Prediction of intra-uterine growth retardation using maternal glucose tolerance and anthropometric data

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Summary

Maternal anthropometric data and the intravenous glucose tolerance test (IVGTT) were investigated as predictors of idiopathic intra-uterine growth retardation (IUGR). Eighty-three eligible subjects without known risk factors for IUGR were enrolled at 30.5 ± 3.8 weeks' gestation and followed up until delivery at 39.3 ± 1.9 weeks, at which stage the infants were assessed.

There were no differences between the IVGTT profiles of mothers of infants which were appropriate for gestational age and those which were small for gestational age (SGA), irrespective of lenient or strict definitions of SGA. Third-trimester weight gain (grams per week) correlated well with both duration of pregnancy and birth weight (P < 0.01). Correlations were also found between maternal weight and birth weight, between maternal height/weight ratio and birth weight, and between birth weight and maternal subscapular skinfold thickness.

Subjects and methods

The subjects were pregnant black women attending the Diepkloof antenatal clinic in Soweto. Subjects were enrolled early in the third trimester because this is when there is a rapid increase in the rate of nutrient transfer to the fetus and any effects of malnutrition are easier to detect. Enrolment was between 28 and 32 weeks' gestation according to the period of amenorrhea and clinical estimation by a midwife. Only women with no known risk factors related to the development of IUGR were included. These factors included chronic maternal disease, previous fetal loss, hypertension, smoking, drug and alcohol abuse and other conventional risk factors. Subjects were enrolled between June and August 1983 and the last infant was born in January 1984.

All eligible subjects were selected from clinic records the day preceding their next visit. They were visited at home by a nursing sister involved in the study. The study was explained to the subjects, instructions were given regarding the IVGTT (including overnight fasting), and informed consent was obtained.

At the clinic a full antenatal history was taken by the same worker who had visited the subject's home. Physical examination was performed by a midwife. Routine antenatal investigations, i.e. measurement of the haemoglobin value, serological testing for syphilis and blood grouping, were performed at the laboratories of the South African Institute for Medical Research.

Anthropometric measurements were performed by the principal investigator. Weight was measured using a Detecto beam balance scale (accurate to within 100 g) and height using a standing board with adjustable headpiece (accurate to within 0.5 cm). Skinfold thickness was measured with a Lange skinfold caliper. The average of three readings was taken from the triceps and subscapular regions bilaterally. Mid-upper arm circumference was measured bilaterally using a non-stretch tape measure. The fasting IVGTT was performed between 08:00 and 10:00. A heparin-lock intravenous cannula was inserted to avoid repeated venepuncture. Glucose (25 g) in a 50% solution was injected into an antecubital vein. Blood samples were obtained before and every 10 minutes after the glucose was injected for a period of 1 hour. The blood glucose level was measured by the glucose oxidase method. Glucose estimations were done in the Paediatric Mineral Metabolism Research Unit at Baragwanath Hospital.

Utilising a system of file markers and patient information cards, close contact was kept with the patients. Routine antenatal examination was done by midwives, and weights were recorded in order to calculate weight gain per week. Anthropometric measurements were repeated once before delivery. All anthropometric measurements were performed by the same investigator.

Subjects delivered at Diepklouf clinic or Baragwanath Hospital, and mother and infant were assessed by the principal investigator after delivery. The following neonatal data were obtained: weight, length, head circumference and gestational age (Dubowitz assessment). Maternal data included weight, height, skinfold thickness and mid-upper arm circumference.
The babies were classified as either appropriate for gestational age (AGA) or SGA. For the purposes of this study, SGA infants were categorised using both lenient and strict criteria. The lenient method involved plotting gestational age versus birth weight on a standard chart in use in the UK. This chart is upward-shifting in comparison with some other charts (e.g., the Lubchenko chart) and consequently yields relatively large numbers of infants falling below the 10th percentile. The strict method involved selection of those infants whose birth weights were > 2 standard deviations (SD) below the mean for the study population.

**Results**

The IVGTT was performed on 96 eligible pregnant women. A frankly diabetic profile was observed in 5 cases—none of these patients had previously been identified as suffering from diabetes, and they were excluded from further analysis. Also excluded were mothers who were lost to follow-up (5 subjects) or suffered fetal loss (1). Two babies which were large for gestational age and their mothers were also excluded from analysis.

