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Effect of Neonatal Testosterone Administration and Beta Adrenergic Stimulation on Adult Prolactin Levels

Neonatal administration of testosterone to female rats induced anovulation in adulthood (1). In these animals, hyperprolactinemia has been described (3). The effectiveness of neonatal steroid administration can be blocked by the simultaneous administration of drugs as reserpine and chlorpromazine (2), tyramine and alpha adrenergic blockers as phentolamine and phenoxybenzamine (5). The mechanism for this protection could be the indirect activation of beta postsynaptic receptors leading to a decrease in hypothalamic testosterone aromatization (6). The present work tries to clarify the relation between anovulation and hyperprolactinemia in neonatal androgenized female rats, and the influence of neonatal noradrenergic manipulation in both alterations. Beta adrenergic receptors were stimulated indirectly, by blocking the presynaptic alpha-2 receptors with yohimbine and increasing thereby the norepinephrine release into the synaptic cleft, or directly by administering the beta agonist orciprenaline.

Female Wistar rats were maintained under controlled light (12 h light - 12 h darkness) and temperature (20 °C). Table I summarizes the different treatments performed in this experiment. Systemic injections were given in a volume of 100 μl, and the intraventricular injections according to NOBLE'S technique (4) were all in a volume of 5 μl. Anovulation was defined as ten or more consecutive days of smears showing cornified cells accompanied by the absence of fresh corpora lutea in the ovaries. The rats were decapitated around the day 100 in the morning of an estrous day. Trunk blood was collected and prolactin in plasma determined in triplicate using a NIAMDD kit. The values were expressed in ng/ml of the reference preparation NIAMDD-Rat-RP-1. All samples were run in the same assay, being the sensitivity 0.1 ng and the intraassay variation 8 %. Results are expressed as means ± SEM. The differences between prolactin levels were analyzed using the analysis of variance and the pairwise test (7) and the differences in the incidence of anovulation were analyzed by X^2.

Neonatal administration of olive oil or NaCl does not induce any change in vaginal cycle nor in Prl values (groups 2 and 3). Orciprenaline adminestered subcutaneously (groups 5 and 6) or intraventricularly (group 7) were also uneffective, indicating that beta adrenergic stimulation during the hypothalamic differentiation period does not affect the organization of the control of gonadotropin and prolactin secretion. Although elevated prolactin levels have been reported in anovulatory syndromes of most origins in the rat, the results now presented show that anovulation induced with low doses of testosterone (25 μg) (group 4) is not associated with hyperprolactinemia.

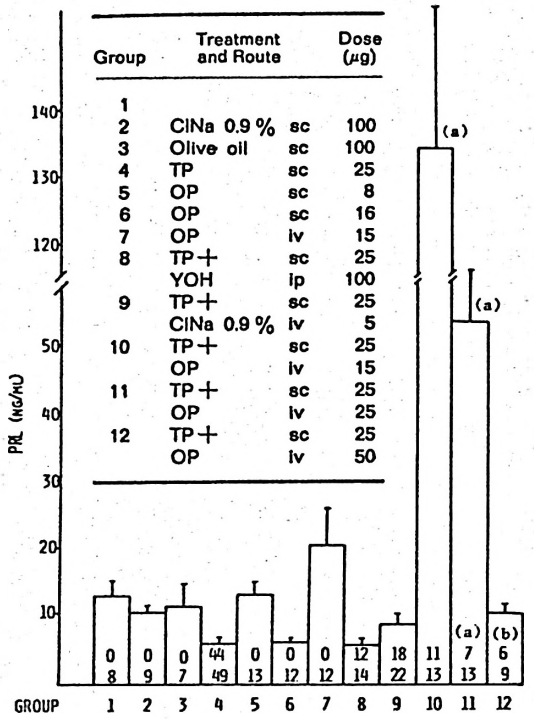

Fig. 1. *Prolactin (PRL) plasma levels and incidence of anovulation in control and experimental groups.*

In the bottom of each bar the number of animals showing anovulation over the total is expressed. (a) $p < 0.01$ and (b) $p < 0.05$ *vs* group 4 respectively. TP = Testosterone propionate; OP = Orciprenaline; YOH = Yohimbine hydrochloride; sc = subcutaneously; iv = intraventricularly; ip = intraperitoneally. The drugs were injected at 10.00 h of day 4, except in groups 5, 6 and 8 (YOH) in which the total dose was administered in four injections (10 and 22 h of days 4 and 5).

Orciprenaline injected intraventricularly in androgenized females induced a biphasic effect depending on the dose used. The lower dose (15 μg) increased ($p < 0.01$) the prolactin levels, without any effect on the incidence of anovulation (group 10). Animals treated with TP and 25 μg of orciprenaline (group 11) showed hyperprolactinemia ($p < 0.01$) and a significant reduction ($p < 0.01$) in the incidence of anovulation. Finally, animals injected with TP and 50 μg of orciprenaline (group 12) showed a reduction in the incidence of anovulation ($p < 0.05$) without changes in Prl values (fig. 1). These results suggest that the two effects of androgens neonatally administered i.e. induction of anovulation and modifications in the mechanisms controlling prolactin secretion, are independent and respond in a different fashion to simultaneous beta adrenergic stimulation. The exact mechanism of the interaction between testosterone and the different doses of orciprenaline remains uncleared.

Key words: Prolactin levels, Testosterone.

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