g was administered. The objective was to investigate glucose tolerance during the second and last trimesters of pregnancy. The last trimester is considered to be a period when glucose tolerance is prone to decrease. Methods were used to determine whether small fluctuations occur. To identify the changes of glucose tolerance in this period, subjects were selected who were pregnant but had neither complications nor episodes related to abnormalities of glucose metabolism.

Judging from the GTT findings in this study obtained during a normal pregnancy, the fasting plasma glucose levels decrease with increasing gestational time, even within the last trimester. Glucose tolerance decreases with increasing gestational time, as is shown clearly by 1) the observation that after the 33rd week of gestation, the peak of the rise in plasma glucose occurs later, at 60 minutes instead of 30 minutes after glucose ingestion; and 2) by the positive correlation between gestational week and plasma glucose at different times after glucose ingestion. The parameter that best reflected the decrease in glucose tolerance was the level 60 minutes after glucose injection, which at 33 gestational

weeks reached the significantly high level of 134 ± 24 mg/dl, compared to 113 ± 30 mg/dl at 28 weeks. This indicates that there is a pronounced decrease in glucose tolerance during the last trimester, beginning at or around the 33rd week. This finding agrees with the clinically observed onset of metabolic disturbances, including ketoacidosis, that begin to increase in frequency at the 34th gestational week in pregnant diabetic females.

Next, the changes in plasma IRI after 75 g GTT were observed. As previously mentioned, the fasting plasma IRI level during pregnancy tends to increase (Spellacy and Goetz, 1963) and the post-glucose loading response is augmented (Daniel et al. 1974; Kalkhoff et al. 1970; Lind et al. 1973; Spellacy and Goetz, 1963; Spellacy et al. 1965; Spellacy et al. 1965). During pregnancy, the anabolic phases in the mother and the fetus are gradually potentiated, while the accelerated secretion of corticosteroids and hPL by the mother after the 20th gestational week brings about a relative potentiation of maternal catabolism (Freinkel et al. 1979). Therefore in the anabolic state caused by glucose loading, greater quantities of insulin are required than when the mother is not pregnant.

Reflecting on this pattern of insulin secretion, the postglucose loading plasma IRI levels tended towards hypersecretion in comparison to non-pregnancy levels. These trends are explained by the rise with increasing gestational time in the post-glucose loading plasma IRI levels at each time of measurement, especially at 60 minutes after the ingestion of glucose (correlation ratio $r = 0.90$). Fig. 5. shows the relationship between gestational week and insulinogenic index, which should closely reflect insulin secretory function. The augmentation of insulin secretion continued to rise sharply from the first trimester through the second trimester until the 31st week, when it plateaued moment

arily and then began another rising phase in the 35th week.

To summarize, a decrease in glucose tolerance, as indicated by the rise in plasma glucose after ingestion of 75g glucose, and the augmented insulin secretion accompanying the rise in plasma glucose both appear to increase gradually during gestation, even during the last trimester. The decrease in glucose tolerance at approximately the 36th gestational week is particularly marked and is accompanied by a pronounced simultaneous increase in insulin requirement.

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