



## The Arbotifacient and Cuddling Potencies of Oxytocin In the Wistar Rat Animal Model

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### ABSTRACT

The anterior pituitary hormone, oxytocin is well reputed for inducing abortion, hastening labor cum parturition, and prepares the subjects for motherhood. The experimental application of tehse is presently tested in the Wistar rat animal model.

Adult female Wistar rats of reproductive age were mated and injected with 0.5ug oxytcin on days 5, 10, 15, 18, 19 and 20 of gestation; hormone potencies and animal behaviours were carefully monitored pre-partum. Oxytocin was least effective in the early days of gestation; however, hormone potencies gradually increased as pregnancy advanced.

Both endogenous secretion and exogenous administration of oxytocin was least effective at the initial and mid-phases of pregnancy in the rat. Perhaps if higher dosage of the hormone were administered, the resulting high plasma concentration might probably override the prevailing physiology in the early phase of pregnancy in the uterus though, and such could be effective enough to elicit response possibly, with the accompanied complications.

**Keywords:** Oxytocin, Abortion; Cuddle; Females; Wistar rat.

Oxytocin is a nine-amino-acid-peptide that is naturally synthesized in hypothalamic neurons of para-ventricular nuclei and transported down axons of the posterior pituitary for secretion into blood. Oxytocin is also secreted from a few other tissues, including the ovaries and testes (Blaffer and Carter, 1995). Vincent du Vigneaud first synthesized oxytocin in 1953, which fetched him the Noble Prize for Chemistry in 1955.

In years past, oxytocin had the reputation of being an 'uncomplicated' hormone with only a few well-defined activities related to birth and lactation. As has been the case with so many hormones, further research has deomosntrated many subtle but profound influences of this little peptide. However, some of its cardinal effects in females include stimulating contraction myo-epithelial cells, causing milk to be ejected into the ducts and cisterns; it's released during labour, when the fetus stimulates the cervix and vagina; and it also enhances contraction of uterine smooth muscle indirectly and helps expedite the normal contractions of spontaneous labor and facilitate parturition or~~o~~ birth. Oxytocin is responsible for uterine contractions, both before and after delivery. The muscle layers of the uterus (myomentrium) become more sensitive to oxytocin near term. Towards

the end of a term pregnancy, levels of progesterone decline, and contractions that were previously suppressed by progesterone begin to be more frequent and stronger. This change in the oxytocin/progesterone ratio is believed to be one of the initiators of labor (Blaffer and Carter, 1995). Oxytocin can be used when labor needs to be induced or if the contractions are not strong enough to progress normally. It is also used to control bleeding after childbirth. Oxytocin also can help to stimulate contractions if there is an incomplete abortion or miscarriage.

The idea that physiological changes might prepare the expectant mother for her new role led to a now classic experiment. In an earlier work, when blood from a rat that had just given birth was injected into a virgin female, the result was a dramatic reduction in the time it took virgins to nurture pups (Cushing and Carter, 1999). On the other hand, most times scientist handling laboratory animals whether novice or experienced, are commonly confronted with aggression by the animals, and wastages such as when wholly sacrificing pregnant animals during experiments just to retrieve embryos/fetal tissue; however, on the alternative, abortion could be induced on a targeted day, to possibly reduce wastes and costs.

The present work was designed to



experimentally study the abortifacient and cuddling potencies of oxytocin in the rat animal model.

## MATERIALS AND METHODS

20 healthy virgin female and 5 male Wistar rats weighing between 200g and 250g were bred in the tidy, well-ventilated animal holdings of the Department of Human Anatomy for the study and given animal mash and clean drinking water adequately. They were mated: 1 male to 4 females and gestation confirmed according to the methods of Asling (1960). 10 pregnant rats were given intra-peritoneal injections of 0.5ug oxytocin, (Amros Pharmaceuticals, Karachi, India) on days 5, 10, 15, 18, 19 and 20 of gestation; dosages were administered following adoption of a modified method of Frayne et al. (1996). The 10 rats used for control were given equivalent dosage of normal saline; daily weights were assessed and the abortifacient and pre-equivalent and pre- and post-partum behavioral effects of oxytocin were closely monitored in the animals. The male rats were only used for mating.

## RESULTS

The oxytocin-treated rats were relatively calm, receptive, and non-aggressive and welcoming compared with the control. although there were cases of mild labor, there were no abortions in any of the rats treated on days 5 and 10; whereas days 15 and 18 rats showed spontaneous labor with nausea and convulsions an tachycardia, and only one rat littered on day 18. However, on days 19 and 20, there were spontaneous labor and prompt littered within 30 minutes of injection. All the litters were spared and nursed well by the mothers. There were no cases of eating up the young ones, safe for the control, that ate up 9 of their pups. All the control rats littered between days 20 to 22 of gestation. Mean weight was 285g 0.02 for the treated rats and 279g 1.04 for the control.

