

# ASSESSMENT OF EFFECTIVENESS OF DIFFERENT DOSAGE REGIMENS OF PANTOPRAZOLE IN CONTROLLING SYMPTOMS AND HEALING ESOPHAGEAL LESIONS OF PATIENTS WITH MILD EROSIIVE ESOPHAGITIS

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**ABSTRACT** - *Background* - Gastroesophageal reflux disease is a very common affection, and esophageal involvement is particularly frequent. The means to effectively control symptoms and improve esophageal inflammation in these patients is to reduce esophageal acid exposure. For this purpose, we use gastric proton pump inhibitor, that can suppress gastric acid secretion. *Aim* - To compare the effectiveness of two different pantoprazole dosage regimens (20 and 40 mg/day), in controlling symptoms and healing esophageal lesions of patients with mild erosive esophagitis. *Material and Methods* - Fifty-seven patients with endoscopically confirmed mild erosive esophagitis characterized as non-confluent erosions in the distal esophagus, were randomly to be treated either with pantoprazole 20 mg/day (group I, 28 patients) or 40 mg/day (group II, 29 patients) over a period of 4 weeks. After treatment completion, the patients were assessed for clinical and endoscopic outcome, i.e., absence of erosions in distal esophagus and improvement of gastroesophageal reflux symptoms. *Results* - At the end of the treatment, 73.1% of the patients in group I and 85.7% of the patients in group II had endoscopic improvement. We also observed, that 88.5% of the patients in group I and 92.9% of the patients in group II had complete elimination of heartburn and regurgitation. *Conclusion* - Pantoprazole dosage regimens of 20 mg/day and 40 mg/day provide equivalent effectiveness in controlling symptoms and healing esophageal lesions of mild esophagitis.

**HEADINGS** - Gastroesophageal reflux, drug therapy. Esophagitis, peptic, drug therapy. Proton pumps, antagonists & inhibitors. Pantoprazole.

## INTRODUCTION

Gastroesophageal reflux disease (GERD) affects approximately 5%-10% of the adult world population, a figure which shows a trend to increase. Several complications may result from GERD, of which esophageal involvement is particularly frequent. The severity of esophageal damage will depend on the acidity of gastric contents flowing backward into the esophagus, the appropriate clearance of gastric

contents from the esophagus, and the time of exposure of the esophagus to refluxate<sup>(5, 6)</sup>.

Clinical manifestations of reflux esophagitis generally include heartburn and acid regurgitation. In spite of the high incidence of reflux esophagitis, most patients have only mild disease forms, characterized by an inflammatory process of the distal esophageal mucosa, either associated with isolated erosions or not. Severe complications of reflux esophagitis, such as hemorrhage, ulceration, stenosis, and Barrett's esophagus, are less common.

Diagnosis and follow-up of reflux esophagitis are best accomplished by means of upper GI endoscopy, which, in addition to providing macroscopic diagnosis of esophageal lesions, enables the collection of biopsy specimens for histopathological analysis<sup>(9)</sup>.

Several dietary and behavioral measures are recommended for the treatment of reflux esophagitis. These however do not seem to play a role in relapse prevention and esophageal lesion healing<sup>(5)</sup>.

The only means to effectively control symptoms and improve esophageal inflammation in these patients is to reduce esophageal acid exposure. For this purpose, we use drugs which suppress gastric acid secretion, in an attempt to neutralize refluxate acidity. Until recently, the only drugs able to inhibit gastric acid secretion were H2 receptor antagonists, largely used to treat GERD. However, since the effect of these drugs is limited to keeping intragastric pH above 4 during 6 of the 24 hours in a day, they provide disappointing results in terms of esophageal healing rate and even symptom relief<sup>(4, 5)</sup>. Association of prokinetic agents to H2 receptor antagonists for the treatment of GERD has also failed to significantly improve therapeutic effectiveness, especially in more severe grades of reflux esophagitis<sup>(8)</sup>.

A new category of antisecretory drugs which exert their effects through gastric proton pump inhibition has been recently made available. These agents show improved ability to control gastric acidity, keeping intragastric pH above 4 for better than 87% of the 24 hours in a day, particularly during daytime and after meals<sup>(2)</sup>. The efficacy of pantoprazole, one of these proton pump inhibitors, has been extensively examined, inclusively with the help of gastric pH monitoring. Clinical investigations have established the optimal therapeutic dose of pantoprazole at 40 mg each morning<sup>(12)</sup>.

## PATIENTS AND METHODS

Fifty-seven GERD patients were selected to participate in this study according to the following criteria:

a. Inclusion criteria:

- age between 18 and 80 years;
- GERD symptoms, particularly heartburn and regurgitation;
- endoscopic confirmation of non-confluent erosions in the distal portion of the esophagus up to five days before inclusion;
- informed consent signature;

b. Exclusion criteria:

- pregnant or nursing women;
- previous gastric and/or esophageal surgery;
- systemic disease associated with GERD;
- use of proton pump inhibitors and/or PPI antagonists and/or H2 receptor antagonists in the last 20 days.

These patients were randomly assigned to be treated either with pantoprazole 20 mg (group I, 28 patients) or 40 mg (group II, 29

patients) every morning before breakfast, over a period of 4 weeks. After treatment completion ( $\pm 3$  days) the patients were assessed for clinical and endoscopic outcome, i.e. absence of erosions in the distal portion of the esophagus and improvement of symptoms (elimination of heartburn and regurgitation).

