

GONADOTROPINIC RESERVE IN WOMEN AFFECTED BY HYPERPROLACTINEMIC AMENORRHEA

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SUMMARY

The Authors have evaluated the hypophysis gonadotropic reserve after stimulation by synthetic GnRH (100 ng) in women affected by functional hyperprolactinemia and by prolactin-secreting adenoma.

The LH response was significantly higher in women affected by functional hyperprolactinemia.

The PRL values seem to have no influence on the gonadotropic reserve except for the cases in which the PRL levels were higher than 200 ng/ml. In all these cases a prolactinoma was present.

The FSH response was similar in the two groups considered.

It is well known that we can contemporaneously have a hyperprolactinemic condition and an alteration of the gonadotropic function, with consequent amenorrhea and sterility.

The eventual relations between the two conditions are not till nowadays clear, neither for what concerns the basal conditions of the gonadotropic secretion, nor for the hypophyseal response to the stimulation by synthetic GnRH, expression of the hypophysis gonadotropic reserve. In fact, while some AA. have experimentally noticed that the response to a GnRH stimulation is not directly correlated with the prolactin blood levels or with the eventual presence of a prolactinoma (^{8, 16}), others have observed that we have not only a different response in case of functional hyperprolactinemia and of hyperprolactinemia due to a prolactinoma, but this response is also as smaller as larger is the adenoma (²).

These different points of view have induced us to conduct a research on the argument, controlling the hypophysis gonadotropic reserve by stimulation with synthetic GnRH in hyperprolactinemiae of functional type or due to an adenoma of the hypophysis.

MATERIAL AND METHODS

We have studied 17 women affected by hyperprolactinemic amenorrhea. 10 were affected by a prolactin-secreting adenoma of the hypophysis, diagnosed radiologically and histologically; the other 7 patients had no radiologic sign of sella's alteration.

Age, parity, period of amenorrhea, eventual presence of galactorrhea and thyroid function are shown in table 1.

The research was conducted by injecting rapidly intravenously 100 ng of synthetic GnRH, after an absolute rest of 20 minutes and always between 8 and 10 a.m.. Blood samples were drawn after 0, 15, 30, 45, 60, 90, 120 minutes.

LH, FSH and PRL were dosed by radioimmunoassay, using common kits.

The patients were divided into groups, on the basis of the presence or not of an adenoma and

Table 1.

	name	age (yr)	parity	duration amenorrhea	galactorrhea	prolactin (ng/ml)	FSH (ng/ml)	LH (ng/ml)	Rx skull
1	D. G.	31	0	14 yr	+	55	1,5	1,5	+
2	C. M.	27	0	9 yr	—	75	1,0	0,8	+
3	D. L.	35	0	2 yr	+	110	3,6	1,1	+
4	C. A. M.	32	0	4 yr	—	132	3,1	0,7	+
5	S. F.	30	0	12 yr	—	180	3,7	2,2	+
6	I. D.	35	0	6 yr	+	200	3,7	1,4	+
7	R. M.	33	0	8 yr	+	240	1,6	0,6	+
8	B. C.	31	0	10 yr	+	615	3,5	0,8	+
9	M. A.	28	2	3 yr	+	1585	0,3	0,2	+
10	S. T.	34	1	7 m	+	20	1,8	2,3	—
11	S. A. M.	24	1	2 yr	+	40	1,9	1,1	—
12	M. N.	32	2	2 yr	+	35	1,8	2,3	—
13	L. D.	26	0	9 m	—	80	3,8	4	—
14	M. R.	31	0	8 m	—	59	3,6	4,2	—
15	M. R.	26	0	2 yr	+	160	4,2	6,5	—
16	P. G.	22	0	2 yr	+	170	2,3	1,8	+
17	M. A.	23	0	6 m	—	27	1,7	1,8	—

TSH was normal in all patients; normal values = 2-16 1,8-3,1 2,1-3,2.

also on the basis of the PRL blood levels: moderately high values (from 20 to 49 ng/ml), mildly high (from 50 to 100 ng/ml), remarkably high (100 ng/ml).

