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Oral glucose tolerance test is a poor predictor of hyperglycemia during pregnancy

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1 Introduction

Gestational diabetes mellitus (GDM) is the most common metabolic disorder in pregnancy. The condition is considered to be associated with increased perinatal morbidity and mortality [6], which may be reduced by adequate diagnosis and management. The diagnosis of GDM is generally established by means of an oral glucose tolerance test (OGTT), that is regarded as abnormal on the basis of predefined criteria. The aim of treatment in gestational diabetic patients is to obtain normoglycemia, which usually requires dietary measures with or without insuline therapy. In an effort to study the efficacy of the glucose tolerance test to detect those patients with GDM who require therapeutic measures to maintain normoglycemia, we compared the results of a glucose tolerance test with those of a glucose profile consisting of three postprandial glucose values, and with pregnancy outcome.

2 Subjects and methods

During a two-year period, from September 1985 to August 1987, we prospectively studied 250 Caucasian pregnant women considered to be at risk for GDM. Each woman had one or more of the following risk factors: a past history of GDM, a previous macrosomic or hypoglycemic infant, a positive family history, age 35 years or more, obesity, recurrent glycosuria, or accelerated fetal growth in the present pregnancy. Patients with known type 1 or type 2 diabetes mellitus, and women with multiple pregnancy were excluded.

Curriculum vitae

CAROLINA JULIA MARIA BACKX, *M. D., was born in Breda, The Netherlands, in 1958. She graduated at the Erasmus University Medical School, Rotterdam, in 1983, and she participated in experimental oncogynaecologic studies at John Hopkins University Baltimore, USA, in 1979. She currently finishes up her specialty training in Obstetrics and Gynaecology at the University Hospital, Dijkzigt, in Rotterdam, and is a member of the Consilium Gynaecologicum et Obstetricum. Her main interest is in high risk obstetrics.*

In all subjects a 50-g OGTT was performed following three days of glucose loading with at least 50 g glucose/day and capillary blood was sampled at 0, 0.5, and 1 hour. On the same day one of the staff nurses taught the women how to take their own capillary blood samples at home. Samples were collected in prelabeled fluoride oxalate tubes, on the following day one hour after breakfast, lunch and dinner. Glucose levels were measured the next day in whole blood using the hexokinase method (Boehringer Mannheim). Only one 50-g OGTT and one home glucose profile (HGP) were obtained from each subject to be used for comparison. The gestational age at the time of testing ranged from 16 to 36 weeks, with a median of 29 weeks.

The OGTT was considered to be abnormal if one or more of the glucose values exceeded the upper limits as used in our institution, of 5.3, 9.1 and 8.7 mmol/L at 0, 0.5 and 1.0 hour, respectively, prior to 28th weeks' gestation, and of 5.5, 8.4 and 9.2 mmol/L thereafter [4]. The home glucose profile (HGP) was considered abnormal if one or more of the glucose values exceeded the value of 7.0 mmol/L [4]. A diagnosis of GDM was rejected when both OGTT and glucose profile were normal, and no treatment was instituted. When both the OGTT and the glucose profile were abnormal, a diagnosis of GDM was made. These patients were treated with dietary measures alone or, if necessary to maintain glucose values at of below 7.0 mmol/L, in combination with insulin. When one of both tests was abnormal, the diagnosis of GDM as well as the necessity for therapeutic measures was considered to be questionable, and a third test was performed.

This third test was used as a gold standard, and consisted of a clinically monitored glucose profile (CGP). Subjects were on a standard hospital diet (approximately 40% fat, 45% glucose, 15% protein, 30 kcal/kg.day) during the test, and capillary whole blood samples were taken one hour after each of the three main meals. GDM was considered to be absent and no specific treatment was given if glucose values did not exceed the level of 7.0 mmol/L. Patients in whom one or more glucose concentrations exceeded the value of 7.0 mmol/L were considered to have gestational diabetes, and therapeutic measures were instituted.

Differences in relative frequencies between groups were tested with the X^2-test, and a p value of < 0.05 was regarded as significant.

