

EFFECT OF METIAMIDE, AN H<sub>2</sub>-ANTAGONIST ON STRESS-INDUCED GASTRIC ULCERS IN RATS

Histamine-induced gastric acid secretion has been shown to be mediated through activation of H<sub>2</sub>-receptors (1) and this action of histamine is antagonized by metiamide an H<sub>2</sub>-receptor antagonist (2). Histamine has also been suggested to play a role in mediating gastric ulcers in rats (4); however, attempts at altering the incidence of experimental gastric lesions by the administration of H<sub>1</sub>-antihistamines or drugs inhibiting histamine synthesis or catabolism have led to controversial results (3,4). In the present study, an attempt was made to investigate the effect of metiamide, an H<sub>2</sub>-antihistamine on the production of stress-induced ulcers.

Albino rats of either sex (150-200 g) were used for the study. The animals were fasted for 24 hr before being subjected to restraint and cold stress as per the method of Senay and Levine (6). At the end of stress period of 4 hr the animals were sacrificed and their stomachs were opened along the greater curvature. Gastric mucosae were observed with the help of magnifying glass for erosions, haemorrhages and ulcers. Ulcers were scored according to the method described by Prino *et al.* (5). Normal saline or drugs were injected intraperitoneally 30 min prior to subjecting the animals to stress. Each group of animals received either normal saline, metiamide or mepyramine. The results were analysed by unpaired 't' test.

The results are presented in Table I. Stress-induced by immobilisation and cold produced gastric ulcers in all the rats belonging to the control group. In metiamide treated group there was a significant ( $P < 0.001$ ) decrease in ulcer score, while the difference in the ulcer score between control and mepyramine treated groups was not significant.

TABLE I: Effect of metiamide and mepyramine on stress-induced gastric ulcers in rats.

Drug (dose mg/kg)	Mean ulcer score $\pm$ S.E.M.	P Value
Normal Saline 0.2 ml/100 g (10)	3.4 $\pm$ 0.43	—
Metiamide 1 (10)	1.25 $\pm$ 0.26	P < 0.001
Metiamide 1.5 (10)	0.14 $\pm$ 0.09	P < 0.001
Metiamide 2 (10)	0.1 $\pm$ 0.06	P < 0.001
Mepyramine 10 (10)	2.7 $\pm$ 0.45	P > 0.2

Figures in parenthesis indicate the number of rats used.

In the present study, the H<sub>1</sub>-antihistamine mepyramine (10 mg/kg) failed to protect rats against stress induced gastric ulcers; while H<sub>2</sub>-antihistamine metiamide significantly decreased the ulcer score. This suggests that histamine plays a major role in the production of stress induced ulcers in rats and this effect is mediated through H<sub>2</sub>-receptors.

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