

Hormonal placental functions and intra-uterine growth retardation in patients with positive contraction stress tests

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Summary

Human placental lactogen (HPL) and urinary and serum oestriol levels were studied in patients in whom the contraction stress test was positive. After birth the infants were assessed for growth retardation. Low PHL, serum oestriol and urinary oestrogen levels were found in 66%, 30% and 15% of patients respectively. Gestational ages were known in 148 patients, of whom 72 (49%) had infants whose weights were below the 10th percentile for gestational age. HPL values were low in 81% of mothers who gave birth to growth-retarded infants, but serum and urinary oestriol levels were low in only 43% and 21% respectively. When both a positive stress test and a low HPL value were present, 69% of infants were growth retarded. The incidence of growth retardation rose to 85% when both HPL and serum oestriol levels were abnormal in patients with positive contraction stress tests. In this study estimation of HPL levels was found to be superior to that of oestrogen levels in detecting growth-retarded infants.

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The relationship between antenatal fetal monitoring, low oestriol and human placental lactogen (HPL) levels and intra-uterine growth retardation still needs to be ascertained. According to Freeman¹ the oxytocin challenge test will usually become positive before a decrease in previously normal urinary oestriol excretion. However, of 137 patients with persistently subnormal urinary oestriol excretion, Chew *et al.*² observed abnormal fetal heart rate (FHR) patterns during Braxton Hicks contractions of moderate intensity in only 24%. Abnormal FHR patterns during strong Braxton Hicks contractions were seen in 25% of these patients. They therefore suggested conservative treatment in patients with normal FHR patterns, even when the oestriol excretion was persistently low. Only a few studies could be found where HPL values were determined in patients with a positive contraction stress test.³⁻⁴ This study was therefore undertaken to examine hormonal placental function tests in patients with a positive contraction stress test.

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Patients and methods

Patients in whom the stress test was positive were studied regarding serum HPL and oestriol values, 24-hour urinary oestrogen levels and intra-uterine growth retardation.

Initially the method of Freeman¹ was used for the performance of the stress tests, but later accelerations of the FHR were also regarded as normal and oxytocin was administered only when non-stressed monitoring revealed a silent pattern.⁵ A positive test was regarded as repeated late decelerations in the FHR in the absence of supine hypotension or hyperstimulation. Unless the fetus was regarded as too immature, it was delivered soon after a positive contraction stress test.

Immediately after a positive test had been observed, blood samples were taken for HPL and serum oestriol estimations. HPL was measured by radio-immunoassay, using a standard kit (HPL and oestriol immunoassay kit, Radiochemical Centre, Amersham, England). Radio-immunoassay was also used to measure total serum oestriol levels, using the same kit. The laboratory's coefficients of variation for HPL and serum oestriol estimations were 7,7% and 12,4% respectively. If done within 4 days before a positive contraction stress test, the 24-hour urinary oestrogen value was also considered. Total urinary oestrogen levels were measured in 24-hour urinary specimens by colorimetry, using the Kober reaction.⁶ Estimation of urinary oestrogen levels after a positive contraction stress test was not taken into consideration. The results of these hormonal tests were plotted on curves used by Tygerberg Hospital, which ranged from 25 to 43 weeks. (These curves were compiled from values of 432 obstetric patients whose gestational ages were known; these patients do not represent a normal population.) Values which fell below the 10th percentile line were regarded as low or abnormal.

Soon after birth, if the condition of the newborn infant was satisfactory, a Dubowitz score was determined to estimate the gestational age.⁷ Weight-for-gestational-age charts of Tygerberg Hospital were used to assess the intra-uterine growth of the neonates.⁸ Those whose birth weights were below the 10th percentile for the specific duration of pregnancy were regarded as small for gestational age (SGA). When both the estimated duration of pregnancy according to the last menstrual period and the Dubowitz score were available, the latter was regarded as more accurate and therefore used to plot the birth weight and hormonal test result against the duration of pregnancy. Intra-uterine deaths were not included in the estimations of growth retardation, since birth weight is not an accurate reflection of fetal weight at the time of intra-uterine death. Serum oestriol and HPL studies were not done on all patients as these tests were not initially available. Urinary oestrogen levels were not available in every case, since in some patients a positive stress test had been obtained soon after admission and delivery was not delayed for 24 hours to collect a urine specimen.

