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**HELICOBACTER PYLORI INFECTION AND GASTRIC SECRETION
IN DUODENAL AND GASTRIC ULCER PATIENTS
— THE EFFECT OF ERADICATION AFTER ONE YEAR**

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The mechanism by which *Helicobacter pylori* (Hp) predisposes to duodenal and gastric ulcers remains still unclear. It is possible that Hp infection impaires gastric secretion. Evaluation of gastric acid and mucus secretion before and after Hp eradication would let to estimate the influence of Hp infection on gastric secretion. To evaluate the effect of Hp infection on gastric acid and gastric mucous secretion before and one year after Hp eradication.

We examined 28 Hp positive peptic ulcer disease patients (10 — gastric ulcer GU, 18 — duodenal ulcer DU) before and one year after antibacterial treatment. Gastric acid output was examined basely (BAO) and in response to pentagastrin (6 µg/kg) (MAO) using Kay's standard method. Some components of gastric mucus as fucose, galactose, hexosamines and sialic acid were measured using calorimetric methods basaly and after pentagastrin stimulation. Plasma gastrin concentration was measured in 20 patients (6-GU, 14-DU) by radioimmunoassay before and one year after eradication. Hp status was determined by rapid urease test (CLO) and histology (Giemsa stain).

One year after Hp successful eradication gastric acid secretion was significantly reduced — BAO: 3,31 vs 1,474 mmol/h; MAO: 19,63 vs 14,85 mmol/h, $p < 0.05$. Plasma gastrin concentration decreased significantly from 9,783 to 6,017 pmol/l, $p < 0.05$. In patients with ineffective eradication we did not observe any significant changes in gastric acid secretion. An evident, but not statistically significant, decrease of sialic acid output in eradicated patients was noted.

The study has shown the significant influence of Hp infection on gastric acid secretion. Those results support the hypothesis that increased gastric acid secretion may be one of the pathogenic mechanism of Hp infection inducing mucosal damage.

Key words: *Helicobacter pylori* infection, gastric acid secretion, mucus gastric secretion, gastrin

INTRODUCTION

Epidemiologic and clinical evidence has shown that infection of *Helicobacter pylori* (Hp) is associated with chronic active gastritis in up to 100% patients, in duodenal ulcer (DU) in 90% to 95%, and in gastric ulcer (GU) in 60%—70% (1). Its eradication decreases recurrence of DU from 80% to less than 2% in a year (2). This fact is a strong evidence that Hp infection is

important in the development and relapse of peptic ulceration. But pathogenic role of bacterial infection in peptic ulcer disease is still poorly understood, being a subject of still not-ending speculations.

The pathogenesis of peptic ulcer disease is based on the long-standing concept that an ulcer occurs as a result of an imbalance between luminal aggressive and mucosal defensive factors. Hp is accepted as one of the acquired factors involved in peptic ulcer disease. But not everybody infected Hp has peptic ulceration. "There is no ulcer, when there is no acid" — said Schwarz in 1910 (3). Hp and gastric acid, two aggressive factors seem to act together to predispose to peptic ulceration. On the other hand, bacterial infection may also impair mucosal defense. According to Slomiany Hp may be responsible for the weakening of gastric mucus gel integrity (4). But Markesich's findings argue against the hypothesis of gastric mucus degradation by Hp (5).

We therefore studied the chosen parameters of gastric secretion in two group Hp positive patients, with DU and GU, before and one year after the treatment of bacterial infection.

The aim of our study was to evaluate the effect of Hp infection on gastric acid and gastric mucus in one year observation of 28 (DU and GU) patients group before and after treatment of bacterial infection.

PATIENTS AND METHODS

28 Hp positive patients with peptic ulcer were included in the study. Subjects were excluded if they had a history of gastrointestinal disease. They all had active, uncomplicated ulcer (diameter less than 2 cm) at endoscopy. There were 10 gastric ulcer patients and 18 duodenal ulcer patients. The range of age was 29—71, mean 46, 13 females, 15 males. None of the subjects had taken antisecretory medication within 14 days of the studies. Patients were treated with dual drug regiment consisting of amoxycillin (1000 mg twice daily) and Omeprazol (20 mg twice daily) given for two weeks.

Determination of Hp status

Hp status was determined by rapid urease test (CLO) and histology (two antral, two body biopsy specimens routinely processed and stained with haematoxylin and eosin and Giemsa stains in Gray modification). Subjects were defined as Hp negative if rapid urease test and histology were negative in every specimens.

Gastric secretion

Gastric secretion was measured using a standard Kay's method (6, 7). Within seven days of the endoscopy and after an overnight fast a nasogastric tube (90—120 cm long, 14 French) was introduced through the nose or mouth and positioned in the stomach. The position was checked fluoroscopically and by recovery of infused saline. Four 15 minute collection of basal secretion were obtained (basal acid output — BAO) and pentagastrin (6 µg/kg) was then administered subcutaneously. Four additional 15 minute gastric secretion were obtained (maximal acid output — MAO) The samples were kept on ice during transfer to laboratory. All aspirates were stored at 4°C until analysed.

