Effect of Exogenous Oxytocin on Contractility of the Female Reproductive Tract of the Rabbit

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Abstract The effect of oxytocin on the contractility of oviductal isthmus, uterus and cervix was investigated in rabbits before and after mating. The oviductal responsiveness to oxytocin was conspicuous during estrus and up to 3-4 days after mating, followed by its gradual decrease; but an abrupt decline was evident in 2 of 5 does on Day 7. Uterine motility was affected by oxytocin until 2 days after mating, and the uterine sensitivity decreased thereafter. Cervical responses to oxytocin were not consistent during estrus and were not noted 3 days after mating.

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Oxytocin has been generally accepted as a stimulator of uterine muscular activity in several species, both *in vitro* and *in vivo*. It has been believed that effects of oxytocin are affected by ovarian hormones. In rabbits, estrogen increases the responsiveness to oxytocin, while progesterone decreases it¹⁻⁵⁾. However, very little is known of the effects of this drug on the oviductal and cervical motility of rabbits during early pregnancy. The purpose of the present investigation is to study the effects of exogenous oxytocin on the contractile activities of the reproductive organs of rabbits before and after mating.

Materials and Methods

Five adult, female Japanese White rabbits were used. Muscular activities of the reproductive organs were recorded *in vivo* by placing polyurethane balloon catheters into the lumina of the oviductal isthmus, uterus and cervix on the ipsilateral side, as reported previously⁶⁾. Following recovery from the surgery for fitting the catheters, intraluminal pressure changes of each organ were simultaneously monitored daily for about 60 min by a multipurpose polygraph (RM-85, Nihon Kohden, Japan) using preamplifiers (RPF-5, Nihon Kohden) and Ailtech pressure transducers (MS-20S, U.S.A.). All animals received intravenous injections of 5 IU of oxytocin (Showa Yakuhin-kako, Japan) one or more days prior to mating, and once each day for 7 days after mating. Human chorionic gonadotrophin (50 IU, Gonatropin, Teikoku-Zōki, Japan) was given intravenously just after mating. Recordings of contractile motilities of three different organs were always started at least 30 min before the oxytocin administration. The day of mating was designated as Day 0.

Oxytocin and Contractility of Reproductive Tract

Fig. 1. Effect of oxytocin administration on contractility of the oviduct (O), uterus (U) and cervix (C) of a rabbit before and after mating (up to Day 3).

Results

Typical pressure changes before and after oxytocin administration are shown in Fig. 1. During estrus, administration of oxytocin elicited a marked response in the oviduct, but relatively small changes occurred in the other two organs. The tone of oviductal contractions increased immediately after oxytocin injection, the magnitude exceeding the mechanical sensitivity (up to 80-100 mm Hg) applied in the present investigation. Similar responsive patterns of oviductal contractions to oxytocin occurred up to Day 3 or 4, and subsequently the duration of increased tubal tone was gradually shortened and the increased contraction amplitude became smaller. In 2 of 5 does, the oviductal responsibility to oxytocin disappeared completely on Day 7.

On the other hand, oxytocin-induced activity of the uterus in estrous rabbits returned to the preinjection level within about 5 min, followed by slightly increased amplitude of contractions. Oxytocin administration on Days 1 and 2 induced slight increases in the uterine contraction amplitude and frequency without a rise in the tone. After Day 2, the uterine motility was not much affected by oxytocin injection.

In contrast to these two organs, the response of the cervix to oxytocin was variable even in estrous rabbits. In many cases (60.5% of 38 trials), the contraction amplitude in the cervix was increased slightly by exogenous oxytocin. However, in some cases (26.3%) the cervix did not respond even if the uterus was responsive, and in other cases (13.2%) the amplitude diminished, indicating a relaxation of the cervix. The effect of oxytocin on cervical motility seemed to disappear on and after Day 3.

Discussion

The present observations confirm the previous findings that uterine sensitivity to oxytocin is diminished under progesterone influence¹⁻⁵. Since plasma concentration of progesterone begins to rise from about 4 days after mating^{7,8}, our data may support the "progesterone-block" theory of CSAPO^{9,10}. This alteration in uterine responsiveness to oxytocin may be coincident with changes in number of oxytocin receptors in the myometrium of rabbits, as reported recently¹¹.

Although COUTINHO *et al.*¹² insisted on the insensitivity of rabbit oviduct to the stimulatory action of oxytocin regardless of the hormonal status, the present data clearly demonstrate that the rabbit oviduct is sensitive to oxytocin and that the tubal responses to this drug are more resistant to endocrine changes following ovulatory stimulus than those of the uterus and cervix.

Effects of oxytocin on cervical motility have been a conflicting matter in the literature. *In vivo* and *in vitro* studies in the human cervix have lacked unity concerning the stimulatory effect of oxytocin¹³⁻¹⁵. NEWTON¹⁶ found that isolated and sliced cervix of goat did not respond *in vitro* to oxytocin, even in very large doses. In contrast, ADLER *et al.*¹⁷ reported, using a small balloon technique, that the cervixes of the rabbit, cat and guinea pig do contract in response to oxytocin in most experi-

mental cases. They pointed out, however, that there is no consistency in the cervical responsiveness to oxytocin: it elicits an increase, a decrease or no change in cervical motility.

The present results show that the effectiveness of oxytocin in the rabbit reproductive tract is organ-dependent, as mentioned by ADLER *et al.*¹⁷⁾. Since the oviduct was more sensitive to oxytocin than were the other two organs, it is possible that exogenous oxytocin may have a role on the control of oviductal egg transport, although TSUTSUMI *et al.*¹⁸⁾ speculated on the inability of oxytocin to alter the rate of egg transport.

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外因性のオキシトシンが雌家兎生殖道の 収縮運動に及ぼす影響

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卵移動に及ぼすオキシトシンの影響を知るために, 卵管峡部, 子宮ならびに子宮頸の収縮運動に対する影響を交配前後の家兎を用いて追求した. オキシトシンに対する卵管の反応性は交配前ならびに交配後3-4日目まで顕著であった. その後, 徐々に低下したが, 5羽の供試兎のうち2羽で交配後7日目に急激な反応性の低下がみられ

た. 子宮運動は交配後2日目までオキシトシンによって影響を受けたが, その後子宮の感受性は低下した. 交配前の子宮頸の反応には一定の傾向がみられなかったが, 交配後3日目では全く反応しなくなった.

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