

OVARIAN AND UTERINE CHANGES INDUCED BY
BROMOCRIPTINE INJECTION TO
PSEUDOPREGNANT RATS

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SUMMARY

Administration of bromocriptine (100 µg) to rats on day 7 of pseudopregnancy (P.P.) caused a marked reduction in P.P. length associated with a significant reduction in ovarian weight and an increase in uterine weight. Structural changes included: a marked increase in the percentage of both antral follicles and atretic corpora lutea, endometrial lining height, stromal and myometrial thickness. The results reaffirm prolactin role in maintaining rat luteal function.

INTRODUCTION

Prolactin has been shown, long ago, to be luteotrophic in the rat, since it is essential for induction and maintenance of P.P. and early pregnancy (Shaik and Yoshinaga, 1970). The role of prolactin has been a subject of controversy in recent years. Serum prolactin level rises only for the first 2-3 days after induction of P.P. and then declines to a very low level (Bast and Melampy, 1972). Moreover, it has been found that P.P. can be induced in the rat even if the initial

rise in serum prolactin was inhibited by injecting ergocornine (Wuttke and Meites, 1972).

In the present investigation bromocriptine, dopamine agonist (Besser and Thorner, 1976) and antiprolactin (Ectors et al., 1972) was injected into pseudopregnant rats for the purpose of obtaining more information on prolactin role in controlling luteal function.

MATERIALS AND METHODS

Twenty adult (8-12 week old) female rats of Wistar strain weighing 200-240 gm were used. They were kept in a temperature (22-26 °C) and light (14 hr light, 10 hr darkness) controlled room. Rats were given the standard dry pellets (Etafia animal feed factory, Baghdad) and tap water *ad libitum*.

Estrous cycles of the experimental rats were followed by vaginal smearing for at least 2 weeks and only regular cyclers were included in the experiment. Bromocriptine* was diluted in physiological saline and injected subcutaneously daily on day 7 of P.P. at a dose of 100 µg, while control animals received physiological saline through the same route. Pseudopregnancy was induced by keeping females, in the afternoon of pro-estrous, overnight with vasectomized males. The day after was considered as the 1st day of P.P. Ten of the rats (5 treated and 5 control) were left till the end of P.P. The remaining ten (5 treated and 5 control) were sacrificed on day 9 of P.P.

Animals were weighed before being sacrificed by neck dislocation. Ovaries and uteri were quickly removed, weighed and then fixed in Bouin's fluid. Tissues were processed in histokinate using routine procedure of

* Paralodel® ; Sandoz AG, Basel, Switzerland.

dehydration, sectioned at 5 μ m (serial sections for ovarian tissue only) and stained with haematoxylin and eosin.

Number of antral and atretic follicles, intact and atretic corpora lutea (C.L.) were counted. Endometrial epithelial lining height, stromal and myometrial thickness were measured. Results were statistically analysed using student's t-test (Shedecor and Cochran, 1967).

RESULTS

The results of this experiment as summarized in table 1 showed that the length of P.P. was significantly shortened ($P < 0.01$). The average length was 10.3 ± 0.61 days in the treated rats compared to 12.7 ± 0.16 in the control.

Table 1 : Effect of bromocriptine on the length of P.P., ovarian and uterine weights in rats.
values are mean \pm standard error.

* $P < 0.01$

group	length of P.P./days	ovarian weight mg/100 gm B.W.	uterine weight mg/100 gm B.W.
control	12.7 ± 0.16	56.56 ± 2.16	121.46 ± 6.19
treated	$10.3 \pm 0.61^*$	$40.84 \pm 0.68^*$	153.83 ± 5.07