Maternal and neonatal data were complete for the remaining 83 subjects. Mean maternal age on entry to the study (± SD) was 30.5 ± 4.1 years. The mean duration of pregnancy on entry was 30.5 ± 3.8 weeks, and at delivery was 39.3 ± 1.9 weeks. Of the infants 25 were classified as SGA according to the lenient criteria described above (mean birth weight 2558 ± 286 g); however, only 9 of them were identified as SGA when the strict criteria were applied (mean weight 2401 g, range 1820 - 2700 g). All of the latter group also fell below the 10th percentile when plotted on the Lubchenko charts. Owing to the small number of subjects delivering before 37 and after 41 weeks, only data for mothers and infants with periods of gestation between these values were included when defining our strict AGA and SGA subgroups, i.e. it was only between 37 and 41 weeks between were adequate to define a population of SGA babies > 2 SD below the mean. The mean birth weights of the AGA groups were 3189 ± 369 g for the lenient group and 3078 g (2520 - 4020 g) for the strict group.

The Fig. 1 shows the glucose profiles for mothers who subsequently delivered AGA or SGA infants, according to the lenient or strict criteria used. Analysis of variance revealed that the profiles were statistically similar for all four groups.

Although the profiles were similar, during the initial analysis it was noted that the differences in the 20- and 30-minute glucose values between strict SGA and AGA groups just reached statistical significance (P = 0.045 and 0.039 respectively). Scrutiny of the data revealed that the differences were due to glucose values which were > 3 SD above the mean in a subpopulation of 6 mothers in the AGA group. Fig. 1 shows the supranormal mean profile for this subgroup. The mothers in this group were not diabetic according to glucose values or according to k values (which describe the glucose disappearance rate). In fact, the k values were almost identical for all five groups shown on Fig. 1 (1.77 - 1.98) and all were well within the normal range (0.94 - 3.31).

Maternal anthropometric data are given in Table I, which shows the mean values of various measurements. Although none of the differences between AGA and SGA groups are significant (irrespective of lenient or strict criteria for SGA), it should be noted that mothers of SGA infants had a tendency towards lower weight, height/weight ratio, weight gain during pregnancy, arm circumference and skinfold thickness. Analysis was by the t-test when data were normally distributed and by the Mann-Whitney U-test when data were skewed or numbers were too small to apply the t-test.

Finally, the various maternal characteristics shown in Table I were considered as independent variables and each was examined in terms of its ability to predict duration of pregnancy and/or birth weight. For the total group, maternal weight gain per week was a good predictor of pregnancy duration (r = 0.52; P < 0.01) and of birth weight (r = 0.31; P < 0.01). Maternal entry weight was a reasonable predictor of birth weight (r = 0.29; P < 0.02). Weaker correlations were between birth weight and maternal height/weight ratios, and birth weight and entry subscapular skinfold thickness.

**Discussion**

It is generally accepted that Third-World population groups in the RSA have LBW rates which are two to three times higher than the 6 - 8% rate in our privileged communities. It is also recognised that most LBW neonates in underprivileged societies are growth-retarded/small-for-dates infants, while in the privileged groups the majority of LBW neonates are appropriately grown premature infants. Using liberal criteria for growth retardation, the present study identified 27.7% of study infants as SGA. This high rate almost certainly demonstrates the inappropriate use of a First-World growth chart in the assessment of a Third-World or transitional community.

Strict criteria for the diagnosis of growth retardation yielded an SGA rate of 12.5%. This figure is also high, particularly when one considers that the study population included only apparently healthy women experiencing normal pregnancies.

Previous data have suggested that the GTT may be of value in predicting IUGR. The use of the test to predict 'idiopathic' growth retardation implies altered carbohydrate metabolism, perhaps on the basis of deficient energy intake. The ability to identify the mother and fetus at risk by means of a relatively simple test would represent an attractive option for the obstetrician and the neonatologist, particularly if part of the solution to the problem is simply nutritional supplementation during pregnancy. In the present study we were unable to demonstrate any abnormality of the IVGTT in mothers who subsequently delivered SGA infants, irrespective of whether liberal or strict criteria for growth retardation were used. However, it should be noted that initial analysis of the glucose profiles in mothers of SGA and AGA infants suggested that the curves were different between 20 and 30 minutes.
Further analysis revealed that the apparent differences were not due to a flatter curve or different k values in the SGA group, but were due to extremely high glucose levels in a subpopulation of AGA mothers. It is not clear whether the same phenomenon has been observed in other studies.

