Concentrations of prostaglandin A-, E- and F-like substances in gastric mucosa of normal subjects and of patients with various gastric diseases

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Summary

1. Prostaglandin A-, prostaglandin E- and prostaglandin F-like substances were determined radioimmunologically in antral biopsy material obtained by endoscopy.

2. In patients with gastritis, the concentrations of prostaglandin (E + A)-like substances were six times as high and of prostaglandin F-like substances twice as high as in normal subjects. In chronic atrophic gastritis, the concentrations of prostaglandin (E + A)-like material was four times as high as in normal subjects whereas prostaglandin F-like material remained unchanged. In acute gastric ulcer, prostaglandin (E + A)-like material reached concentrations four times higher than in normal subjects, accompanied by a fivefold increase of prostaglandin F-like substances. After healing of the gastric ulcer, prostaglandins returned to normal values.

3. There was no correlation between gastrin and prostaglandins in all biopsy specimens.

Key words: duodenal ulcer, gastric ulcer, gastrin, gastritis, prostaglandins, ulcer.

Introduction

Prostaglandin E₂-like substances are present in concentrations up to 36 ng/mg of soluble protein in human gastric mucosa (Bennett, Murray & Wyllie, 1968; Bennett, Stamford & Unger, 1973), whereas in the submucosa the concentrations are much lower. In normal subjects and in duodenal ulcer patients, prostaglandin E₂-like material in basal gastric juice reached concentrations of 2.4 ± 0.85 (SE) ng/ml (Bennett et al., 1973) or 443.8 ± 49.0 pg/ml (Peskar, Holland & Peskar, 1974). The concentrations of these substances in biopsy material taken from patients with acute gastric ulcers have not been measured previously. Naturally occurring prostaglandins of types E and A, and their analogues such as 15-methyl and 16,16-dimethyl compounds, inhibit gastric secretion in man (Nylander & Andersson, 1976; Karim & Fung, 1976; Karim, Carter, Bhana & Ganesan, 1973a; Nylander & Andersson, 1974), dog (Robert, 1976; Robert, Nezamis & Phillips, 1967) and rat (Robert, 1976; Robert, Nezamis & Phillips, 1968). In the dog the inhibition was demonstrated against a variety of gastric stimulants (Robert, 1976). In humans, prostaglandin A₁ and E, revealed a dose-dependent inhibitory effect on basal gastric secretion and secretion stimulated by histamine (Wilson, Phillips & Levine, 1971) or pentagastrin (Classen, Koch, Bickhardt, Topf & Dempling, 1971). 15-Dimethyl-prostaglandin E₂ methyl ester and 16,16-dimethyl-prostaglandin E₂ methyl ester were also shown to be potent inhibitors of gastric secretion both in animals (Robert, 1976; Robert, Nezamis & Phillips, 1967) and man (Nylander & Andersson, 1976; Karim & Fung, 1976; Karim, Carter, Bhana & Ganesan, 1973b).

The same prostaglandins were reported to prevent formation of ulcers and to favour ulcer healing (Nylander & Andersson, 1976; Karim

In the present study prostaglandin E-, A- and F-like compounds were measured in antral atrophic gastritis and acute gastric and duodenal ulcers.

Material
Ten patients with gastritis, 10 with chronic atrophic gastritis, 13 with acute gastric ulcer and 16 with duodenal ulcer were studied. They comprised men and women aged 35–80 years. The diagnosis was made on the basis of the clinical history, radiography and endoscopy. Eight subjects with normal mucosa served as controls. At endoscopy all of these eight control patients had macroscopically normal vascular patterns and histologically no tissue destruction. Five patients with healed gastric ulcer and with normal mucosa were also studied. None of the subjects took anti-acids or other drugs before or during the investigation.

The mucosal biopsies were taken by gastrointestinal biopsy forceps and were examined histologically. They were all obtained from the antrum along the major curve at least 4 cm from any macroscopic pathological lesion. The biopsies were placed in ice-cold sodium chloride solution (150 mmol/l) and extracted immediately with ethyl acetate or by boiling. The ethyl acetate extracts for prostaglandin determination were made by the method of Orczyk & Behrman (1972). The boiling at 100°C in a water bath for gastrin extraction was done by the method of Creutzfeldt, Arnold, Creutzfeldt & Track (1975).

Analytical procedures
Prostaglandin extracts were chromatographed by the method of Jaffe & Behrman (1974) and then determined by radioimmunoassay, also as described by Jaffe & Behrman (1974).

