Carbohydrate metabolism in twin pregnancy

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Summary

Carbohydrate metabolism was evaluated in 26 women with a twin pregnancy and 26 women with a singleton pregnancy. The groups were similar in respect of age, parity and gestational age. Each woman had an oral glucose tolerance test. No significant differences in venous blood sugar values or insulin responses were found between singleton and twin pregnancies.

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It is well known that pregnancy is associated with alterations in carbohydrate metabolism. These changes are best reflected by blood glucose and insulin patterns. Fasting blood glucose levels become slightly lower during pregnancy, whereas plasma insulin levels after a glucose challenge are significantly elevated, most markedly so towards the end of gestation.[1] Pregnancy is therefore associated with a decreased sensitivity to insulin. The cause of this insulin insensitivity in pregnancy is unknown, but one possible explanation is the rise in the level of human placental lactogen (HPL) that accompanies gestation.[2]

Spellacy *et al.*[3] showed that HPL levels are even higher in pregnancies with two or more placentas. Subsequently, in a study of carbohydrate metabolism in twin pregnancies, Spellacy *et al.*[4] using an intravenous glucose tolerance test (GTT) showed that HPL levels were significantly higher and fasting glucose levels were significantly lower in women with twin pregnancies as compared with singleton pregnancies.

The present study was undertaken to determine: (*i*) whether carbohydrate metabolism as determined by an oral GTT was significantly altered in twin pregnancy as compared with singleton pregnancies at the same gestation; and (*ii*) the nature of the relationship between blood glucose, insulin and HPL levels in twin gestation.

Patients and methods

Informed consent was obtained from 52 Black women in the last trimester of pregnancy who were attending the antenatal clinic at King Edward VIII Hospital, Durban, and were quite sure of the date of their last menstrual period.

Twenty-six women had the diagnosis of twin pregnancy confirmed by ultrasonography after multiple pregnancy was suspected on clinical grounds. The other 26 had singleton pregnancies. Both groups were matched for age, parity, weight and gestational age. None of the women included in the study was on any form of drug therapy except for prophylactic iron and vitamin therapy. The subjects were encouraged to partake of a high carbohydate diet for at least 1 week prior to the GTT.

After the overnight fast venous blood samples were withdrawn from a peripheral vein in which a 'butterfly cannula' was inserted. The cannula was flushed and kept open with a solution of heparinized saline. Blood samples were taken for glucose, insulin and HPL estimations initially. A 50 g glucose load dissolved in 300 ml water was given to the patient and blood samples for glucose and insulin were withdrawn at half-hourly intervals for 3 hours.

Laboratory methods

The samples for glucose were taken in tubes containing sodium fluoride and potassium oxalate while the specimens for insulin and HPL were taken in tubes containing no preservative. Plasma glucose was measured by the ferricyanide method on the AutoAnalyzer.[5] HPL was assayed in duplicate by radio-immunoassay techniques (Radiochemical Centre, Amersham, UK). Serum insulin levels were measured in duplicate by a radioimmunoassay in which the antibody was coupled to a solid phase (Pharmacia, Uppsala, Sweden). A control was incorporated in each assay undertaken.

Statistical analysis

The areas under the insulin and glucose curves were computed according to the method of Chiles and Tzagournis.[6]

The glucose results were analysed with Student's *t* test; the insulin data, following a positively skewed distribution, were analysed with the Mann-Whitney U test.

Results

The characteristics of the two groups are shown in Table I.

Plasma HPL levels were significantly higher in women with twin pregnancies than in women with singleton pregnancies.

Plasma glucose response. Analysis of the blood glucose results is shown in Table II and Fig. 1. There was no significant difference between the two groups throughout the period of testing.

Plasma insulin response. Analysis of the plasma insulin responses is shown in Table III and Fig. 2. Although at most points the values tended to be lower for the twin pregnancy group, these differences did not attain significance. Furthermore, while the area under the insulin curve in the twin group (5 790 μU/min) was lower than in the singleton pregnancies (7 080 μU/min) this did not attain significance at the 5% level ($0,1 > P > 0,05$).