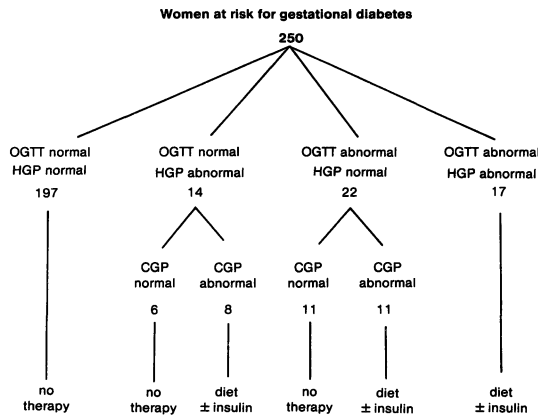

Figure 1. Diagnosis and management of GDM. OGTT oral glucose tolerancetest HGP home-monitored glucose profile. CGP clinically monitored glucose profile.

3 Results

The glucose test results are shown in figure 1. Both OGTT and HGP were normal in 197 women and abnormal in 17 women, while in 36 women only one of the two tests was found to be abnormal. These 36 women were tested again, using the CDP as a gold standard. Of these 36 women, only 19 had an abnormal CGP and were treated with diet with or without additional insulin therapy.

Fetal outcome as related to the OGTT and HGP test results is presented in table I. An abnormal OGTT was associated with the birth of a large-for-gestational age infant (weight > 90th centile) in 6 of 39, or 15% of cases, a normal OGTT with 21 of 214 large infants (no significant difference). An abnormal HGP preceded the birth of a large infant in 7 of 31, or 23% of cases,

Table I. Fetal outcome related to glucose test results

	n	> 90th percentile infant		instrumental delivery		5'-Apgar score		perinatal deaths	
		n	(%)	n	(%)	n	<7	n	(%)
OGTT + HGP normal	197	18	(9.1)	35	(17.8)	4	(2.0)	3	(1.5)
OGTT or HGP abnormal	36	5	(13.8)	7	(19.4)	0	(0.0)	0	(0.0)
OGTT + HGP abnormal	17	4	(23.5)	3	(17.6)	0	(0.0)	1	(5.3)
Total	250	27	(10.8)	45	(18.0)	4	(1.6)	4	(1.6)

while a normal HGP was associated with 20 of 219, or 9%, large-for-gestational age infants, again no significant difference. The frequency of occurrence of instrumental deliveries was similar between groups. Four perinatal deaths occurred (1.6%). In three of these cases both OGTT and HGP had been normal and fetal or neonatal death appeared to be unrelated to glucose metabolism (one second trimester birth due to cervical insufficiency, one stillbirth of a severely growth retarded fetus, one asphyxiated infant born after placental abruption). In the fourth case both OGTT and HGP had been abnormal. Despite treatment with diet and insulin, the infant had a birth weight of 4380 g at 39 weeks (> P 90). The infant was in good clinical condition and had normal glucose levels during the first 48 hours after delivery, but died suddenly on the third day after birth. Postmortem examination failed to demonstrate the cause of death.

4 Discussion

Patients with GDM tend to deliver large babies, which may increase the risk of perinatal morbidity [3] and mortality [6]. The most important risks are: prolonged labor and delivery, hyperbilirubinemia, traumatic injury and neonatal hypoglycemia [3]. In order to reduce these risks, considerable effort is put into the detection and treatment of GDM. However, no agreement exists about the criteria on which the diagnosis should be based, about the question how accurate the diagnosis can predict increased risks, or on the effectiveness of treatment to reduce those risks [2, 7].

The diagnosis of GDM is usually based on a abnormal OGTT. However, important differences exist with regard to patient selection, optimum timing, dose and duration of glucose loading, site and frequency of sampling, method of glucose assay, and normal ranges [1]. An abnormal OGTT does not necessarily mean that glucose values under less unphysiologic circumstances, that is on a normal diet, are abnormal. In addition, healthy pregnant women at no increased risk of GDM have a 2.3% risk of an abnormal test if 2 standard deviations above the mean in uncomplicated pregnancy is used as a cut-off level. In the present study the OGTT was abnormal in 39 of 250 women, or 16%, at risk for GDM. However, 11 of these 39 women (or 28%) with a abnormal OGTT subsequently had two normal glucose day profiles (HGP and CGP). Consequently, the OGTT overestimated the occurrence of hyperglycemia by 28%.

