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EVOLUTION OF GASTRIC AND DUODENAL ULCERS AT PATIENTS WITH *HELICOBACTER PYLORI* INFECTION, AFTER TREATMENT WITH PROTON PUMP INHIBITORS AND AN ASSOCIATED TREATMENT

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ABSTRACT. Modern antiulcer therapy consists in a combined treatment aims both to decrease gastric acid secretion and to eradicate *Helicobacter pylori* infection. In this paper we comparatively studied the clinical, the endoscopic, and the secretory evolution of two groups of patients with gastro-duodenal ulcers who were treated with Nexium (Esomeprazole) a single dose of 40 mg / day for 21 days, respectively with Nexium a single dose of 40 mg / day, associated with anti-*H. pylori* therapy (metronidazole 250 mg bid + amoxicillin 750 mg bid. The study results show that after associated treatment with PPIs and anti-*H. pylori* therapy, reduction of basal acid secretion is greater. The pain persists longer in patients who received treatment with PPIs alone without anti-*H. pylori* therapy. In case of 84% of patients with GU and 91% of those with DU, endoscopic healing of ulcer niche took place after 21 days of treatment with Nexium, respectively in case of 89% of patients with GU and 96% of those with DU after combination therapy.

Keywords: protons pump inhibitors, *Helicobacter pylori*, gastric ulcer, duodenal ulcer, basal acid secretion

INTRODUCTION

Hydrochloric acid secretion is a unique feature of the parietal gastric cells, being the only exocrine cells with such a function (Hersey et al., 1995). In order to exercise this function, parietal cell has an abundant mitochondrial device which ensures intense energy metabolism and a specialized tubulo-vesicular device able to concentrate hydrogen ions and a complex transport system. In descriptive terms, the secretory process can be divided in two stages: formation of HCl, storage and transport of H+ (Besancon et al., 1993). Regardless the production mechanism, H+ ions will be taken by the tubule-vesicular system, and the bicarbonate ions will be removed through the serous membrane in exchange for Cl- ions. The amount of bicarbonate arrived in circulation corresponds to the level of H+ secretion in the gastric lumen and produces a deflection of blood to alkaline pH (Soll, 1998). This is defined as "alkaline tide" and its measurement may be an indirect test for assessing the gastric secretory capacity Proton pump inhibitors (PPIs) are the most powerful anti-secretory known to date (Lindberg et al., 1986, Sachs et al., 1988). Drugs of this class inhibit the final stage of HCl secretion, regardless the initial stimulus. It was called "acid pump", now known as the H+/K+-ATP-ase (Lorentzon et al., 1987; Lindberg et al., 1990; Bytzer, 1998). Modern antiulcer therapy consists in a combined treatment aims both to decrease gastric acid secretion and to eradicate Helicobacter pillory infection (Wallmark et al., 1983, Keeling et al., 1987). In this paper we comparatively studied the clinical, the endoscopic, and the secretory evolution of two groups of patients with gastro-duodenal ulcers treated with protons pump inhibitors, respectively with protons pump inhibitors associated with anti- H pylori therapy.

MATERIALS AND METHODS

The study was conducted on two groups of patients, as follows:

Group 1: consisted of 25 patients, including 10 with gastric ulcer and 15 with duodenal ulcer who were treated with Nexium (Esomeprazole), a single dose of 40 mg/day for 21 days.

Group 2: consisted of 29 patients, including 12 with gastric ulcer and 17 with duodenal ulcer who were treated for 21 days with a single dose of Nexium 40 mg/day, associated with anti *H. pylori*, metronidazole 250 mg bid + amoxicillin 750 mg bid.

Distribution of patients is described in table and Chart 1 bellow.

Table 1

Distribution of patients surveyed according to disease and the treatment applied

Disease	Gastric ulcer	Duodenal ulcer	Total
No. Patients treated with Nexium	10	15	25
Nr. Patients treated with Nexium + anti *H. pylori*	12	17	29

Antiulcer drugs administration was made after single-blind research method.

Among patients contained in this study, 21% were at the incipient phase of the disease and in case of 79% the disease started 1 to 20 years ago.

Positive diagnosis for gastric and duodenal ulcer was made using clinical, secretory, and endoscopy criteria.

