MODIFICATION OF VASCULAR RESPONSE TO SYNTHETIC OXYTOCIN BY OESTROGEN IN RABBIT

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Summary: Intravenously administered oxytocin caused a dose-related fall in blood pressure of the rabbit. When oxytocin was administered in oestrogen-primed animals, the depressor response was converted to a pressor one - "Oxytocin reversal". The "oxytocin reversal." was abolished after treatment with dihydroergotamine, hexamethonium or adrenalectomy. The "oxytocin reversal" did not appear in reserpinized animals.

Key words: oxytocin rabbit blood pressure oestrogen

INTRODUCTION

Lloyd (8,9), Lloyd and Pickford (10,11) and Fullerton and Morrison (4) have shown that the vascular action of oxytocin in male or dioestrous female rat may be converted to a pressor action by previous treatment with an oestrogen. This is also seen during natural oestrous cycle and latter half of the pregnancy indicating that the vascular responses to oxytocin varies with the concentration of the ovarian hormones. In view of this, it was thought of interest to study the vascular response to oxytocin in rabbit and its interaction with oestrogen.

MATERIALS AND METHODS

The experiments were done in rabbits of either sex weighing 1.5—2 *kg* anaesthetized by pentobarbitone (40 *mg/kg*, i.v.). The arterial blood pressure was recorded from a common carotid artery by means of Condon's mercury manometer and all injections in a volume not exceeding 0.5 *ml* were made in the cannulated femoral vein. Some of the experiments were conducted in rabbits of either sex primed with oestrogen (0.5 *mg/kg* s.c.) twenty four hr prior while in some of the acute experiments water soulble oestrogen (Styptanon, Organon) was used (0.5 *mg/kg*, i.v.) 10 min before the experimentation. For each set of experiment a minimum of 5 animals were used (n).

RESULTS

Responses to synthetic oxytocin (n=10) :

A definite sharp and transient fall in carotid blood pressure in rabbit of either sex was a consistent response to intravenously administered oxytocin in doses of 100 *mU*, 200 *mU* and 400 *mU* (Fig. 1).

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Effect of synthetic Oxytocin in oestrogen primed rabbit (n=5) :

Priming the rabbit with oestrogen 18—24 hr before experimentation or administra of water soluble oestrogen during the course of an acute experiment produced "oxytocin reversa i.e., the hypotensive response to oxytocin was converted to a pressor action which was also d dependent. Oxytocin in the dose of 100 *mU*, 200 *mU*, and 400 *mU* produced a dose depend pressor response (Fig. 1).

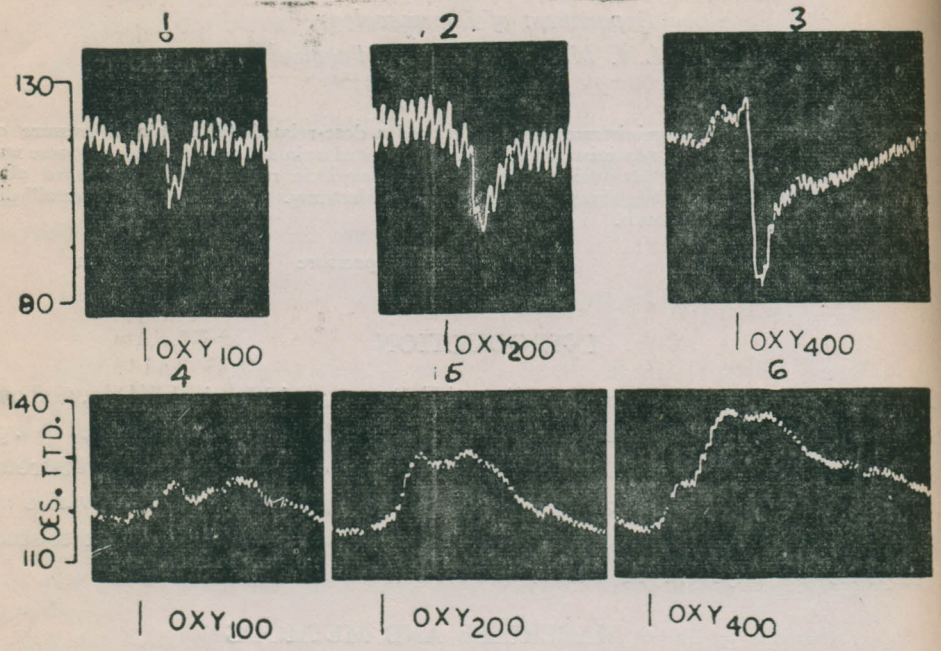

Fig. 1: Records of blood pressure (mm Hg) of rabbits anaesthetised with pentobarbitone sod (40 *mg/kg* i.v.). Panels 1, 2 and 3 show the effects of three doses of oxytocin (oxy 100, 200 and 400 *mU* respectively) in normal rabbit. Panels 4, 5 and 6 show the effects of same doses of oxytocin in rabbit primed with oestrogen.