Gastric acid output

Titratable acidity was measured by titration to pH 7.0 with 0,01 M sodium hydroxide. Acid output was calculating taking the mean of all four 15 minute samples before (BAO) and after pentagastrin infusion (MAO).

Gastric mucus determination — the chosen components

The components of gastric mucus as fucose, galactose, hexosamines and sialic acid were measured in gastric juice using calorimetric methods basaly and in response to pentagastrin (8—13). The samples of gastric juice with blood or bile were excluded.

Plasma gastrin concentration

Blood was collected into chilled tubes containing EDTA and the plasma was separated promptly and frozen at -20°C . Plasma gastrin concentration was measured by radioimmunoassay with antibody G17. The basal gastrin value for 20 patients (10 DU, 10 GU); after the treatment: Hp positive — 8, Hp negative — 12) was measured by taking blood samples before the treatment and one year after.

Statistical methods

Normally distributed data are expressed as means and Student's unpaired t test used to compare the significance of the difference between the group means.

Ethics

The protocol was approved by local ethical committee and all patients gave written informed consent. The study was conducted according to the guidelines of the Declaration of Helsinki.

RESULTS

Clinical

At repeat endoscopy after 4 weeks after the end of the treatment ulcers had held in all patients. 16 patients (13 DU, 3 GU) stayed Hp positive after a year. None ulcer recurred in Hp negative group during one year of observation. One gastric ulcer and 5 duodenal ulcer occurred in Hp positive group 1 year after the ineffective treatment.

Gastric acid output

Basal and stimulated acid output were significantly lower ($p < 0.05$) in one year after eradication of Hp in group of 12 patients (GU-7, DU-5) from 3,31 mmol/l (BAO 1) to 1,474 mmol/l (BAO 2), and from 19,63 mmol/l (MAO 1) to 14,85 mmol/l (MAO 2). There were no significant changes in gastric acid output in 16-patients group (GU-3, DU-13) when eradication failed (*Tab.1, Fig. 1*).

Table 1. Gastric acid output (mmol/h), basal plasma gastrin concentration (pmol/l), fucose and sialic acid concentration (mg%), fucose A and sialic acid A output (mg/h) before (1) and in 1 year after eradication (2), n — number of patients, /S.E/

		Hp negative (patients n = 12)			Hp positive (patients n = 16)		
		total	GU	DU	total	GU	DU
HCl	BAO 1	3,3*/0,95/	4,4	1,8	3,64	3,64	5,8
	BAO 2	1,47*/0,41/	1,9	0,8	3,4	3,4	4,6
	MAO 1	19,6*/3,37/	17,6	22,4	16,9	16,9	20,6
	MAO 2	14,8*/2,92/	15,2	14,3	24,2	23,4	24,4
GASTRIN	1	9,8*/2,2/	10,7	8,7	8,2	7,0	8,6
	2	6,0*/1,1/	7,2	4,8	7,8	6,0	8,3
FUCOSE	BAO 1	33,8	29,9	39,3	32,8	35,8	32,1
	BAO 2	39,5	25,4	59,2	24,3	25,2	24,1
	MAO 1	24,6	13,6	40,1	14,9	17,3	14,3
	MAO 2	24,9	14,2	40,0	10,7	13,8	10,1
SIALIC ACID	BAO 1	5,3	6,17	4,2	7,0	10,1	6,3
	BAO 2	5,3	16,1	6,8	5,7	5,6	5,8
	MAO 1	5,3	6,0	4,0	4,0	6,7	3,4
	MAO 2	8,1	12,8	6,8	3,6	4,9	3,3
FUCOSE A	BAO 1	14,2	17,1	19,6	28,7	19,3	30,9
	BAO 2	20,3	21,6	18,6	21,3	16,0	22,6
	MAO 1	22,8	15,9	32,6	26,8	17,3	29,0
	MAO 2	24,6	19,9	31,3	21,4	25,7	20,7
SIALIC ACID A	BAO 1	3,1	3,0	3,2	4,5	4,6	5,6
	BAO 2	3,8	3,1	4,0	4,7	3,1	5,1
	MAO 1	8,5	8,1	9,1	12,9	6,1	14,4
	MAO 2	3,5	4,2	2,5	9,8	8,4	10,2

