LETTER TO THE EDITOR

ISOLATED TERMINAL GUINEAPIG ILEUM - AN IN VITRO MODEL TO DEMONSTRATE DALE’S REVERSAL PHENOMENON

(Received on August 17, 1979)

Adult guineapigs of either sex (250-300 g) were used. All experiments were done on pieces obtained from the last 6 cm portion of the terminal ileum adjacent to the ileo-caecal junction. The tissue pieces, 2-3 cm long were suspended in 10 ml bath containing Tyrode solution kept at 37°C and bubbled continuously with oxygen. Isotonic contractions against 0.5 g tension and magnified 6-fold, were recorded on a slow moving kymograph.

Adrenaline hydrochloride (0.01-3 μg/ml). 5-hydroxytryptamine creatinine sulphate (0.1-0.3 μg/ml) and carbachol (0.05-0.1 μg/ml) were used as agonists. Phenoxybenzamine (0.1-1 μg/ml), dihydroergotamine (0.1-1 μg/ml), pronethalol (0.5-1 μg/ml), propranolol (0.5-1 μg/ml), cyproheptadine (0.5 μg/ml) and atropine (1 μg/ml) were used as blockers.

Smaller doses (0.01-0.03 μg/ml) of adrenaline relaxed the intestine (Fig. 1-A). Subsequent exposure to the same dose ether resulted in tachyphylaxis or produced contraction. However, doses from 0.1 μg/ml and above elicited dose-dependent contractions (Fig. 1-A). Contractile responses were also evident with 5-hydroxytryptamine and carbachol.

The α-blockers, phenoxybenzamine or dihydroergotamine completely blocked, in about 15 min, the contractile responses to adrenaline and usually reversed them to...
relaxation (Fig. 1-B); in this respect, phenoxybenzamine was more potent than dihydroergotamine. The resultant relaxant effect could be blocked by β-adrenoceptor blockers propranolol or pronethalol (Fig. 1-B). Though cyproheptadine completely abolished the excitatory effect of 5-hydroxytryptamine, in the doses used, it had no effect on the response to adrenaline. Also, phenoxybenzamine and dihydroergotamine did not alter the 5-hydroxytryptamine-induced contractile responses. Further, neither cyproheptadine nor phenoxybenzamine modified the responses of the tissue to carbachol. Atropine in concentrations sufficient to abolish the contractile responses to carbachol was without effect on the responses to adrenaline and 5-hydroxytryptamine.

The excitatory response to high doses of adrenaline and its blockade/reversal by phenoxybenzamine or dihydroergotamine indicate that this response is mediated through α-adrenoceptors. The abolition of subsequent relaxation by β-blockers (propranolol or pronethalol) suggest the β-inhibitory receptor involvement. The initial relaxant responses to smaller doses of adrenaline could not be explained in terms of its β-receptors mediation because of the development of quick tachyphylaxis. However, no such tachyphylaxis was observed following α-blockade.

The involvement of 5-hydroxytryptamine in guineapig ileum study, though cyproheptadine did not alter those of adrenaline reversed the adrenaline responses. This, therefore, supports the specific involvement of the adrenaline responses.

The results of the present study to those with spinal cat block to adrenaline. The greater sensitiveness to low doses of adrenaline is increased, upon the former.

Thus, the terminal pith model to demonstrate the

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The involvement of 5-hydroxytryptamine in the mediation of the excitatory effect
of adrenaline in guinea pig ileum has been suggested (6,7). However, in the present
study, though cyproheptadine could effectively block the responses to 5-hydroxytryptamine,
it did not alter those of adrenaline. Similarly, the doses of phenoxybenzamine which
reversed the adrenaline responses did not modify the 5-hydroxytryptamine-induced
contractions. This, therefore, negates the involvement of tryptaminergic receptor and strongly
supports the specific involvement of \( \alpha \)-excitatory and \( \beta \)-inhibitory receptors in mediating
the adrenaline responses.

The results of the present study on guinea pig ileum demonstrate a close resemblance
to those with spinal cat blood pressure preparation in relation to reversal of responses
to adrenaline. The greater sensitivity of \( \beta \)-adrenoreceptors on the vascular smooth muscle
which results in fall in blood pressure to small doses of adrenaline is well known. Likewise,
our findings suggest that probably the \( \beta \)-receptors present in this part of the ileum are
much sensitive to low doses of adrenaline, resulting in relaxation; however, as the dose
of adrenaline is increased, the contraction mediated by \( \alpha \)-component is superimposed
upon the former.

Thus, the terminal portion of the guinea pig ileum is suitable for use as an in vitro
model to demonstrate the Dale's adrenaline reversal phenomenon.

ACKNOWLEDGEMENTS

Thanks are due to the Head of the Division and to the Director of this Institute
for providing the necessary facilities and to Dr. B.B. Mahapatro for kindly sparing adrenaline
hydrochloride. Thanks are also due to Professor M. Sabir, College of Veterinary Sciences
and Animal Husbandry, Mathura for helpful suggestions.

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REFERENCES


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**LETTER TO THE EDITOR**

**HYPOTENSIVE EFFECT**

(Receiv. 13.10.1970)

Sir,

Glucagon reduces vascular resistance in man (1) and dogs (2) is also observed in rats and dogs is reported here.

Male albino rats (250-300gm) were used. The jugular vein was cannulated and blood pressure was recorded with a Con道 manometer. Blood pressure was measured by cannulating the right carotid artery.

In experiments with rats (Fig. 1), intravenous or subcutaneous administration of glucagon (1.5mg/kg) produced a fall in blood pressure which was significant in both species. The hypotensive effect of glucagon lasted for approximately 2-4 minutes (Fig. 1). Pre-treatment with propranolol (3mg/kg) in eight dogs caused the pressure to fall to a lower level which remained unaffected after pretreatment. The hypotensive effects were found to last for 15-20 min with each

The work confirms that the hypotensive effect of glucagon is not blocked by propranolol and lasted longer. In rats and dogs, the effect is only seen in doses which are not toxic. In both species, hypotensive effects are not blocked by propranolol.