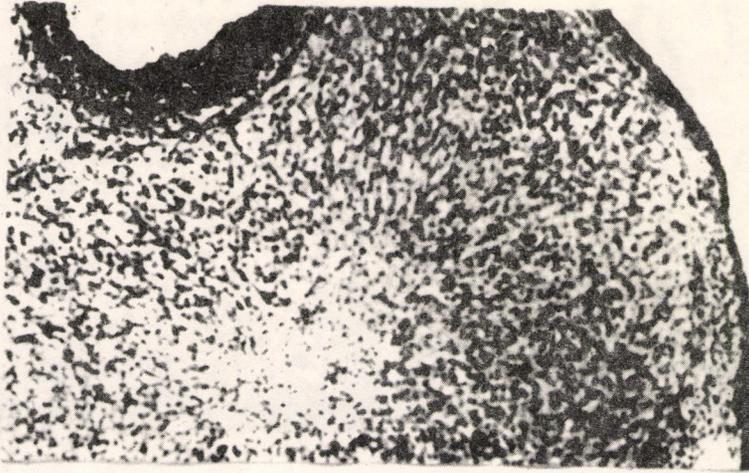


Fig.1: A section in an ovary of treated rat showing degenerating corpus luteum (x 100).

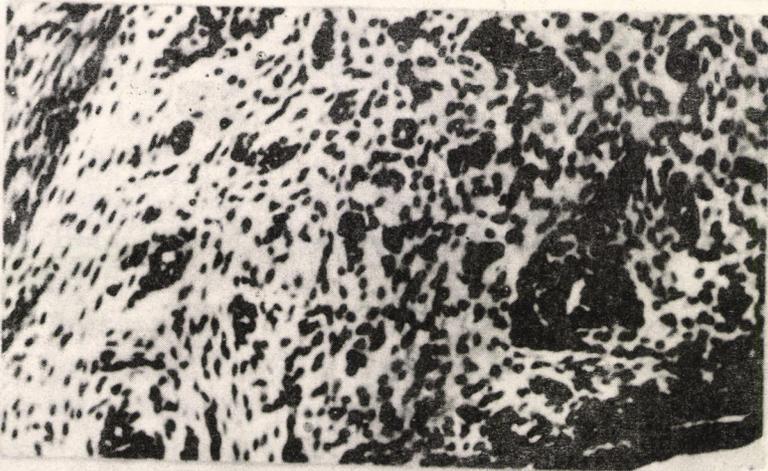


Fig.2: Transverse section in the uterus of a control rat (x 230).

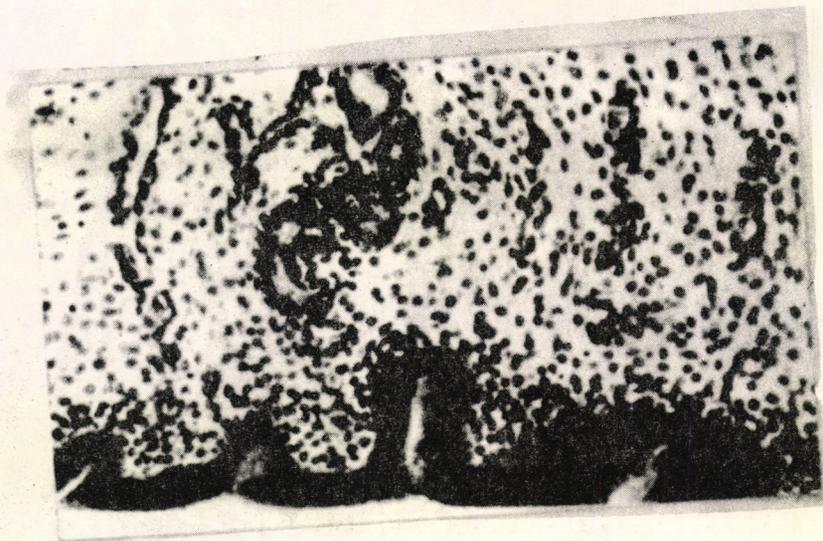


Fig.3: Transverse section in the uterus of a treated rat showing clear endometrial development (x 230).

There was a significant reduction ($P < 0.01$) in ovarian weight in the treated rats compared with the control while uterine weight showed a significant increase ($P < 0.01$) (table 1).

