A standardised breakfast tolerance test in pregnancy: comparison with the 75 g oral glucose tolerance test in unselected mothers and in those with impaired glucose tolerance

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SUMMARY

There is still disagreement concerning the optimal procedure for the diagnosis of milder degrees of hyperglycaemia in pregnancy. We have compared the results of a 75 g oral glucose tolerance test (OGTT) and a standardised breakfast test performed one week apart in 102 non-diabetic women with a singleton pregnancy. There was poor correlation between the two tests (r=0.15) at two hours, and neither test was predictive of adverse maternal or fetal outcome. One hundred and four patients with impaired glucose tolerance, diagnosed at 30 weeks' gestation by 75 g OGTT, subsequently had a breakfast and lunch meal profile. There was no significant correlation between the two-hour OGTT value and either the two hour post-breakfast value (r=0.35) or the maximum profile value (r=0.33). Using the WHO diagnostic criterion of >8 mmol/l for the OGTT and a maximum glucose concentration >6.8 mmol/l for the meal profile, there was no relationship between an abnormal result in either test and pregnancy outcome. In our obstetric environment, the 75 g OGTT, a standardised breakfast test, and a structured meal profile, all failed to provide a useful indication of pregnancy outcome in mothers not already known to have diabetes.

INTRODUCTION

We have previously reported that, in our obstetric population, fetal outcome is not adversely affected by maternal impaired glucose tolerance as defined by the current WHO criteria.[1,2] The most important pathological aspect of carbohydrate intolerance in pregnancy is likely to be hyperglycaemia associated with normal eating habits, and the oral glucose tolerance test (OGTT) does not necessarily reflect this. We have investigated the relationship between the response to the 75 g OGTT and a standardised breakfast test in a group of unselected pregnant women, and related the glucose responses to maternal morbidity and fetal outcome. We have also studied a selected group of mothers who had impaired glucose tolerance by the WHO criteria.[3]

PATIENTS AND METHODS

1) Unselected pregnancies

One hundred and fifteen women attending an antenatal clinic were studied. The patients were contacted by telephone at about 28' weeks gestation and asked to participate.

The only exclusion criteria were multiple pregnancy, pre-existing diabetes, and treatment with steroids or antihypertensive agents. Each patient underwent a 75 g OGTT and a 300 Calorie standardised breakfast test at 30 - 32 weeks' gestation. The tests were performed one week

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apart, after an overnight fast. The order of the tests was alternated by number of entry into the study. The 75 g glucose was in the form of dextrose monohydrate and had the same calorific value as the standardised breakfast. The latter contained 45 g carbohydrate, 10 g protein and 9 g fat, as a portion of breakfast cereal with milk, toast and butter, and a cup of tea.

2) Impaired glucose tolerance pregnancies

Nine hundred and thirty six patients had a 75 g OGTT performed at about 30 weeks' gestation because of positive clinical screening criteria according to the protocol in use at our hospital at that time.[4] The criteria were glycosuria in a second fasting sample, family history of diabetes in a first degree relative, maternal weight >90 kg, history of congenital malformation or unexplained stillbirth, or a previous baby weighing 4.5 kg or more. One hundred and seventeen of these 936 women were found to have impaired glucose tolerance using the WHO two-hour cut off of 8.0 mmol/l. One hundred and four of these patients subsequently had a breakfast/lunch profile with venous samples for plasma glucose measurement before and two hours after each meal: both breakfast and lunch contained 300 Calories and had identical nutrient content.

RESULTS

1) Unselected pregnancies

Thirteen of the 115 patients recruited into the study were unable to complete both tests; in a few cases this was due to vomiting of the glucose load, but several patients did not keep the second appointment. The mean age of the remaining 102 women was 27.7 years (range 18-40 years). Parity varied from 0-3. The mean booking weight was 64.6 kg (range 43.6-107.4 kg), and the mean body mass index at booking was 24.8. The majority of patients attended for the booking visit between six and 16 weeks' gestation.

Forty eight of the women had the OGTT performed before the breakfast test, and 54 had the breakfast test first: there was a greater number of withdrawals among the patients who had the OGTT first, which may indicate that this test was less acceptable to the patients. There was no significant difference in age, parity, weight or body mass index with respect to the order in which the tests were performed.

