Acta Genet Med Gemellol 33:571-574 (1984)

SHORT NOTE

Received 9 June 1983
Final 30 March 1984

Screening for Multiple Pregnancy

Determination of Human Chorionic Gonadotropin (hCG), Alpha-Fetoprotein (α-FP) and Human Placental Lactogen (hPL) in Blood During the Second Trimester of Pregnancy

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Abstract. The value of single determinations of serum hCG, hPL, and αFP for the detection of multiple pregnancy was investigated in a consecutive series of 992 women between the 14th and 24th week of pregnancy. With the 90th percentile as referent value, all twin pregnancies (n = 10) were detected by the combined results of the three determinations. Considered separately, hPL proved to be the most useful indicator of multiple gestation; the sensitivity of hPL alone was 70% and the predictive value of hPL concentrations above the 90th percentile was 8.1.

Key words. Chorionic gonadotropin, Alpha-fetoprotein, Human placental lactogen, Twin pregnancy

INTRODUCTION

Early diagnosis of multiple pregnancy is a prerequisite for adequate antenatal care. Although second-trimester echography provides the only accurate and safe method of diagnosis, screening methods may be valuable. The increased placental and fetal mass in multiple pregnancies is predictably associated with higher levels of several pregnancy hormones. Determination of hCG [3], hPL [2,5] and αFP [4,8] has been claimed to be helpful in the early detection of multiple pregnancies.

In the course of a prospective study of hormonal screening for neural tube defects and fetoplacental dysfunction now in progress we performed a retrospective analysis of the predictive value of the serum hCG, hPL, and αFP concentrations in the second trimester of pregnancy for the detection of twin pregnancies.

PATIENTS AND METHODS

In a consecutive series of 992 pregnant women, blood was collected for hormonal analysis at the time

of a routine antenatal visit scheduled between the 16th and 20 th week of pregnancy. The data of patients who were lost to follow-up or in whom blood was sampled more than four weeks behind schedule were not taken into consideration. Serum hCG levels were determined by radioimmunoassay according to the dioxane precipitation method [7], and results were expressed in international units of the 2nd International Standard of hCG (MRC, London). For the assay of hPL and αFP, commercial radioimmunoassay kits were used (Amersham International, Buckinghamshire, UK).

Because the hormonal concentrations were not always normally distributed, the referent value for normal singleton pregnancies was expressed in percentiles. An incidence of twin pregnancies of 1/80 was taken for calculation of the predictive value of the hormonal screening test.

RESULTS

The data for 806 singleton pregnancies and 10 twin pregnancies were available and appropriate for analysis. The serum concentrations of hCG, hPL, and αFP in the 10 twin pregnancies and the 80th percentile for the corresponding gestational week in singleton pregnancies are given in Table 1.

Table 1 - Serum Levels of hCG, hPL, and αFP in 10 Twin Pregnancies and the Corresponding 80th Percentile for Normal Singleton Pregnancies

Patient	Gestational week	hCG (IU/ml)	Percentile 80th	hPL (ug/ml)	Percentile 80th	α FP (ng/ml)	Percentile 80th
1	14	104.2***	60.4	1.04	1.16	25.2	28.5
2	16	75.1**	53.5	2.76***	1.40	85.1***	43.1
3	16	34.8		1.45*		92.9***	
4	17	75.0***	37.7	1.60**	1.43	75.4***	48.0
5	17	53.5**		1.54*		68.5**	
6	19	21.1	27.6	3.97***	1.67	71.9*	71.0
7	22	10.6	23.2	4.97**	3.44	154.7**	101.6
8	22	54.4***		5.72***		232***	
9	24	35.1**	31.6	8.32***	4.42	115.7	154.6
10	24	25.8		6.42**		141.3	

* above the 80th percentile
** above the 90th centile
*** above the 95th centile

The sensitivity, the predictive value of a positive result, the false-positive rate (100 minus the predictive value) for the three hormones were calculated for three cut-off levels (80th, 90th, and 95th percentiles) (Table 2). With the 90th percentile taken as cut-off level, hPL alone detected 7 of the 10 twin pregnancies. The sensitivity of the test was increased to 90% by parallel determination of hCG and hPL or αFP and hPL; the increased sensitivity is, however, attained at the cost of a lower specificity and predictive value.

DISCUSSION

At the present, the best method for the diagnosis of twins is routine ultrasound screening of the whole obstetric population at some time during the second trimester of pregnancy. Ancillary screening tests may, however, be of value where ultrasound examination is not readily available for all patients. Because the concentrations of fetal and placental hor-

Table 2 - Twin-Pregnancy Screening Value of Serum hCG, hPL, and αFP at Three Levels of Specificity

hCG	Cut-off level (percentile)	Sensitivity	Predictive value of a positive result	False-positive rate
	80	60	3.7	96.3
	90	60	7.1	92.9
	95	30	7.1	92.9
hPL	80	90	5.4	94.6
	90	70	8.1	91.9
	95	50	11.2	88.8
αFP	80	70	4.2	95.8
	90	60	7.1	92.9
	95	40	9.2	90.8
Combination of hCG and hPL	80	100	6.0	94.0
	90	90	10.2	89.8
	95	70	15.1	84.9
Combination of hCG and αFP	80	90	5.4	94.6
	90	80	9.2	90.8
	95	50	11.2	88.8
Combination of αFP and hPL	80	90	5.4	94.6
	90	90	10.2	89.8
	95	70	15.1	84.9

mones in twin pregnancies are nearly twice those in singleton pregnancies, hormone assays can be expected to have screening value. The efficiency of a screening test depends on its sensitivity (percentage of twin pregnancies with a positive result) and its specificity (percentage of singleton pregnancies with a negative result). These two variables are conversely related: maximal sensitivity is associated with minimal specificity and vice versa. The optimal levels of sensitivity and specificity depend on the results of cost-benefit analysis in economic and medical terms with respect to early diagnosis. Although the number of twin pregnancies in our series is rather small, the results of the three hormonal screening tests indicate that hPL determination is the most useful for the detection of twin pregnancy. At a specificity level of 90%, 7 out of 10 twin pregnancies will be detected and 8.1% (predictive value) of the hPL concentrations using above the 90th percentile will be associated with a twin pregnancy. Similar results have been reported for hPL, determined between the 29th and 30th week of pregnancy [5].

Although the mean concentrations of serum hCG [1,6] and αFP [4] are significantly higher in twin pregnancies, the sensitivity of these two hormones for the detection of twins is low. In this respect, neither of them can serve for practical screening purpose. Even if used in combination with hPL, they do not contribute to greater screening efficiency.

From our data it may be concluded that the determination of hPL in the second trimester of pregnancy has a screening function for the detection of twin pregnancies. This approach may be useful where screening of all pregnant women by ultrasound is not feasible or used for its indicator value when placental hormones are measured for other indications.

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