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LHRH Test in Ovariectomized Women with and without Treatment of Sex Hormones

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The modulatory effect of sex hormones on the LHRH test, has been studied on ovariectomized women, randomly divided into groups which received estrogen (E_2), progesterone (P) and E_2 + P respectively. One group was left untreated. Menstruating women in follicular phase were also studied. The LHRH test was performed on all women and FSH, LH levels were measured in the blood.

The LH levels in the blood following the LHRH test showed an increase in all the groups under investigation, including the ovariectomized untreated one. This suggests that, after ovariectomy, the hypophysis does not reach its maximum capacity for gonadotrophin release.

The FSH response to the LHRH test was very low in all the groups studied, including the ovariectomized without treatment. It thus could be suggested that FSH needs other stimuli besides LHRH for its physiological release.

The concentration of sex steroid hormones in blood seems to modify the gonadotrophin response to a dose of LHRH (LHRH test) (1).

Recent studies, performing the LHRH test for the secretion of gonadotrophins have proved that women low oestrogen levels have a small gonadotrophin response after LHRH administration (10, 12). In contrast, the response appears to be amplified if the test is performed on days preceding ovulation (4, 6, 14) when the levels of estrogen are high and when there is a slight progesterone increase.

In order to study the modulatory effect of sex hormones on the LHRH test, we chose women who had undergone an ovariectomy; on whom therefore the influence of steroid and non steroid products from the ovary did not exist.

The women were randomly divided into groups and, except for one untreated group, they received estrogen (E_2), progesterone (P) and E_2 + P respectively. After these treatments the LHRH test was performed and FSH and LH blood levels were measured.

Materials and Methods

Has been studied twenty one women between the ages of 30-40 who, for var-

ious reasons, had undergone an ovariectomy and thirteen menstruating women in follicular phase. Ten ml of blood were collected in menstruating and ovariectomized women. In these last women the blood were collected before the ovariectomy and on the 3th, 5th, 7th, 15th, 30th and 60th days thereafter. When the gonadotrophin rise had been stabilized (day 60). These ovariectomized women were divided into 4 groups:

A) 7 women did not undergo any hormonal treatment. *B*) 6 women were administered 0.1 mg of ethynyl estradiol for a period of 10 days. *C*) 5 women were administered 20 mg of progesterone (dihydrogesterone) for a period of 10 days. *D*) 3 women were administered 0.1 mg ethynyl estradiol for a period of 10 days and 20 mg of progesterone on day 11.

The LHRH test. 100 μg of synthetic LHRH was administered intravenously to all the women under investigation. In women treated the LHRH test was made immediately after treatment. The blood samples to determine FSH and LH were taken just before the injection and at intervals of 20, 60, 90 and 120 minutes thereafter.

Sample collection and methods. The blood samples, after coagulating at room temperature were centrifugated in order to obtain serum which was frozen at —20° C until the analyses were performed. The FSH and LH concentrations were measured by RIA using Cea-Ire-Sorin kits without modification. The coefficients of variation of these methods were 7 % and 14 % respectively.

Statistical study. The statistical analysis of the results was done using the Student's paired «t» test.

Results

The serum level of FSH and LH increased significantly after the 5th and 7th

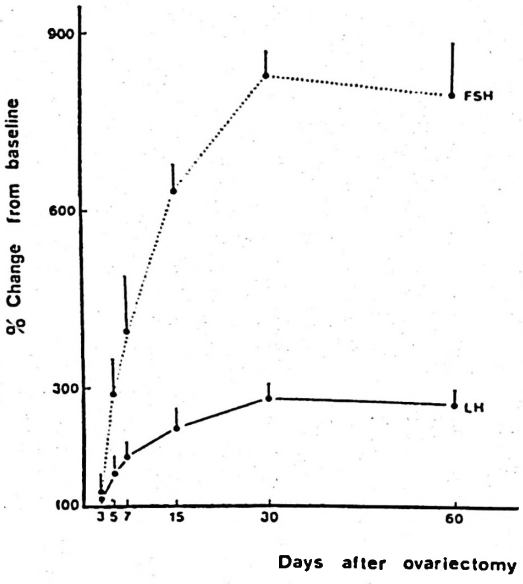

Fig. 1. *Plasma levels of LH and FSH after ovariectomy.*
The data are expressed as mean ± SE.

