

PROGNOSTIC VALUE OF hCG, PROGESTERONE, 17-BETA ESTRADIOL AND THE ECHOSCOPIC EXAMINATION IN THREATENED ABORTION DURING THE FIRST TRIMESTER

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SUMMARY

The Authors refer on the validity of echoscopic examination and hCG, progesterone and 17-beta estradiol values in the prognosis of threatened abortion during the first trimester of pregnancy in 62 patients.

The echoscopic examination allowed a prognosis to be made in accordance with the clinical evolution of threatened abortion in 90% of the cases; the plasma levels of hCG and progesterone in 87% of the cases; 17-beta estradiol in 83% of the cases.

The Authors conclude that the simultaneous assay of hCG, progesterone and 17-beta estradiol plasma levels does not improve the prognostic validity of echoscopy but, in some cases, can provide essential details on the etiology of threatened abortion itself.

Spontaneous abortion during the first trimester occurs in about 15% of all pregnancies; the vitality of the embryo is already compromised, in one out of two cases, at the first appearance of clinical signs of threatened abortion and about six out of ten abortions seem to be due to chromosomal anomalies (^{1,9}).

The prognostic and clinical evaluation of threatened abortion is closely related to the data of physical and biochemical monitoring.

The echoscopic evaluation can result in the following pictures:

1) the gestational sac is morphologically normal and there are signs of the embryo's vitality;

2) the embryo's vitality is certain but there are anomalies in the trophoblast insertion or the presence of two embryos;

3) the embryo's vitality can be neither denied nor confirmed; in this case the examination is repeated after a few days;

4) pregnancy is clearly interrupted.

It is known that the ovum implantation, its development and the subsequent constitution of the fetoplacental unit are responsible for remarkable hormonal modifications.

Undoubtedly endocrine monitoring is at present the qualified way to study and carry out the prognostic evaluation of threatened abortion and to dispel the not infrequent doubts arising during the echoscopic examination, particularly at the initial stage of pregnancy.

Although the studies carried out often come to differing conclusions, it can be generally said that hCG, progesterone (P) and 17-beta estradiol (E₂) are excellent hormonal parameters to formulate the diagnosis and prognosis of threatened abortion.

It must be remembered that hCG, secreted six days after the conception, reflects the precocious function of trophoblast (²) and is already doseable ten days after ovulation, approximately when the ovum implantation occurs (^{11,12}).

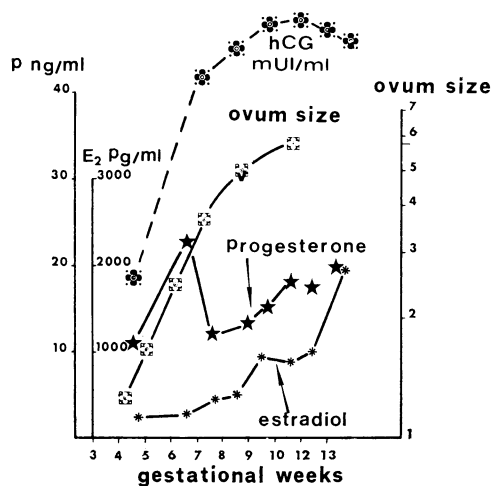


Fig. 1. — Observation of Mrs G. Thècle, *J. Gyn. Obst. Reprod.*, 1980.

HCG secretion doubles every 1.4 days and, according to Chartier, is a sign of the ovum vitality during the first week of gestation⁽⁴⁾. A more or less significant alteration of its increase rate can be a biological sign of a constitutional anomaly of the ovum.

HCG secretion occurs between the eighth and the twelfth week of gestation and its secretion curve, expressed in semi-logarithmic co-ordinates, appears as a line that reaches the axis of the abscissa towards the eighth-ninth day after the ovulation coinciding with the moment of implantation⁽²⁻¹³⁾.

From the echoscopic point of view it is important to remember that the representation of the longest diameter of the gestational sac (already evaluable at the fourth gestational week) runs closely parallel to the hCG secretion line (fig. 1).

Although its action is not yet completely clear, it is known that hCG serves to prolong the life of the corpus luteum and stimulate its steroidogenesis. As mentioned before, its precocious alterations are bad omens; moreover, a scarce original production of hCG generally in-

dicates the occurrence of chromosomic abortion (fig. 2).