For the prostaglandin (E + A)-like material the same antibody was used as described by Kantrowitz, Robinson, McGuire & Levine (1975) (gift of Dr L. Levine). Prostaglandin F-like compounds were determined by a highly specific antibody (Kirton, Cornette & Barr, 1972) (gift of Dr K. T. Kirton).

Gastrin extracts were also determined by radioimmunoassay by a method of Raptis, Dollinger, von Berger, Schlegel, Schröder & Pfeiffer (1975). The antibody reacts with non-sulphated and sulphated forms of gastrin, 100% with human gastrin (G 17) and 35% with human gastrin (G 34). There was no cross-reaction with pancreozymin, secretin, insulin or glucagon.

The protein was estimated by the method of Lowry, Rosebrough, Farr & Randall (1951). Concentrations of prostaglandin and gastrin were calculated per mg of mucosal protein. All values were corrected for losses. Student’s t-test for unpaired data was used for statistical comparisons. Mean results ± sem are shown unless otherwise stated.

Results
In normal subjects the amounts of prostaglandin (E + A)-like material per mg of gastric mucosal protein varied from 21 to 83 ng and the amounts of prostaglandin F-like material from 2 to 17 ng (Fig. 1).

In gastritis, significantly higher concentrations of prostaglandin (E + A)-like compounds (312 ± 40 ng/mg, n = 10; P < 0.005) were demonstrated, accompanied by slightly increased prostaglandin F-like compounds (20 ± 4 ng/mg, n = 10; P < 0.025). Significantly high concentrations of prostaglandin (E + A)-like compounds (206 ± 39 ng/mg, n = 10; P < 0.0025) were also found in patients with chronic atrophic gastritis, whereas prostaglandin F-like compounds were not changed significantly.

Concentrations in mucosa of patients with gastric ulcer were 203 ± 21 ng/mg (n = 13; P < 0.01) for prostaglandin (E + A)-like material and 44 ± 7 ng/mg (n = 13; P < 0.01) for prostaglandin F-like material.

In patients (n = 5) with healed gastric ulcer (confirmed endoscopically and histologically), prostaglandin E + A was normal, but prostaglandin F was still significantly increased (58 ± 7 ng/mg, n = 5; P < 0.02). In patients with duodenal ulcer (n = 16) all gastric mucosa prostaglandin concentrations remained low. The concentrations of gastrin estimated by radioimmunoassay (range 2–4200 pg/mg of protein) in the same antral biopsies did not correlate with concentrations of prostaglandin E + A or of prostaglandin F (r = 0.074).
Discussion

The results show that prostaglandin (E+A)-like substances are increased in the antral mucosa in gastritis, chronic atrophic gastritis and acute gastric ulcer and do not correlate with concentrations of gastrin. This evidence does not support the finding that mucosal prostaglandins are decreased in gastric lesions and acute gastric ulcer (Karim & Fung, 1976). It has been reported that gastric ulcers are caused by a prostaglandin deficiency after treatment with non-steroidal anti-inflammatory drugs (Karim & Fung, 1976; Robert, 1976). The ulceration could be prevented by application of various naturally occurring prostaglandins (Robert, 1976). The present findings neither support nor contradict the hypothesis that prostaglandin deficiency may be a factor in genesis of peptic ulcer because in these studies prostaglandins were measured in the acute phase.

On the other hand, prostaglandins seem to be involved in pathogenesis of gastric inflammation. Our data also support this hypothesis. This inflammatory effect of prostaglandins has to be independent of gastric secretion because prostaglandins do not alter concentrations of gastrin (also confirmed by our results) while they are inhibiting gastric secretion (Robert, 1976) and one can speculate that the increased concentrations of prostaglandins found under these circumstances might also play a role in the healing process as follows.

Damage to the gastric mucosa may stimulate increased prostaglandin formation in the neighbourhood of the destroyed tissue. There may even be an activating factor favouring production of prostaglandin E+A, since concentrations of prostaglandin F are not markedly influenced in inflammation. If ulcers develop as a result of prostaglandin deficiency, the normal tissue could counteract by increasing the concentrations of prostaglandin E+A to start the proliferation phase.

Studies of prostaglandin E+A concentrations before ulcer formation or gastritis, during the acute phase and the healing process would test this hypothesis and might define the prostaglandin concentrations necessary to cure ulcer.

The problem in defining the action of prostaglandins in the stomach is that although they have a potent inflammatory effect (Vane, 1976), they are necessary for the protection of the gastric mucosa (Cohen, 1976; O’Brien & Carter, 1975). Prostaglandins might therefore be decreased during ulcer development and low...
in the ulcer crater, but increased during the inflammatory and healing phase of gastritis, chronic atrophic gastritis and gastric ulcer.

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References