* — Asterisk indicates significant difference $p < 0.05$

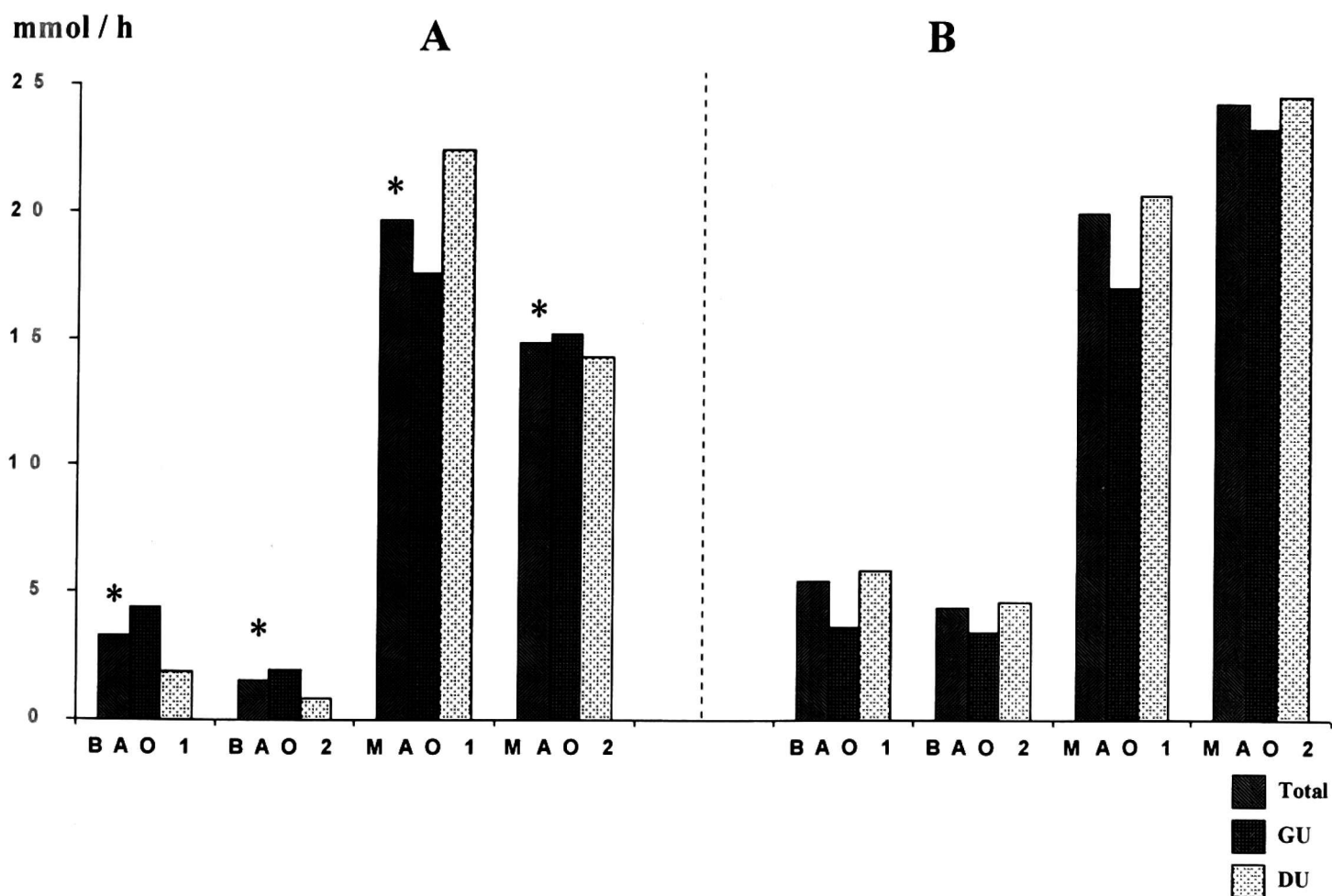


Fig. 1. Gastric acid output, mean value, (mmol/h) before (1) and in 1 year after eradication (2), A — successful eradication, B — failed eradication.
* — Asterisk indicates significant difference $p < 0.05$

