SHORT COMMUNICATION

INFLUENCE OF RESERPINE AND GUANETHIDINE ON THE RESPONSES OF THE ISOLATED RAT ILEUM TO CATECHOLAMINES

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Summary : The sensitivity of the isolated ileum of the rat to catecholamines has been investigated using normal, reserpinized and guanethidine treated animals. Both reserpine and guanethidine treatment produces supersensitivity to adrenaline, noradrenaline and to a greater extent to isoprenaline.

Key words : guanethidine supersensitivity reserpine rat ileum

INTRODUCTION

Supersensitivity of various tissues to the action of catecholamines after treatment with sensitizing agents such as reserpine and guanethidine, have been reported in the literature. Rat ileum is a suitable model for the assay of catecholamines. However, reports are not available for the assesment of supersensitivity to catecholamines on this preparation. We investigated the supersensitivity of rat ileum to catecholamines after reserpine and guanethidine pretreatment.

MATERIAL AND METHODS

Preparation of animals : Male albino rats of the Holtzman strain weighing 200 to 300 *gm* were used in all experiments. Animals were equally divided into three groups. Animals in the control group received 0.2 *ml* of normal saline (ip) on two alternate days and were killed on the 4th day. Animals in the second group received reserpine similarly

in two doses of 1 *mg/kg* (ip). Animals in the third group received guanethidine similarly in two doses of 20 *mg/kg*. These doses of reserpine and guanethidine were the maximal doses tolerated by the animals.

Rat Ileum preparation : ileum from the freshly killed rats was suspended in a 10 *ml* organ bath containing aerated Tyrode solution at 37°C.

Estimation of activity of drugs : The entire dose response curve of adrenaline was plotted by its capacity to reduce the maximum contraction produced by acetylcholine (100 *ng/ml*) when added to the bath one min before acetylcholine. On separate tissues dose-response curves of noradrenaline and isoprenaline were elicited and compared with adrenaline. The potency of the three catecholamines was measured by using parallel line assay method.

RESULTS

Table I shows the ED_{50} of adrenaline, noradrenaline and isoprenaline on the three types of tissues. Comparison of ED_{50} of the three catecholamines were determined and relative potency was found out (Table II). On the normal tissue the sensitivity of adrenaline and isoprenaline was 1.5 and 5.7 times more than noradrenaline respectively. The sensitivity of reserpinized tissue when compared with the normal tissue was increased by 17.6, 17.9 and 360.7 times for adrenaline, noradrenaline and isoprenaline respectively. Similarly the sensitivity of the guanethidine treated tissue was also increased by 9.3, 6.6 and 87.6 times for adrenaline, noradrenaline and isoprenaline, respectively.

TABLE I : Doses of adrenaline, noradrenaline and isoprenaline causing equal Inhibition of acetylcholine induced contraction of rat ileum after treatment with reserpine and guanethidine.

Drugs	*N*	*Control*	*Reserpine treated*	*Guanethidine treated*
		ED_{50} *in ng/ml*	ED_{50} *in ng/ml*	ED_{50} *in ng/ml*
Adrenaline	10	928.7±37.3	52.6±2.8	98.8±4.4
Noradrenaline	10	1418±42.1	78.9±3.3	213±11
Isoprenaline	10	245.3±10.7	0.68±0.11	2.8±0.16

N : Number of experiments.

ED_{50} was calculated for 50% inhibition of acetylcholine induced contraction.

TABLE II : Comparison of relative potencies of adrenallne (Ad), noradrenaline (Na) and isoprenaline (Iso) observed by different workers on isolated tissues and intact preparations.

Preparation	*Relative potencies*									*References*
	Control			*After reserpine*[a]			*After guanethidine*[a]			
	Ad	*Na*	*Iso*	*Ad*	*Na*	*Iso*	*Ad*	*Na*	*Iso*	
Rat fundus	1	1	5							Vane (5)
Rat fundus	1	1.2	20	6	3.4	3125	10	1.2	984	Khan & Asmae (4)
Rabbit ileum				3	2	2.5				Flemming & Schimidt (3)
Rat fundus	1	1	9.4	4	2	2515				Darabi & Haque (1)
Rat fundus	1.06	1	9.4				7.7	1.3	676	Darabi & Haque (2)
Rat arterial B.P.									2-3	Von Euler & Purkhold (6)
Rat ileum	1.5	1	5.7	17.6	17.9	360.7	9.3	6.6	87.6	Present study

[a] In terms of control.

DISCUSSION

In our study the potency of adrenaline is 1.5 times more than noradrenaline while the potency of isoprenaline is 5.7 times more than noradrenaline. This result agrees with the observations of Vane (5), Khan and Asmae (4) and Darabi and Haque (1) (Table II) on different tissues. The increase in activity of the three catecholamines after reserpinization agrees with the results of Khan and Asmae (4), Flemming and Schimidt (3) and Darabi and Haque (2) on different tissues (Table II) except in production of different grade of supersensitivity of different tissues to isoprenaline. The increase in activity of catecholamines noted after guanethidine treatment agrees with the results of Khan and Asmae (4) and Darabi and Haque (2) on different tissues with (Tabla II).

Supersensitivity to isoprenaline after reserpine and guanethidine treatment seen in this work is interesting. This study would support the view that reserpine and guanethidine treatment may increase the sensitivity of rat ileum to isoprenaline by the mechanism which may be independent of the uptake and depletion of storage of catecholamines in the sympathetic nerve endings.

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