While IVGTT evidence for deficient energy intake was not apparent in mothers of SGA infants, Table I shows that there was a tendency for these mothers to weigh less and have lower height/weight ratios, less weight gain during pregnancy, smaller arm circumference values and lower skinfold measurements. This trend was present whether strict or liberal SGA criteria were used. It is likely that larger patient numbers would have shown the differences to be statistically significant and have confirmed that mothers who subsequently delivered SGA infants were certainly leaner, if not actually malnourished.

In terms of prediction of the outcome of pregnancy, this study confirms the value of monitoring maternal weight gain during pregnancy.33,34 Our data showed a significant correlation between weight gain (expressed as grams per week) and both birth weight and duration of pregnancy.

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REFERENCES

Prostaglandin E₂ vaginal gel — a new formulation for the induction of labour

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Summary

In order to evaluate the efficacy of prostaglandin E₂ vaginal gel in the induction of labour it was compared with a routine method of induction by oxytocin titration. A total of 50 patients were randomly allocated to two groups; 25 patients received intravaginal prostaglandin E₂ gel and 25 oxytocin infusion. In both groups amniotomy was performed once the patient was in the active phase of labour. Successful outcome was regarded as established labour within 12 hours of commencement of the trial. In the oxytocin group this was achieved in 88% of multiparas and 75% of primigravidae. In the prostaglandin group the outcome was successful in 82% of multiparas and 75% of primigravidae.


It is well established that the uterine cervix undergoes marked biophysical and biochemical changes towards late pregnancy which result in increased cervical compliance. These changes, so-called 'ripening of the cervix', greatly influence the outcome of induced labour. Ripening of the cervix, however, shows great individual variation and at least 5 – 10% of women will reach term with an 'unripe' uterine cervix. Induction of labour under such circumstances is hazardous,1 and many authors therefore recommend the use of prostaglandins to ripen the cervix before formal induction. Several studies have shown that prostaglandins, applied either extra-amniotically or intravaginally, may not only improve the state of the cervix but also induce labour. In these studies the vehicle used to release prostaglandins has varied from Tylosole gel as the slow-release medium to wax-based pessaries and vaginal tablets. There has, however, been concern regarding the homogeneity and chemical stability of the gel and the irregular absorption of the tablets and wax-based pessaries. In contrast, the vehicle Cabosil gel has the advantage of homogeneity and chemical stability. The latter can be maintained at 4°C, thus avoiding the need to prepare a gel and prostaglandin mixture before induction. We compared the efficacy of prostaglandin E₂ in Cabosil gel against a standard method of oxytocin titration for the induction of labour.

Patients and methods

Informed consent was obtained from 50 patients requiring induction of labour at term. Patients with a history of antepartum haemorrhage, those who had previously undergone uterine surgery, and those with a history of bronchospasm or glaucoma or who were known to be hypersensitive to prostaglandins were excluded from the study, as were patients who had undergone previous attempts at induction in the index pregnancy. All patients included in the study were randomly allocated to two groups. Twenty-five patients received intravaginal prostaglandin E₂ in Cabosil gel (group A) for induction of labour. The gel consisted of a mixture of triacetin and colloidal silicone dioxide supplied by Upjohn (Europe), was supplied in specially made syringes for direct insertion, containing either 1 or 2 mg prostaglandin E₂ and was stored at 4°C. At the onset of induction, the 'favourability' of the cervix was assessed by the Bishop score and 1 – 2 mg prostaglandin E₂ gel was inserted around the cervix. If the patient was not in the active phase of labour as judged by a change in cervical dilatation of 3 cm or more 6 hours after the initial dose, then either 1 or 2 mg more gel was inserted; 1 mg was used if there was a change in the Bishop score and 2 mg if there was no change.

The other 25 patients (group B) were assigned to induction of labour by oxytocin titration, starting with 2 mIU/min and doubling the dose every 30 minutes until optimal uterine contractions were obtained. The Bishop score was assessed before induction.

Management

The blood pressure and pulse rate were recorded at half-hourly intervals and the fetal heart rate was recorded continuously.