For the OGTT, the mean (± SEM) venous plasma glucose at 0, 1 hour and 2 hours was 4.4 mmol/l (± 0.04), 7.4 mmol/l (± 0.17) and 6.1 mmol/l (± 0.12), and for the breakfast test 4.4 mmol/l
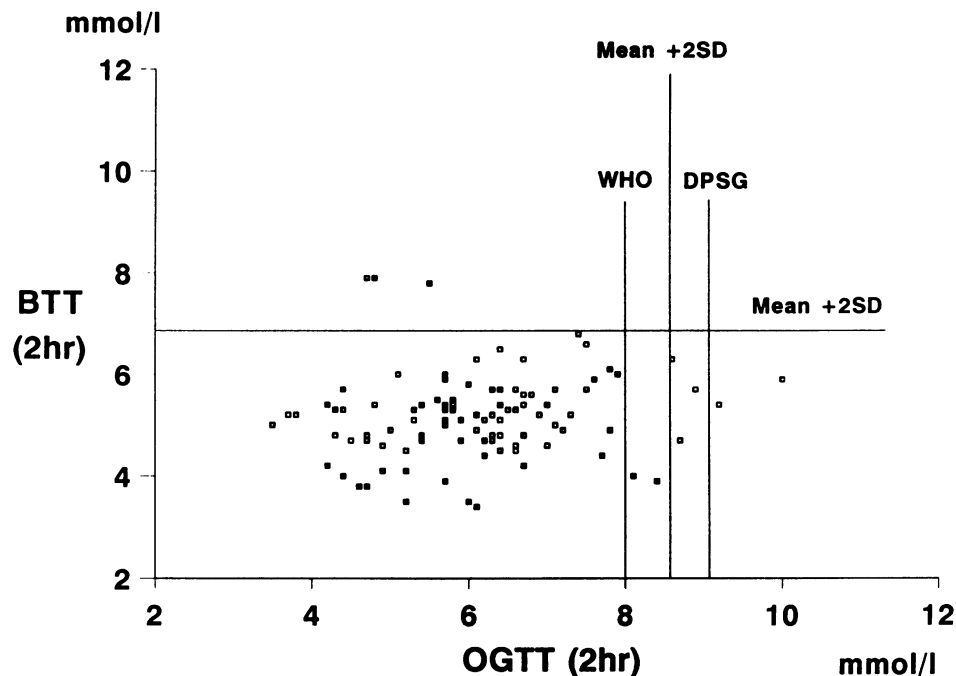

Fig 1. Comparison of the glucose concentrations at 2 hours in the 75 g oral glucose tolerance test (OGTT) and the standardised breakfast tolerance test (BTT): r=0.15.

WHO: World Health Organisation definition of impaired glucose tolerance in pregnancy (>8.0 mmol/l).

DPSG: Diabetes Pregnancy Study Group definition of impaired glucose tolerance in pregnancy (>9.0 mmol/l).

The definition of diabetes is a 2 hour plasma glucose concentration >11 mmol/l.

(± 0.05), 6.2 mmol/l (± 0.12) and 5.2 mmol/l (± 0.08). In general the one-hour glucose concentration was higher than the two-hour level, and the glucose load caused a greater rise in plasma glucose than the isocaloric standardised breakfast. There was poor correlation between corresponding OGTT and breakfast test values within patients; r=0.53 for the fasting values, r=0.36 at 1 hour and r=0.15 at 2 hours.

Figure 1 relates the 2 hour OGTT and breakfast test values. Using the WHO cut-off level of 8 mmol/l for the 75 g OGTT, seven women had impaired glucose tolerance. If the modified cut-off level of 9 mmol/l suggested by the Diabetic Pregnancy Study Group[5] is used, this number is reduced to two. The mean + 2SD value for 2 hour plasma glucose in the OGTT in this study was 8.6 mmol/l. No patient was found to have diabetes (2 hour value >11.0 mmol/l). No patient had a 2 hour glucose concentration above 8 mmol l^{-1} in the breakfast test; the mean + 2SD level for the 2 hour plasma glucose was 6.8 mmol/l and there were three patients with a value above this.

Only eighteen of the women (17%) had a clinical indicator to have an OGTT using the previous standard hospital criteria. The most common criteria were a family history of diabetes and maternal weight greater than 90 kg, but the presence of such indicators was not predictive of either impaired glucose tolerance or abnormal breakfast tolerance.

The results of both tests were analysed against pregnancy complications and fetal outcome. Five women had a urinary tract infection, seven had pregnancy-induced hypertension and two had polyhydramnios, but none of these mothers had either impaired glucose tolerance or abnormal breakfast tolerance by any of the previously defined criteria. There were no significant differences between those with normal and impaired glucose tolerance or normal and abnormal breakfast tolerance with regard to gestation at delivery, onset of labour or mode of delivery.

