

SERIAL DETECTION OF PLASMA-FACTOR XIII LEVELS DURING THE OVULATORY CYCLE AND ESTROPROGESTATIVE CONTRACEPTION

P. F. BOLIS, M. FRANCHI, L. MARINO,
A. M. M. PAGANELLI, P. SAMPALO

Institute of Obstetric and Gynaecologic Clinic,
University of Pavia (Italy)

SUMMARY

The Authors examine the variations of plasma F. XIII levels during the physiological cycle and estroprogestative contraception. Their data show steady elevated levels in patients on oral contraception compared to normally ovulating women; in normal cycles, besides, a decrease was noted during the preovulatory phase.

The results suggest a possible action of steroid hormones on plasma F. XIII levels, and consequently on the process of fibrino-stabilization.

INTRODUCTION

Plasma Factor XIII (or F.S.F., or Laki-Lorand's Factor, or Fibrinolygase, or F. XIII) is a plasma protransglutaminase which, after the activation by thrombin in the presence of Ca^{++} ions, has fibrin as physiologic substrate (^{1, 2, 3}).

After the action of activated F. XIII, the stabilized fibrin shows increased resistance, mechanical (⁴) and to directly by plasmin and indirectly by streptokinases induced lysis (^{5, 6}), and becomes insoluble in urea and in weak acids (^{7, 8, 9, 10, 11}).

The interest bound to the study of coagulation during hormonal contraception induced the Authors, also considering the few data in the literature (¹²), to detect the possible different behaviour of Plasma F. XIII levels during the physiologic cycle and the estroprogestative contraception.

MATERIAL AND METHODS

Have been taken and tested peripheral venous blood samples from:

— 8 women, aged between 21 and 26 years, assuming for more than 3 months combined estroprogestative pill (Ethinilestradiol 0.003 mg, Levonorgestrel 0.15 mg) for birth control;

— 10 healthy women, aged between 23 and 29, normally ovulating, as documented by basal temperature.

All the subjects were free of relevant diseases, and were advised of the aim of the study.

Every subject underwent 4 venopunctures during the same month: the first time between day 6 and 10 from menstruation or bleeding, the second time between day 13 and 15, the third time between day 20 and 23, the fourth time between day 27 and 29.

Each blood sample was treated with NaEDTA 2% 1:10 v/v and centrifuged at 1000 g for 15 minutes to obtain Platelets Poor Plasma which was defibrinated according Sheltawy (¹³).

The Platelets Poor Plasma defibrinated was stored at -20°C until the time of detection of Plasma F. XIII levels.

Plasma F. XIII levels have been detected performing Nalli's method based on fibrin-agarose gel diffusion (^{14, 15}).

The Plasma F. XIII levels of the samples were measured as fibrino-stabilizing activity percentage, while 100% was considered the fibrino-stabilizing

Table 1. — *Serial detection of Plasma Factor XIII from normally ovulating women.*

	Age	Proliferative phase (day 6-10)	Perioviulatory phase (day 13-15)	Secretive phase (day 20-23)	Premenstrual phase (day 27-29)
A. P.	23 yrs.	75%	62%	75%	75%
L. B.	27 yrs.	80%	60%	75%	80%
A. M.	25 yrs.	100%	75%	90%	100%
P. S.	29 yrs.	80%	60%	75%	75%
G. G.	23 yrs.	100%	75%	90%	100%
P. B.	23 yrs.	95%	60%	85%	95%
D. C.	24 yrs.	100%	70%	95%	100%
S. S.	23 yrs.	80%	65%	80%	80%
P. B.	27 yrs.	105%	75%	90%	100%
M. F.	27 yrs.	105%	70%	95%	
Mean value	92%	67.2%	85%	89.4%
Range	75-105%	60-75%	75-95%	75-100%
Standard Deviation	11.8	6.5	8.1	11.5

activity of Plasma Pool taken from 10 healthy men, aged between 19 and 27, and treated according Sheltawy's method⁽¹³⁾.

The progressive dilutions of this Plasma Pool, necessary for the standard measure curve, were obtained with Tris HCl 0.05 M (pH 7.5) buffer.

The statistical analysis of the results was evaluated by Student's T test.

RESULTS

The Plasma Factor XIII levels in women normally ovulating and under treat-

ment with estroprogestative for birth control are reported in table 1 and 2 and in figure 1.