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TABLE I. CHARACTERISTICS OF THE TWO GROUPS IN THE STUDY

	Singleton	Twin	Significance
Age (yrs)*	26,3 ± 5,9	26,2 ± 5,5	$P > 0,20$
Parity†	2 (0 - 7)	1,5 (0 - 7)	$P > 0,20$
Weight (kg)*	71,8 ± 11,1	74,9 ± 18,6	$P > 0,20$
Gestational age (wks)*	33,6 ± 3,1	34,1 ± 2,9	$P > 0,20$
HPL (μg/ml)*	5,8 ± 1,4	8,5 ± 1,6	$P > 0,001$

*Results expressed as mean ± SD. Groups compared using Student's *t* test.
†Result expressed as median (minimum - maximum). Groups compared using the Mann-Whitney U test.

TABLE II. ANALYSIS OF THE BLOOD GLUCOSE LEVELS (mmol/l) DURING AN ORAL GTT*

Time	Singleton	Twin	Significance
Fasting	4,20 ± 0,51	3,96 ± 0,56	$0,10 > P > 0,05$
½ h	6,35 ± 1,17	6,00 ± 1,07	$P > 0,20$
1 h	6,72 ± 1,22	6,47 ± 1,02	$P > 0,20$
1½ h	6,06 ± 1,27	6,00 ± 1,07	$P > 0,20$
2 h	5,33 ± 1,27	5,55 ± 1,02	$P > 0,20$
2½ h	4,52 ± 1,07	4,88 ± 1,10	$P > 0,20$
3 h	3,93 ± 1,12	4,06 ± 1,02	$P > 0,20$
Area under glucose curve (mmol/min)	993,52±135,38	985,85±133,47	$P > 0,20$

*Results expressed as mean ± SD. Groups compared using Student's *t* test.

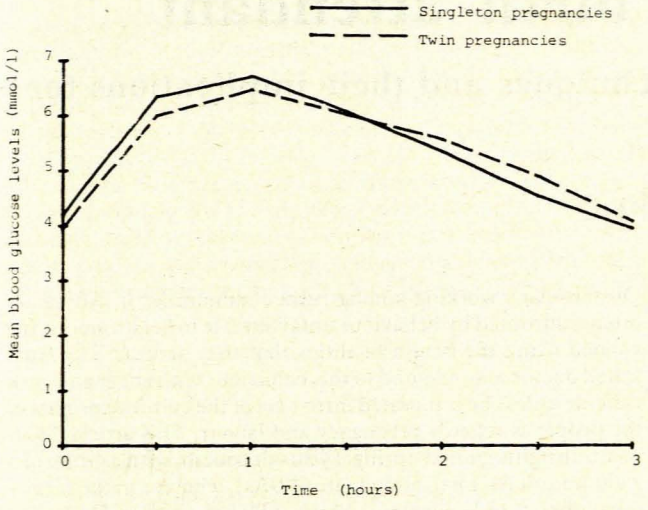

Fig. 1. Blood glucose levels during an oral GTT.

Correlations between HPL and glucose and insulin areas. There was no significant correlation between the HPL levels and the areas under the insulin curve ($r = -0,33$; $P > 0,05$) and between HPL and glucose curves ($r = 0,15$; $P > 0,05$).

Discussion

A brief survey of the literature on carbohydrate metabolism in multiple gestation shows very little data on this subject. MacGillivray *et al.*[7] point out that chemical gestational diabetes is more common in women with twin pregnancy and recommend that all women with multiple gestation have a GTT in the third trimester of pregnancy. However, at King Edward VIII Hospital,

TABLE III. ANALYSIS OF THE PLASMA INSULIN (μU/ml) DURING AN ORAL GTT*

Time	Singleton	Twin	Significance
Fasting	14,0 (8,7 - 36,0)	12,6 (5,0 - 60,0)	$P > 0,20$
½ h	48,0 (12,0 - 145,0)	43,0 (6,5 - 160,0)	$P > 0,20$
1 h	48,5 (24,0 - 110,0)	39,5 (8,7 - 135,0)	$P > 0,05$
1½ h	37,5 (15,0 - 132,0)	34,5 (12,0 - 100,0)	$P > 0,20$
2 h	30,0 (11,0 - 164,0)	35,0 (8,0 - 65,0)	$P > 0,20$
2½ h	21,5 (10,8 - 116,0)	20,0 (7,0 - 50,0)	$P > 0,20$
3 h	13,5 (7,4 - 54,0)	14,0 (1,5 - 33,0)	$P > 0,20$
Area under insulin curve (μU/min)	7 080 (4 380 - 19 560)	5 790 (1 810 - 15 315)	$0,10 > P > 0,05$

*Results expressed as median (minimum - maximum). Groups compared using Mann-Whitney U test.