Fetal outcome in relation to the 2-hour OGTT and breakfast test results is shown in Figure 2. Neither test was of value in predicting adverse fetal outcome. The one stillbirth and two major fetal malformations (Fallot's tetralogy and tracheo-oesophageal fistula) occurred to mothers with normal glucose tolerance and breakfast tolerance.

All of the mothers of the 11 infants who required admission to the special care baby unit had a normal breakfast test and 10 had a normal OGTT.
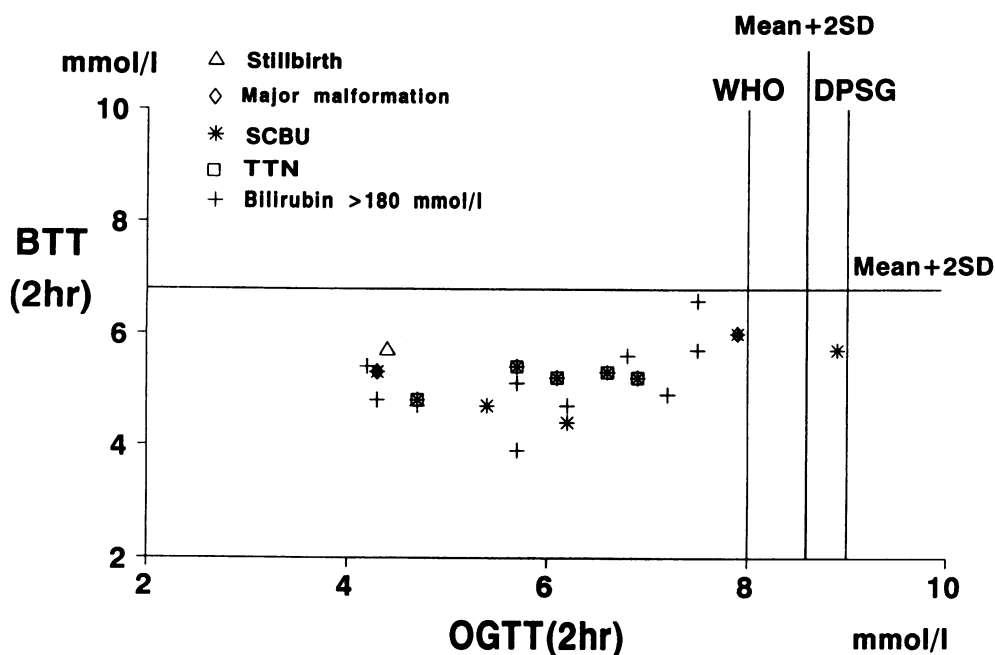

Fig 2.   Fetal outcome in relation to the 2 hour glucose concentrations during the 75 g oral glucose tolerance test (OGTT) and breakfast tolerance test (BTT). Outcomes are stillbirth, major congenital malformation, admission to special care baby unit (SCBU), transient tachypnoea of the newborn (TTN), and serum bilirubin >180 mmol/l. The WHO and DPSG criteria are as defined in Figure 1.
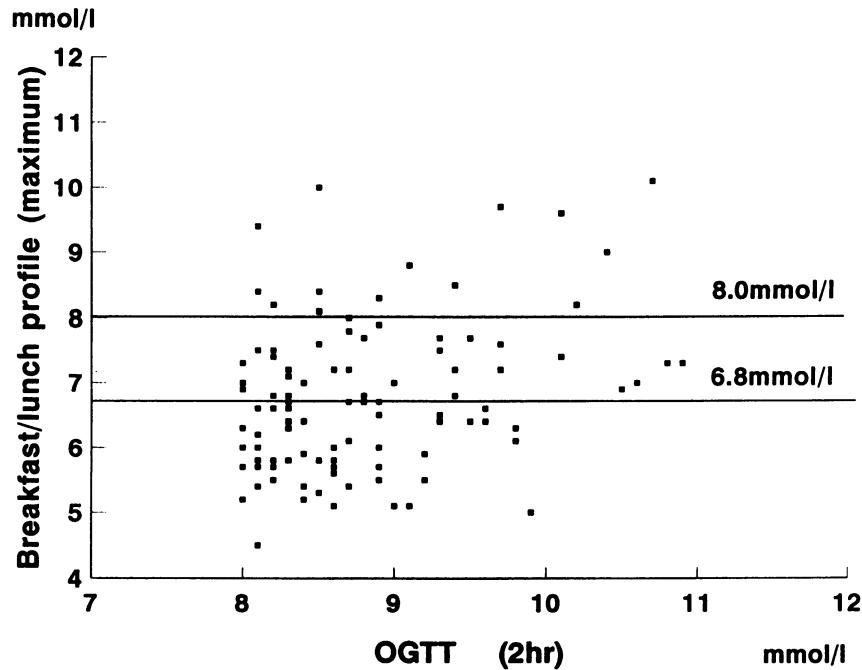
mmol/l