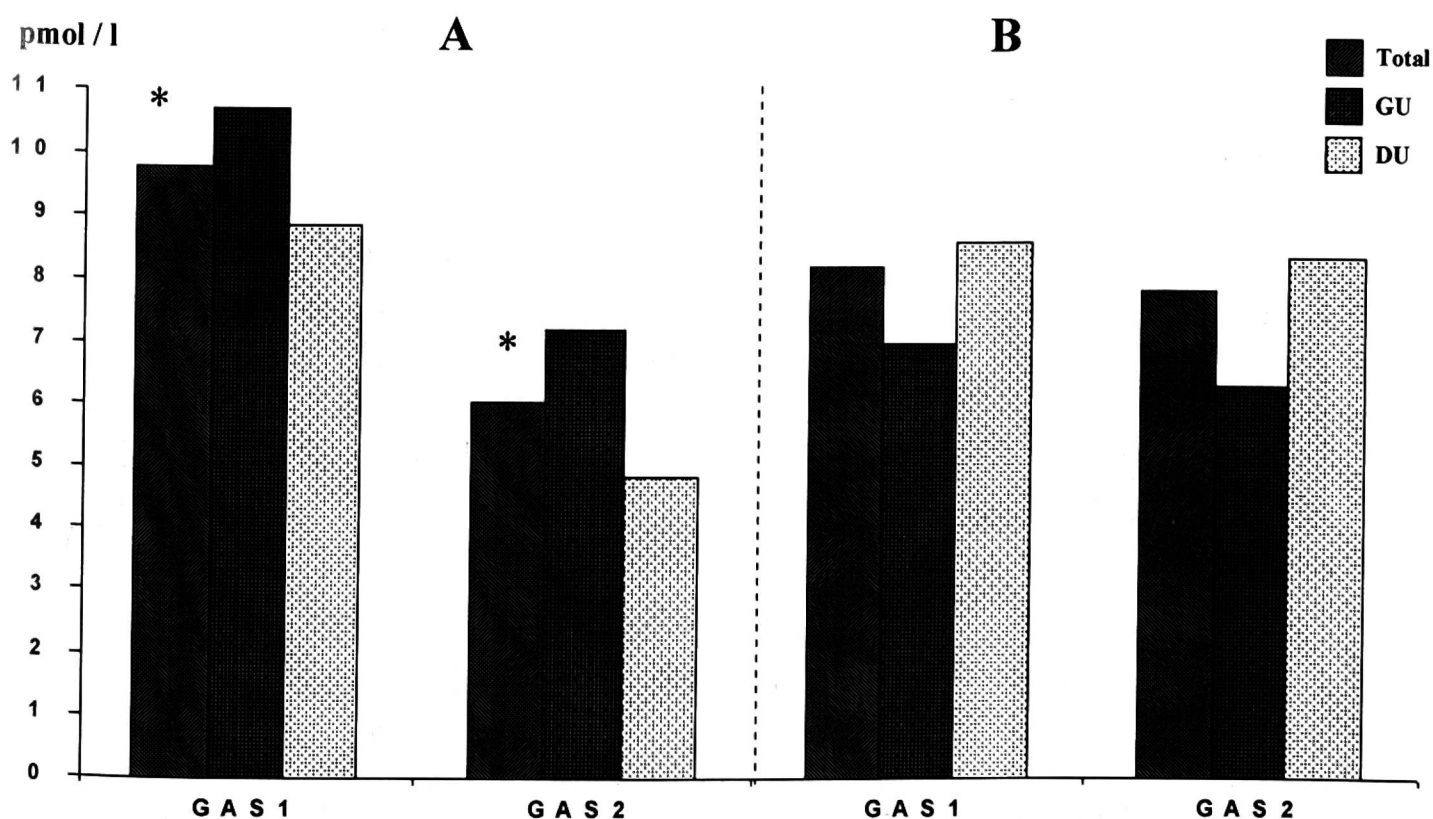


Fig. 2. Basal plasma gastrin concentration, mean value, (pmol/l) before (1) year after eradication (2), A — successful eradication, B — failed eradication.
* — Asterisk indicates significant difference $p < 0.05$

Basal plasma concentration

Basal plasma gastrin concentrations fell significantly after the eradication of Hp. The median plasma gastrin concentration before treatment was 9,783 pmol/l, compared with 6,017 pmol/l after ($p < 0.05$). There were none significant changes in Hp positive group of patients one year after treatment (Tab. 1, Fig.2).

Mucus components (mg%) before and one year after successful eradication

There was no statistically significant influence of Hp eradication on examined components of gastric mucus in a year after successful treatment. Evident decrease of sialic acid output in all GU and DU eradicated patients