Structural changes in the ovaries of treated rats reflected a marked increase in the percentage of antral follicles accompanied by a decrease of the same magnitude in the percentage of atretic follicles compared with the control (table 2). Percentage of intact and degenerated C.L. showed a marked increase in the treated rats as compared with the control (table 2 and fig.1).

Uterine changes included a significant increase ($P < 0.05$) in both endometrial lining height and myometrial thickness in treated rats as compared with control (table 2, fig.2 and 3). However, endometrial thickness showed an insignificant increase in the treated animals.

Table 2: Ovarian and uterine changes associated with bromocriptine (100 µg) injection daily to rats on day 7 of P.P. and killed on day 9.

group	ovarian changes		uterine changes (µm) *		
	Percentage of follicles	percentage of corpora lutea	lining	stroma	myometrium
control	70.8	29.2	7.863 ± 0.294	102.44 ± 5.643	54.6 ± 0.318
treated	85	15	8.571 ± 0.24	126.0 ± 6.847	80.66 ± 6.187

* P < 0.05
values of uterine thickness are mean ± S.E.

DISCUSSION

Results of the present investigation provided further evidence supporting the hypothesis concerning the vital role of prolactin in maintaining rat P.P. The significant reduction in the length of P.P. as a result of bromocriptine administration, seems to agree with previous reports using similar prolactin inhibitors (Meites *et al.*, 1972; Janssens, 1986). Inhibition of prolactin release as a result of bromocriptine administration may have caused a reduction in luteal support, since prolactin is known to be the major luteotrophic hormone in rodents (Canong, 1985). The decrease in luteal function in the treated rats was evidenced by the marked decrease in the percentage of intact C.L. accompanied by an increase of the same magnitude in the percentage of atretic C.L. Reduction in luteal function may explain the significant reduction in ovarian weight in treated rats, since C.L. are known to constitute the major part of ovarian weight (Malven, 1969).

The significant increase in uterine weight in treated rats, on the other hand, is a clear indication of an estrogenic effect (Welschen *et al.*, 1975). Increased estrogenic level may have been brought about in the treated rats by FSH released after removal of the negative feedback exerted by prolactin on FSH release (Campbell and Schwartz, 1977).

It is well known (McDonald, 1975), that FSH stimulate follicular growth. High level of FSH brought about by prolactin secretion inhibition as a result of bromocriptine administration may have been the reason behind the increased percentage of antral follicles and the decrease in percentage of atretic follicles. The marked increase in the percentage of atretic follicles in

the control rats may be attributed to the effect of prolactin on ovarian follicles. It is known that a high serum level of prolactin in the rat is associated with a decrease in follicular activity and an early appearance of follicular atresia (Uilenbroek and Linden, 1984).

All uterine changes obtained as a result of bromocriptine administration are clearly indicative of increased estrogen secretion (Madjerek, Z.S. 1971), brought about by increased FSH secretion.

In conclusion, results obtained in this investigation reaffirm once again the importance of prolactin for normal activity of rat corpus luteum.

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تغيرات مبيض ورحم الجرذان في حالات الحمل الكاذب

المرافقة لحقن البروموكريبتين

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الخلاصة

حقنت اناث جرذان بالغة في اليوم السابع من الحمل الكاذب
بجرعة 100 مايكروغرام من مادة البروموكريبتين. اظهرت النتائج
اختزال واضح في طول فترة الحمل الكاذب في كافة الحيوانات
المعاملة ورافق ذلك انخفاض معنوي في وزن المبيض وزيادة في كل
من وزن الرحم والنسبة المئوية للجريبات ذات التجوييف والنسبة
المئوية للاجسام الصفراء المتكسدة وسماك بطانة الرحم وخلايا المنطقة
السدوية بالاضافة الى عزل الهرم. تؤكد هذه النتائج اهمية هرمون
البرولاكتين للمحافظة على فعالية الجسم الاصفر في الجرذان.