SHORT COMMUNICATION

EFFECT OF SOME ANTIHISTAMINIC DRUGS ON THE OESTROUS CYCLE OF RATS

K. SAMBASIVARAO AND M. SABIR

Division of Pharmacology & Toxicology,
Indian Veterinary Research Institute, Izatnagar-243122

Summary: The effect of some antihistaminic drugs namely antazoline hydrochloride, diphenhydramine hydrochloride and mepyramine maleate has been investigated on the oestrous cycle in albino rats. On daily intraperitoneal administration, for 6 days, all the three drugs (10 *mg/kg*) significantly ($P<0.001$) prolonged the duration of oestrous cycle. The duration of subsequent cycle returned to near normal.

Key words: oestrous cycle, antihistaminics, histamine involvement, oestrogen action

INTRODUCTION

Histamine has been reported to play some role in the mediation of the actions of reproductive hormones (5, 6, 9). On daily parenteral administration, for eight days, histamine produces histological changes in the vagina of rats which are characteristic of pro-oestrus and oestrus, and concurrent administration of antihistaminic drug pyrilamine maleate results in a quiescent vaginal mucosa characteristic of dioestrus and metoestrus (4). Like histamine, the intraluminal application of oestradiol produces hyperaemia, vasodilation and oedema in the uterus and antihistamines, like diphenhydramine and chlorpheniramine, block these changes (8). Further, uterine histamine concentration is significantly reduced during oestrus phase of the cycle (2,6,7) as also during oestradiol-induced oestrus (3, 6, 7) in rats. These findings suggest that the action of oestrogens in the regulation of oestrous cycle is possibly mediated through the local release of endogenous uterine histamine. The present investigation deals with the effect of some antihistaminic drugs on the duration of oestrous cycle in normally cyclic rats.

MATERIALS AND METHODS

Healthy female albino rats (120-180 *gm*) maintained at room temperature (23-33°C) were screened for the regularity of oestrous cycle for 20-25 days. Rats with regular oestrous cycle of 4-5 days were selected for further study. Distilled water was instilled into the vagina, the vaginal contents were aspirated out and smears prepared. Different phases of the oestrous cycle were detected by the microscopic examination of the vaginal smears. The criteria used for differentiating the stages of the oestrous cycle were those of Allen (1). Separate smear records were maintained for individual animals.

The drugs (10 *mg/kg*) were injected, intraperitoneally, in two divided (9.30 AM and 5.30 PM) doses, daily, for six days, and the vaginal smears were examined during and after this period till the individual animals showed normal oestrous cycle. Thus, each rat served as its own control.

RESULTS

The results are presented in Table I. The duration of oestrous cycles in untreated control rats was 4-5 days. All the three antihistaminic drugs significantly ($P<0.001$) prolonged the duration to 11-12 days. However, the duration of the subsequent oestrous cycle returned to near pre-antihistamine level and, thereafter, animals had normal and regular cycles.

TABLE I: Effect of intraperitoneally administered antazoline, diphenhydramine and mepyramine on duration of the oestrous cycle of albino rats. P values calculated by student's 't' test. (5 rats in each group).

Drugs	*Average ± S.E. duration (days) of oestrous cycle*	
	Before treatment	*During treatment*
Antazoline hydrochloride	4.60 ± 0.13	11.00 ± 0.90*
Diphenhydramine hydrochloride	4.20 ± 0.29	11.00 ± 1.00*
Mepyramine maleate	4.90 ± 1.00	11.60 ± 1.10*

SE.— Standard error

* — $P<0.001$

DISCUSSION

In the present study, all the three antihistaminics (antazoline hydrochloride, diphenhydramine hydrochloride and mepyramine maleate) significantly ($P<0.001$) prolonged the oestrous cycle. Significant changes in the uterine (2, 8) and blood (5,6) histamine levels have been observed during different phases of the oestrous cycle. Also, antihistaminics block the oestradiol (8) and histamine (4)-induced histological changes in the uterus and vagina. It is, therefore, likely that the prolongation of the duration of oestrous cycle by the antihistaminic drugs, as observed here, may possibly be due to their ability to block the action of oestrogen-influenced endogenously released histamine.

ACKNOWLEDGEMENTS

Sincere gratitudes are due to Dr. N.K. Bhattacharyya for helpful suggestions. Thanks are due to the Director of this Institute for providing necessary facilities. Thanks are also due to Messrs Ciba-Geigy, Bombay for antazoline hydrochloride, to Messrs Parke-Davis, Bombay for diphenhydramine hydrochloride and to Messrs May & Baker, Bombay for mepyramine maleate.

REFERENCES

1. Allen, E. The oestrous cycle in the mouse. *Amer. J. Anat.*, **30**: 297-348, 1922.
2. Kapila, K. Histamine content of albino rat uterus during oestrous cycle and early pregnancy. *Ind. J. Physiol. Pharmac.*, **11**: 127-128, 1967.
3. McKercher, T.C., L.S. Van, R.K. Bhatnagar and J.P. Burke. Estrogen induced biogenic amine reduction in rat uterus. *J. Pharmacol. Exp. Ther.*, **185**: 514-522, 1973.
4. Oppo, G.T. *Boll. Soc. itali. biol. Sper.*, **32**: 1365, 1956 (Cited by Spaziani and Szego, 1959).
5. Prasad, S.P., V. Raviprakash, M. Sabir and N.K. Bhattacharyya. Changes in blood histamine and bradykininogen levels during different periods of oestrous cycle in goats. *J. Reprod. Fert.*, **42**: 229-232, 1975.
6. Singh, N.P. and M. Sabir. (Under publication).
7. Spaziani, E. and C.M. Szego. The influence of oestradiol and cortisol on uterine histamine of the ovariectomized rats. *Endocrinol.*, **63**: 669-678, 1958.
8. Spaziani, E. and C.M. Szego. Further evidence for mediation by histamine of estrogenic stimulation of the rat uterus. *Endocrinol.*, **64**: 713-723, 1959.
9. Szego, C.M. Role of histamine in mediation of hormone action. *Fed. Proc.*, **24**: 1343-1352, 1965.