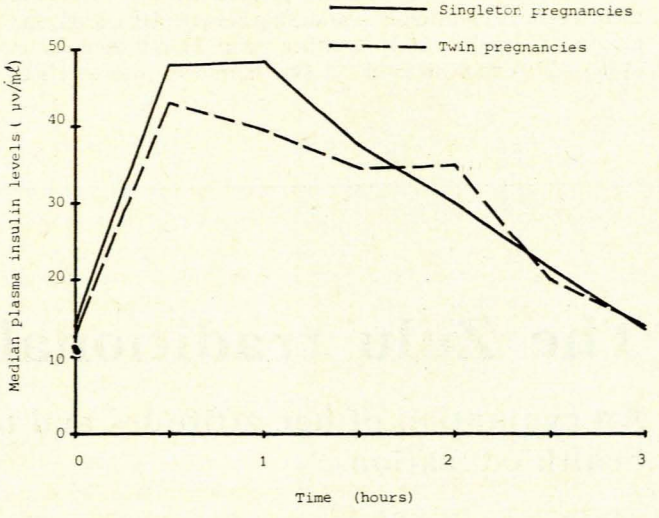

Fig. 2. Plasma insulin levels during an oral GTT.

where the incidence of multiple pregnancy is very high (1 out of 26 pregnancies) the clinical impression is that the frequency of carbohydrate intolerance is not increased in multiple pregnancy.

Spellacy *et al.*[4] also showed that the woman carrying twins is not at higher risk of clinical hyperglycaemia. They performed an intravenous GTT using a 25 g glucose load on 24 women with twin gestation and found no difference in glucose and insulin profiles when compared with a group of 24 women with singleton pregnancies matched for age, parity, weight and gestational age. One of the criticisms of their study is the use of the intravenous GTT. Arguments for its use are that it gives values more influenced by glucose disposal than the oral GTT, both variations in rate of absorption and the problem of nausea from ingestion of glucose being avoided. However, most extensive studies for detecting gestational diabetes have used the oral GTT, and it would seem that its use has become firmly entrenched. More importantly, the oral GTT is more physiological since absorption of glucose is a necessary stimulus for the entero-insular axis which is part of the total metabolic cycle being tested.

The present study was therefore undertaken to determine if there was an alteration in carbohydrate metabolism in twin pregnancy using the 50 g oral GTT. No significant differences in venous blood sugar or insulin profiles were found between singleton and twin gestations, which supports the clinical impression that the woman carrying twins is not usually at high

risk of clinical hyperglycaemia. There was a tendency however for the insulin levels to be lower in multiple than in singleton pregnancies. These results are very similar to those of Spellacy *et al.*[4] Why these changes occur is difficult to define; the altered hormonal milieu of pregnancy is usually held to be responsible and this is probably so. Certainly the changes revert to normal.[8] One of the many explanations for the high levels of insulin in pregnancy is the rise in HPL levels that accompanies gestation. HPL has been described as having a 'diabetogenic' effect.

Beck and Daughaday[9] infused non-pregnant women with HPL and demonstrated an impairment in glucose tolerance together with an increased insulin response. However, the HPL had to be given by infusion for a minimum of 12 hours and some of the subjects had an unusual response to an oral glucose load prior to the investigation. Despite reservations about this study, HPL is regarded by many authors as a major factor causing insulin resistance in pregnancy. HPL levels are even higher in multiple gestations; the belief therefore arises that twin gestations have a high incidence of diabetes. The present study does confirm that HPL levels are much higher in women carrying twins than in those with singleton pregnancies ($P < 0{,}001$) but there was no demonstrable relationship between HPL levels and glucose and insulin profiles in either group. Thus it would be an over-simplification to hold any one hormone, such as HPL, responsible for the carbohydrate intolerance in pregnancy; the whole complex of altered maternal adaptations, including changes in protein and fat metabolism, probably combine to influence changes in carbohydrate metabolism.

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