Other investigators screen for GDM by sampling at one or several occasions during the day, either at random, or before and after one of the main meals, or after a glucose load [5]. Again, 2.3% of healthy pregnant women will have abnormal test results by statistical definition in many studies. In the present study, 11 of 219 women, or 5%, with a normal HGP, had both an abnormal OGTT and an abnormal CGP. This suggests that the HGP in this study underestimated the occurrence of hyperglycemia by 5%.

Even if one assumes that the OGTT overestimates by 28%, and the HGP underestimates by 5% the chance of hyperglycemia, this still leaves unanswered the question as to what extent mild to moderate hyperglycemia increases the risks in the perinatal period, or how effective treatment of such hyperglycemia is to prevent these risks. Our study cannot provide the answer to this question, because all women in whom hyperglycemia was identified, were treated. The percentages of large-for-gestational age infants, instrumental deliveries, low Apgar scores, and perinatal deaths, were slightly, but not significantly, higher than those in the normoglycemic, untreated group. Although this could indicate that treatment was indeed effective, alternative explanations are that the numbers were too small to allow valid statistical comparison, or that outcome would have been just as good without therapy. Twenty-one large-for-gestational age infants were born from 214 normoglycemic untreated mothers. This suggests that one cannot effectively identify the 10% largest infants in the population by screening for GDM.

The percentages of instrumental deliveries, low Apgar scores and perinatal deaths in the normoglycemic women are comparable to those in the population of pregnant women in our high-risk obstetric unit; they were apparently not related to birth weight. This suggests that in women considered to be at increased risk for GDM also other risk factors than poor glycemic control alone may contribute to a fetal outcome that is less favorable than that in the general population [6].

Although several authors have argued that treatment of GDM should result in improved out-

come, the effect of treatment can only be demonstrated in a large randomized study in which the hyperglycemic controls remain untreated. Considering the inconvenience, anxiety and costs of glucose tolerance testing for the patient, a randomized controlled study of the efficacy of screening and treatment programs for GDM may be warranted and ethically justified.

Abstract

In an effort to assess the efficacy of the oral glucose tolerance test to detect patients with gestational diabetes mellitus who require therapeutic measures to maintain normoglycemia, we compared the results of an oral glucose tolerance test with those of a home glucose profile consisting of three postprandial glucose values in 250 pregnant women.

The OGTT overestimated the occurrence of hyperglycemia by 28%, while the home glucose profile underestimated the occurrence of hyperglycemia by 5%. Pregnancy outcome was not significantly different between spontaneously normoglycemic women and those who required therapy. One cannot effectively identify the ten percent largest infants in the population by screening for gestational diabetes.

Keywords: Diabetes and pregnancy, diabetes screening, gestational diabetes, glucose tolerances test.

Zusammenfassung

Oraler Glukose-Toleranztest als Parameter mit geringer Aussagekraft für eine Hyperglykämie in der Schwangerschaft

Um die Effizienz eines oralen Glukose-Toleranztestes zur Aufeckung eines Gestationsdiabetes, der therapeutische Maßnahmen zur Einhaltung normoglykämischer Werte erfordert, zu überprüfen, verglichen wir die Ergebnisse des oralen Glukose-Toleranztestes mit denen von Blutzuckerprofilen in häuslicher Umgebung.

Prospektiv wurden 250 Schwangere mit Risikofaktoren für einen Gestationsdiabetes (GDM) untersucht. Bei allen Patientinnen wurde nach 3 Tagen glukosereicher Ernährung ein oraler Glukose-Toleranztest (50 g) mit Blutentnahmen bei 0, 0.5 und 1 Stunde durchgeführt. Um ein häusliches Glukoseprofil zu erhalten, wurde am folgenden Tag jeweils eine Stunde nach Frühstück, Mittag- und Abendessen Blut abgenommen. Von einem pathologischen OGTT gingen wir aus, wenn die Werte vor der 28. Schwangerschaftswoche höher als 5.3, 9.1 und 8.7 mmol/l bei 0, 0.5 und 1 Stunde lagen, später wurden die Grenzwerte bei 5.5, 8.4 und 9.2 mmol/l angesetzt. Das häusliche Glukose-Profil (HGP) galt als pathologisch, wenn mindestens einer der Werte 7.0 mmol/l überstieg. Fiel nur einer der beiden Tests pathologisch aus, wurde die Diagnose GDM in Zweifel gezogen. In diesen Fällen wurde ein dritter Test durchgeführt, wobei ein klinisch überwachtes Glukoseprofil (CGP) erhoben und als Gold-Standard benutzt wurde.

