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Glucose Tolerance in Twin Pregnancy

Doris M. Campbell, Ian MacGillivray

Department of Obstetrics and Gynaecology, University of Aberdeen, UK

The hypothesis of a slower rate of glucose disappearance after intravenous glucose injection has been tested and proved in a sample of 54 women with twin pregnancies. Different standards for glucose tolerance being therefore required for these women, care should be taken before labelling them as diabetic.

Key words: Glucose tolerance, Twin pregnancy, Diabetes

Many changes are known to occur in carbohydrate metabolism in normal singleton pregnancies. For example, fasting plasma glucose is lower [10], there is a decrease in tolerance to both oral and intravenous glucose loads [10], and the insulin response increases progressively as pregnancy advances [6].

These latter factors are indicative of insulin antagonism by specific pregnancy factors and decreased sensitivity of the peripheral tissues to insulin. The pregnancy factors that have been implicated are the placental hormones, human placental lactogen, oestrogen, and progesterone. As all of these are known to be increased in twin pregnancy [7, 12, 16], it is possible that there would be a greater insulin antagonism in multiple pregnancy with a further alteration in response to glucose loading. It was therefore postulated that there would be a slower rate of disappearance of glucose from the circulation, and this study was devised to test this hypothesis.

METHODS

Fifty-four women with twin pregnancies were selected for study, and the incidence of preeclampsia in the cases is shown in Table 1. It was felt necessary to define the groups according to the development of preeclampsia, as it has previously been shown [13] that in singleton pregnancies with proteinuric preeclampsia there is a greater tendency to an abnormal glucose tolerance test. However, this is not so if the test is performed prior to the onset of proteinuric preeclampsia [3]. The test was repeated in 26 of the women, the first test performed before, and the second test after 30 weeks, at an interval of approximately four weeks.

A rapid intravenous glucose tolerance test was used. Two fasting samples were taken, followed by an intravenous injection of 25 g of glucose. Plasma glucose was then estimated at 4, 10, 20, 30, 40, 50, and 60 minutes after injection. The results can here be expressed by the increment index [4] or K value [1].

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RESULTS

There was a significant decrease in the mean fasting plasma glucose levels for all patients between 24 to 27 weeks' and 33 to 36 weeks' gestation, a difference of 0.4 mmole/liter or 7 mg% ($t = 3.27$, $P < 0.01$: Table *2a*). In the group who remained normotensive (Table *2b*) there was a similar fall of 0.3 mmole/liter.

There was a significant difference in the fasting plasma glucose between the first and second tests of the 26 women who were tested twice (Table 3).

There was a small insignificant decrease in the increment index as gestation advanced when all cases were considered, and also when only the normotensive group was analysed (Tables 4 *a, b*). Similarly, when the results were expressed as K values (Tables 4 *c, d*). This was also found in the 26 women who were tested twice (Table 5). The distribution pattern of increment index in twin and singleton pregnancies (Figure) differ, in that there is a tendency for lower values of increment index to be found in the twin pregnancies. The singleton values were obtained from 500 consecutive glucose tolerance tests carried out recently in pregnancy in Aberdeen on the basis of indicators of potential diabetes [15].

In 9.3% of women with twin pregnancies there was a family history of diabetes in first-degree relatives, compared with 7.3% in singletons (Table 6) [15]. There was a greater tendency to obesity in the women with twin pregnancies according to Kemsley [11] scales for weight for height centiles above both the 75th and 85th. None had glycosuria.

