INHIBITING EFFECT OF ATROPINE ON PROLACTIN BLOOD LEVELS AFTER STIMULATION WITH TRH

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SUMMARY

With this study, the Authors, have demonstrated that atropine has an inhibiting action on the hypophysis response and that such inhibition is correlated to the lenght of time between the i.m. injection of anticholinergic and the intravenous administration of TRH.

Such results make believe that in human, as in the animal the cholinergic system plays a role, maybe important, in the prolactin release.

The neural influences on prolactin secretion (HPRL) are mainly of inhibiting type.

In fact it is well known that deconnexion of the hypophysis from the Central Nervous System (CNS) causes a rise in the plasmatic HPRL levels.

This and other experimental situations have suggested that in the hypothalamus there is a prolactin inhibiting factor (PIF), which would be present in higher concentrations in the medial eminence, near to the supraoptic nucleus.

The role of cathecolamines in the control of prolactin secretion is a very studied problem.

Concerning dopamine, is now widely ascertained that it exerts an inhibiting action.

In fact, it is well known that dopaminergic drugs as L-DOPA ([9]), apomorphine ([10]) and particularly bromocryptine ([5]) cause a decrease in the plasmatic prolactin levels both in normal and hyperprolactinemic subjects. On the other hand the administration of drugs with an antidopaminergic action as sulpiride and metoclopramide ([8]) is followed by a rapid rise of prolactinemia.

Concerning the role of histamine on prolactin secretion, it has been recently showed that the intraventricular injection of H_2 blocking can cause a HPRL rise ([1]).

In agreement with these observations, the intravenous injection, in normal subjects, of cimetidine stimulates the prolactin release ([3]).

It seems that serotonine, in opposition to dopamine, has a stimulating effect on the HPRL release, in fact, the administration of methysergide and methergoline, well known antiserotonin drugs, can reduce the prolactin rise during the lactation ([16]).

Recent studies suggest that even γ-aminobutyric acid (GABA) can increase the prolactin release ([14]).

Finally, even the intraventricular injection of endorphine and enkephaline stimu-

Table 1. — *Prolactin blood levels after the administration of 200 μg of TRH.*

Time	Men	Women
0 (basal)	4,5 ±0,80	7,5 ±0,45
20′	21,4 ±1,88	30,7 ±1,32
30′	24,28±1,36	54,68±1,42
60′	20,01±1,72	35,83±1,04
90′	13,25±1,04	22,48±1,15
120′	6,48±0,84	12,31±0,75
180′	5,23±0,61	8,4 ±0,80

lates the release of prolactin, this response is blocked by naloxone, a drug which blocks the opiate receptors ([3]).

The aim of our study is to verify, in human, an eventual action of the cholinergic system on the prolactin release.

MATERIAL AND METHODS

Our research was conducted on 12 adult healthy women, not affected by endocrinologic diseases, aged between 20 and 35 years, and on 12 adult men, healthy and not affected by endocrinologic diseases, aged between 25 and 46 years.

The phases of our research were:

1) At 8 a.m. the 24 volunteers, in conditions of absolute rest and fasting since midnight of the day before, underwent the test with 200 micrograms of intravenous TRH. The blood samples for the HPRL dosages were drawn at o' (basal), 20′, 30′, 60′, 90′, 120′, 180′.

2) One week later the 24 volunteers, under the same condition, received again 200 micrograms of TRH, preceded by an intramuscular injection of 1 mg of atropine 10 minutes before the test.

The blood samples for the HPRL dosage were drawn at time 0 (basal pre-atropine), 10 minutes after the injection of atropine and just before the TRH one, at 20′, 30′, 60′, 90′, 120′, 180′.

3) One more week later, the 24 volunteers received 200 micrograms of TRH, preceded by the administration of 1 mg of atropine 2 hour before the test.

The blood samples for the HPRL dosage were drawn at time 0 (basal pre-atropine), 1 hour after atropine and just before the TRH, then at 20′, 30′, 60′, 90′, 120′, 180′, from the beginning of the stimulation test. The HPRL was dosed by radioimmunoassay. The statistical analysis was conducted by « t » student test.

RESULTS

In the first phase (tab. I and fig. 1), both men and women have a normal response of the HPRL to the stimulation test.

In the second phase (tab. II and figure 2), after the test with TRH preceded 10 minutes before by the administration of 1 mg of atropine, both groups have showed a notable decrease in the prolactin response to TRH.

On the contrary, in the third phase, in which the anticholinergic was administered 1 hour before the TRH test, no inhibiting effect was observed in the prolactin release (tab. III and fig. 3).

DISCUSSION

The results reported on the relation between acetylcholine and prolactin are contradictory.

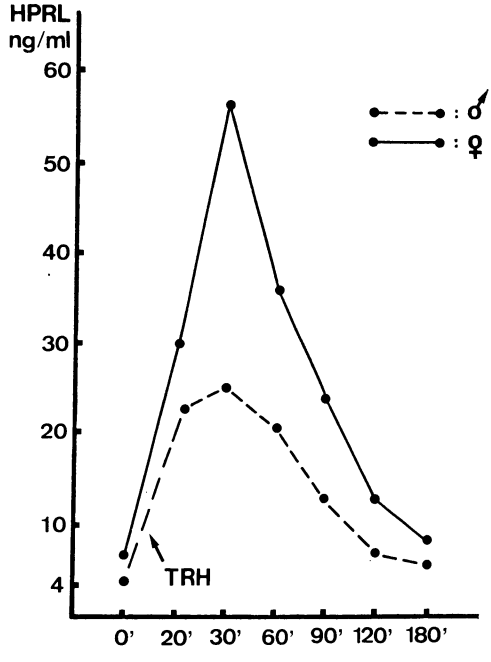

Fig. 1. — PRL blood level after the administration of 200 μg of TRH.