The detection of Plasma F. XIII levels from 10 women normally ovulating resulted in the following mean values:

- proliferative phase:
(day 6-10) 92% (range 75-105%)
- perioviulatory phase:
(day 13-15) 67.2% (range 60-75%)
- secretive phase:

Table 2. — *Serial detection of Plasma Factor XIII from women under estroprogestative treatment.*

	Age	End of 1st week (day 7-8)	End of 2nd week (day 13-15)	End of 3rd week (day 20-22)	End of 4th week (day 27-29)
P. L.	23 yrs.	135%	135%	135%	135%
D. E.	22 yrs.	100%	100%	100%	100%
B. A.	24 yrs.	100%	100%	100%	100%
P. R.	22 yrs.	135%	140%	140%	140%
G. D.	25 yrs.	100%	100%	100%	100%
B. M.	26 yrs.	110%	110%	110%	110%
R. P.	26 yrs.	100%	100%	100%	100%
P. P.	21 yrs.	120%	120%	120%	120%
Mean value	112.5%	113.1%	113.1%	113.1%
Range	100-135%	100-140%	100-140%	100-140%
Standard Deviation	15.5	16.6	16.6	16.6

- (day 20-23) 85% (range 75-95%)
- premenstrual phase:
(day 27-29) 89.4% (range 75-100%).

The statistical evaluation of mean values has documented: highly significant decrease of Plasma F. XIII during periovulatory phase when compared with either proliferative phase ($p < 0.001$) or secre-

- end of 2nd week:
(day 13-15) 113.1% (range 100-140%)
- end of 3rd week:
(day 20-22) 113.1% (range 100-140%)
- end of 4th week:
(day 27-29) 113.1% (range 100-140%).

For this group of women no significant differences have been found.

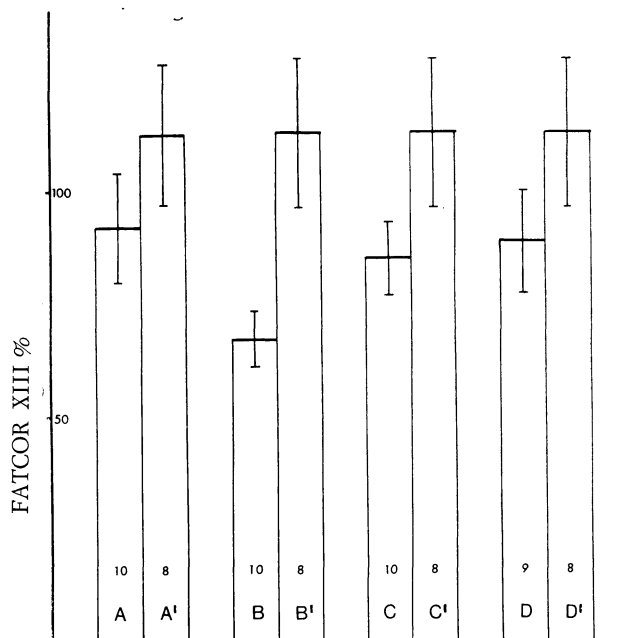


Fig. 1 — Serial detection of plasma-factor XIII levels, mean values: A: Proliferative phase (day 6-10); A': End of 1st week (day 7-8); B: Periovulatory phase (day 13-15); B': End of 2nd week (day 13-15); C: Secretive phase (day 20-23); C': End of 3rd week (day 20-22); D: Premenstrual phase (day 27-29); D': End of 4th week (day 27-29). A, B, C, D: normally ovulating women. A', B', C', D': women under treatment with estroprogestative.

tive and premenstrual phases ($p < 0.001$); no significant differences were found between secretive and premenstrual phases and between proliferative and premenstrual phases.

The detection of Plasma F. XIII levels from 8 women under treatment with estroprogestative for birth control resulted in the following mean values:

- end of 1st week from bleeding:
(day 7-8) 112.5% (range 100-135%)

Comparing the mean values of Plasma F. XIII levels of the two groups of women, have been found highly significant differences between periovulatory phase and 2nd week ($p < 0.001$) and between secretive phase and 3rd week ($p < 0.001$), significant difference between premenstrual phase and 4th week ($p < 0.01$), and no significant differences between proliferative phase and 1st week; the mean values resulted higher for the women

under treatment with estroprogestative in every serial sample (fig. 1).

DISCUSSION

Plasma F. XIII levels have shown significantly different values in women under treatment with estroprogestative for birth control when compared with normally ovulating women.

For the latter ones a significative decrease has been found during periovulatory phase, as a result of not constant Plasma Factor XIII levels.

On the contrary, for women under treatment with estroprogestative Plasma Factor XIII levels showed no changes in serial assays, and resulted significantly higher than in normally ovulating women.

Even if a previous study⁽¹²⁾ found no changes in Plasma F. XIII levels for women under estroprogestative treatment for birth control, the results here reported suggest a possible action of steroid hormones on Plasma F. XIII levels, and through it on the last step of coagulation process, the fibrinostabilization.

However it is not yet known the cause of low Plasma F. XIII levels during periovulatory phase (increased utilization or decreased synthesis?) and of its stable higher levels during estroprogestative treatment for birth control.

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