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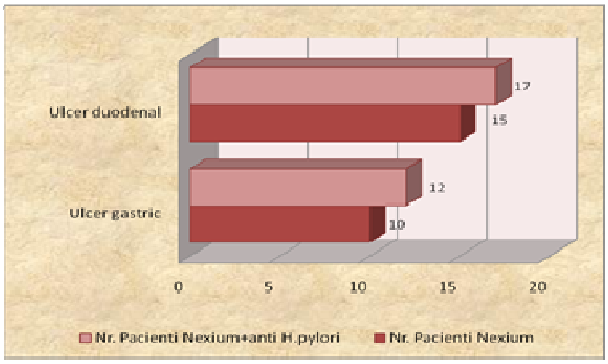

Chart 1. Distribution of patients surveyed according to disease and the treatment applied

Results assessment criteria

In order to assess the treatment efficiency we have monitored the following parameters:

• Fading of pain;

• Changes in basal acid output after 14 and 21 days of treatment (Ghosh et al., 2011);

• Changes in hydrogen ion secretion after 14 and 21 days of treatment (Ghosh et al., 2011);

• Ucer endoscopical healing after 14 and 21 days of treatment;

Endoscopic examinations were performed by means of an Olympus video endoscope, model EVIS 100.

Statistical analysis of the data obtained was done by means of a Student Test (Zimmerman et al., 1997).

RESULTS AND DISCUSSIONS

Clinical evolution of pain in patients with gastro-duodenal ulcer after treatment with Nexium, Nexium + therapy anti- *H. pylori* is described in tables 2, 3 and in graphics 2, 3.

Table 2

Pain fading in patients with gastric ulcer

Treatment	3 days	5 days	10 days	15 days	20 days
Nexium	62%	71%	82%	86%	92%
Nexium+anti *H. pylori*	68%	79%	88%	91%	95%

After 14 days of treatment with Nexium the pain is fading in 86% of patients with gastric ulcer, whereas the patients who had been treated with Nexium associated with anti H pylori therapy, the pain disappears in 91 % of patients with gastric ulcer surveyed.

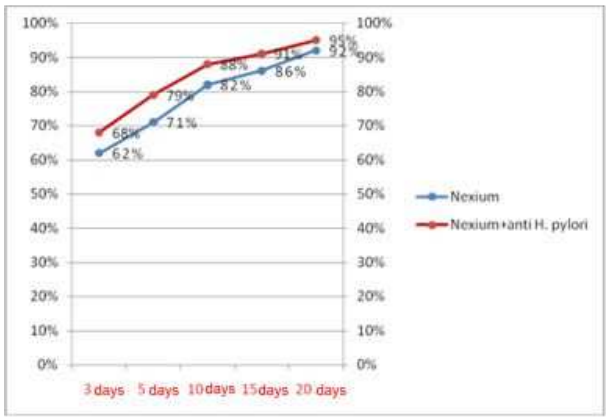

Chart 2. Pain fading in patients with gastric ulcer

At 91% of patients with duodenal ulcer treated with Nexium pain is fadinf after 14 days of treatment, whereas in patients treated with combination therapy pain disappears at a rate of 93% of patients. After 21 days of treatment this percentage increases to 96%.

Table 3

Disappearance of the pain in patients with duodenal ulcer

Treatment	3 days	5 days	10 days	15 days	20 days
Nexium	68%	76%	85%	91%	94%
Nexium+anti *H. pylori*	73%	82%	90%	93%	96%

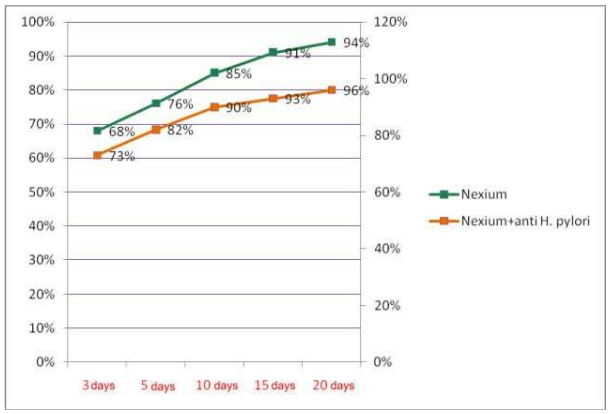

Chart 3. Pain fading in patients with duodenal ulcer

Gastric acid secretion (BAO) decreased significantly both in patients treated with Nexium and those with combination therapy (see Tables 4, 5 and Charts 4, 5).