RESULTS

Fig. 1 shows the different hypophyseal response to the GnRH test in case of functional hyperprolactinemia and of hyperprolactinemia due to adenoma.

In fact, this response was significantly higher in the first group. As normally happens, the higher increase to stimulation was observed 30 minutes later.

The FSH response to the GnRH test did not point out any significant variation between the two groups examined (Fig. 2).

Fig. 3 shows that the PRL basal level does not influence the test behaviour in the two groups examined; in fact, the response is always higher in functional cases, independently from the PRL values considered.

It is important to notice that in 3 cases of adenoma with PRL levels higher than 200 ng/ml, LH values are always low and the response to the GnRH test is absent.

CONCLUSIONS

The good behaviour of the GnRH test in women affected by functional hyperprolactinemia induces to consider that the defect of the hypothalamus-hypophysis-ovary axis is not at hypophyseal level, where there is a gonadotropic reserve which is normally released after stimulation, but at hypothalamic level for an insufficient or absent GnRH action. If is a matter of a primitive alteration involving contemporaneously the GnRH function and the PIF one and not an inhibiting action of the hyperprolactinemia on the GnRH increment, is still to be defined.

To explain the amenorrhea, besides the mechanism above mentioned, one must

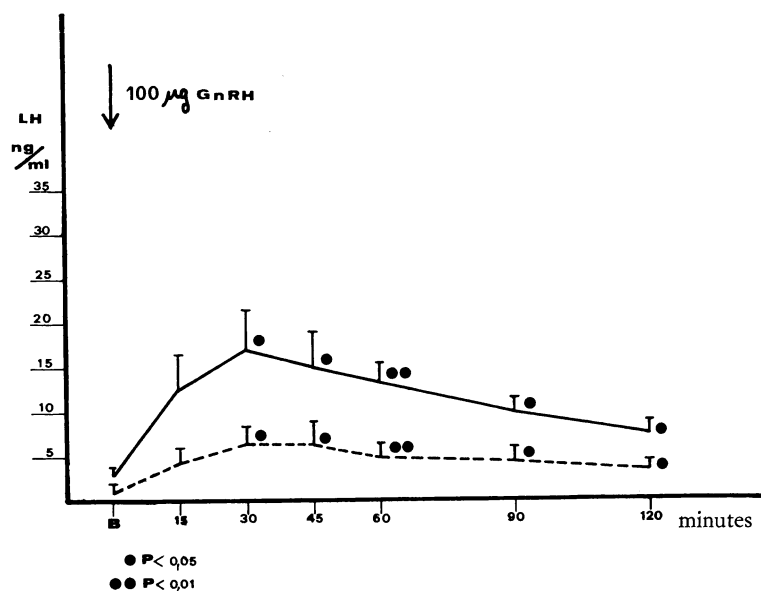


Fig. 1. — Mean plasma LH response to intravenous GnRH injection in 7 women with functional hyperprolactinemia (—) and in 10 women with prolactin-secreting microadenoma (---).

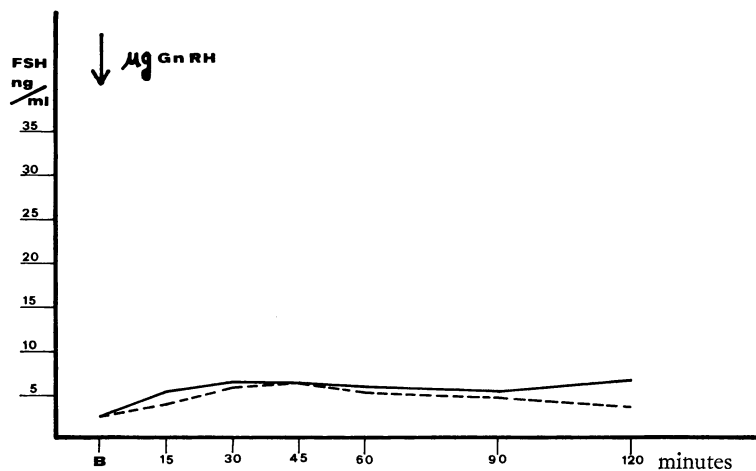


Fig. 2. — Mean plasma FSH response to intravenous GnRH injection in 7 women with functional hyperprolactinemia (—) and in 10 women with prolactin-secreting microadenoma (---).

