Milk Let-Down Activity of Synthetic Oxytocin (Syntocinon) and Relaxin in Lactating Rats.* (23684)

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A recent investigation(1) showed Nembutal was able totally to inhibit milk let-down in the lactating rat but the young were able to obtain milk when oxytocin (Armour) was injected intravenously while the offspring were actively sucking. Values thus obtained when compared with normal let-down data(2) suggested the amount of oxytocin released by lactating rats in response to nursing stimuli was in the range of less than .02 to .1 USP/kg. It occurred to us such a procedure could serve as a method of bioassay for substances possessing milk let-down activity. With this in mind, we have assayed, in the present study, a new synthetic oxytocin (Syntocinon) which has been demonstrated to possess all other properties of natural oxytocin(3-7) and relaxin which has been claimed to have milk let-down activity(8).

Materials and methods. Forty primiparous albino lactating rats weighing 280-320 g were used. Shortly after birth each litter was reduced to 6 young and when 14 days old was isolated from their mother for 10 hours. Each mother was injected with Nembutal (4.5 mg/100 g) i.p. 10-20 minutes prior to end of isolation period and when completely anaesthetized, laid on her side and her litter replaced. Thirty rats received Syntocinon‡ in dose of .02, .05 or .1 USP/kg *i.v.* in a volume not exceeding .06 ml. into the superior epigastric vein a few minutes after the young had been replaced and while they were actively sucking. Ten others similarly received either 600 or 1200 Guinea Pig Units (GPU) releasin.§ After each litter had been nursed for 30 minutes, they were removed, weighed, killed by decapitation and stomach contents removed and weighed.

Results. Syntocinon injected *i.v.* into anesthetized lactating rats a few minutes after the young had commenced to nurse resulted in milk let-down after a latent period of 5-8 seconds and seemed to persist 4-5 minutes. After milk flow apparently had ceased, they became quiet and sucked intermittently the remainder of the nursing period. Amount of milk thus obtained expressed as percent litter body weight is shown in Table I and is compared with data similarly obtained previously(1) with natural oxytocin. Syntocinon resulted in same magnitude of milk let-down using our 3-point method of assay, as did natural oxytocin. No milk was obtained during 30 minutes very active sucking by young of anaesthetized lactating rats injected *i.v.* with large doses of a relaxin preparation (Table I).

Discussion. Previous workers have found equivalent responses for natural oxytocin and Syntocinon in regard to oxytocic activity(3-5) the synthetic product having much less pressor and antidiuretic effects(3,4,6,7). The observation in the present study that Syntocinon is capable of causing milk let-down in anaesthetized lactating rats of the same magnitude as natural oxytocin indicates further the physiological similarity of the two compounds and, in addition, indicates the reliability of our method of assay in determining milk let-down. A variety of other compounds will initiate milk let-down in isolated perfused cow's udder(9,10), or will cause local alveolar contraction of mammary glands of rats, mice, guinea pigs and rabbits when applied topically(11). Recently, Shaffhausen *et al.*, (8) have suggested relaxin may also effect contraction of mammary alveoli of sheep for after obtaining all milk possible by hand milking, they were able to secure additional milk by hand milking following intraarterial injection of 500 GPU of a relaxin prepara-

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§ Relaxin preparation W1164A of Warner-Chilcott Lab, Lot No. 53, assaying 30 GPU/mg.

TABLE I. Comparison of Milk Removal by Litters of Anaesthetized Nursling Rats Injected with Natural Oxytocin, Syntocinon and Relaxin on 14th Day Postpartum.

Treatment	No. of rats	Avg wt (g) Litters	Milk	Avg % Wt of milk / Wt of litters
Controls*	40	144.0	5.5	3.8 ± .19
Nembutal†	14	164.5	.0	.0
" + 600-1200 GPU Relaxin	10	133.4	.0	.0
" + .02 USP/kg oxytocin†	11	159.0	4.7	3.0 ± .82
" + " " Syntocinon	10	174.9	5.6	3.2 ± .21
" + .05 USP/kg oxytocin†	11	164.2	6.3	3.8 ± .20
" + " " Syntocinon	10	159.4	6.0	3.8 ± .27
" + .1 USP/kg oxytocin†	5	168.8	9.8	5.9 ± .45
" + " " Syntocinon	10	179.3	10.3	5.7 ± .46

* Data from Grosvenor and Turner(2). † Data from Grosvenor and Turner(1).

tion. However, if relaxin in doses used in the present investigation was capable of contracting mammary alveoli or directly activating pituitary release of oxytocin, then nursling rats should have obtained milk. Since none was obtained, it is concluded relaxin, under the conditions of this experiment, has no milk let-down activity in the lactating rat.

Summary. 1) A synthetic oxytocin, (Syntocinon, Sandoz), injected *i.v.* into Nembutal anaesthetized lactating rats in doses of .02, .05 and .1 USP/kg a few minutes after the young had commenced to nurse resulted in milk let-down after a latent period of 5-8 seconds and seemed to persist 4-5 minutes. Amount of milk thus obtained expressed as percent litter body weight corresponded very well with data similarly obtained previously with same doses of natural oxytocin. It is concluded Syntocinon and natural oxytocin possess equivalent milk let-down activity. 2) Relaxin injected *i.v.* in dose of 600-1200 Guinea Pig Units into 10 anaesthetized lactating rats failed to initiate milk let-down.

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