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SHORT COMMUNICATION

EFFECT OF ANGIOTENSIN CONVERTING ENZYME INHIBITOR (CAPTOPRIL) ON GASTRIC ULCER PRODUCTION IN PYLORUS LIGATED RATS

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Abstract: Intraperitoneal injection of Angiotensin Converting Enzyme inhibitor, captopril, reduced significantly (P<0.001), the production of gastric ulcers in pylorus-ligated albino rats, compared to the control groups, irrespective of the dose schedule - single or quadruple. In the light of evidence available in the literature, it is reasonable to hypothesise that the anti-ulcer effect of captopril may be mediated through prostaglandins.

Key words: captopril pylorus ligation ulcer index

INTRODUCTION

Angiotensin Converting Enzyme (ACE) was discovered in 1954 and is the enzyme responsible for the formation of Angiotensin II from Angiotensin I, components of Renin Angiotensin System (RAS). The former is a potent vasoconstrictor and stimulates the release of aldosterone and ADH and hence has an inportant role in the regulation of arterial blood pressure and of fluid and electrolyte homeostasis. Recent data has expanded the traditional endocrine actions of RAS to include effects on local tissues (paracrine), cells of origin (autocrine) and intracellular organelles (intracrine) (1). It is, therefore, pertinent to state that RAS can influence the functions of several organs in the body, stomach included, acting systemically or/and locally. In view of these facts, the present study was planned to identify the role of ACE inhibitor, captopril, on the production of gastric ulcers in pylorus-ligated rats. For, the administration of captopril is expected to reduce or block the formation of Angiotensin II which has so far not been shown to have any direct or indirect influence on gastric secretion.

METHODS

Thirty healthy albino rats of Wistar strain of either sex, weighing 150-250 gms, were divided into three groups of 10 each. The first group served as controls-subjected to pylorus ligation (vide infra); the effect of a single dose of intraperitoneal injection of captopril (Wockhardt) 35 mg/kg body weight (2) on the production of gastric ulcers was studied in the second group and in the third group, the effects of four doses of captopril - once a day for 4 dyas - was studied. In case of rats that received Captopril injection, the last single dose was given just before they were subjected to pylorus ligation.

Ulcer production: The pylorus was ligated after a fast for 36 hrs (3). Animals were killed 8 hrs after the operation. This interval allowed the formation of severe ulcers in the forestomach (shay ulcers).

Determination of ulcer index: The stomach was removed, opened along the greater curvature, cleaned and spread on a cardboard with the mucosal surface upwards and

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smoothened free of corrugation. The area of the entire gastric mucosa and that of the ulcers were estimated using a mm grid, with the help of a monocular magnifying lens. The ratio of the total area of the ulcers divided by the area of the gastric mucosal surface yielded the ulcer index value.

The mean ulcer index value ± SEM for each group was calculated and the statistical analysis was by Student's 't' test. The results are shown in Table I.

TABLE I : Influence of captopril on gastric ulcer index in rats Mean ± SEM.

Group n = 10		*% Incidence of ulcers*	*Ulcer index***
I	Control	100%	0.037 ± 0.0036
II	Single dose of Captopril	90%	0.01 ± 0.0027*
III	Four doses of Captopril	90%	0.015 ± 0.0047*

* P<0.001 compared to Group I.
** Ulcer Index : Area of ulcers/total area of gastric mucosa.

RESULTS

All the animals in the control group developed gastric ulcers on pyloric ligation while 90% of them did so in the other two groups. The ulcer index values in the experimental groups were less compared to the control group, the difference being highly significant statistically (P<0.001). Between the two experimental groups, the number of doses of captopril did not produce any significant difference in the ulcer index. No histological study was done on the ulcers.

DISCUSSION

The results of the study show that captopril can reduce the incidence of gastric ulcers following pyloric ligation and the effect does not appear to be dose-dependent. The causation of ulcers in the gastric mucosa due to pyloric ligation may be two-fold: stress-induced increase in gastric hydrochloric acid secretion and stasis of the acid. The presence of the acid in the stomach has been shown to be a prerequisite for the formation of stress ulcers (4). Whether acid alone is the offending and causative mechanism is not clear; for, in one study on traumatized patients, acid secretion is normal or decreased (5). It is reasonable to surmise that in pylorus ligated rats, stasis is the major offending factor for ulcerogenesis. The mode of action of ACE inhibitor, captopril, is probably through strengthening of the gastric mucosal barrier or/ and maintaining blood flow through the stomach. Histological and biochemical studies have to be carried out to prove the former hypothesis. Clinical and experimental studies in critically ill and normal man and animals demonstrated clearly that gastric mucosal integrity is determined to a great extent by gastric blood flow (5). Since the therapeutic action of captopril is to block the formation of Angiotensin II, especially under stressful condition and therefore its vasoconstrictor action, the resulting change in systemic arterial blood pressure can alter gastric blood flow (6).

Recent evidence indicates that prostaglandins possess potent gastric anti-ulcer properties, independent of their known inhibitory effects on acid secretion by strengthening gastric mucosal barrier, stimulation of gastric mucin and bicarbonate secretion and enhancing gastric mucosal blood flow (7). Prostaglandin E_1 has been shown to prevent formation of gastric ulcers in pylorus ligated rats and the rat stomach is known to release PGE_1 (3). It is, therefore, possible that ACE inhibitor, through some unknown mechanism, may increase the local concntration of PGE_1 in the rat stomach. Captopril is known to release prostaglandins, particularly, prostacyclin, into the systemic circulation (8). However, a definite link between ACE inhibitor and gastric PGE_1 needs to be established.

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