Experimental gastric ulcers and uropepsinogen excretion in the rat

Excretion of uropepsinogen has been examined in animals and man (Müller & Braun, 1964; Calandra, Fonnesu & Cozzolino, 1965; Pastor Franco, 1966; Abbott, Harrisson & Brogle, 1967) and though it is generally accepted that its excretion rises in patients with gastric or duodenal ulcers, the value of the parameter as a diagnostic test has not been assessed.

Table 1. *Relation between gastric ulcers and uropepsinogen excretion in the rat.* The urines were collected for 18 h after the administration of reserpine or hydrochlorothiazide; after the second administration of phenylbutazone and the tenth injection of prednisolone; after 4 fasting days; after the plaster bandage and 24 h after the injection of CCl_4 or renal monolateral lesion respectively from 20 h fasted rats. Atropine and oxyphencyclimine were given simultaneously to the reserpine or to the second phenylbutazone administration. Morphological examination was made at the end of the urine collection.

Treatment	Uropepsinogen (mg tyrosine/rat/18 h) mean ± s.e.	Morphological examination Ulceration Index mean ± s.e.	% Ulcerated animals
Controls	1·65 ± 0·20 (20)	0·15 ± 0·08 (20)	15
Hydrochlorothiazide (5 mg/kg orally	1·51 ± 0·19 (20)	0·10 ± 0·07 (20)	10
Controls	1·53 ± 0·21 (20)	0 (20)	0
Renal monolateral	1·67 ± 0·17 (20)	0 (20)	0
Controls	1·70 ± 0·20 (20)	0 (20)	0
CCl_4 (4 mg/kg, i.p. as 1 : 1 v/v) mixture with olive oil)	1·73 ± 0·17 (20)	0 (20)	0
Controls	1·55 ± 0·20 (20)	0 (20)	0
Plaster bandages	2·53 ± 0·21 (20)*	3·25 ± 0·28 (16)	100
Controls	1·38 ± 0·12 (20)	0·10 ± 0·07 (18)	10
Fasting (4 days)	2·49 ± 0·16 (20)*	1·74 ± 0·40 (19)	63·1
Controls	0·78 ± 0·09 (10)	0 (10)	0
Prednisolone (10 mg/kg daily s.c. for 10 days)	1·28 ± 0·11 (10)*	2·00 ± 0·44 (10)	80
Controls	1·91 ± 0·18 (20)	0 (20)	0
Reserpine (5 mg/kg, i.p.)	4·02 ± 0·27 (20)*	2·35 ± 0·23 (20)	100
Reserpine (5 mg/kg, i.p.) + atropine (10 mg/kg orally)	2·78 ± 0·42 (20)*†	0·90 ± 0·23 (20)*	95
Reserpine (5 mg/kg, i.p.) + oxyphencyclimine (10 mg/kg orally)	2·22 ± 0·30 (20)†	0·35 ± 0·13 (20)*	45
Controls	1·03 ± 0·14 (20)	0 (20)	0
Phenylbutazone (100 mg/kg orally twice in 8 h)	2·55 ± 0·25 (20)*	3·40 ± 0·21 (20)	100
Phenylbutazone (100 mg/kg orally twice in 8 h) + atropine (10 mg/kg orally)	1·28 ± 0·07 (20)†	2·05 ± 0·33 (20)*	85
Phenylbutazone (100 mg/kg orally twice in 8 h) + Oxyphencyclimine (10 mg/kg orally)	1·24 ± 0·05 (20)†	1·90 ± 0·38 (20)*	65

* Significance relative corresponding control group, † Significance relative to reserpine or phenylbutazone treated group ($P \leqslant 0·01$). Numbers of animals are in parentheses.

We now report the results of experiments made in rats in which different kinds of experimental gastric ulcers have been induced and in some instances treated with anti-acetylcholine drugs. We also examined the effect of the diuretic hydrochlorothiazide on the rate of uropepsinogen excretion in normal rats, and also the influence of lesions other than gastric ulcers on the assay of acid proteolytic enzyme activity in the urine of rats with hepatic or renal damage.

Male or female Sprague-Dawley rats, 160–170 g, had gastric ulcers produced by reserpine (Radouco-Thomas, Lataste-Dorolle & others, 1960), by phenylbutazone, by prednisolone, by fasting or by immobilization in plaster bandages (Müller & Braun, 1964). Groups of rats with reserpine- or phenylbutazone-induced ulcers were treated orally with atropine sulphate or oxyphencyclimine (1-methyl-1,4,5,6-tetrahydro-2-pyrimidylmethyl-α-cyclohexyl-α-phenylglycolate hydrochloride) both solubilized in 5% acacia gum. Further groups of normal rats were treated with hydrochlorothiazide; the hepatic damage was produced by CCl_4 and a monolateral renal lesion according to Coppi, Bonardi & Fresia, (1966). Uropepsinogen activity was measured with the haemoglobin method of Anson (1963) and the amount of uropepsinogen excreted was expressed as mg of tyrosine/rat per 18 h. On additional groups of rats in the same experimental conditions the number of animals with gastric lesions and the severity of these graded by an arbitrary scale from 0 to 4+ was recorded. All the results were statistically evaluated by the Student's *t*-test.

Hydrochlorothiazide, CCl_4 or renal lesion did not affect the uropepsinogen excretion or the integrity of the gastric mucosa (Table 1).

The excretion of uropepsinogen always increases in animals with any gastric ulcers, however induced. Oxyphencyclimine and, to a lesser extent, atropine decreased the ulceration index as well as the excretion of uropepsinogen in the animals given reserpine or phenylbutazone. In these groups there was a good relation between the enzyme excretion and the severity of gastric lesions, although the two parameters were not always in proportion.

Thus the evaluation of the uropepsinogen excretion, together with a morphological examination, could provide a useful tool in the screening of anti-ulcer drugs.

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