EVIDENCE FOR NON-INVOLVEMENT OF CENTRAL CATECHOLAMINES IN COPPER ACETATE INDUCED OVULATION

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Abstract—The effect of reserpine and phenoxybenzamine pretreatment has been studied on copper acetate induced ovulation in rabbits. It has been observed that neither reserpine nor phenoxybenzamine prevented the ovulatory response of the copper salt. These findings indicate that copper induced ovulation does not appear to be mediated through the involvement of central adrenergic mechanisms.

Fevold and co-workers (1) were the first to report the ovulatory effect of copper in rabbits. Harris (2) induced ovulation in rabbits by injecting subthreshold amounts of copper salts into the third ventricle. Later on Hiroi et al. (3) localized the site of ovulatory action of copper salts to the posterior median eminence region. The presence of catecholamines in the median eminence of rabbit (4) and their role in spontaneous and reflex ovulation (5–6) led us to investigate the effect of a catecholamine depletor, reserpine and an α-adrenergic receptor blocking agent, phenoxybenzamine (dibenzyline) on copper acetate induced ovulation in rabbits.

METHODS

This study was conducted on adult, healthy female, non pregnant albino rabbits weighing from 1.4 to 1.6 kg. The animals were kept on an ad libitum standard diet plus water. The animals were divided in different groups according to the treatment schedule. All the animals were given oestradiol dipropionate 100 μg s.c. for 2 days prior to the i.v. injection of copper acetate (10 mg) or normal saline. Reserpine was administered i.p. in a dose of 0.5 mg/kg for one, two or three days prior to the injection of copper acetate or normal saline. Phenoxybenzamine was administered in a dose of 10 mg/kg i.p. one hr prior to the injection of copper acetate.

All animals were laparotomized under ether anaesthesia 24 hr after injection of copper acetate or normal saline. Ovulation was detected by direct observation of the ovaries for the presence of fresh corpora haemorrhagica and recovery of ova in the Fallopian tube flushings. The abdomen was closed and animals were allowed to recover.

RESULTS

The results of this study are presented in Table 1. The rabbits on oestradiol
dipropionate and normal saline (group A) failed to ovulate, whereas ovulation was observed in all the rabbits receiving oestradiol dipropionate and copper acetate (group B). The pretreatment of rabbits with reserpine for one, two or three days prior to the injection of copper acetate in oestradiol dipropionate treated rabbits failed to block ovulation (groups D, F and G). Four out of five rabbits on reserpine for 3 days and copper acetate on 4th day were found dead on the morning of 5th day before a laparotomy could be attempted. The remaining rabbit showed signs of ovulation (group G). There was no indication of ovulation in rabbits treated with oestradiol dipropionate, reserpine for one or two days and normal saline (group C and E). Copper acetate was also found to induce ovulation in all the rabbits treated with oestradiol dipropionate and phenoxybenzamine (group H).

**DISCUSSION**

Several workers have reported that reserpine blocks ovulation and prolongs oestrous cycle in various species of animals (7-10). The antiovulatory effect of reserpine can be antagonized by pretreatment of animals with monoamine oxidase inhibitors (11, 12). These findings indicate that reserpine blocks ovulation through the depletion of central monoamines. Bhargava and Gupta (5) proposed that central catecholamines play a role in the release of the luteinizing hormone releasing factor (LRF). Recently Kamberi et al. (13) have reported an increase in LRF concentration in portal blood after injection of dopamine into the 3rd ventricle of rat. Furthermore, the central adrenergic receptors concerned in the physiological control of ovulation have also been identified. Gupta et al. (6) were
the first to report that the α-adrenergic receptor blocking agents when administered i.p. prolonged the duration of oestrous cycle in mice and prevented post-coital ovulation in rabbits on intracerebroventricular administration. On the other hand, β-adrenergic receptor blocking agents given by the same routes neither prolonged the duration of oestrous cycle in mice nor prevented post-coital ovulation in rabbits. Recently Schneider and McCann (14) have also reported that dopamine induced increase in LRF can be blocked by the α-adrenergic receptor blocking agent and not by the β-adrenergic receptor blocking agent. Recently Gupta et al. (15) have reported induction of ovulation by administration of dopamine intravenously or intracerebroventricularly in rabbits. This dopamine-induced ovulation was found to be blocked by prior administration of α-adrenergic receptor blocking agents e.g. phenoxybenzamine and dihydroergotamine. Haloperidol (a dopaminergic receptor blocking agent) was also found to block dopamine induced-ovulation. Thus, it can be presumed that reserpine blocks ovulation through the depletion of central catecholamines, however, Hopkins and Pincus (16) have reported that reserpine renders the ovary refractory to the actions of exogenous gonadotropins in immature rats. The induction of ovulation in reserpinized animals, as observed in the present study, indicates that reserpine does not make the ovary refractory to the actions of gonadotropins. The results of our study with reserpine appear to rule out the role of catecholamines in copper-induced ovulation. This is further supported by the fact that phenoxybenzamine, which blocks post-coital ovulation in rabbits (6) does not block copper acetate induced ovulation (see Table 1). Sawyer and Markee (17) have also reported the failure of dibenamine to block ovulation induced by intrahypophyseal injection of copper salt.

In conclusion it may be stated that copper induced ovulation in rabbits is not mediated through central adrenergic mechanisms.

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