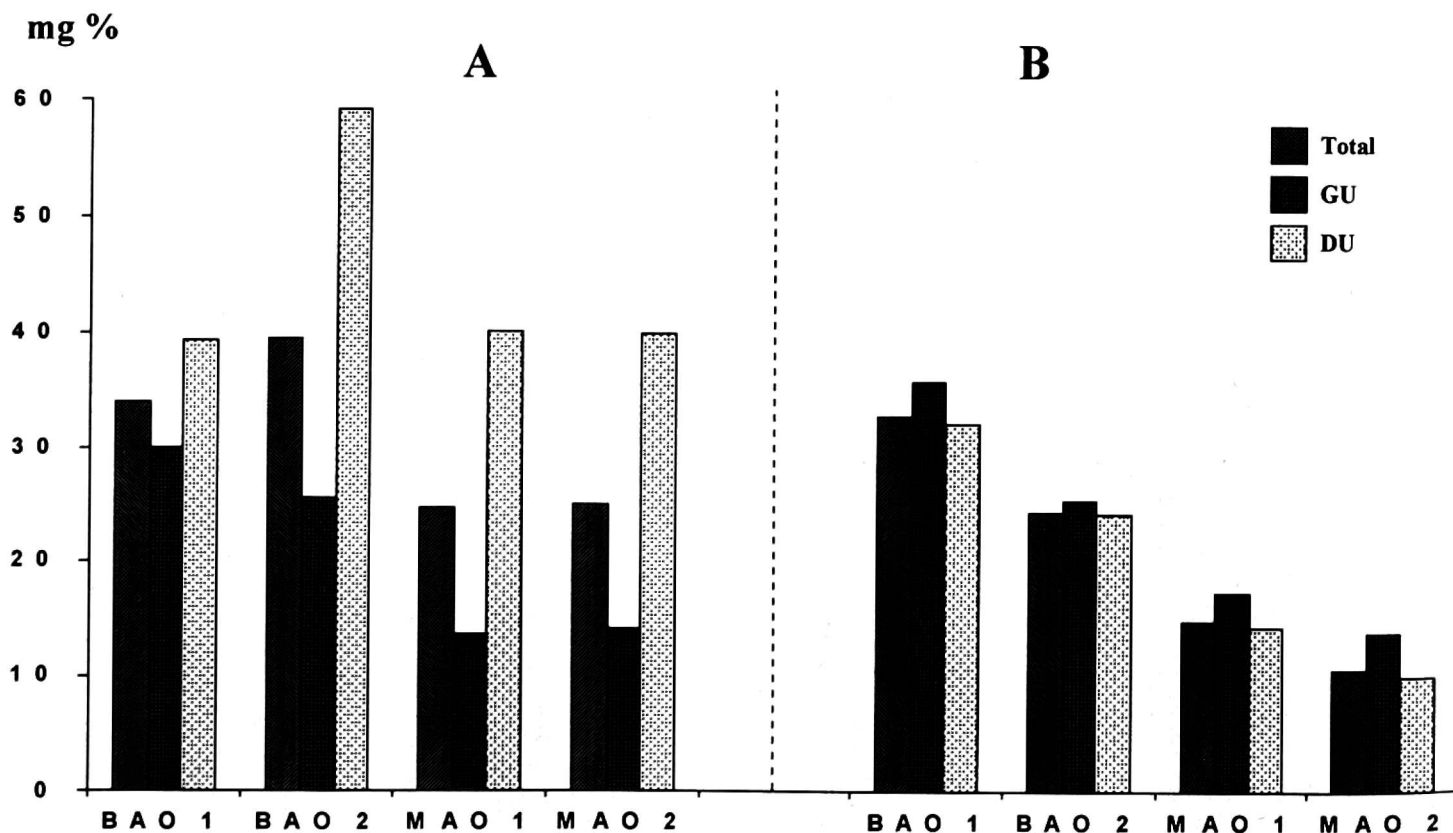


Fig. 3. Fucose concentration, mean value, (mg%) before (1) and in 1 year eradication (2), A — successful eradication, B — failed eradication.

was observed. However the concentration of sialic acid in GU patients after effective treatment increased. In DU eradicated patients increasing of fucose concentration was noticed. There were no changes in fucose output (Tab 1., Fig. 3, 3A, 4, 4A).

