SHORT COMMUNICATION

HISTAMINE RECEPTORS IN GUINEA-PIG ISOLATED URINARY BLADDER

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Summary: Spasmogenic action of histamine, 2-(2-aminoethyl) pyridine (H_1 receptor agonist) and 4 methyl-histamine (H_2 receptor agonist), have been studied in guinea pig isolated urinary bladder in the presence of mepyramine (H_1 antagonist) and metiamide (H_2 antagonist) to identify the presence of H_1 and H_2 receptors. The study suggested the presence of H_1 as well as H_2 receptors in this preparation.

Key words : histamine urinary bladder H_1 and H_2 receptors

INTRODUCTION

The classical antihistaminics (mepyramine and diphenhydramine) do not block certain actions of histamine (1,3,4,6). The discovery of burimamide by Black *et al.* (2) showed the involvement of H_2 receptors mediating these actions. The present work was undertaken to identify and type the histamine receptors in guinea-pig urinary bladder.

MATERIAL AND METHODS

Isolated bladder of male guinea-pig was mounted according to the method of Ursillo and Clark (7) except that the bath temp was maintained at $35 \pm 0.5°C$ and the magnification was 8 to 10 times.

The spasmogen was in contact with the tissue for 30 sec. The agonist response/ wash cycle was of 5 min. Mepyramine was present in the bath for 2 min only once, whereas metiamide was added every time to the bath 5 min before recording the response to the spasmogen.

For each set of experiments, a minimum of six observations was made. Student's 't' test was used to statistically evaluate the results. Concentrations mentioned in the text are those of the salts.

RESULTS AND DISCUSSION

Histamine acid phosphate, 2-(2-aminoethyl) pyridine dihydrochloride (H_1 agonist) and 4 methyl histamine dihyrochloride (H_2 agonist) produced dose dependent contractions. The sensitivity of the tissue to histamine was 0.1 $\mu g/ml$. to H_1 agonist 2 $\mu g/ml$ and to H_2 agonist 15 $\mu g/ml$. Addition of 1 $\mu g/ml$ of metiamide produced a partial blockade of responses to histamine (0.1 to 0.4 $\mu g/ml$) and considerable blockade of responses to H_2 agonist (40 to 160 $\mu g/ml$) but failed to produce any significant blockade of responses to H_1 agonist (2 to 8 $\mu g/ml$). Further addition of mepyramine (0.1 $\mu g/ml$) produced an additional blockade of responses to histamine and H_2 agonist. Mepyramine produced significant blockade of the H_1 agonist response (Table I).

TABLE I : Actions on guinea-pig urinary bladder of histamine, H_1 agonist and H_2 agonist and their modification by metiamide and metiamide plus mepyramine.

Agonist	*Dose of agonist ($\mu g/ml$)*	*Response (mm ± S.E.)*			*% Inhibition*	
		Control	*After metiamide*	*After metiamide and mepyramine*	*After metiamide*	*After metiamide and mepyramine*
Histamine	0.1	32.66 ± 2.06	24.16 ± 1.95*	11.00 ± 2.25*	29.26	66.31
	0.2	44.16 ± 2.16	35.00 ± 1.06*	21.66 ± 2.03*	18.18	50.95
	0.4	58.00 ± 3.19	50.00 ± 2.19*	38.63 ± 1.70*	13.94	36.50
2-(2-aminoethyl) pyridine	2	34.00 ± 2.00	33.00 ± 1.16	19.00 ± 0.47*	03.00	44.11
	4	54.00 ± 2.17	52.00 ± 2.00	37.00 ± 0.60*	03.70	31.48
	8	73.00 ± 2.89	70.00 ± 2.20	55.00 ± 1.02*	04.28	24.65
4-methyl histamine	40	29.00 ± 2.07	18.00 ± 0.47*	8.00 ± 1.22*	37.93	72.41
	80	40.00 ± 2.12	30.00 ± 1.60*	17.00 ± 1.18*	25.00	57.50
	160	51.00 ± 3.10	40.00 ± 1.22*	26.00 ± 1.92*	21.56	49.19

Each value depicts the mean of 6 experiments.

* $P < 0.01$

Log dose response curve of histamine showed a parallel shift to the right in the presence of metiamide as well as mepyramine suggesting the competitive nature of the antagonism.

Acetylcholine chloride was used in all these experiments to show the specificity of the antagonists. The acetylcholine 0.1 $\mu g/ml$ responses were not modified by both the antagonists to any significant degree.

It was observed that in the presence of metiamide the initiation of the response was delayed by about 10 sec.

Dose dependent contractions with histamine were partially blocked by metiamide (H_2 antagonist) as well as mepyramine (H_1 antagonist) suggesting the presence of H_1 as well as H_2 receptors in this preparation.

The dose dependent contractions with 2-(2-aminoethyl) pyridine a selective H_1 agonist were blocked only by mepyramine. Metiamide failed to block the responses to H_1 agonist.

The responses to 4-methyl histamine, a H_2 agonist were partially blocked by metiamide as well as mepyramine since it is reported to have some stimulant effect on H_1 receptors also (5).

It appears that both H_1 and H_2 receptors are present in this preparation subserving a common response, though the sensitivity to the H_1 and H_2 agonist is of a low order.

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