Table 4

Changes in basal acid output (BAO) in patients with gastric ulcer

	NEXIUM			NEXIUM + Anti H.pylori		
	Initial	14 days	21 days	Initial	14 days	21 days
Acid output (mEq/h)	4.38 ± 0.97	3.17 ± 0.59	1.94 ± 0.25	2.68 ± 0.48	0.17 ± 0.09	0.14 ± 0.05

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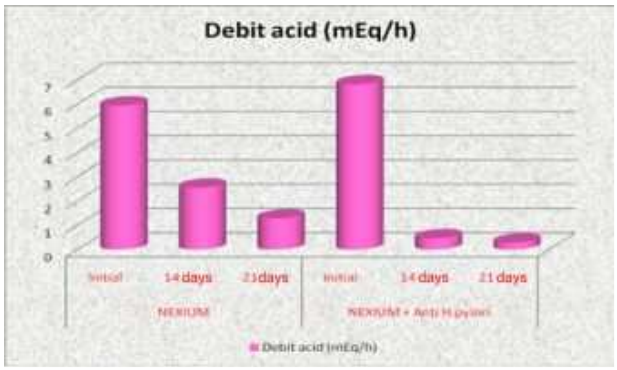
Graphic 4. Changes in basal acid output (BAO) in patients with gastric ulcer

Table 5

Changes in basal gastric acid secretion in patients with duodenal ulcer

	NEXIUM			NEXIUM + Anti *H. pylori*		
	Initial	14 days	21 days	Initial	14 days	21 days
Acid output (mEq/h)	5.94 ± 1.76	2.55 ± 0.59	1.28 ± 0.12	6.82 ± 1.84	0.46 ± 0.19	0.28 ± 0.06



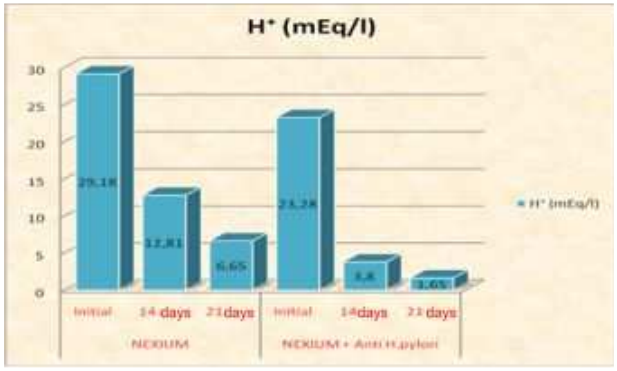
Graphic 5. Changes in basal acid output in patients with duodenal ulcer

Changes in hydrogen ions secretion are shown in Tables 6, 7 and Charts 6, 7.

Table 6

Changes in hydrogen ion secretion in patients with gastric ulcer

	NEXIUM			NEXIUM + Anti *H. pylori*		
	Initial	14 days	21 days	Initial	14 days	21 days
H^+ (mEq/l)	46.12 ± 22.14	8.60 ± 3.17	5.05 ± 1.19	47.08 ± 29.54	4.30 ± 2.10	3.15 ± 1.04

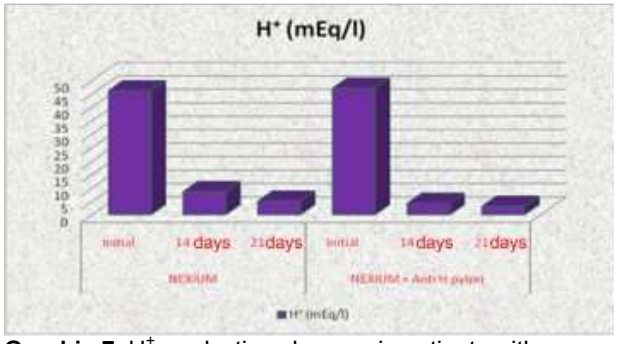


Graphic 6. Changes in hydrogen ion secretion in patients with gastric ulcer

Table 7

Changes in hydrogen ion secretion in patients with duodenal ulcer

	NEXIUM			NEXIUM + Anti H. pylori		
	Initial	14 days	21 days	Initial	14 days	21 days
H^+ (mEq/l)	46.12 ±22.14	8.60 ±3.17	5.05±1 .19	47.0 8±29 .54	4.30 ±2.1 0	3.15 ±1.0 4



Graphic 7. H^+ production changes in patients with duodenal ulcer

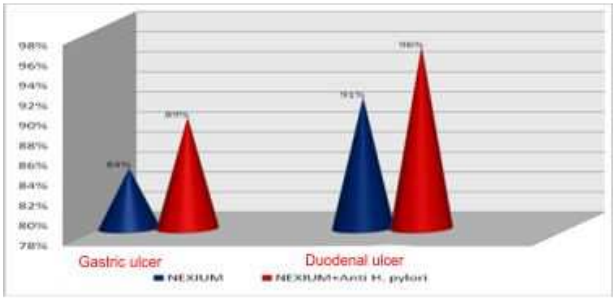
Nexium treatment, both alone and in combination with anti *H. pylori* therapy decreases considerably the production of H+.

