PROLACTIN PLASMA LEVELS AND ORAL CONTRACEPTIVES AT LOW DOSAGE

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SUMMARY

In the present study the Authors consider whether estroprogestins at low dosage may influence the basal levels of plasma Prolactin in a group of patients subdivided on the basis of their different ways of life. The results show that oral contraceptives containing 30 microgrammes of EE do not induce modifications on PRL levels; however these are significantly ($p \leqslant 0.01$) lower in the smoker group. It has therefore been hypothesised that smoke may interfere with the regulatory mechanisms of PRL, even if the practical effects of such action in the ambit of the physiopathology of reproduction is not yet clear.

After the first indication by Shearman (1966) ([1]), numerous other Authors ([2, 3]) reported in literature cases of hyperprolactinemia, amenorrhea, and sometimes galactorrhea after estroprogestin treatment.

The estrogens can in fact increase both the synthesis and the release of PRL ([4]), with a dose-dependent effect; this explains the higher plasma levels that are met in the female sex in physiological conditions such as the post-puberal age ([5]), the phase of ovulation ([6]) and pregnancy ([7]).

The administration of exogenous estrogens in fact induces significant increases in prolactin levels ([8]) and the successive stimulation with TRH produces further increases both at basal levels and at the prolactin peak ([9]).

We have therefore thought it opportune, considering the vast diffusion of these compounds of contraceptive aim, to enquire if estroprogestins at low dosage may also have an influence on the plasma levels of prolactin in a group of normal patients.

MATERIAL AND METHODS

Our study was carried out on 110 normoprolactinemic women, of ages comprising 18 to 40 years, who came to our out-patients departments for contraceptive advice.

All the patients had taken an estroprogestin compound containing 0.15 mg of Levonorgestrel and 0.03 mg of ethinyl estradiol for a period of time varying from a minimum of 24 to a maximum of 36 months.

These were divided into three groups on the bases of their ways of life. In the 1st group, formed of 55 women, we included those who were taking only oral contraceptives (OC); in the 2nd group, consisting of 30 subjects, those who were taking oral contraceptives and who smoked 10 or more cigarettes a day (OC+smoke); and in the 3rd group, composed of 25 subjects, those who, besides oral contraceptives habitually drank alcoholic beverages (OC+alcohol).

The dosage of plasma Prolactin was determined before and after treatment, with samples at 8 in the morning during the first phase of the menstrual cycle. The assay was carried out by RIA with the double anti-body method. The

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TABLE 1. — *Plasmatic levels of PRL in patients treated with oral contraceptives at low dosages.*

Group	No. cases	Period of dosage	Average ng/ml	D.S.	Δ
OC	55	Before treatment	10.67	±3.20	
		After treatment	10.91	±4.76	—
		Difference	0.24	n.s.	
OC + smoking	30	Before treatment	8.92	±2.59	
		After treatment	8.77	±3.16	2.14 **
		Difference	0.15	n.s.	
OC + alcohol	25	Before treatment	10.80	±2.82	
		After treatment	10.40	±4.21	—
		Difference	0.40	n.s.	

OC : Group taking oral contraceptives at low dosage.
n.s. : Insignificant statistical difference.
** : Difference statistically significant by $p<0.01$.
Δ : Difference in respect to the group taking only OC.

normal range for our laboratory varies from 5 to 25 ng/ml.

The data obtained were elaborated according to the method of the analysis of variance.

RESULTS

The results obtained are summarized in table 1.

In the 1st group (OC) the average value of plasma Prolactin gave the result of 10.67 ± 3.20 ng/ml before treatment and 10.91 ± 4.76 ng/ml after treatment.

There was no significant statistical difference.

In the 2nd group (OC + smoke) the average value of plasma Prolactin was 8.92 ± 2.59 ng/ml before treatment and 8.77 ± 3.16 ng/ml after treatment.

There was no significant statistical difference.

In the 3rd group (OC + alcohol) the average value of plasma Prolactin was 10.80 ± 2.82 ng/ml and 10.40 ± 4.21 ng/ml, respectively before and after treatment.

There was no significant statistical difference.

The comparisons among the various groups showed a significantly statistical difference of $p \leqslant 0.01$ in the 2nd group (OC + smoke), where the Prolactin levels gave results inferior to the other two groups.

In all the cases, however, the plasma values of Prolactin were within the limits of the normal range.

DISCUSSION

From the results obtained it seemed clear in our series that treatment with oral contraceptives of low dosage had not significantly modified the basal value of Prolactin in the various groups examined.

Several Authors ([10, 11, 12]) have clearly demonstrated that the administration of estroprogestins containing not more than 50 microgrammes of ethinylestradiol does not increase prolactinemia.

In a study undertaken by Mishell *et al.* ([13]), using different combinations of estroprogestins, no significant differences at all emerged in the basal levels of Prolactin between the group taking OC and the control group; however a statistically significant increase was noted in the release of PRL after dynamic tests with hypoglycemia and with TRH in the group

that had been using OC for a long period of time.

In a recent work ([14]) carried out on patients who took OC containing 150 micrognammes of Levonorgestevel and 30 micrognammes of Ethinylestradiol, an increase in Prolactin levels was reported only in the group of patients who had shown hypertension during the course of estroprogestin treatment.

In our study we met with neither cases of hypertension nor modifications of basal levels of Prolactin.

On the other hand we noticed a diminution of prolactinemia in the 2nd group of our patients (OC+smoke).

It is not easy for us to give a reliable explanation of this datum; the most plausible hypothesis is that smoke interferes at the level of the hypothalamic neurotransmitters, both directly, and through the regulatory system of the PIF, causing an inhibitory effect on the release of PRL.

However, Andersen and Schioler ([15]), in a study carried out on puerperae during nursing, noted a statistically significant reduction in Prolactin levels among the smokers compared with the non-smokers. In agreement with these results various epidemiological studies ([16]) have shown that women who smoke cigarettes nurse their babies for a shorter period than the non-smokers; besides, in studies ([17, 18]) carried out on animals it appeared that nicotine inhibits the response of PRL to lactation.

In conclusion, these data of ours allow us to affirm the absolute safety of the use of OC in low dosage, since they have not shown any significant effect on the release of PRL, and they suggest a reflection on the reduction of PRL in smokers, an effect which deserves further study.

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