Intrauterine Fetal Growth Retardation: A Comparison of Human Placental Lactogen Urinary Oestriol and Biparietal Diameter Measurements

H. P. ROBINSON, W. R. CHATFIELD*, R. W. LOGAN AND FRANCES HALL
Departments of Obstetrics and Biochemistry, Queen Mother's Hospital, Glasgow, G3 8SJ

Forty-two 'at risk' pregnancies were serially monitored by sonar biparietal cephalometry, 24 h urinary oestriol assays and determination of serum human placental lactogen. The results were assessed by a scoring system, and it was found that a combination of sonar cephalometry and 24 h urinary oestriol assays gave the most reliable prediction of intrauterine growth retardation.

In a previous communication, Robinson et al. (1973) compared the value of five methods of fetal monitoring in respect of their ability to differentiate between normal and growth-retarded pregnancies in a small series of patients. These tests included sonar biparietal cephalometry, 24 h urinary oestriol assays and determination of serum oxytocinase, total alkaline phosphatase and heat-stable alkaline phosphatase activities. In order to evaluate the results, a preliminary scoring system was devised where points were allotted to the overall level and to the trend of the results. Using this system it was found that a combination of sonar cephalometry and urinary oestriol assays gave the most reliable prediction of intrauterine fetal growth retardation. No individual test satisfactorily separated the normal from the abnormal pregnancies and, in particular, the enzyme tests were found to be of little clinical value.

During the course of the investigation, reports appeared stressing the apparent value of human placental lactogen (HPL) as a test of placental function (Keller et al., 1971; Letchworth and Chard, 1972). It was, therefore, decided to measure the HPL concentration in the sera already collected and to apply to the results a scoring system similar to that previously described, and thereby to compare the resulting scores with those obtained using biparietal cephalometry and urinary oestriol assays.

MATERIAL AND METHOD

Of the 45 patients in the original series, insufficient HPL results were available from three of the 34 normal pregnancies to allow their inclusion in the scoring system, although the individual values in the three cases were used when compiling the HPL range in normal pregnancies. It was possible, however, to include all 11 cases involving intrauterine growth retardation. An average of 4.3 weekly estimations were performed on each patient.

The methods employed in measuring the biparietal diameters and urinary oestriol levels, the scoring system as applied to these parameters, and the diagnosis of intrauterine growth retardation have already been described (Robinson et al., 1973).

HPL method

The sera were stored at −20°C prior to determination of the HPL concentration by the commercially available Phadebas HCS Test kit. Analyses were performed in duplicate and the means of the paired results were used when constructing the normal range and in the assessment of all values. Determined in this fashion, the coefficient of variation for an individual result averaged 6%. One hundred and eleven results from the 34 normal pregnancies were used to construct a normal range between 30 and 40 weeks of gestation. In common with other workers, we found that the normal values followed a log-normal distribution and transformation was effected as previously described (Robinson et al., 1973) before depicting the median values and 95% confidence limits.

Scoring system

In the absence of data from a large series which could be used to assign appropriate weighting factors to each parameter, it was decided to employ an arbitrary scoring system similar to that described in the original series, whereby high scores were associated with abnormality.

A score of one point was allotted where the majority of results fell below the median and above the lower confidence limit, and two points where the majority fell below the lower confidence limit. High levels (above the median) scored no points. Abnormal trends were allotted two points as it has been found from experience that deterioration of placental function compares in importance with a very low absolute level. A trend was taken to be abnormal when, during a period of three weeks prior to delivery, the increment in HPL results...
failed to parallel the appropriate normal curve, and attained values of less than 85% of those expected. A deviation of 15% from the normal trend was selected as indicating a significant fall in HPL for two reasons.

The error of the method when performed in duplicate has been shown to be small and the biological variation in any one healthy subject is also low. This latter feature contrasts with urinary oestriol assays where a significant fall was deemed to have occurred only when the result fell to 50% of the value previously recorded and this fall was confirmed by at least two consecutive estimations. So, too, an increment in biparietal diameter equal to or less than 50% of that normally expected, in most cases being assessed over a two-week period and involving at least three separate measurements, was judged to be abnormal.

RESULTS

Of the 42 patients studied, there were nine who delivered babies with weights below the tenth percentile on Lubchenco's tables of normal gestational weights (Lubchenco et al., 1963) and two whose babies had weights between the twenty-fifth and tenth percentiles but showed the clinical signs of intrauterine growth retardation.

