It has been reported that ovulation of rats can be blocked by morphine (1), and administration of ovulation blocking drugs to the proestrous rats was shown to inhibit the spontaneous release of luteinizing hormone (LH) which occurs during the afternoon of the day of proestrus (2). Peak levels in serum follicle-stimulating hormone (FSH) and prolactin also are seen on the afternoon of proestrus in the rat (3). Such being the case, we carried out studies to determine whether or not morphine, an ovulation blocking drug, would change serum LH, FSH and prolactin levels of proestrous rats.

Female Wistar rats, 12 weeks old, were housed under controlled lighting conditions (lights on 0600 to 1800 hr). Estrous cycles were monitored by daily vaginal smears taken between 0900 to 1000 hr, and only animals showing 3 or more consistent 4-day cycles were used. At 1355 hr on proestrus, rats were given morphine hydrochloride (50 mg/kg) or saline (5 ml/kg) s.c. and were decapitated at 1800 hr. Injection of morphine sulfate (50 mg/kg) between 1200 to 1400 hr of the day of proestrus was reported to block ovulation (1). As we intended to determine the changes of serum gonadotropins and prolactin levels when ovulation is blocked by morphine, we chose a condition of morphine administration similar to that previously reported (1). We did not confirm however, that morphine actually blocks ovulation. Serum samples were stored frozen at 80 C until the assay of hormones. Hormones were determined using radioimmunoassay kits kindly provided by NIAMDD, NIH and the standard procedure supplied with the kits was followed. Values were expressed in terms of NIAMD-Rat LHRP-1, FSHRP-1 or ProlactinRP-1. Results were statistically analyzed using Student's t-test.

Administration of morphine at 1355 hr decreased the serum levels of LH, FSH and prolactin of proestrous rats at 1800 hr, although the decrease in FSH levels was not significant (Table I). This means that morphine blocked the late afternoon rise in serum LH, FSH and prolactin of proestrous rats, although we cannot exclude the possibility that morphine merely delayed the rise in these hormones. A similar decrease of LH levels by morphine was observed by Pang et al. (4). Since it was suggested that acute administration of a narcotic drug results in an indirect inhibition of dopaminergic receptor activity (5) and that in the intact proestrous rat, any interruption of central dopaminergic impulse flow significantly
TABLE 1. Effect of morphine on serum LH, FSH and prolactin levels in proestrous rats

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of rats</th>
<th>LH (mean ± S.E.) (ng/ml)</th>
<th>FSH (mean ± S.E.) (ng/ml)</th>
<th>Prolactin (mean ± S.E.) (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline</td>
<td>10</td>
<td>623 ± 105</td>
<td>206 ± 37</td>
<td>947 ± 154</td>
</tr>
<tr>
<td>Morphine</td>
<td>7</td>
<td>15 ± 3</td>
<td>110 ± 11</td>
<td>144 ± 52</td>
</tr>
</tbody>
</table>

*P < 0.001

decreased LH and FSH secretion and inhibits ovulation (6), it may be that morphine inhibits ovulation by decreasing the proestrous LH and FSH surges through effects on a central dopaminergic pathway. As the increased prolactin levels in plasma may cause a stimulation of hypothalamic prolactin inhibiting factor (PIF) synthesis and/or release, which is followed by an inhibition of prolactin release (7), and acute administration of morphine to male rats increases serum prolactin levels (8), morphine may suppress the proestrous serum prolactin surge by stimulating the PIF synthesis and/or release. The possibility of a direct action of morphine on the pituitary cannot be excluded and the mechanism of morphine which inhibits the proestrous LH, FSH and prolactin surges remains to be elucidated.

Our finding suggests the possibility that morphine blocks ovulation by inhibiting the preovulatory LH surge. The role of lowered FSH and prolactin levels of morphine-treated proestrous rats in the blockade of ovulation is now being investigated.

REFERENCES


INHIBITION OF PROSTAGLANDIN SYNTHETASE SYSTEM IN THE RABBIT RENAL MEDULLA BY PSYCHOTROPIC DRUGS

Haruo TACHIZAWA, Tadashi SAITO and Takeshi AKIMOTO
Research Institute, Daiichi Sankyo Co., Ltd., Edogawa-ku, Tokyo 132, Japan
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It has been reported that chlorpromazine and desipramine, a major tranquilizer and antidepressant, respectively, exert anti-inflammatory activity in animals (1, 2) and that chlormezanone, a minor tranquilizer, has a more potent analgesic activity than aspirin (3). Vane has proposed that the pharmacodynamic activities of non-steroidal anti-in-