ABSTRACT

Carbohydrate metabolism in normal pregnancy

and preeclampsia

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Carbohydrate metabolism is altered in normal pregnancy as indicated by the impairment of glucose tolerance and this is exacerbated by preeclampsia. Two cross-sectional studies (Studies I and II) and a longitudinal study (Study III) were designed to observe features of altered carbohydrate metabolism during and preceding the onset of preeclampsia. Studies I and II had preeclamptic (PE) primigravidae subjects and normal pregnant (NP) controls, Study III followed normal primigravidae subjects through pregnancy at 12(T1), 24(T2) and 36(T3) weeks gestation and at 12 (T4) weeks post-partum. Insulin receptor binding to white blood cells (WBC) and red blood cells (RBC), plasma insulin and glucose in the fasted state and after an oral (OGTT) or intravenous (IVGTT) glucose load were observed in Studies I and III. Plasma C-peptide in the fasted state and after an

IVGTT was observed in Studies II and III. Two way analysis of variance (ANOVA) was used to examine the data in all studies. The percentage of insulin specifically bound (%SB) to its receptors on WBC in the PE was significantly lower compared to the NP, ($p<0.05$). In Study III, at T1 the (%SB) to WBC in those women who became preeclamptic (BPE) was significantly higher compared to those who had a normal pregnancy (BNP), ($p<0.01$). The (%SB) to RBC for pooled data of the BPE was significantly lower compared to the pooled data of the BNP, ($p<0.005$).

Plasma insulin in the fasted state was significantly higher in the PE compared to the NP, ($p<0.05$) in both Studies I and II. At T2 and T3 the plasma insulin in the fasted state was significantly higher in the BPE compared to the BNP, ($p<0.05$) and ($p<0.0001$) respectively. On calculating the predictive use of the basal hyperinsulinaemia at T2, there was a 80% sensitivity and 57% specificity and at T3 there was a 100% sensitivity and a 43% specificity for predicting preeclampsia. Plasma glucose in the fasted state in the PE was similar to that in the NP in Studies I and II, also at all study periods in Study III in the two groups. Plasma C-peptide in the fasted state in the PE was similar to that in

the NP in Study II and also between the BPE and the BNP in Study III.

The rate of glucose disappearance K_G in pooled data of the BPE was significantly lower compared to the BNP, ($p<0.05$).

In conclusion, basal hyperinsulinaemia was observed in preeclampsia and also occurring, from as early as the second trimester of pregnancy, in the women destined to become preeclamptic. This finding was not the result of increased insulin secretion since the plasma C-peptide levels in the fasted state were similar in the preeclamptics or those destined to develop preeclampsia compared to the normal pregnant women. As a marker or predictor for preeclampsia, the basal hyperinsulinaemia although displaying a high sensitivity had a low specificity which devalued its use as a predictor. This hyperinsulinaemia was observed under normoglycaemic conditions, establishing preeclampsia as an insulin resistant state. The lowered binding of insulin to its receptors on white blood cells, in preeclampsia, may be another indicator of peripheral insulin resistance. Impaired glucose tolerance as observed in the decreased rate of glucose disappearance (K_G) in the preeclamptics was confirmed as a feature of preeclampsia.