Endoscopic healing of ulcer niche is shown in the table and graphic 8.

Table 8

Endoscopic healing of ulcer niche in patients with gastric and duodenal ulcers

Treatment	Endoscopic healing after 21 days	
	Gastric Ulcer	Duodenal Ulcer
NEXIUM	84%	91%
NEXIUM + Anti *H. pylori*	89%	96%



Graphic 8. Endoscopic healing of ulcer niche in patients with gastric and duodenal ulcers

In case of 84% of patients with gastric ulcer and 91% of those with duodenal ulcer, endoscopic healing of ulcer niche occurred after 21 days of treatment with Nexium, respectively to 89% of patients with gastric ulcer and 96% of those with duodenal ulcer following combined therapy.

The treatment with PPIs therapy alone and in combination with anti- *H. pylori* has led to considerable decrease in the production of hydrogen ions and therefore hydrochloric acid in gastric juice. This inhibition occurs after 3 days of treatment and increases progressively and, after 14 days, it will be very intense. Reducing gastric acid secretion is more pronounced in patients who received associated treatment for eradication of *H. pylori* infection too. Ulcer pain fading is also higher in patients with combination therapy, respectively Nexium and anti- *H. pylori*. Healing of gastric ulcers in 80% of cases and duodenal ulcers in 90% of cases after treatment with Nexium or Nexium and anti-*H. pylori* therapy, demonstrates superior efficacy of this inhibitor therapy compared with older therapies (i.e. histamine H2 receptor antagonists, such as ranitidine) (Kim et al., 2004).

One should also mention that the associated treatment with anti-secretory and anti-*H. pylori* is very important because it decreases the appearance of recurrence, which in a year is 10 times lower in patients who received such treatment, as against those who were treated with only with IPPs. This is explained in specialised literature by the fact that recurrence of *H. pylori* infection is a prediction factor for ulcer recurrence (Penston, 1996). In other words the recurrence of *H. pylori* infection increases the chances for ulcer recurrence (Basu et al., 2011). According to a meta-analysis of 30 studies checked (Hopkins et al., 1996), the annual rate of endoscopic duodenal ulcer recurrence decreases down to 7% (extreme 0-22%) versus 61% (extreme 20-100%), in case of persistent bacteria. In gastric ulcer recurrence, annual rate is 5% (extreme 0-7%) in case of successful eradication, and 46% (extreme 44-75%) in patients with *H. pylori* (Bretagne, 1996). Therefore the confirmation of eradication of *H. pylori* infection is mandatory if one wishes to prevent ulcer recurrence. Furthermore, treatment of *H. pylori* infection is required in patients with gastric ulcers refractory to various therapies because refractory ulcers are frequent *H. pylori* positive or appears after the use of NSAIDs. Control endoscopy and biopsy can confirm the eradication of *H. pylori*; for this medical check should be done at 2 months after eradication (Jinda et al., 2011). Recent studies in patients with gastric or duodenal ulcers showed that recurrence after 6-12 months is over 80% in patients with *H. pylori* positive and 5% in those with *H. pylori* negative. Therefore the impact of *H. pylori* eradication on ulcer recurrence is very high. Ulcer recurrence risk does not decrease even one year after ulcer healing even if the maintenance treatment was performed correctly. The duration of maintenance therapy for gastric and duodenal ulcers with PPIs is 1-3 years. The highest risk of recurrence occurs in the first 6 months of maintenance therapy. If *H. pylori* cannot be eradicated or if the patient is required to use NSAIDs, maintenance treatment may be extended over five years. If recurrences are asymptomatic and occasional, intermittent treatment schemes can be used for a shorter period (Buffet, 2003).

CONCLUSIONS

After a combined treatment, PPIs therapy and anti *H. pylori* therapy the decrease of basal acid secretion is greater. The pain persists longer in patients who received treatment with PPIs alone without anti-*H. pylori* therapy. To 84% of patients with gastric ulcer and 91% of those with duodenal ulcer, endoscopic healing of ulcer niche occurred endoscopic after 21 days of treatment with Nexium, respectively in 89% of patients with gastric ulcer and 96% of those with ulcer duodenal after combination therapy.

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