Results

Positive tests of 161 patients were analysed. The indications for the tests were mainly pre-eclampsia (38,3%), suspected intra-

uterine growth retardation (16,5%), postdatism (12,8%), poor maternal weight gain during pregnancy (10,1%), and hypertension (9,0%). In the remaining 13,3% of patients most of the indications were antepartum haemorrhage and diabetes. The gestational age was known in 148 patients, of whom 72 (49%) were delivered of growth-retarded infants. HPL values were available for 77 patients, of whom 51 (66%) had values below the 10th percentile. Of the 53 plasma oestriol estimations done, 16 values (30%) were low. Urinary oestrogen estimations were done in 46 patients, of whom 7 (15%) had abnormal values. The differences in incidence of these abnormal tests are significant ($\chi^2 = 14,6$, with 2 degrees of freedom; $P < 0,001$). In the infants with appropriate birth weights for gestational age (AGA), 47% of HPL values were below the 10th percentile line. However, when they were small for dates, 81% of HPL values were low (Table I). These differences are statistically significant ($P < 0,01$).

TABLE I. HORMONAL PLACENTAL FUNCTION TESTS AND FETAL GROWTH

Hormonal test	Fetal growth		
	AGA	SGA	Total
Human placental lactogen			
Normal	18 (53%)	8 (19%)	26
Below 10th percentile	16 (47%)	35 (81%)	51
Total	34	43	77
	$\chi^2 = 9,94$ (1 degree of freedom); $P < 0,01$		
Plasma oestriol			
Normal	20 (87%)	17 (57%)	37
Below 10th percentile	3 (13%)	13 (43%)	16
Total	23	30	53
	$\chi^2 = 5,66$ (1 degree of freedom); $P < 0,02$		
Urinary oestrogen			
Normal	17 (95%)	22 (79%)	39
Below 10th percentile	1 (5%)	6 (21%)	7
Total	18	28	46
	Numbers too small for statistical analysis		

Abnormal plasma oestriol values occurred in 13% of AGA infants but in 43% of SGA infants ($P < 0,02$) (Table I). Urinary oestrogen values were low in 5% of the AGA infants and 21% of the SGA infants (Table I). These numbers were too small for statistical analysis.

The HPL value was below the 10th percentile in 51 patients and 35 of these (69%) were delivered of growth-retarded infants. Low plasma oestriol values were seen in 16 patients, of whom 13 (81%) had growth-retarded neonates. Urinary oestrogen values were below the 10th percentile in 7 patients, of whom 6 (86%) had SGA babies (Table II).

Both HPL and plasma oestriol estimations were done in 61 patients whose gestational ages were known. Both values were below the 10th percentile in 13 patients. Eleven of these (85%) were delivered of growth-retarded infants. All three tests were done in 27 patients. The values of all tests were below the 10th percentile in 5 patients, of whom 4 were delivered of growth-retarded infants.

Intra-uterine death occurred in 6 patients. HPL values were determined in 3 of these patients, all of which were below the 10th percentile. Plasma oestriol values were also determined in 3 patients, of whom 2 had levels below the 10th percentile. Urinary

TABLE II. PREDICTION OF GROWTH RETARDATION

Test	Growth retardation		%
	Patients	%	
Contraction stress test alone	148	72	49
Low HPL	51	35	69
Low plasma oestriol	16	13	81
Low urinary oestrogen	7	6	86
Low HPL and oestriol	13	11	85
All tests low	5	4	80

oestriol estimations were done in 5 patients, of whom only 1 had a level below the 10th percentile.

Discussion

Infants had appropriate birth weights for gestational age in 53% of cases of normal HPL values and in 47% of patients with abnormal HPL values. Abnormal HPL values were also observed in 81% of patients with small-for-dates infants. The differences between normal and abnormal values in AGA and SGA infants were significant, but many values in AGA infants were also low. However, normal values in SGA infants were obtained less frequently. Most of the AGA infants had normal oestriol levels, but 57% of SGA infants also had normal levels. Although plasma oestriol values were less frequently 'falsely high' in AGA infants, normal values occurred in many cases of intra-uterine growth retardation. There were too few urinary oestriol estimations for statistical analysis, but it seemed as if a high percentage of growth-retarded infants also had normal urinary oestriol values. However, some urinary oestrogen estimations were done a few days before the stress test, while plasma oestriol and HPL estimations were done immediately after a positive test had been observed. Better correlation can therefore be expected when urinary oestriol levels are estimated immediately before a positive stress test.