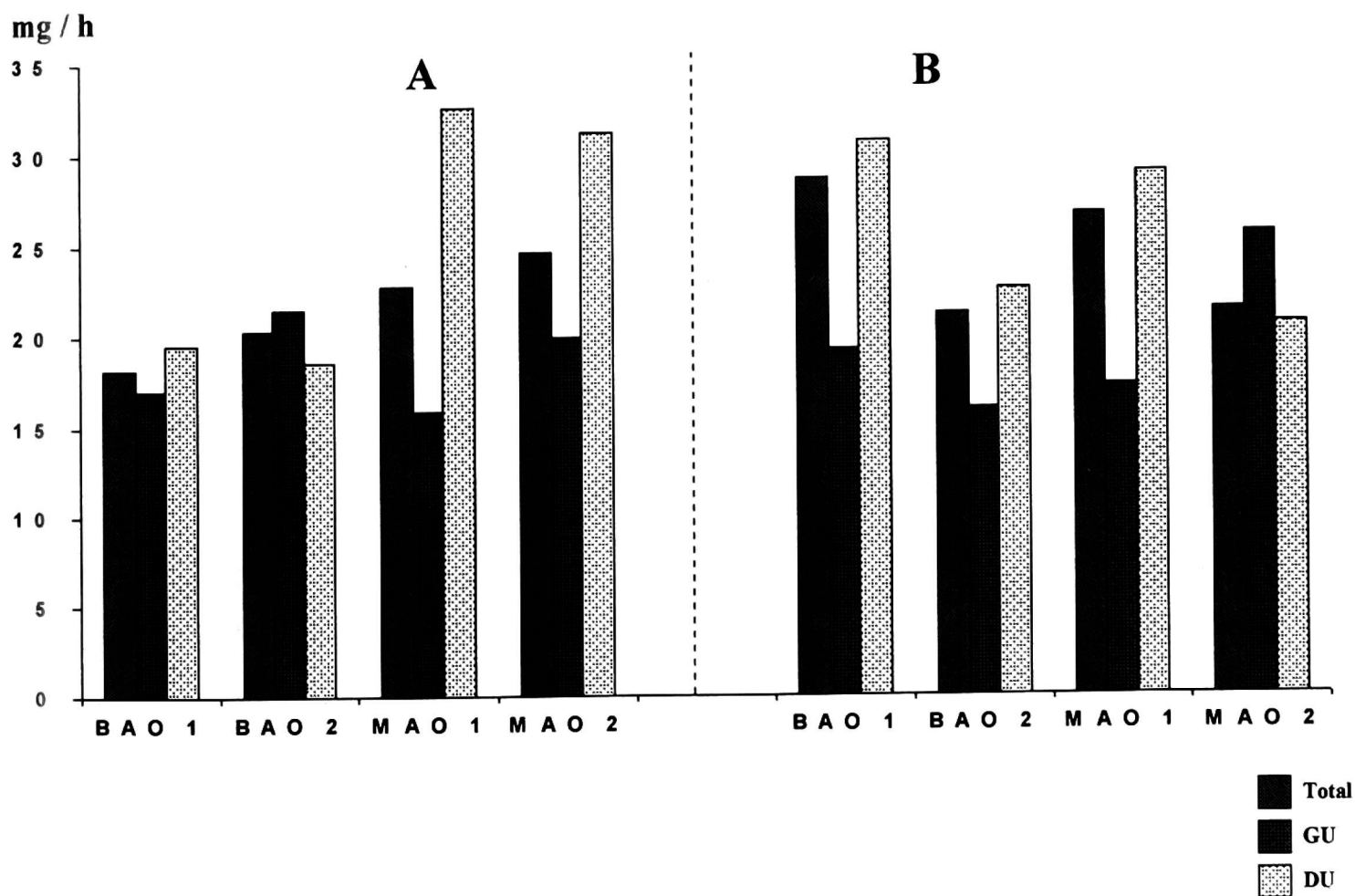


Fig. 3A. Fucose output, mean value, (mg/h) before (1) and in 1 year eradication (2), A — successful eradication, B — failed eradication.