Combined scores of two or more in individual tests and four or more in pairs of tests were found to separate the normal from the growth-retarded pregnancies with the least number of false results. The numbers of false negative and false positive results with each test and pairs of tests are shown in Table 1 together with the total percentage of false results for each.

DISCUSSION

The estimation of serum HPL concentration is theoretically an attractive test of placental function. It is produced solely by the syncytiotrophoblast (Sciarra et al., 1963) and Saxena et al. (1969) have shown a significant correlation between HPL concentration and placental weight. It has a very short biological half life of only 29 min. (Spellacy et al., 1966) with no circadian rhythm (Kaplan and Grumbach, 1965) thus justifying the use of serum assays. Furthermore, the high recovery rate and the accuracy of the radioimmunoassay permits reliance to be placed on individual results and the recent simplification of the technique (Letchworth et al., 1971) allows large numbers of samples to be processed in a relatively short period of time.

Spellacy and his co-workers (1971) in a large prospective series reported that using this test they were able to identify those patients with severe pre-eclampsia whose babies were at most risk from intrauterine death, and they advocated its widespread use as a screening test. Saxena et al. (1969) also found HPL assays to be of value stating that subnormal levels would almost invariably be found after 28 weeks in growth-retarded pregnancies. No mention was made, however, of false positive or false negative results. In the present series the general level of the results in the growth-retarded pregnancies was below the median in nine out of the 11 cases but very low levels were only observed in two of these. The corresponding figures for the 31 normal pregnancies were 14 and two respectively.

In a comparative series Keller et al. (1971) assessed the efficiency of urinary oestriol and pregnanediol assays, the dehydroepiandosterone sul-

<table>
<thead>
<tr>
<th>False result rate %</th>
<th>Test and pairs of tests</th>
<th>Pregnancies with a growth-retarded fetus (11 patients)</th>
<th>Normal pregnancies (31 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Correct result</td>
<td>False negative result</td>
</tr>
<tr>
<td>26</td>
<td>Serum H.P.L.</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>12</td>
<td>Urinary oestriol</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>10</td>
<td>Biparietal cephalometry (B.P.D.)</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>H.P.L. and oestriol</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>12</td>
<td>H.P.L. and B.P.D.</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>0</td>
<td>Oestriol and B.P.D.</td>
<td>11</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 1. Analysis of results achieved by monitoring normal pregnancies and pregnancies with a growth-retarded fetus.
phate loading test, and serum heat-stable alkaline phosphatase and HPL levels in their ability to detect placental dysfunction in ‘risk’ pregnancies. Using broad criteria for the diagnosis of fetoplacental dysfunction they found that HPL concentration gave no false negative results, but a 35% false positive rate, while oestriol levels had 31% false negative and 12% false positive rates respectively. The remaining three tests were considered to be of lesser value. When oestriol and HPL concentration were considered in combination they found no cases in which both tests were false negative and only 7% in which both were false positive.

In our series, although the criteria for fetoplacental dysfunction were more stringent, there was an appreciable false negative rate of 36% (four instances in 11 cases) using HPL levels, while the false positive rate was lower at approximately 22% (seven instances in 31 cases). The error rate for oestriol levels, on the other hand, was of a similar magnitude to that quoted by Keller et al. (1971). We were unable, however, to confirm the low rate of false results as reported by these workers using the combination of HPL and oestriol assays, and found in contrast that the error rate of oestriol assays alone was not significantly improved by the addition of HPL results.

Sonar biparietal cephalometry in our series appeared to be the most valuable single test, but when taken in combination with HPL its efficiency actually decreased. The combination of urinary oestriol measurement and cephalometry did, however, provide complete separation of the normal from the growth-retarded pregnancies.

It may, therefore, be concluded from this limited series that the use of HPL as an isolated test is of doubtful value and that its addition to either oestriol assays or biparietal cephalometry as assessed by our scoring system seems to add nothing to the efficiency of either test.

We thank our obstetrical colleagues and the nursing staff of the Queen Mother’s Hospital, without whose co-operation this study could not have been undertaken.

H. P. Robinson thanks the Medical Research Council who are providing continuing support for sonar research in the Department of Obstetrics, Queen Mother’s Hospital, Glasgow.

REFERENCES


