The effect of carbohydrate intolerance on neonatal birth weight in pregnant women without gestational diabetes mellitus

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Background: There is still no consensus on screening, threshold levels and treatment of gestational diabetes mellitus. Furthermore, the importance of a positive 50-g glucose screening test in patients who had a negative 100-g oral glucose tolerance test remains controversial. We investigated the impact of the 50-g glucose screening test results on neonatal outcome in pregnant women with uncomplicated pregnancies, who had no risk factors according to ACOG criteria.

Patients and Methods: Three hundred eighty-six pregnant women with singleton pregnancies were prospectively screened with 50-g glucose challenge test between 24 and 28 weeks. If the test result was >140 mg/dl, a 100-g 3-hour oral glucose tolerance test was performed. Patients with a positive screening test, but not diagnosed as gestational diabetes mellitus constituted the study group, and patients with a negative screening test constituted the control group. Cesarean rates, neonatal birth weights and complications were compared between these groups.

Results: The cesarean delivery rates were not statistically different between the study and control groups (8.3% vs. 6.4%, $P>0.05$). The rates of macrosomic births were 10.0% in the study group, and 6.4% in the control group ($P>0.05$), but the mean birth weight (3451.67 ± 355.70 g) in the study group was significantly higher than the mean birth weight (3296.29 ± 365.14 g) in the control group ($P=0.003$). Neonatal hypoglycemia and hyperbilirubinemia was also encountered more often in babies of pregnant women with a positive 50-g glucose challenge test but negative 100-g glucose tolerance test.

Conclusion: Because of similarities with gestational diabetes mellitus on the basis of perinatal outcomes, the non-diabetic pregnant women with 50-g glucose screen test result over 140 mg/dl but a negative 100-g OGTT should be followed closely.

Key words: Diabetes mellitus, glucose challenge test, carbohydrate intolerance, neonatal outcome

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The accepted method of screening for gestational diabetes mellitus (GDM) is the 1-hour 50-g glucose challenge test (GCT) adapted by O'Sullivan et al.[1] in 1973. Universal screening for GDM has been extensively studied and is supported by most obstetricians.[2] The current strategy calls for screening pregnant women between 24 and 28 weeks with 1-hour 50-g GCT without regard to the time or amount of the last meal.[2] If the result is over 140 mg/dL threshold value, the patient should undergo a 3-hour 100-g oral glucose tolerance test (OGTT), according to National Diabetes Data Group (NDDG) criteria.[3] The American College of Obstetricians and Gynecologists (ACOG) recommends selective screening of pregnant women, and selective screening has gained popularity in recent years.[4]

Although no longer a problem with modern obstetric techniques, previous studies noted an increased frequency of maternal morbidity and mortality in women with GDM.[5-7] However, whether fetal and neonatal morbidity and mortality is improved is uncertain, despite improved metabolic control in GDM.[8-12] Patients who do not meet NDDG criteria are excluded from the high risk group for GDM. Nevertheless, carbohydrate intolerance, as determined by the 50-g GCT, might affect pregnancy outcome, birth weight and neonatal outcome. Previous studies have shown that patients with a 1-hour 50-g GCT higher than 140mg/dL but who are negative on the 100-g OGGT had more macrosomic babies and babies with neonatal complications.[13-15] However, these studies do not report whether the ACOG criteria were followed. Furthermore, pregnant women with complications that may affect birth weight were included in some of the studies.

For this reason, we investigated the impact of a positive GCT but negative OGTT on pregnancy outcomes in women who did not have risk factors according to ACOG criteria and did not have pregnancy complications in follow-up.

Patients and methods

Five hundred and three pregnant women with singleton pregnancies were admitted to our clinics before 24 weeks gestation between February 2001 and September 2002. Height, pregnancy weight, gravidity, parity, and risk factors for GDM[4] were recorded. The body mass index was calculated by dividing pre-pregnancy weight by the height squared. Seventy-four pregnant women who had ACOG risk factors (obesity, previous GDM history, DM in first degree relatives, macrosomic baby, congenital anomaly, habitual abortus, and unexplained stillbirth) and 7 pregnant women with overt DM were not included in the study.

A 50-g GCT was performed between 24 and 28 weeks in 386 pregnant women who were followed-up regularly. The 50-g GCT results were >140mg/dL in 85 pregnant women. These women received a 150-g carbohydrate diet for 3 days and then a 100-g OGTT was performed after an overnight fast. Sixteen women were excluded because they had GDM according to NDDG criteria. The remaining 69 pregnant women with a positive GCT but negative OGTT formed the study group. The 301 pregnant women with a negative 50-g GCT results served as a control group. Nine women from the study group and 18 women from the control group were excluded because of pregnancy complications like pre-eclampsia, intrauterine growth restriction, and preterm birth that may have influenced birth weight and neonatal outcome. The final statistical analysis included 60 patients in the study group and 283 patients in the control group.