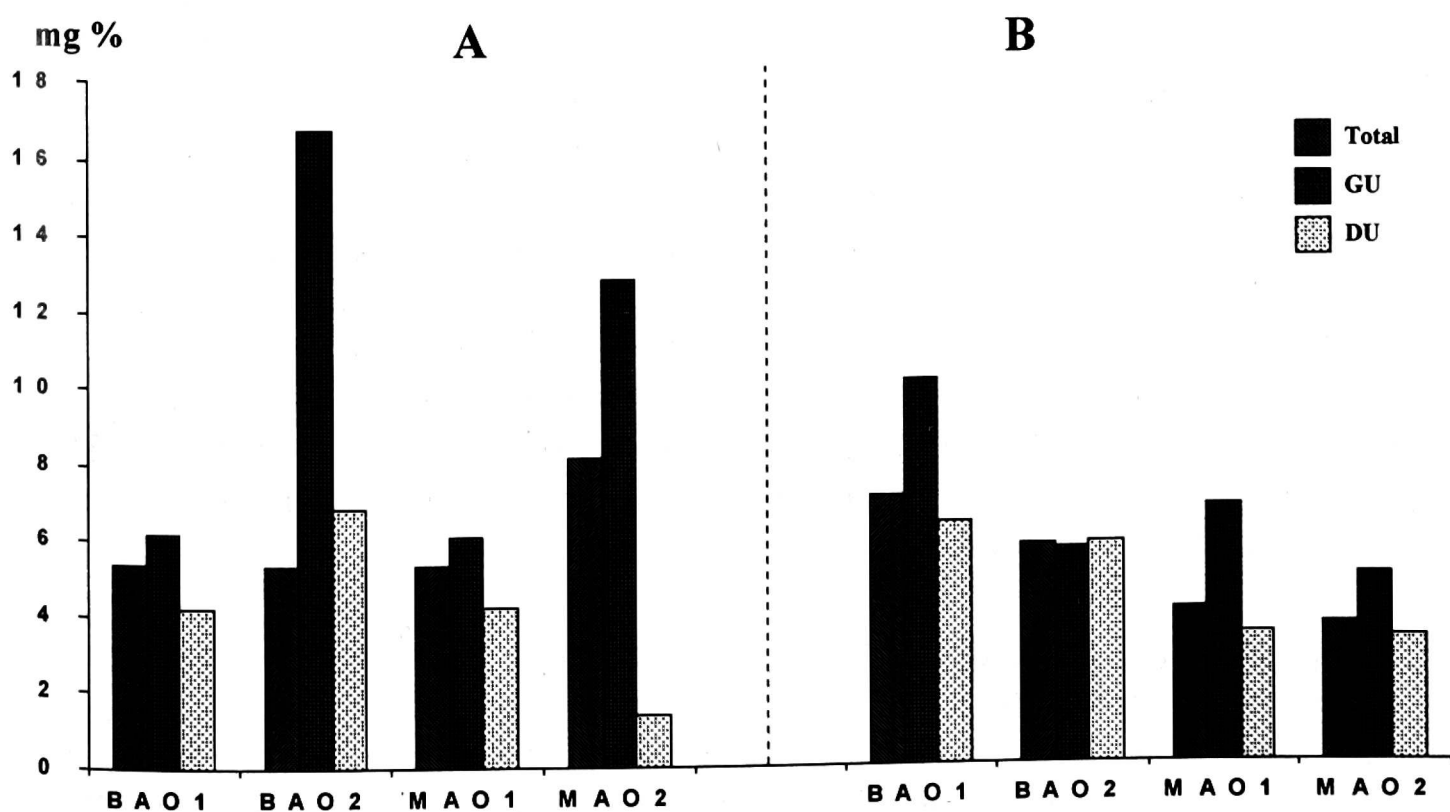


Fig. 4. Sialic acid concentration, mean value, (mg%) before (1) and in 1 year eradication (2), A — successful eradication, B — failed eradication.

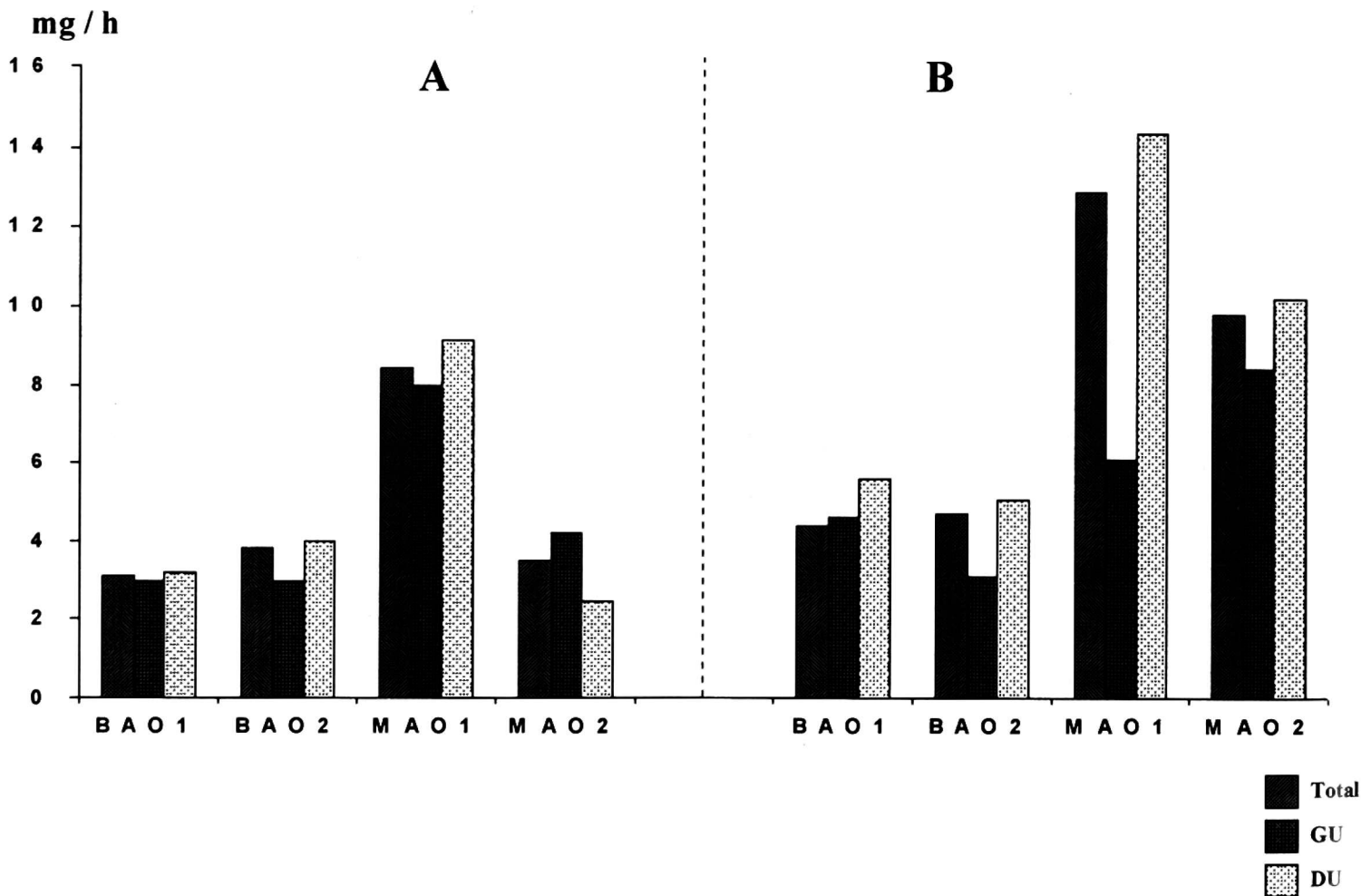


Fig. 4A. Sialic acid output, mean value, (mg/h) before (1) and in 1 year eradication (2), A — successful eradication, B — failed eradication.