As regards progesterone, its importance in maintaining the initial pregnancy is already well known. Csapo and Erdos⁽⁶⁾, Csapo and Pulkinen⁽⁷⁾, Thau and coll.⁽¹⁴⁾ proved in candidates for pregnancy interruption that the ablation of the corpus luteum causes abortion only before the seventh week; subsequently the steroidogenic secretion is assured by the fetoplacental unit⁽¹⁰⁾.

The progesterone level is significantly higher between the tenth and the fifteenth week after ovulation; at about the fifth-sixth week progesterone levels can decrease to minimum values of 11.5-12 ng/ml. This drop can explain the presence of small metrorrhagies in the first trimester, when echoscopic and objective uterine evolutions are normal. At the end of the tenth week the secretion of progesterone increases regularly thanks to the activity of the fetoplacental unit and its

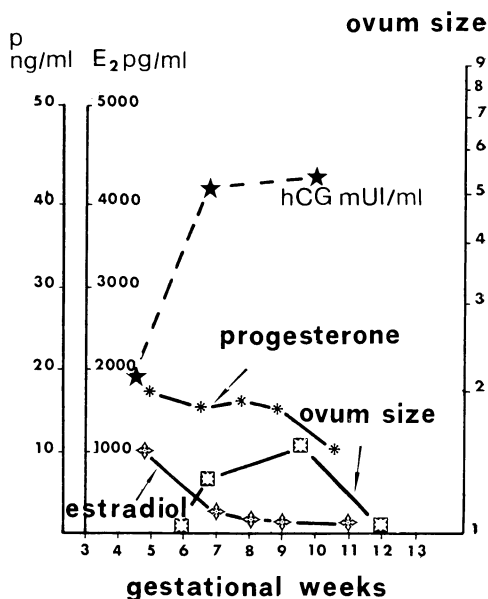


Fig. 2. — Observation of Mrs T. Agnès, *J. Gyn. Obst. Reprod.*, 1980.

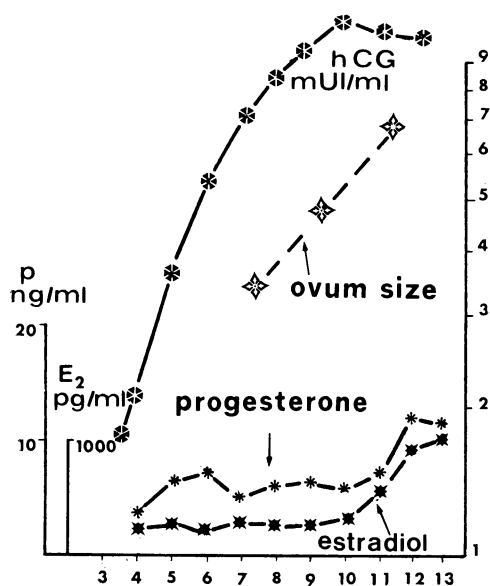


Fig. 3. — Observation of Mrs. V. Catherine, *J. Gyn. Obst. Reprod.*, 1980.

average values pass from about 25 ng at the second week to 34 ng/ml at the thirteenth week (fig. 1).

A few production of progesterone without anomalies of the gestational sac and with normal hCG secretion shows the presence of primitive and real luteal insufficiency (fig. 3).

The estrogenic secretion of the corpus luteum is stimulated by hCG, but its effect on 17-beta estradiol secretion is slower than on progesterone secretion; in fact a significant increase in the E₂ level, that exceeds the limit of 120 pg/ml, observed in the menstrual cycle, occurs on the fourteenth day after ovulation.

E₂ increases regularly over the first trimester of pregnancy and its levels are close to 190 pg/ml at the third week, 550 pg/ml at the sixth week, 1300 pg/ml at the ninth week and 3100 pg/ml at the thirteenth week⁽¹³⁾ (fig. 1).

The purpose of this study is verifying the validity of the echoscopic examination

and hCG, P, and E₂ assay in the diagnosis and prognosis of threatened abortion during the first trimester.

MATERIAL AND METHODS

This study was carried out on 62 patients showing clinical signs of threatened abortion, between the fifth and the thirteenth completed week of gestation.