Neonatal birth weight, cesarean rates for cephalopelvic disproportion and early neonatal complications like hyperbilirubinemia, hypocalcemia, respiratory distress syndrome, and hypoglycemia rates were assessed. Neonates over 4000 grams were considered macrosomic. Neonatal blood glucose and calcium levels were assessed only in symptomatic babies (lethargy, atony, suckling problems, convulsion, etc). Neonatal hypoglycemia was defined as a blood glucose level lower than 35 mg/dL. Neonates who had to receive phototherapy for at least 24 hours were considered hyperbilirubinemic.

Group characteristics and neonatal birth weights were compared with Student's *t* test. Rates of cesarean delivery, macrosomia, hypoglycemia and hyperbilirubinema were compared with Fisher's exact test with Yate's correction. Statistical significance was a *P* value <0.05. We used SPSS 10.0 (SPSS Inc, Chicago).

Table 1. Characteristics of the pregnant women by response to the 50-g glucose challenge test.

	50-g GCT		
	<140 mg/dl Mean±SD (n=283)	140 mg/dl Mean ±SD (n=60)	*P* value
Age (years)	28.81 ± 4.24	29.70 ± 4.85	0.15
Gravida	2.47 ± 0.94	2.57 ± 1.96	0.56
Parity	1.15 ± 0.66	1.07 ± 1.01	0.42
Height (cm)	159.34 ± 11.85	161.93 ± 5.06	0.10
Weight (kg)	63.99 ± 16.33	62.07 ± 9.19	0.38
Body mass index (kg/m^2)	23.94 ± 3.04	23.86 ± 3.18	0.87
Maternal weight at birth (kg)	75.68 ± 8.90	75.87 ± 9.88	0.82
Gestational weeks at birth	39.50 ± 1.06	39.70 ± 0.98	0.18

Table 2. Neonatal outcomes by response to the 50-g glucose challenge test.

	50-g GCT		
	<140 mg/dL n = 283 [n (%)]	140 mg/dL n = 60 [n (%)]	*P* value
Cesarean delivery rate for CPD*	18 (6.4%)	5 (8.3%)	0.57
Neonatal birthweight (g) [mean ±SD]	3296.29 ±365.14	3451.67 ±355.70	0.003
Macrosomia	15 (5.3%)	6 (10.0%)	0.23
Hypoglycemia	2 (0.7%)	3 (5.0%)	0.05
Hyperbilirubinemia	11 (3.9%)	7 (11.7%)	0.02

* CPD, cephalopelvic disproportion

Results

The mean age of the study and control groups were 29.7±4.85 years (range, 21-40 years) and 28.81±4.24 years (range, 19-39 years), respectively. There was no statistically significant difference between the study and control groups in age, gravidity, parity, height, BMI, maternal weight at birth, or gestational weeks at birth (P>0.05, Table 1).

The mean neonatal birth weight of the babies in the study group was significantly higher than the babies in the control group (3451.67±355.70 vs. 3296.29±365.14, P=0.003) (Table 2). The rate of macrosomic babies was 10% (6/60) in the study group and 5.3% (15/283) in the control group; the difference was not statistically significant. Likewise, the rates of cesarean delivery for cephalopelvic disproportion were not statistically different between the study and control groups (8.3% vs. 6.4%, P>0.05). There was no case of respiratory distress syndrome or hypocalcemia in either group. Three babies (0.7%) in the study group and two babies (5.0%) in the control group needed intravenous glucose for intractable hypoglycemia, and the difference was statistically significant (P<0.05). Eleven babies (3.9%) in the control group and 7 babies (11.7%) in the study group received phototherapy for hyperbilirubinemia (P<0.05, Table 2).

Discussion

Gestational diabetes mellitus is still a controversial disease despite ongoing research for 30 years. There is still no consensus on screening methods, threshold values, diagnostic criteria or universal versus selective screening. Some authors suggest that GDM is not responsible for increases in perinatal morbidity and mortality.[16] One group of investigators suggested that maternal obesity, rather than GDM, was responsible for macrosomia even though patients were diagnosed and treated for GDM.[17,18] Many reports indicate that there is a high incidence of macrosomia and cesarean delivery rates in untreated GDM.[19,20] Umbilical artery acidosis may be encountered more often in untreated GDM.[21] In one study, birth weight, the rate of macrosomia, shoulder dystocia and caesarean delivery rates were increased in improperly treated GDM.[17] Despite the controversy, most clinicians believe that treatment of GDM decreases maternal and neonatal complications.

