PROGNOSTIC VALUE OF PLASMA PROGESTERONE-R.I.A. IN THREATENED ABORTION

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SUMMARY

In a study carried out on Progesterone plasma levels in two groups of women (222 controls and 76 patients affected with threatened abortion) between the 7th and 14th gestational week, the Authors affirm the poor prognostic utility of Progesterone assay. The predictive value for pregnancy interruption of Progesterone levels below the 10th centile resulted to be of 53.00%.

The luteal body is already proved to be the main source of pregnancy Progesterone till about the 7th gestational week, after which the placenta is showed to be concerned in the hormone almost total production.

Maternal cholesterol is converted into Pregnenolone and then into Progesterone in placental mitochondria; Progesterone is transformed into 6-alpha-OH-Progesterone by the placenta only in a negligible amount, while the main metabolic way let it pass into the maternal organism, by which it is mainly cleared as pregnanediol-glucuronide.

Only after being transformed into 20-alpha-OH-Progesterone through reduction and hydroxylation processes, it can be oxydized to Progesterone again in the placenta, or be utilized as a precursor of corticosteroidal and androgen hormones in fetal tissues.

The role of Progesterone in maintaining pregnancy is essential: after being released at the placental-uterine interface, it impregnates the myometrium and makes it keep relaxed until pregnancy-term, probably through an inhibiting action on prostaglandin synthesis ([1]).

Progesterone treatment of threatened abortion seems to find its rationale in its just described mode of action, even if double-blind studies carried out with Progesterone and placebo don't seem to point out that the endocrine therapy achieves better results ([2]).

If we consider that almost 50-60% of spontaneous abortions, mainly when they are extremely precocious, can be ascribed to a genetic disorder ([3, 4]), we should suggest a Progesterone therapy only for those cases of threatened abortion in which low Progesterone plasma levels could be surely regarded as the main factor responsible for the disease, and not as an aspecific sign of a generic placental damage.

The several studies carried out to find reliable parameters for a prognostic evaluation of threatened abortion, often reach

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contrasting conclusions on the usefulness of plasma Progesterone-R.I.A.; the lack of certainties existing in literature justifies this research we carried out in our Department to verify whether plasma Progesterone-R.I.A. may be practically useful in the prognostic evaluation of clinically and echographically monitored patients affected with threatened abortion.

MATERIAL AND METHODS

Two groups of patients were studied: the first one (control) consisted of 222 women with a physiological pregnancy, and the second one of 76 patients with a clinical and echographic picture of threatened abortion.

The blood drawing for Progesterone-R.I.A. was performed from every patient's cubital vein between 08.00 and 10.00 in the period between the 7th and the 14th gestational week. Blood samples were centrifuged and plasma stored at −20 °C until dosage.

Plasma Progesterone-R.I.A. was performed by Serono Biodata Kit (Code 1274 – ethylic ether extraction – polyethylenglicole precipitation).

The pregnancy outcome was controlled for every patient in both groups, and the cases in which it resulted unknown were preliminarily excluded from our study.

It is noteworthy to say that every patient affected by threatened abortion underwent, after the blood drawing, a parenteral therapy with Progesterone 200 mg/day i.m., at least till the 16th gestational week, unless, of course, pregnancy spontaneously broke off before.

RESULTS

The values from Progesterone-R.I.A. in the controls at different gestational ages were elaborated through 2nd degree polynomial approximation and represented under the form of centiles (table 1).

Out of the 76 cases of threatened abortion in which at least one plasma Progesterone-R.I.A. was performed, 34 (44.7%) aborted before the 20th gestational week while 42 (55.3%) reached the term of pregnancy.

Plasma Progesterone levels at the different gestational weeks were below the 10th centile in 19 cases, that is in the 25% of threatened abortions (fig. 1); 10 out of them aborted (13.15%) while 9 could end their pregnancy (11.85%). In particular, the true positives were 10, the true negatives 33, while the false positives were 9 and the false negatives 24. The statistical analysis did not show any statistically significant difference ($\chi^2=0.64$). The method resulted to have a sensitivity of 29%, a specificity of 79% and a predictive value of 53%.

TABLE I. — *Plasma Progesterone.*

10th centile: $4.54-0.88\chi + 0.07\chi^2$
50th centile: $28.15-4.29\chi + 0.24\chi^2$
2nd degree approximation

Gest. week	10th	50th
7	1.92	9.82
8	2.12	9.10
9	2.47	8.87
10	2.96	9.10
11	3.60	9.82
12	4.38	11.01
13	5.31	12.68
14	6.38	14.82

DISCUSSION AND CONCLUSION

Our results point out a remarkable overlapping of Progesterone values in plasma from patients with threatened abortion independently from their pregnancy outcomes, what makes this assay useless for a correct diagnostic procedure; in fact, Progesterone levels below the 10th centile could predict the miscarriage only in 53% of cases.

Our data contradict Kunz and Keller's [5] statements according to which low Progesterone levels would predict the abortion in 89% of cases, and the results of Juppila [6, 7] who states a predictive value of 93% for low plasma Progesterone levels between the 6th and the 20th gestational week.