12

11

10

9

8.0mmol/l

8

6.8mmol/l

7

6

5

4

7   8   9   10   11   12

Breakfast/lunch profile (maximum)

OGTT   (2hr)   mmol/l

Fig 3. Comparison of the 2 hour plasma glucose concentration for the 75 g oral glucose tolerance test (OGTT) with the highest breakfast/lunch profile glucose: r=0.33. The lines at 8.0 mmol/l and 6.8 mmol/l represent the established abnormal and mean +2SD values for the breakfast tolerance test.

All five infants who had transient tachypnoea of the newborn, all 10 who had hyperbilirubinaemia, and all three who had a birthweight >4.5 kg had mothers in whom both tests were normal.

2) Impaired glucose tolerance pregnancies

The 2-hour post breakfast glucose was the highest of the four breakfast/lunch profile values in 69 (66%) of the women. As with the unselected pregnancies, there was no significant correlation between the two-hour OGTT glucose concentration and the two-hour post-breakfast value (r=0.35). There was also no significant correlation between the two hour OGTT glucose and the maximum concentration recorded during the breakfast/lunch profile (r=0.33). Comparing the two-hour OGTT glucose with the highest meal profile glucose (Figure 3), only 15 of the 104 mothers with impaired glucose tolerance had a meal profile glucose greater than 8.0 mmol/l, but 44 had a value greater than 6.8 mmol/l. These cut-off levels of 8.0 mmol/l and 6.8 mmol/l were respectively the established abnormal value and the mean +2SD glucose concentration for the breakfast tolerance test. There were no perinatal deaths in this group, and the only baby with a congenital malformation (hydronephrosis due to ureteric reflux) was born to a mother with a normal profile. Mean birthweights in those with

maximum profile values above and below 8.0 mmol/l were not significantly different, 3634 g and 3706 g respectively.

DISCUSSION

There continues to be concern about the value of the OGTT in diagnosing hyperglycaemia in pregnancy. There is much logic in the concept that hyperglycaemia in response to the normal food intake of the mother is the only relevant clinical criterion. An OGTT which gives a large unphysiological load of glucose is a stress test, and the diagnosis of impaired or abnormal glucose tolerance is thus based on conditions not experienced in day to day life. Other medical disorders in pregnancy, such as hypertension, are diagnosed by observations made in the unstressed state. The study by Nelson-Piercy and Gale[6] in the North East Thames region of London showed very great variation in the screening protocols and interpretation used in a number of maternity units in the UK. If there is to be any logical development and ultimate agreement in this field, a structured approach to the diagnosis of hyperglycaemia in pregnancy will have to be followed.[7]

Whole day profiles of blood glucose in normal pregnancy and selected mothers known to have

gestational diabetes have been undertaken and do show consistent differences.[8] The post-prandial hyperglycaemia in gestational diabetes is reflected in a mild but consistently higher basal glucose level throughout the night.

A number of workers have studied the use of more physiological challenges. Hollingsworth used an isocaloric breakfast meal (400 Calorie) and also a 2000 Calorie 24 hour diet programme.[9] This defined that pregnant women with gestational diabetes mellitus (criteria of O'Sullivan et al[10]) had a delay in the release of insulin, but there was considerable heterogeneity, particularly in relation to obesity. The Aberdeen group have simplified the concept with a standardised prepacked formula meal given as a breakfast test containing 58 g carbohydrate and 453 Calories. They found the meal test to be readily accepted by pregnant women, and the plasma glucose response to be highly reproducible within subjects.[11] In unselected pregnancies they showed that the glycaemic response to this standardised breakfast test differed from that to a 75 g OGTT and related better to fetal birthweight percentile.[12] In the clinical field, Peterson and Jovanovic-Peterson have studied the glycaemic response by self-monitored blood glucose one hour after a series of meals in pregnancy, and found that the glucose response to a mixed meal in mothers with gestational diabetes is highly correlated with percentage carbohydrate in the meal, but varies greatly between individuals and between breakfast, lunch and dinner.[13]

In the present study we have identified normal values for a standard breakfast test which is closely related to the normal food for this Belfast population. The most relevant measurement in screening for hyperglycaemia appears to be a 2 hour post breakfast value >6.8 mmol/l (mean + 2 SD). There was a poor correlation between the results of the OGTT and the breakfast test when performed in the same pregnant women, one week apart in the third trimester. The question of whether one test is more appropriate than the other can only be answered by reference to measures of outcome in a large series of patients. In this small study, neither test was predictive of maternal morbidity or poor fetal outcome.