Table 2. — *Prolactin blood levels after the administration of 200 μg of TRH, preceded by 1 mg of atropine i. m. 10 minutes before the test.*

Time	Men	Women
0 (basal pre-atropine)	3,71±1,08	6,51±0,92
10′ (after atropine and pre-TRH)	4,11±0,71	6,92±0,81
20′	5,44±1,27	13,10±1,2
30′	9,92±0,47	23,21±1,92
60′	6,63±0,95	18,07±0,42
90′	4,85±0,78	14,71±1,18
120′	4,64±0,14	11,18±1,06
180′	3,90±0,72	8,02±0,75

Grandison ([6]) and Grandison and Meites ([7]) report that acetylcholine lowers the HPRL levels in the rat. According to McCann ([12]) inhibiting effect occurs even using eserine, and it is blocked by treating the animals with sulphate atropine, a drug which can pass the haemato-encephalic barrier.

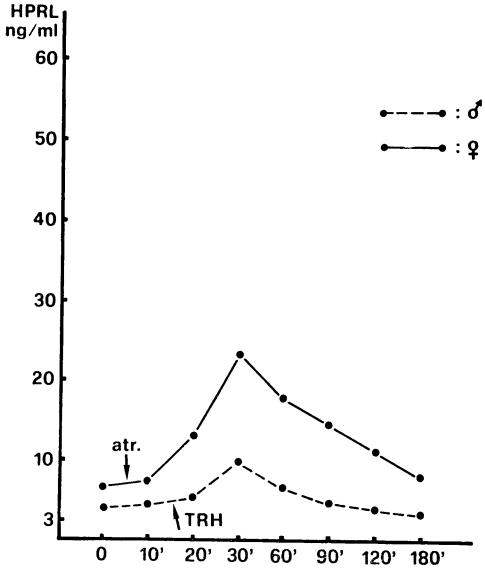

Fig. 2. — PRL blood levels after the administration of 200 μg of TRH, preceded by 1 mg of atropine i.m. 10 minutes before the test.

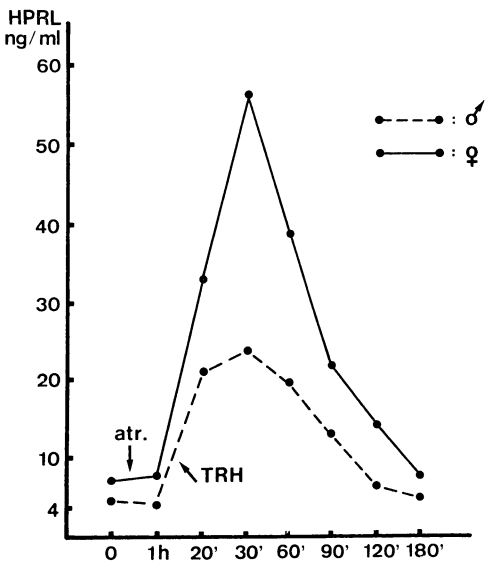

Fig. 3. — PRL blood levels after the administration of 200 μg of TRH, preceded by 1 mg of atropine i.m. 60 minutes before the test.

According to Mc Cann ([12]) these cholinergic drugs exert their effect at CNS level on the muscarinic receptors, probably involving the dopaminergic system.

In fact the systemic administration of pilocarpine and the intraventricular ad-

Table 3. — *Prolactin blood levels after the administration of 200 μg of TRH, preceded by 1 mg of atropine 60 minutes before the test.*

Time	Men	Women
0 (basal pre-atropine)	4,67±0,56	7,84±1,2
1 h. (after atropine and pre-TRH)	4,38±0,41	7,91±2,1
20′	20,91±1,40	32,1 ±2,15
30′	23,8 ±1,05	56,31±3,12
60′	19,8 ±1,92	37,1 ±2,98
90′	13,75±0,25	21,89±2,32
120′	6,58±0,28	14,21±2,92
180′	5,07±0,37	9,6 ±1,98

ministration of acetil-choline do not modify the HPRL levels in animals pretreated with pimozide or alpha-methyl-tyrosine; however pimozide reestablishes the response to stress which was abolished by pilocarpine. In contrast with these results, atropine can prevent the HPL surge in the premenstrual phase.

Furthermore, Mc Lean ([13]) reported that high doses of atropine inhibit the HPRL nocturnal surge, effect which was blocked by the pretreatment with eserine.

Our studies conducted in order to show an eventual interference of atropine on prolactin normal response to the stimulation test with TRH, have clearly demonstrated that atropine has an inhibiting action on the hypophysis response and that such inhibition is correlated to the lenght of time between the intramuscular injection of anticholinergic and the intravenous administration of TRH.

In fact, administering atropine 10′ befor the stimulation test a clear inhibiting effect on the prolactin response to TRH was observed. On the contrary, the injection of atropine one hour before the test, did not show modifications in comparison to the only administration of TRH.

Under a statistical point of view, the « t » Student test carried out between the averages of the first phase values and the averages of the second phase values, has pointed out a statistical significance, for a $P<0.001$, among all the comparisons, except for the averages of the values at time 0, in men.

In the women it was noticed a statistical significance between the averages of the first phase values and those of the second one, fo a $P<0.001$, only in the central times, while the comparison between the averages of time 0 and 180′ are significative for a $P<0.005$.

On the contrary, no significance was observed between the first and third phase of the experiment both in men and women.

In conclusion our results show that in human, as in the animal, the cholinergic system plays a role, maybe important, in the prolactin release.

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