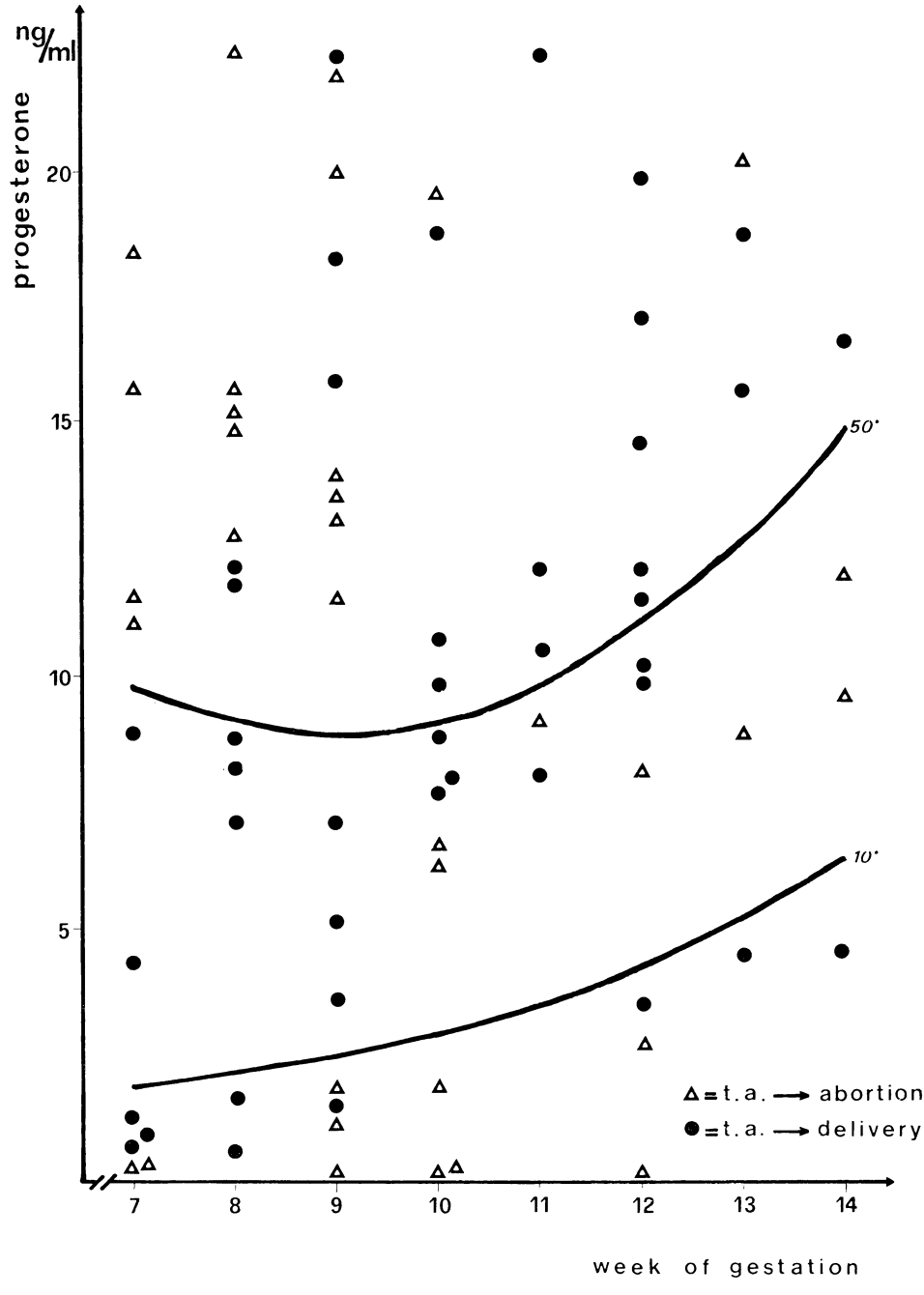

Fig. 1. — Plasma progesterone trend between the 7th and the 14th week of gestation (10th and 50th centile). The cases are represented of threatened abortion which ended in miscarriage (△) or had positive outcomes (●).

Soyama and Coll. ([8]) and Jovanovic and Coll. ([9]), on the contrary, at the end of a complete endocrine study on patients affected with threatened abortion, report data similar to ours and state that plasma Progesterone-R.I.A. does not increase the predictive value on pregnancy outcome, already provided by the R.I.A. of plasma hCG, E2 and PRL.

Also Nygren and Coll. ([10]) affirm that plasma Progesterone and Estradiol-R.I.A. neither gives additional news, nor modifies in any degree the good predictive value already gained through plasma hCG assay, while Miyakawa and Coll. ([11]) seem to assign an higher prognostic value to plasma Progesterone levels, when they come from a correct, seriate monitoring of the single affected patients after the 16th gestational week, and are carefully examined in their longitudinal trend.

Independently from the contrasting data in literature, the analysis of the data from our series let us only confirm that plasma Progesterone-R.I.A. is hardly useful for a prognostic evaluation of threatened abortion.

As to the utility of Progesterone therapy to which we submitted all the 76 patients affected with threatened abortion, we can say "a posteriori" that it was probably useless in the patients whose Progesterone levels were over the 10th centile, a part of which (31.57%) nevertheless aborted; yet, we can say nothing about its usefulness in the cases with Progesterone levels below the 10th centile: as we know, 10 of them aborted in spite of the terapy; but as to the 9 patients whose pregnancies had normal outcomes (11.85%) in spite of low Progesterone levels, it is impossible to ascertain whether the treatment could modify the ominous prognosis of threatened abortion, or these pregnancies normally reached their term independently from exogenous Progesterone supply.

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