## DISCUSSION

The uterine muscles did not give swift response to oxytocin at the early stages of

pregnancy, possibly due to yet high levels of progesterone and estrogen which suppresses oxytocin, since oxytocin is responsible for uterine contractions, both before and after delivery, hence the spontaneous response to oxytocin on days 19 and 20. oxytocin is a potent stimulator of myomentrium via its direct action, it increases sodium influx into the uterine myofibril, hence, activates the muscle contractility; moreso, its direct action on endometrium promotes increased arachidonic acid metabolism with subsequent synthesis of prostaglandins F2a and E2 (Chan and Chen, 1992). Towards term pregnancy, increase plasma oxytocin is preceded by marked rise in oxytocin receptors levels in both the endometrium and myometrium and this coincides with increased potency of oxytocin and the expulsive phase of delivery, (Fuchs et al., 1992). Moreso, a great deal had been revealed about what goes on inside female mammals as they prepare for motherhood: during the last third of pregnancy, when a cascade of endocrinological events readies and motivates mothers. Prominent in this maternal cocktail are the steroid hormones estrogen and progesterone, manufactured by the placenta and essential for maintaining pregnancy as they suppress uterine contraction, this could explain the non-effectiveness of oxytocin in the earlier days of gestation. However, as pregnancy advances, progesterone and, a little later, estrogen levels fall around the time of birth, hence, oxytocin becomes effectual. (Parry et al., 1996).

Oxytocin means 'rapid birth'. It is a synthetic hormone named for the natural posterior pituitary hormone. Oxytocin is released during labor when the fetus stimulates the cervix and vagina, and it enhances contraction of uterine smooth muscle to facilitate parturition or birth. Moreso, males too synthesize oxytocin in the same regions of the hypothalamus as in females, and also within the testes and perhaps other reproductive tissues. Pulses of oxytocin can be detected during ejaculation. Evidences available from earlier work suggests that oxytocin is involved in



facilitating sperm transport within the male reproductive system and perhaps also in the female, due to its presence in seminal fluid. It may also have effects on some aspects of male sexual behaviour, (Frayne et al., 1996).

In both male and female rats oxytocin usually exerts potent physiological anti-stress effects; such is presently seen in the virtually relaxed, non-aggressive oxytocin-treated-rats, this could possibly explain the relatively higher weight gain. If daily oxytocin injections are repeated over a 5-day period, blood pressure is decreased by 10-20mmHg, the withdrawal latency to heat stimuli is prolonged, cortisol levels are decreased and insulin and cholecystokinin levels are increased. These effects last from one to several weeks after the last injection. These after-effects properties of oxytocin may probably enhance the cuddling behaviours and care for the pups rather than resorting to cannibalism by the mother rats. After repeated oxytocin treatment, weight gain may be promoted and the healing rate of wounds increased. However, oxytocin antagonists can block most of the behavioural and physiological effects induced by oxytocin. In contrast, the anti-stress effects cannot, suggesting that unidentified oxytocin receptors may exist, (Uvnas-Moberg, 1998; Komisaruk and Whipple, 1998).

Presently, when the mother first greets her emerging offspring, it continues to be released whenever she nurses. Oxytocin released into the brain is known to promote calming and positive social behaviours, such as pair bonding. During breastfeeding or suckling, maternal oxytocin levels are raised by somatosensory stimulation. Oxytocin may, however, also be released into the plasma, and cerebrospinal fluid by non-noxious stimuli such as touch and warm temperature, (Sarnyai and Kovacs, 1994; Kovacs et al., 1998).

For instance, when first presented with pups, in the absence of oxytocin, a virgin female laboratory rat generally ignores them; she may appear afraid of the tiny, squirming, naked creatures and, occasionally, may even eat them. Only after being introduced to pups many times

over several days can a virgin rat be conditioned to tolerate and care for them licking them, crouching protectively over them, retrieving them when they stray from her side. In contrast, a pregnant rat responds within minutes to pups, even prior to delivery of her own, prompted by the secreted endogenous oxytocin (Cantor et al., 1999).

The study builds upon previous knowledge of the important role oxytocin plays in the reproductive life of mammals. The hormone facilitates nest building and pup retrieval in rats, acceptance of offspring in sheep, and the formation of adult pair-bonds in prairie voles. In humans, oxytocin stimulates milk ejection during lactation, uterine contraction during birth, and is released during sexual orgasm in both men and women (Turner et al., 1999).

During parturition, there is an increase in concentration of oxytocin in cerebrospinal fluid, and oxytocin acting within the brain plays a major role in establishing maternal behaviour. Oxytocin released into the brain is known to promote calming and positive social behaviours, such as pair bonding. Previous studies in domestic sheep had provided the most complete picture we have of the behavioral effects of oxytocin: as a lamb moves down the birth canal, nerves stimulated during the passage trigger the release of oxytocin in the mother's nervous system. Only if oxytocin is present at birth or injected so that it reaches the brain at the same time a mother meets her newborn, will she bond with her offspring. If release of oxytocin is blocked, the ewe rejects her lamb. In addition, high levels of oxytocin also are found in mother's milk, raising the possibility that this hormone plays a role in making the mother-infant attachment mutual (Turner and McGuinness, 1999; Kosfeld et al., 2005).

In conclusion, it appears that both the endogenous and exogenous oxytocin is least potent to induce labour at early pregnancy, in particular, with the present dosage in the rat; a higher dosage if employed, could probably be more potent, though this might be accompanied by complications if not mortality in the animals;



whereas, the cuddling effects are well expressed pre-and post partum. The observations in this experiment are invariably applicable to humans, being eutherian mammals.

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