## RESULTS

Of 28 patients (16 females and 12 males) in group I, only 26 completed study – one patient had an allergic reaction to pantoprazole and one patient dropped out. Of 29 patients (17 females and 12 males) in group II, 28 completed study – only one patient dropped out.

Subjects included in this study were aged in average 49.2 years (range 19-80). Figures for individual groups were 45 (19-69) years (group I) and 49 (19-69) years (group II).

As for endoscopic healing of esophageal erosions at the end of the treatment, 19 (73.1%) of 26 patients in group I and 24 (85.7%) of 28 patients in group II had endoscopic improvement.

Upon treatment completion, 88.5% of patients in group I and 92.9% of patients in group II reported complete elimination of heartburn and regurgitation. Table 1 shows the endoscopic and clinical outcome in both groups.

Table 2 summarizes the results of statistical tests used to compare the variables observed in both groups, as well as their significance.

## DISCUSSION

Assessment of therapeutic effectiveness of pantoprazole 20 mg/day has been the object of various studies. Dosage regimens based on 20 mg/day and 40 mg/day have been described as equivalently

TABLE 1 – Endoscopic and clinical outcome

	Endoscopic healing	Symptoms relief
Group I (20 mg/day)	73,1%	88,5%
Group II (40 mg /day)	85,7%	92,9%

TABLE 2 – Comparison of variables in treatment groups

Variable	Statistic test	Result ( $\alpha < 0.05$ )
Age	Student's <i>t</i> test	$P = 0.27$
Sex	Chi-square	$P = 0.6708$
Endoscopic improvement	Fisher's exact test	$P = 0.3198$
Symptom improvement	Fisher's exact test	$P = 0.6633$

effective in preventing relapse of the esophageal condition in patients with reflux esophagitis treated conventionally<sup>(4, 11)</sup>.

Previous studies have shown pantoprazole 20 mg/day to be more effective than ranitidine in usual doses, both in healing esophageal lesions and relieving symptoms of reflux esophagitis<sup>(3,13)</sup>. The optimal dosage regimen of pantoprazole was established by means of intragastric pH monitoring at 40 mg/day, equivalent in effectiveness to 80 mg/day. However, the same studies show that a daily dose of 20 mg is less effective than the conventional dosage regimen in controlling gastric acid secretion over 24 hours<sup>(10, 12)</sup>.

By means of objective criteria (symptom improvement and esophageal lesion healing), our results have shown that a dosage

regimen of 20 mg of pantoprazole per day provides therapeutic results in mild erosive esophagitis which are similar to those achieved with the conventional dosage regimen. The use of a lower pantoprazole dose for the treatment of mild erosive esophagitis may represent a less expensive alternative for this significant assemblage of patients.

## CONCLUSION

Pantoprazole dosage regimens of 20 mg/day and 40 mg/day provide equivalent effectiveness in controlling symptoms and healing esophageal lesions of mild erosive esophagitis.

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Moretzsohn LD, Brito EM, Reis MSF, Coelho LGV, Castro LP. Avaliação da eficácia do uso de diferentes doses de pantoprazol no controle de sintomas e cicatrização das lesões esofágicas em portadores de esofagite erosiva de grau leve. *Arq Gastroenterol* 2002;39(2):123-125.

**RESUMO – Racional** – A doença do refluxo gastroesofágico é afecção muito comum e o acometimento do esôfago muito freqüente. A maneira mais eficiente de controlar os sintomas e cicatrizar as lesões esofágicas nesses pacientes, é reduzir a exposição do esôfago ao ácido. Dessa forma, são utilizadas drogas que bloqueiam a secreção ácida gástrica, como os bloqueadores de bomba protônica. **Objetivo** - Comparar a eficiência do uso de diferentes doses de pantoprazol (20 e 40 mg/dia), no controle dos sintomas e cicatrização das lesões esofágicas, em portadores de esofagite erosiva de grau leve. **Material e Métodos** - Cinquenta e sete pacientes com esofagite erosiva de grau leve, caracterizadas endoscopicamente pela presença de erosões não confluentes em esôfago distal, foram randomizados e tratados com pantoprazol 20 mg/dia (grupo I, 28 pacientes) ou 40 mg/dia (grupo II, 29 pacientes), por período de 4 semanas. Ao término do tratamento, os pacientes foram avaliados quanto a melhora clínica e endoscópica, ou seja, ausência de erosões em esôfago distal e melhora dos sintomas de doença do refluxo gastroesofágico. **Resultados** - Ao fim do tratamento, 73,1% dos pacientes do grupo I e 85,7% dos pacientes do II apresentaram melhora endoscópica. Observaram-se, também, que 88,5% dos pacientes do grupo I e 92,9% dos pacientes do grupo II relataram melhora completa dos sintomas da doença do refluxo gastroesofágico. **Conclusão** - O uso de pantoprazol nas doses de 20 mg/dia e 40 mg/dia tem eficácia semelhante no controle dos sintomas e cicatrização da esofagite de grau leve.

**DESCRIPTORIOS** – Refluxo gastroesofágico, quimioterapia. Esofagite péptica, quimioterapia. Bombas de próton, antagonistas & inibidores. Pantoprazol.

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