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SHORT COMMUNICATION

Antihistamine protection against histamine-induced gastric ulceration in the guinea-pig

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IT is generally believed that antihistamines have no protective action against histamine-induced gastric ulceration (Ivy, Grossman & Bachrach 1952). Evidence has been based on animal experiments in which acute gastric ulcers were produced over periods ranging from 24 hr to 40 days and in which repeated large doses of histamine, usually in a beeswax and oil base, were used (Halpern & Martin, 1946; Friesen, Baronofsky & Wangensteen, 1946; Crane, Lindsay & Dailey, 1947; Winter & Mushett, 1948).

We have studied in the adult guinea-pig the protective effect of mepyramine maleate on gastric ulceration produced in less than 6 hr by a much smaller single dose of histamine in aqueous solution.

METHODS

Male albino guinea-pigs of 700 g average body weight were used. In most of the experiments, fasted animals were used. They were deprived of food for about 10 hr before the start of each experiment and wore loosely fitting perspex collars to prevent coprophagy. Non-fasted animals wore no collars. All animals received water *ad lib.*

Gastric ulceration was induced by a single injection of histamine acid phosphate (HAP) in aqueous solution (1 mg/ml) given either intramuscularly or intraperitoneally according to the method previously described (Eagleton & Watt, 1964). The dose by intramuscular injection was 1 mg/kg and by the intraperitoneal route either 1 mg or 5 mg/kg. Animals protected with mepyramine maleate were given 10 mg/kg intramuscularly 1 hr before and again 2 hr after the injection of histamine.

All animals were killed by a sharp blow on the head 6 hr after the administration of the histamine. The occurrence of ulceration was assessed after fixation of the stomach in formol-saline.

RESULTS

The incidence of histamine-induced ulceration and the protection afforded by mepyramine maleate are shown in Table 1. Protection was greatest (100%) in the animals which received 1 mg HAP/kg intraperitoneally. In the fasted and non-fasted animals which received 5 mg HAP/kg intraperitoneally, the antihistamine drug reduced the incidence of ulceration (and greatly lessened the severity of lesions). In addition, the protected animals showed no signs of abdominal discomfort as observed in control groups which received only histamine intraperitoneally.

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TABLE 1. THE INCIDENCE OF HISTAMINE-INDUCED GASTRIC ULCERATION IN MALE ADULT GUINEA-PIGS WITH AND WITHOUT ANTIHISTAMINE PROTECTION (2×10 mg/kg i.m.)

Histamine acid phosphate mg/kg	Without mepyramine		With mepyramine	
	No. of animals with gastric ulcers	% with gastric ulcers	No. of animals with gastric ulcers	% with gastric ulcers
1 i.m.	8/11	73	1/6	16
1 i.p.	7/10	70	0/9	0
5 i.p.	15/15*	100	2/5*	40
	10/10†	100	1/6†	16

* Fasted animals. † Non-fasted animals.

DISCUSSION

Our results do not support the current belief that antihistamines are ineffective in preventing histamine-induced gastric ulceration. In contrast with other workers, we used smaller amounts of histamine which were nonetheless effective in producing ulcers. This permitted the effective antagonistic ratio of antihistamine drug to be increased and by restricting the period of ulcerogenesis to not more than 6 hr, this ensured a high concentration of antihistamine throughout the experiment. Provided adequate doses of antihistamine are given it seems possible that protection can be afforded against histamine ulceration produced over longer periods than were used in our experiments. Thus, in work that appears to have been overlooked, Van Meter & Oleson (1949) observed that the antihistamine chlorothen citrate (Tagathen) caused a marked reduction in the incidence and severity of gastric ulcers induced by histamine over a period of several days.

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