All patients presented metrorrhagia, with uterine contractions in some cases, with no modification of the cervix.

Threatened abortions due to uterine malformations or systemic diseases of the mothers were excluded.

After the clinical examinations all patients observed went through echoscopic examinations (U.S.) (Vidoson System by Siemens) and radio-immunologic assay of hCG, progesterone (P) and 17-beta estradiol (E₂).

RESULTS

28 out of 62 patients had a regular pregnancy evolution whereas 34 aborted between the second and the fifteenth day since the beginning of symptomatology.

Echoscapy

The echoscopic examination allowed us to make a satisfactory prognostic evaluation, considering that there were only four

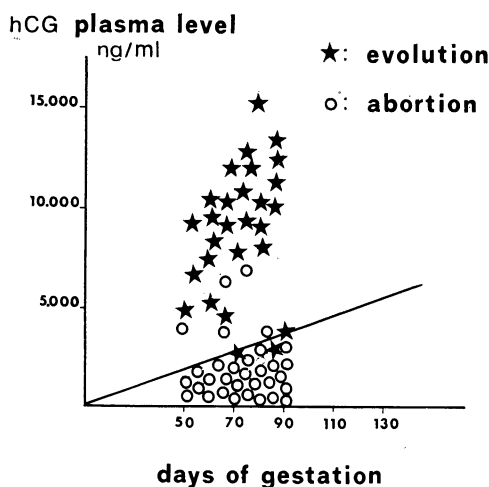


Fig. 4. — hCG plasma levels in function of the gestational and the clinical evolution.

false positives and two false negatives (tab. 1).

Table 1.

	No. of cases	Normal evolution	Abortive evolution
U.S. normal	30	26	4
U.S. negative	32	2	30
Total	62	28	34

Thus, in 56 patients, accounting for about 90 %, the clinical evolution of threatened abortion agreed with the echoscopic examination.

HCG

Plasmatic levels of hCG (fig. 1) showed five false positives and two false negatives (tab. 2).

Table 2.

	No. of cases	Normal evolution	Abortive evolution
Normal hCG	30	25	5
Low hCG	32	3	29
Total	62	28	34

Concordance between hCG values and the clinical evolution was found in 54 cases, accounting for about 87%.

Progesterone

Progesterone values (fig. 5) were normal in relation with the gestational age in 30 cases, but we found six false positives; the same values were low in 32 cases, with two false negatives (tab. 3).

Table 3.

	No. of cases	Normal evolution	Abortive evolution
Normal progesterone	30	24	6
Low progesterone	32	2	30
Total	62	26	36

prog. ng/ml

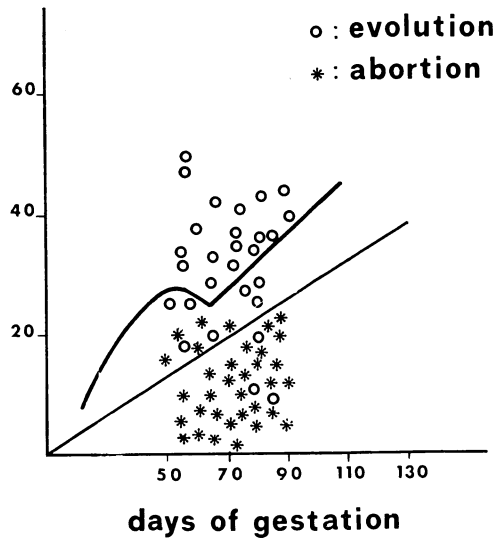


Fig. 5. — Plasma levels of progesterone in function of the gestational age and the clinical evolution.

Concordance between progesterone values and clinical evolution was found in 54 cases accounting for about 87%.

17-beta estradiol

E₂ values (fig. 6) were normal in 26 cases, with four false positives, and low in 36 cases with six false negatives (tab. 4).

Table 4.

	No. of cases	Normal evolution	Abortive evolution
Normal 17-β E ₂	26	22	4
Low 17-β E ₂	36	6	30
Total	62	28	34

Concordance between E₂ values and the clinical evolution was found in 52 cases, accounting for about 83%.