Abb. 1 zeigt die Ergebnisse. Beide Tests waren bei 197 Frauen normal und bei 17 Frauen pathologisch, während bei 36 Frauen lediglich einer der beiden Tests pathologisch ausfiel. Diese 36 Frauen wurden nochmals mit einem CGP als Gold-Standard überprüft, der bei 19 Frauen pathologisch ausfiel. Hier wurde eine Diät und, wenn erforderlich, eine Insulintherapie angesetzt. Der OGTT war bei 39 von 250 Frauen mit Risikofaktoren pathologisch, das entspricht 16%. Jedoch hatten 11 dieser 39 Frauen ($\cong$ 28%) anschließend zwei normale Blutzuckertagesprofile (HCP und CGP). Das heißt, daß der OGTT in 28% das Auftreten von Hyperglykämien überschätzte.

Es gab keinen signifikanten Unterschied bezogen auf das Schwangerschaftsoutcome zwischen spontan normoglykämischen Frauen und denen, wo eine Therapie erforderlich war. Ein Screening auf Gestationsdiabetes ist in der Tat keine effektive Methode, um die 10% hypertropher Kinder in der Population zu identifizieren.

Schlüsselwörter: Diabetes-Screening, Diabetes und Schwangerschaft, Gestationsdiabetes, Glukose-Toleranztest.

Résumé

Le test de tolérance au glucose par voie orale est un mauvais prédicateur de l'hyperglycémie au cours de la grossesse

Nous avons comparé les résultats d'un test de tolérance au glucose par voie orale avec ceux d'un cycle glycémique à domicile afin d'évaluer l'efficacité du test de tolérance au glucose par voie orale à dépister les patientes présentant un diabète sucré gestationnel qui nécessitent des mesures thérapeutiques pour maintenir une normoglycémie.

Nous avons étudié 250 femmes enceintes à risque de diabète gestationnel. Une H. G. P. O. (50 g) a été réalisé

chez tous les sujets après 3 jours de charge en glucose et des prélèvements sanguins ont été réalisés à 0; 0,5 et 1 heure. Pour le cycle glycémique des prélèvements sanguins ont été effectués le lendemain une heure après le petit déjeuner, le déjeuner et le diner. Les H. G. P. O. ont été considérées comme anormales si l'une ou plus des valeurs de la glycémie dépassaient 5,3; 9,1 et 8,7 mmol/L respectivement à 0; 0,5 et 1 heure avant la 28è semaine et 5,5; 8,4 et 9,2 mmol/L après. Le cycle glycémique était considéré comme anormal si l'une ou plusieures glycémies dépassaient 7 mmol/L. Lorsqu'un seul test était anormal, le diagnostic de diabète gestationnel était considéré comme sujet à caution. Dans ces cas, un troisième test était réalisé à savoir un cycle glycémique surveillé cliniquement et servait de standard de référence.

Les résultats des tests sont représentés dans la figure 1, chez 197 femmes les deux, H. G. P. O. et cycle glycémique, sont normaux et anormaux chez 17 femmes, alors que chez 36 femmes, un seul des deux tests est trouvé comme anormal. Ces 36 femmes ont été étudiées de nouveau, en prenant le cycle glycémique surveillé cliniquement comme standard de référence. Parmi ces 36 femmes, seules 19 avaient un cycle anormal et ont été traitées par le régime avec ou sans insulinothérapie additionnelle.

L'H. G. P. O. était anormale chez 39 des 250 femmes, soit 16%, à risque de diabète gestationnel. Toutefois, 11 parmi ces 39 femmes (soit 28%) avec H. G. P. O. anormale présentaient ensuite deux cycles glycémiques normaux. De telle sorte que, l'H. G. P. O. surrestime l'occurence de l'hyperglycémie de 28%.

L'évolution de la grossesse n'est pas significativement différente entre les femmes spontanément normoglycémiques et celles ayant necessité une thérapeutique. En pratique, on ne peut identifier les 10% d'enfants macrosomes dans la population à l'aide de dépistage du diabète gestationnel.

Mots-clés: Dépistage du diabète, diabètes et grossesse, diabètes gestationnels, test de tolérance au glucose.

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