Because of the potential impact of GDM on maternal and fetal morbidity, the Third International Workshop Conferecence on Gestational Diabetes and the American Diabetes Association recommended routine screening of all pregnancies for GDM by 1-hour 50-g GCT between 24 and 28 weeks of gestation, using a threshold value of 140 mg/dL (7.8 mmol/L), without regard to the time and nature of the previous meal.[2,22] In a retrospective analysis of the data from a group of 752 women who underwent both the GCT and oral GTT from 1956 to 1957, the GCT threshold level was established at 143 mg/dL and later rounded down to 140 mg/dL for ease of recollection. Nevertheless, the merits of universal screening over selective screening continue to be contested. ACOG has recommended a selective screening policy that includes all pregnant women more than 29 years old and younger women with historic and clinical risk factors.[4] A selective screening policy fails to detect over a third of gestational diabetics. O'Sullivan et al.[1] found the incidence of glucose intolerance to be comparable in patients with and without risk factors for GDM, and they found that adding maternal age (>29 years) would have left 23% of cases of GDM. Two large, population-based studies by Lavin[23] and Coustan[24] et al. confirmed the findings of O'Sullivan et al., and demonstrated that universal screening could be performed with a modest increase in cost.

Cost-effectiveness is important, but the goal of management is to improve both maternal and neonatal outcomes. There are many studies on the impact of the selective vs. universal screening on the diagnosis of GDM. However, there are limited data on the effect on neonatal outcomes of a positive GCT but negative OGTT, a condition that might be described as mild gestational glucose intolerance.[13-15] Furthermore, to the best of our knowledge, there is no study on the impact of mild gestational glucose intolerance on neonatal outcome in patients who do not carry ACOG risk factors. For this reason, we attempted to determine the impact of mild gestational hyperglycemia on neonatal outcomes in pregnant women who do not have the ACOG risk factors.

Sermer et al[15] found that the incidence of macrosomic babies and cesarean rates are increased in pregnant women with positive 50-g GCT, but a negative 100-g OGTT. However, patients less than 24 years old were excluded from the study due to a low risk of GDM. They found a macrosomia incidence as high as 17.2% in patients with 50-g GCT values over 140 mg/dL. Similar results were obtained by Kaufmann[13] and Berkus[14] et al. They defined only one abnormal value in the 100-g GTT as mild gestational hyperglycemia, and concluded that mild gestational hyperglycemia is associated with macrosomia and poor neonatal outcome. Kaufmann found that the incidence of birth weight greater than 4000 g is 20% or greater in the infants of mothers who had only one abnormal GTT value and only 12.4% in controls. In another study, Bevier et al.[25] studied 103 pregnant women with a positive 50-g GCT and a negative 100-g OGTT, who were randomly separated into two groups. One group received dietary therapy, while the other group was left to routine follow-up. They found a decreased HbA1c level and decreased incidence of macrosomic babies in women who received standard dietary therapy.

In our study, there was no statistically significant difference in the rates of cesarean delivery and macrosomia

between the study and control groups. The rate of cesarean delivery in the study group was 11.7%, whereas this rate in the control group was 9.3%. (P>0.05). Although the rate of macrosomia was higher in the study group than in the control group (10% vs. 4.9%), this difference did not reach statistical significance (P>0.05). This may result from an insufficient number of patients in this study group. Nevertheless, we found that the babies of non-gestational diabetic women with positive 50-g GCT had a mean birthweight of 3451.67±355.70 g, whereas the babies of the control group had a mean birthweight of 3296.29 ±365.14 g (P=0.003). This may reflect the impact of mild gestational glucose intolerance as determined by a positive 50-g GCT on neonatal birthweight.

We found an increased incidence of neonatal hypoglycemia and hyperbilirubinemia in babies of women with positive 50-g GCT but a negative 100-g OGTT. The rate of neonatal hypoglycemia was 0.7% in the control group, and 5.0% in the study group (P=0.05). Likewise, the rates of neonatal hyperbilirubinemia requiring phototherapy in the study and control groups were 11.7% and 3.9%, respectively (P=0.02). Sermer et al.[15] found that 9.4% of neonates of mothers with GCT values over 140 mg/dL received phototherapy. Rey et al.[26] found an incidence of 10% for hypoglycemia and 21.7% for hyperbilirubinemia in patients with impaired glucose tolerance.

Our data suggests that neonatal birthweight and rates of neonatal hypoglycemia and hyperbilirubinemia are increased in babies of pregnant women with a positive 50-g GCT and a negative 100-g OGTT, but larger, prospective studies are needed for confirmation. In future studies, the threshold value of 140 mg/dL may not be sufficient to exclude all GDM cases, and it might be lowered. It is possible that subtle changes in glucose metabolism in pregnant women may also affect neonatal outcome. For this reason, the neonatologist should be aware of the possibility of this subtle metabolic alteration in patients with a positive 50-g GCT but negative 100-g OGTT.

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