Effect of dihydroergotamine, hexamethonium, adrenalectomy and reserpinization on Oxytoci reversal (n=5) :

The oxytocin reversal in oestrogen primed rabbits was abolished 30 min after dihydroer gotamine (D.H.E. 0.5 *mg/kg*, i.v.) and 15 min after hexamethonium (5 *mg/kg*, i.v.). Similarly oxytocin reversal did not appear in oestrogen primed rabbits after bilateral adrenalectomy and after reserpinization (1 *mg/kg* on the 1st day followed by 0.5 *mg/kg* for the next 2 days). After adrenalectomy a stabilizing period of about 60 min was allowed in every experiment before giving oxytocin (Fig. 2).

DISCUSSION

Oxytocin reversal shown by Lloyd and Pickford (10,11) after administration of oestrogen in the rat is confirmed in the present study with the rabbit.

Bilateral adrenalectomy abolished the "oxytocin reversal". It is possible that adrenal medulla contributes to the release since such a possibility has already been suggested for other

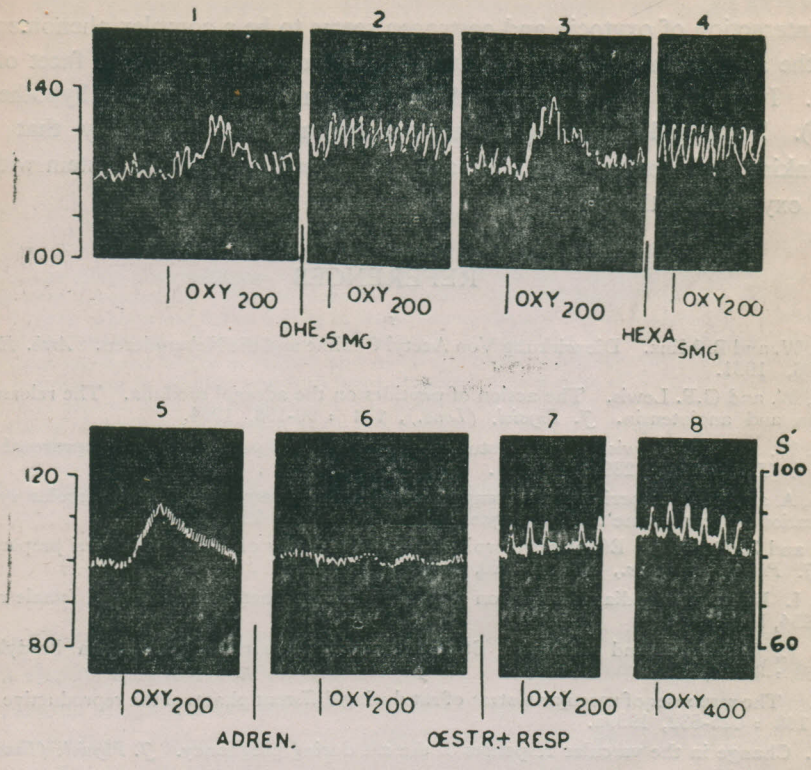

Fig. 2: Records of blood pressure (mm Hg) of rabbits anaesthetised with pentobarbitone sod (40 *mg/kg* i.v.). All records are from oestrogen-primed rabbits. Oxytocin (200 *mU*) was given as indicated in the panels. The records shown in panels 7 and 8 were obtained in reserpinized animals. Panels 1, 3, 5 and 7 show the control effects of oxytocin and panels 2, 4, 6 and 8 show the effects of oxytocin after DHE, hexamethonium (Hex), adrenalectomy (ADREN) and reserpinization respectively. 'S' represents scale for panels 6, 7 and 8.

hypotensive substances viz. acetyl choline (1) bradykinin (2,3) and histamine (12,13). Further, bradykinin has also been reported to release medullary hormone in the rabbit (7). Since oxytocin reversal was abolished after ganglion blockade the possibility of stimulation of sympathetic ganglia cannot be ruled out. The pressor action caused by other depressor substances like histamine and pilocarpine has been reported as due to the action of these agents on sympathetic ganglia and adrenal medulla (14).

It appears that oestrogen by sensitizing the sympathetic ganglia and adrenal medulla releases catecholamines because oestrogen treatment has been reported to stimulate the activity of adrenal glands (6). This suggestion is further supported by the observation that "oxytocin reversal" did not appear in reserpine-treated rabbits although it is possible that oestrogen-induced hypersensitivity of the adrenal medulla and sympathetic ganglia was reduced after reserpine-treatment since

oestrogen induced hypersensitivity of smooth muscles is known to be reduced after reserpine treatment (5).

The interaction of oxytocin and oestrogen seems to be a complex phenomenon and sensitization of the adrenal medulla or sympathetic ganglia may be only one facet of the complex relationship. It has also been suggested that oestrogen may be a part of hypothetical oxytocin receptor (15). Llyod and Pickford (11) have put forward the possibility that adrenaline is the factor linking both the gonadal state and peripheral sympathetic system with this type of response to oxytocin in the rat.

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