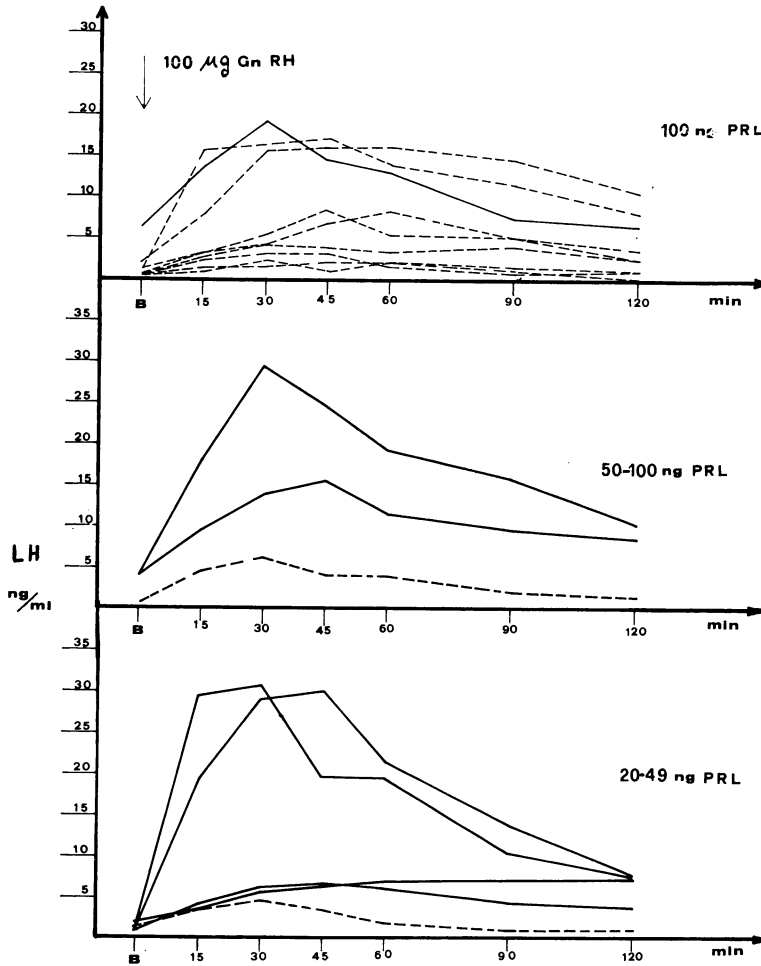


Fig. 3. — Plasma LH response to intravenous GnRH injection in 17 women with functional hyperprolactinemia (—) and with prolactin-secreting microadenoma (----) with varying levels of prolactin: (20-45 ng), (50-100 ng), (100 ng).

also remember the prolactin inhibiting action on the steroidogenesis (^{1, 4, 5}).

On the contrary, in case of prolactinoma, the hypophyseal function seems to be altered, its gonadotropic reserve results to be lower and it seems logical to admit that this is a consequence of the compression mechanism.

The gonadotropic cells would be the first to suffer from this state of things for

topographic reasons (development of the prolactinoma close to the « hypophysis gonadotropic zone ») or by supposition, for the higher biologic vulnerability of these cells in comparison with the other components of the hypophysis.

The compression mechanism seems to be convincing also for the interpretation of the cases of adenoma with PRL blood levels higher than 200 ng/ml in cases in

which, as we have observed, not only the LH basal levels are low, but also the response to the test resulted negative.

In fact, if by supposition there is a relation between functioning mass of the adenoma and quantity of PRL produced, one must retain that to a higher PRL blood level corresponds a higher volume of the tumor and consequently a higher damage due to compression.

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