DISCUSSION

The values of fasting plasma glucose found in the twin pregnancies are very similar to those quoted for singleton pregnancies. The controlling factors of fasting plasma glucose in pregnancy are not well defined, but it has been suggested that the fasting plasma glucose

TABLE 1. Details of Twin Pregnancies Studied

	Primigravidae (n = 14)	Multigravidas (n = 40)	Total (n = 54)	
Normotensives	6	26	32	59.3%
Mild preeclampsia	5	10	15	27.8%
Proteinuric preeclampsia	3	4	7	13.0%

TABLE 2. Twin Pregnancy Fasting Plasma Glucose (mmoles/litre) by Gestation

Weeks of gestation	Mean	SD	N
a) All patients			
24–27	4.16	0.37	16
28–32	3.97	0.39	28
33–36	3.77	0.38	30
> 37	3.96	0.29	6
b) Normotensive patients only			
24–27	4.07	0.34	9
28–32	3.91	0.41	16
33–36	3.78	0.33	19
> 37	3.74	0.18	3

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TABLE 3. Twin Pregnancy Paired Fasting Plasma Glucose (mmoles/litre)

	Mean (n = 26)	SD	
First test	4.04	0.43	Paired t = 2.50 P < 0.02
Second test	3.81	0.38	

TABLE 4. Twin Pregnancy: Increment Index (a and b) and K Values (c and d) by Gestation

Weeks of gestation	Mean	SD	N
a) All patients			
24–27	4.14	0.79	16
28–32	4.38	1.48	28
33–36	3.83	0.78	30
> 37	4.07	0.55	6
b) Normotensive patients only			
24–27	4.16	0.92	9
28–32	4.51	1.76	16
33–36	4.01	0.84	19
> 37	3.86	0.27	3
c) All patients			
24–27	1.97	0.35	16
28–32	1.99	0.45	28
33–36	1.87	0.29	30
> 37	1.83	0.3	6
d) Normotensive patients only			
24–27	1.97	0.38	9
28–32	2.08	0.50	16
33–36	1.92	0.29	19
> 37	1.80	0.25	3

TABLE 5. Twin Pregnancy: Paired Increment Index

	Mean (n = 16)	SD	
First test	4.25	1.42	Paired t = 1.65
Second test	3.82	0.66	

TABLE 6. Twin Pregnancy: Indicators of Potential Diabetes

	N	%
Family history of diabetes: First degree relative	5	9.3
Obesity: > 75th centile weight for height	19	35.2
> 85th centile weight for height	15	27.8
Glycosuria: either fasting or random	0	0.0
Previous heavy-for-dates baby	2	3.7

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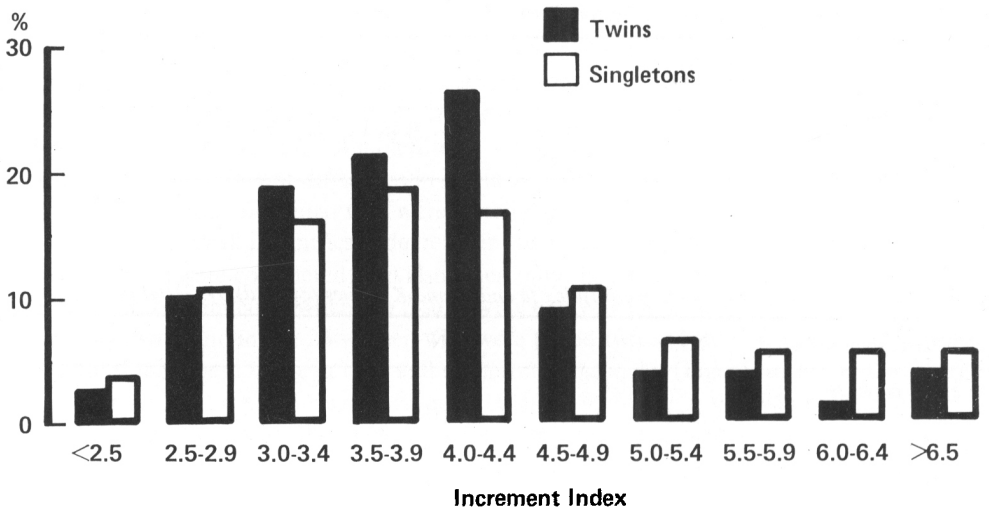

Figure. Distribution of increment index in singleton and twin pregnancies in Aberdeen.

both in diabetic and normal pregnancy is related to birth weight [14]. As the combined birth weight in twin pregnancies is much greater than in singletons, this suggestion cannot apply to twin pregnancies.