DISCUSSION

This study demonstrates that eradication of *Hp* is associated with a marked and sustained fall in basal and pentagastrin stimulated acid output in both duodenal and gastric ulcer patients. We observed this in one year after successful eradication of bacterial infection. The decrease of acid output was accompanied by the significant fall of fasting plasma gastrin concentration. We did not observe any significant changes in gastric secretion in group of subjects where eradication failed. There were also no statistically significant changes in gastric mucus secretion both in eradicated and uneradicated patients, but after eradication a tendency of the increasing of fucose and sialic acid concentration in gastric mucus was noted.

GASTRIC ACID SECRETION

BAO

Eradication of *Hp* in peptic ulcer patients (DU, GU) was accompanied by statistically marked decrease in BAO, what is consistent with the report by

Moss and Calm and recent study of El-Omar (14—16). According to El-Omar increased basal gastric acid output in DU patients is caused by Hp infection because it resolves fully after eradication of bacterial infection (14).

MAO

El-Omar found in his study of DU patients that acid output in response to gastrin releasing peptide fell of 80% 1 year after eradication (14). In our study we measured the response after the stimulation of pentagastrin, which fall significant in a year after eradication of Hp. The hypothesis under our test was that MAO after pentagastrin stimulation would decrease in a year after eradication. It did in our study, what is against the results of Chiba (17). The study did not show a significant fall in acid output after pentagastrin one month after eradication of bacterial infection, what the study of ours and Harris' did (2). The essential of our study was one year of observation, in Harris'-six months. This suggests that the lack of gastric secretion changes in previous study perhaps may due to a short follow up period.

Basal plasma gastrin concentration

This study demonstrates that eradication of Hp is associated with marked and sustained fall in basal plasma gastrin concentration in peptic ulcer patients. A similar fall in fasting gastrin concentration has been noted by Oderda after Hp eradication in children (18). Results of Levi argues this fact (19). The fall of fasting gastrin concentration associated with the significant fall of BAO in a year after eradication is convincing evidence that bacterial infection results in increased circulating levels of gastrin. But in view of high prevalence of Hp in healthy subjects the currently accepted physiological range for plasma gastrin should be re-assessed in non-infected subjects (20).

It is important to consider the possible mechanism of the abnormalities of gastric acid secretion associated with Hp infection in peptic ulcer patients. El-Omar pointed the increased acid response after GRP stimulation, which measure the combined functional response of the antrum (G and D cells) and the body (parietal cells) to endogenous gastrin (16). This fact may be the clue to pathophysiology of Hp infection. GRP plays two roles in physiology of gastric secretion; it stimulates the G cells to release gastrin. The opposite role is the inhibitory control on gastric secretion. It does this by stimulating the release of several peptides (cholecystokinin, secretin, gastric inhibitory peptide, vasoactive intestinal polipeptide, neurotensin, enteroglucagon) that

inhibit gastric secretion, acting via somatostatin (21, 22). Perhaps the impaired balance of GR stimulating and inhibiting function in gastric secretion is the essential in Hp infection. In summary, the abnormalities of hormones involved in gastroduodenal secretion, acquired during Hp infection may explain the predisposition to peptic ulcer disease in Hp positive patients.

Gastric mucus secretion

A number of studies have suggested that Hp can damage the protective mucus coat lining the gastric mucosa. Damage to the mucus gel may be the cause of back-diffusion of aggressive luminal contents such as gastric acid, pepsin and exogenous factors, giving in result tissue injury and ulcer formation (23—26). Hp proteases have been described that degrade mucus glycoproteins. Slomiany was the first, who demonstrated proteolytic activity of Hp. He also reported the degradation of gastric mucus glycoproteins and serum albumin Hp (23, 26). This observation was confirmed and supplemented by Sarosiek (24). There was a gradual loss mucus viscosity and an increase of H⁺ permeability after incubation of mucus with Hp. The results of the study of Nilius showed no proteolytic activity in any of 10 Hp strains tested within a wide pH range (pH 2—9) (27). Markesich have recently demonstrated that gastric mucus from DU patients with Hp infection is more viscous than from those in whom the bacterial infection has been eradicated (5). It is in contradiction to *in vitro* work suggesting that Hp degrades mucus gel (24, 27). The result of Goddard supports finding, as the eradication of Hp leads to increased gastric juice viscosity (28). So until now the evidences of degradation of gastric mucus gel caused the infection of Hp are insufficient.

In our present study an evident decrease of sialic acid output in eradicated patients was observed. However the concentration of sialic acid in GU patients after effective treatment increased. In DU eradicated patients increasing of fucose concentration was noticed. There was no changes in fucose output.

Eradication of Hp infection in DU and GU patients produces a statistically significant fall in basal and stimulated gastric acid secretion one year after the treatment. No evident changes of gastric acid secretion in not eradicated patients were observed. In eradicated DU and GU patients a tendency of the fall of sialic acid output was noted. Our results suggest that the effect of Hp infection on gastric acid secretion and mucus components plays the important role in the pathomechanism of mucosal damage. However further studies are needed.

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