Table I. *LH Response to LH-RH in ovariectomized and menstruating women.*
The data are expressed in ng/ml and as M ± SDM.

Subject	N.°	Basal	20′	60′	90′	120′
Ovariectomized women						
Without treatment	7	12.4±3.8	40.0±14.6 **	41.3±14.6 **	35±13 **	28±11 **
Treated with E_2	6	7.4±2.0	17.8±7.0 **	26.2±6.0 **	29.2±6.0 **	29.7±4.0 **
Treated with P	5	9.48±2.6	22.0±9.0 **	26±9.7 **	23±8.4 **	16.2±5.0 **
Treated with E_2 + P	3	9±2.6	54±12 **	47±14.4 **	37±11.5 **	32±11.3 **
Menstruating women	13	2.98±0.3	13±2.12 **	11±1.65 **	8.5±1.6 **	5.4±0.3 **

** $p < 0.01$.

Table II. *FSH Response to LH-RH in ovariectomized and menstruating women.* The data are expressed in ng/ml and as M ± SDM.

Subject	N.°	Basal	20′	60′	90′	120′
Ovariectomized women						
Without treatment	7	21±5.6	28±7.6	32±9.2 *	33±9.3 *	29±7.1
Treated with E_2	6	8.2±2.0	8.3±1.0	11.2±3.0	11.9±3.0	12.6±2.0
Treated with P	5	13.5±3.7	17.4±6.0	17.5±3.8	17.8±5.2	17.5±7.0
Treated with E_2 + P	3	12.8±1.2	23.6±5.6 *	22±8.0 *	22±5.6 *	22.6±3.0 *
Menstruating women	13	2.28±0.26	3.66±0.58 *	3.84±0.53 *	3.23±0.46 *	2.12±0.2

* $p < 0.05$.

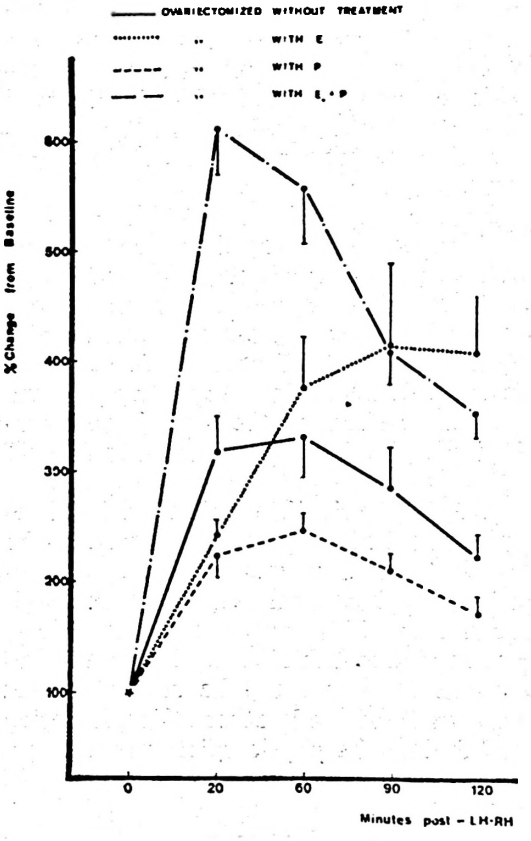

Fig. 2. *Effect of E_2, P and E_2 + P pretreatment upon LH response to LHRH in ovariectomized women.*
The data are expressed as mean ± SE.

days respectively postovariectomy. Both gonadotrophins reach a plateau after day 30 (fig. 1).

Table I shows the LH response to LHRH test in ovariectomized and menstruating women in absolute values. After administration of LHRH the levels of LH in the blood increased significantly as compared to the basal values on the minutes 20, 60, 90 and 120, in all the groups.

Table II shows the FSH response to LHRH test in ovariectomized and menstruating women in absolute values. After administration of LHRH test the levels of FSH in the blood increased significantly as compared to the basal values on the minutes 20, 60, 90 and 120 in the group treated with E_2 + P. In the group without treatment the levels of FSH increased significantly on the 60 and 90 min. In the group of menstruating women the FSH levels increased significantly on the 20, 60 and 90 minutes.