It is known that in singleton pregnancies the increment index and K values diminish as pregnancy progresses from the first, to the second, and to the third trimesters [5]. In the twin pregnancies, however, the fall in increment index and K value was less and did not reach statistical significance. Similarly, the distribution pattern of increment index is different, in that the twin pregnancies can give lower values of increment index than the singleton pregnancies.

The indicators of potential diabetes were not any greater in the twin pregnancies than in the singletons. This finding is contrary to that of Gedda et al [8], who found that there were more women with a twin pregnancy with a family history of diabetes. The greater tendency to obesity in the women with twin pregnancies was not unexpected, as it has already been shown that obese women are more likely to have a twin pregnancy [2]. It is interesting that none of the women with twin pregnancy had either fasting or random glycosuria, because it has been shown that there is an increased glomerular filtration rate in twin pregnancies [9]. It is therefore concluded that there must be increased tubular absorption with perhaps an alteration in the renal threshold for glucose in women with twin pregnancies. The number of women with a previous heavy-for-dates baby was as expected.

It is concluded that the hypothesis suggested at the beginning of the study, that there is a slower rate of glucose disappearance after an intravenous glucose injection in women with twin pregnancies compared to singleton pregnancies, has been proved. It is postulated that this is due to the increase in the placental hormones. Different standards are therefore required for glucose tolerance in women with twin pregnancies, and care should be taken before labelling such patients as diabetic. Women with twin pregnancies do not have more indicators of potential diabetes than those with singleton pregnancies.

REFERENCES

1. Amatuzio DS, Stutzman FL, Vanderbilt MJ, Nesbitt S (1953): Interpretation of the rapid intravenous glucose tolerance test in normal individuals and in mild diabetes mellitus. J Clin Invest 32:428–435.
2. Campbell DM, Campbell AJ, MacGillivray I (1974): Maternal characteristics of women having twin pregnancies. J Biosoc Sci 6:463–470.
3. Campbell DM, MacGillivray I (1976): Glucose tolerance before the onset of preeclampsia. Eur J Obstet Gynecol Reprod Biol 6/5:235–237.
4. Duncan LJP (1956): The intravenous glucose tolerance test. Q J Exp Physiol 41:85–96.
5. Fisher PM, Hamilton PM, Sutherland HW, Stowers JM (1974): The effect of pregnancy on intravenous glucose tolerance. J Obstet Gynaecol Br Commonw 81:285–290.
6. Fisher PM (1976): Glucose induced insulin response studies in relation to human pregnancy and diabetes mellitus. MD Thesis, University of Aberdeen, Chpt 1.
7. Garoff L, Seppälä M, (1973): Alphafetoprotein and human placental lactogen levels in maternal serum in multiple pregnancies. J Obstet Gynaecol Br Commonw 80:695–700.
8. Gedda L, Segni G, Andreani D, Casa D, DiMarco G (1969): Diabete e gemellogenesi. Acta Genet Med Gemellol 14:87–90.
9. Gomez E, Swapp GH (1972): Personal communication.
10. Hytten EE, Lind T (1973): Indices of carbohydrate metabolism. Diagnostic indices in pregnancy. Documenta Geigy p 55.
11. Kemsley WFF, Billewicz WZ, Thomson AM (1962): A new weight for height standard based on British anthropometric data. Br J Prev Soc Med 16:189–195.
12. Masson GM (1973): Plasma oestriol in normal and preeclamptic multiple pregnancies. Obstet Gynaecol 42:568–573.
13. Singh MM (1976): Carbohydrate metabolism in preeclampsia. Br J Obstet Gynaecol 83:124–131.
14. Sutherland HW (1974): Paper to Scientific Meeting of Royal College of Obstetricians and Gynaecologists, Aberdeen, September.
15. Sutherland HW, Stowers JM (1975): The detection of chemical diabetes during pregnancy using the intravenous glucose tolerance test. In "Carbohydrate Metabolism in Pregnancy and the New Born." London: Churchill Livingstone, p 163.
16. Van der Molen HJ (1963): Determination of plasma progesterone during pregnancy. Clin Chim Acta 8:943–953.