To investigate this further, we studied breakfast and lunch profiles in selected mothers who were identified to have impaired glucose tolerance by the WHO criteria. Less than half of these would have been classified as having an abnormal meal profile using the normal range established from the breakfast test. There was again no relationship between impaired glucose tolerance or abnormal meal profile, and maternal morbidity or fetal outcome. It has long been recognised that the glucose rise after the first meal of the day is the greatest and the results of the profiles confirmed that there is no value in continuing the test into the pre and post lunch period.

Our data are relevant to Northern European caucasian populations. The much greater prevalence of hyperglycaemia in pregnancy in other ethnic groups and in other parts of the world makes it desirable that these relationships between blood glucose responses to oral glucose and normal foodstuffs be investigated in more detail, so that the most appropriate diagnostic tests can be identified to detect hyperglycaemia and prevent the associated fetal morbidity.

REFERENCES

1. Hadden D R: Screening for abnormalities of carbohydrate metabolism in pregnancy 1966-77: the Belfast experience. *Diabetes Care* 1980; **3**: 440-6.

2. Roberts R N, Moohan J M, Foo R, Harley J M G, Traub A I, Hadden D R. Fetal outcome in mothers with impaired glucose tolerance in pregnancy. *Diabet Med* 1993; **10**: 438-43.

3. WHO Expert Committee on Diabetes Mellitus. *WHO Technical Report Series* 1980; **646**: 8-12.

4. Hadden D R, Harley J M G. Potential diabetes and the fetus: a prospective study of the relation between maternal oral glucose tolerance and the foetal result. *J Ostet Gynaec Br Comm* 1967; **74**: 669-74.

5. Lind T, Phillips P R. Diabetic Pregnancy Study Group of the European Association for the Study of Diabetes. Influence of pregnancy on the 75 g OGTT. a prospective multicenter study. *Diabetes* 1991; **40** (Suppl 2): 8-13.

6. Nelson-Piercy C, Gale E A M. Do we know how to screen for gestational diabetes? current practice in one regional health authority. *Diabet Med* 1994; **11**: 493-8.

7. Hadden D R. Research clinical methodologies in diabetic pregnancy. In: Research Methodologies in Human Diabetes, Vol 2. (Mogensen C E and Straudl E, eds.) Walter de Gruyter, Berlin 1995: 147-67.

8. Maresh M J A, Gillmer M G D, Beard W, et al. The effect of diet and insulin on metabolic profiles of women with gestational diabetes mellitus. *Diabetes* 1985; **34 (Suppl 2)**: 88-93.

9. Hollingsworth D R, Ney D, Stubblefield N, Fell T. Metabolic and therapeutic assessment of gestational diabetes by two-hour and twenty-four-hour isocaloric meal tolerance tests. *Diabetes* 1985; **34 (Suppl 2)**: 81-7.

10. O'Sullivan J B, Mahan C M, Boston A B. Criteria for the oral glucose tolerance test in pregnancy. *Diabetes* 1964; **13**: 278-85.

11. Sutherland H W, Pearson D W M, Lean M E J, Campbell D M. Breakfast tolerance test in pregnancy. In: Carbohydrate metabolism in pregnancy and the newborn. (Sutherland H W and Stowers J M, eds.) Churchill Livingstone, Edinburgh 1984: 267-75.

12. Campbell D M, Sutherland H W, Turtle S. Standardised test meal in human pregnancy. In: Carbohydrate metabolism in pregnancy and the newborn. (Sutherland H W and Stowers J M, eds.) Churchill Livingstone, Edinburgh 1984: 256-66.

13. Peterson C M, Jovanovic-Peterson L. Percentage of carbohydrate and glycaemic response to breakfast, lunch and dinner in women with gestational diabetes. *Diabetes* 1991; **40 (Suppl 2)**: 172-4.