The LH response to the LHRH test in all the groups of ovariectomized women studied is expressed as a percent of the basal value. The maximum LH secretion is recorded 20 min after the test in the women treated with E_2 + P (fig. 2). In the remaining groups there is a maximum LH secretion between 20 and 60 min with the exception of the group treated with E_2 whose maximum secretion is recorded 90 min after the LHRH.

Figure 3 shows the FSH response to LHRH in all the groups of ovariectomized are women. These responses are more lower than LH responses. The maximum FSH secretion is recorded on the group treated with E_2 + P.

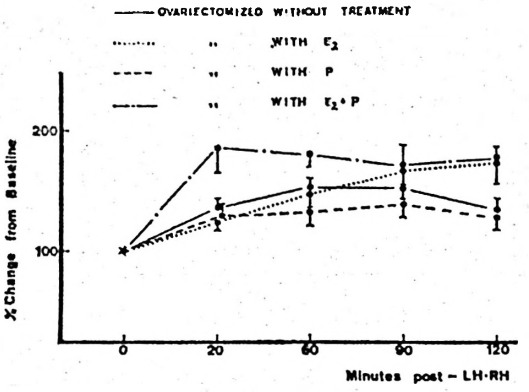

Fig. 3. *Effect of E_2, P and E_2 + P pretreatment upon FSH response to LHRH in ovariectomized women.*
The data are expressed as mean ± SE.

Discussion

Our results show that there is a rise in the LH blood levels after the administration of LHRH in all the groups, including the one which did not receive any treatment. Menopausal women show a similar response (unpublished observation).

This suggests that after the ovariectomy, when the hypothetic negative feedback produced by the ovarian hormones does not exist (fig. 1), the hypophysis does not reach its maximum capacity for gonadotrophin release. It is clear on the other hand that the gonadotrophin concentration in the blood has reached a plateau 30 days after the ovariectomy when oestrogen and progesterone levels are very low in the blood, results which agree with others previously published (2, 15, 16). This raise the questions concerning the factors which induce and determine the plateau of gonadotrophin in the blood of these women.

The gonadotrophin plateau could be due to the stabilization of LHRH caused by the adaptation of the neurons to the steroid hormones produced by the adrenal cortex. A further possibility is that the LH-RH needs the collaboration of high steroid hormone levels in order to stimulate the gonadotrophin cells to their maximum (5, 7, 9).

There is a delay in the highest peak of LH caused by the administration of LHRH to the group of women treated with estradiol when compared with the group of ovariectomized women who did not receive any treatment (fig. 2). The same results have been observed by other authors in normal women (11). In the women treated with progesterone (8, 13), a lower response to LHRH is observed (fig. 2), this perhaps being one of reasons for the anovulatory effect of the gestagens.

In the women treated with estradiol and progesterone together, the LH response to LH-RH is the highest (fig. 2). This data is in agreement with that obtained by other authors after the administration of LHRH at ovulation (17). It is possible that these two steroids have a synergic effect on the hypophysis thereby increasing its responsiveness to LHRH (3).

We find it significant that the FSH response to LHRH is very low even in the ovariectomized women who did not receive any hormonal treatment (table II, fig. 3). In this group there was neither estrogen nor inhibine to lower the response. It thus could be suggested that perhaps FSH needs other stimulus beside LH-RH for its physiological release.

Resumen

Se estudia el efecto modulador de las hormonas sexuales sobre la secreción de gonadotrofinas tras la administración de LHRH, en mujeres ovariectomizadas sin tratamiento, tratadas con estradiol (E_2), con progesterona (P) y con E_2 + P, respectivamente. Después de estos tratamientos se hizo el test de LHRH y se midieron los niveles en sangre de FSH y LH. El mismo test se realizó también en mujeres nor-

males en la fase folicular del ciclo ovárico.

En todos los grupos estudiados, incluso en ovariectomizadas sin tratamiento, se observa un aumento de los niveles de LH tras LHRH, lo cual sugiere que después de la ovariectomía la hipófisis no alcanza su capacidad máxima para la liberación de gonadotrofinas.

La respuesta de FSH al test de LHRH es muy baja en todos los grupos estudiados, incluyendo el de ovariectomizadas sin tratamiento. Esto podría sugerir que la FSH necesita otro estímulo además de LHRH para su liberación fisiológica.

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