If it is postulated that all positive stress tests are indicative of placental insufficiency and therefore used as a standard, HPL seems to be a more reliable hormonal test because low values were obtained more frequently than with oestriol estimations. The fact that 66% of patients had low HPL values also indicates that stress tests are able to indicate an at-risk fetus.

A combination of stress tests and HPL estimations was more accurate in detecting growth retardation than a stress test alone. A combination of a positive stress test and plasma or urinary oestriol estimation was even more accurate.

All 3 patients in whom intra-uterine death occurred had low HPL values; 2 out of 3 had low plasma oestriol values, but urinary oestriol levels were normal in 4 out of 5 cases of intra-uterine death. These facts also demonstrated that estimation of HPL was more sensitive than that of oestriol.

Percentile lines used in this study were not obtained from a normal population but from hospitalized patients in whom the stress test had been negative. If patients with positive stress tests were to be compared with a normal population, the prevalence of abnormal placental function tests would probably be higher.

Reports in the literature regarding urinary oestriol levels in patients in whom the oxytocin stress test had been performed are controversial. Decreased or low urinary oestriol levels were found by some workers⁹⁻¹³ in the majority of patients, while others found a disappointing correlation between oestriol levels and positive stress tests.¹⁴⁻¹⁶ When the results of all these publications were pooled, 76 out of 127 patients had low oestriol levels. Since false-positive tests are well recognized and several clinical and pharmacological conditions may influence urinary

oestriol excretion, a better correlation may be found by careful elimination of patients with false-positive stress tests or false low urinary oestrogen levels.

Two recent publications indicated that HPL measurements provide the best biochemical index of fetal well-being,¹⁷ and that a greater proportion of small-for-dates infants with high oestriol levels was observed than with HPL estimation.¹⁸ Spellacy *et al.*³ reported a good correlation between positive oxytocin challenge tests and low HPL levels. In this study it was also found that HPL values were more sensitive in patients with positive stress tests. The fact that low HPL values were found in 66% of patients with a positive test indicates that an at-risk fetus can be detected by antenatal fetal monitoring. The best results in diagnosing the growth-retarded fetus antenatally were obtained with a combination of antenatal FHR monitoring and hormonal placental function tests.

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The selection of patients at the Grootte Schuur Maternity Hospital

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Summary

The Peninsula Maternity and Neonatal Service (PMNS) was established on 1 January 1980 as a result of the regionalization of obstetric and neonatal services in the Cape Peninsula. Some 20 000 deliveries per annum occur in the 5 maternity hospitals and 3 Midwife Obstetric Units (MOUs) under the aegis of the PMNS. As part of the reorganization of the service the booking and referral criteria have been revised, taking into account the function of the Grootte Schuur Hospital Maternity Block as the high-risk unit. The concept

of risk in perinatology is discussed. The booking and referral criteria are detailed under the headings of booking criteria for hospital and for MOUs and referral criteria from the MOU to hospital — antenatally, in labour, in the puerperium and for neonatal problems.

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In Cape Town, as in most of the Third World, there is a continuing need to select high-risk obstetric patients for antenatal care and delivery at a high-risk maternity hospital. This need is twofold. Firstly, there is a grave shortage of beds which is unlikely to be relieved. Secondly, the development and expansion of the Midwife Obstetric Units (MOUs)¹ has created a demand for better selection of low-risk patients who may be delivered in them. The MOUs are becoming increasingly popular with the community. It is far less time-consuming and far less costly to visit the local MOU than a far-off hospital, and the staff are generally better known to the patients. Most importantly, the MOUs are safe, with an enviable perinatal mortality rate.

This article describes the booking and referral criteria currently used in the Departments of Obstetrics and Gynaecology and Paediatrics and Child Health (Neonatal Section), University of Cape Town and Cape Provincial