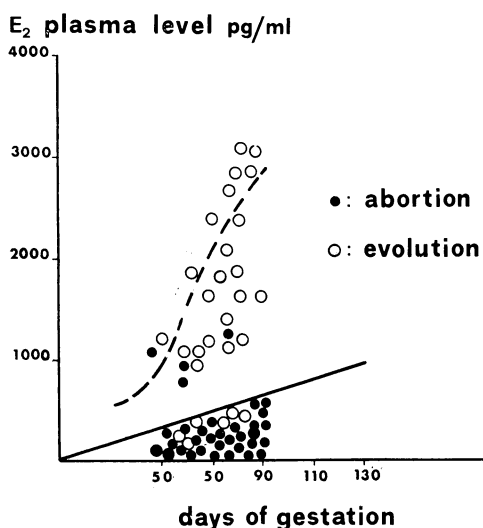


Fig. 6. — Plasma levels of 17-beta estradiol in function of the gestational age and the clinical evolution.

DISCUSSION

In our survey the use of echoscopic examination allowed us to make correct diagnoses and prognoses in about 90% of the cases examined.

This percentage is close to those published in the literature over the last few years⁽⁸⁾ (tab. 5).

Table 5. — *Prognostic value of echographic examination in threatened abortion during the first trimester.*

Levi and Coll.	1973	84%
Duff	1975	85%
Lichtenegger and Weiss	1975	95%
Schlensker and Coll.	1977	95%
Villière and Coll.	1978	90%
Schaap and Piront	1979	88%

It is important to stress that the percentages differ widely in series based on a single examination and in those based on repeated examinations.

Repeated control by echoscopy allowed many Authors to express valid prognoses in 100% of the cases.

Therefore, in most cases, the echoscopic examination provides essential data for the diagnosis and prognosis of threatened abortion evolution during the first trimester.

With regard to hCG, as early as in 1940, Rakoff stressed the relation between placental function and serum and urine levels of hCG, that were then determined by biological methods.

Subsequently various Authors proved that in the case of threatened abortion in the first trimester, during the week preceding the expulsion of the conception product, hCG serum levels are low in relation to the gestational age at least in nine out of ten cases.

As referred above, concordance between hCG values and pregnancy evolution was found in 87% of the cases of threatened abortion.

Various Authors (tab. 6) report different percentages of this prognostic validity.

Table 6. — *Prognostic value of hCG serum levels in threatened abortion during the first trimester.*

Nygren and Coll.	1973	97%
Crosignani and Coll.	1974	94%
Kunz and Keller	1976	79%
Braunstein and Coll.	1978	89%
Chartier and Coll.	1978	85%
Gerhard and Runnebaum	1978	90%
Villière and Coll.	1978	98%
Gaspard	1979	91%

A more precise prognostic judgment is reached when two or more successive dosages are performed⁽³⁾. It must be noted that if the evaluation of hCG (α and β) is performed on different fractions, the quality of the prognostic judgment does not improve significantly⁽⁸⁾.

These facts show that the prognosis of threatened abortion during the first trimester does not vary in a statistically si-

gnificant way if echoscopic examination and hCG dosage are performed simultaneously. In fact, as already said, the plasma levels of hCG are closely related to the echoscopic picture in that the normal growth of the gestational sac is almost constantly matched by the exponential increase of hCG.

Furthermore, in agreement with most of the literature, our experience confirms the existence of a close relation between hCG and P. The relation is weaker between hCG and E₂. Moreover our results showed no close relation between P and E₂, whereas, according to some Authors, the association of a P level higher than 10 ng/ml and a E₂ level higher than 50 pg/ml justify the prognosis of a favourable evolution for a threatened abortion during the first trimester⁽⁵⁾.

In conclusion, according to our survey, from the prognostic point of view, P and E₂ assay does not improve the prognostic significance of hCG.

CONCLUSIONS

In 90% of the cases observed the echoscopic examination contributes considerably to the diagnosis and prognosis of threatened abortion during the first trimester⁽⁵⁾.

HCG assay can be useful when echoscopy is uncertain and provides excellent information on the immediate prognosis of pregnancy, though with some possible discordances.

In conclusion, the simultaneous determination of hCG, P and E₂ levels does not improve the prognostic validity of

echoscopy but provides essential details on the etiology of the threat, thus making it possible to analyze more clearly the cases of primitive luteal insufficiency in abortions due to a primitive anomaly of the ovum.

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