HK J Paediatr (new series) 2023;**28**:3-7

Original Article

Investigation of the Efficacy of Short-term Use of Lansoprazole in the Treatment of Reflux Esophagitis in Children

A ***Basturk***

Abstract

Purpose: The aim of this study was to compare the efficacy and side effects of short- and long-term use of lansoprazole recommended for use in the treatment of reflux esophagitis in the pediatric age group. ***Methods:*** This study included a total of 148 patients aged 8 to 18 years, who were diagnosed with reflux esophagitis through endoscopy between January 2017 and January 2018. Patients were consecutively divided into two groups. A single oral 15 mg/day dose lansoprazole was administered for children with a weight of <30 kg whereas 30 mg/day dose was administered for those with a weight of >30 kg. The drug was administered for four weeks in Group 1 and eight weeks in Group 2. Control endoscopy was performed at the end of the treatment in both groups. Esophagitis levels classified according to the Los Angeles classification were compared. Headache, abdominal pain, diarrhoea, vomiting, bloating, and upper respiratory tract infections that were not present initially but developed after drug use were considered as side effects. ***Findings:*** The 118 patients remaining after those who did not meet the inclusion criteria were excluded from the study were consecutively divided into groups. Group 1 consisted of 58 patients and Group 2 consisted of 60 patients. The recovery rate was 89.5% after four weeks in Group 1 while this rate was 91.2% after eight weeks in Group 2. The difference between the groups was not statistically significant ($p>0.05$). The most common side effects in both groups were abdominal pain, headache, and diarrhoea, which were seen at a rate of 3.4%, 3.7%, and 3.1% in Group 2, respectively. In Group 1, these rates were found to be 1.6%, 2.1%, and 1.9%, respectively. Although the difference between the groups was not statistically significant, the incidence of side effects was low in Group 1. ***Conclusion:*** In children who develop reflux esophagitis due to gastroesophageal disease, four-week lansoprazole treatment is as effective as the eight-week treatment. However, further randomised controlled trials are needed to confirm the finding of this study.

Key words *Child; Lansoprazole; Reflux*

Department of Pediatric Gastroenterology, Faculty of Medicine, Gaziantep University, Universite Bulvari-Campus 27310, Gaziantep, Turkey

A **Basturk** *MD*

Correspondence to: Dr A **Basturk**
Email: drahmetbasturk@hotmail.com

Received May 14, 2020

Introduction

Gastroesophageal reflux (GER) is defined as the physiological transition of gastric content into the esophagus.[1] The GER caused by temporary relaxation of the esophageal sphincter is a normal physiological process that occurs at least once a day in healthy infants at three and four months of age. It can occur in association with a wide variety of physiological and pathological conditions

since this deficiency is normal in infants. This normal event causes approximately one in five caregivers to seek medical help.[2] As a separate clinical entity, GER may also be associated with GER disease (GERD). However, unlike GER, GERD may manifest with extraesophageal symptoms such as cough, laryngitis, pharyngitis, sinusitis, recurrent otitis media, and dental erosions.[1] Underlying conditions associated with GERD include comorbid disorders such as neurological impairment, esophageal atresia, and prematurity in more than three quarters (80%) of children requiring long-term GERD treatment.[2,3] In patients with these signs and symptoms, endoscopically diagnosed esophagitis, food aversion, feeding difficulties, repeated regurgitation episodes, nutrient loss, and poor weight gain may help to establish a definitive diagnosis of GERD.[1] Acid-suppressing agents have been the main treatment when pharmacologic therapy is required in cases of GERD.[2] When used properly, acid-suppressing agents such as histamine-2 receptor antagonists (H2RAs) and proton pump inhibitors (PPIs) are effective at reducing gastric acidity and healing esophageal erosions in children with GERD.[1] The H2RAs may need to be administered twice or three times daily due to their short duration of action and it may show less efficacy in continuous use. Unlike H2RAs, long-term use does not diminish the acid-suppressing effects of PPIs. The use of omeprazole, lansoprazole, and esomeprazole are approved for the treatment of children at one year of age and older in North America and few studies have shown that it can be used in infants younger than one year of age.[2] A total of four-eight oral PPI therapy is recommended for reflux esophagitis caused by GER.[2] However, prolonged use of PPI may lead to the development of resistance to treatment and of drug-related side effects over time.[4,5] The aim of this study was to compare the efficacy and side effects of short- and long-term use of lansoprazole recommended for use in the treatment of reflux esophagitis in the pediatric age group.

Materials and Methods

This study included a total of 148 patients aged eight to 18, who were diagnosed with reflux esophagitis through endoscopy between January 2017 and January 2018 in a hospital providing secondary care. Before the study, approval was obtained from the ethics committee and written/verbal consent were obtained from the families of the children. During the endoscopy procedure, two or three biopsy samples were taken from the esophagus. In patients, who were found to have erosive esophagitis through endoscopy, the classification was made according to the Los Angeles classification.[6] Patients with reflux and without erosive esophagitis in endoscopic evaluation were defined as non-erosive GERD. As a result of histopathology, patients diagnosed with Crohn's disease and eosinophilic and infectious esophagitis were excluded from the study (Table 1). Lifestyle modifications and diet were recommended to the patients with reflux. Patients were consecutively divided into two groups. A single oral 15 mg/day dose lansoprazole was administered for children with a weight of <30 kg whereas 30 mg/day dose[7] was administered for those with a weight of >30 kg. The drug was given for four weeks in Group 1 and eight weeks in Group 2. Control endoscopy and histopathology was performed at the end of the treatment in both groups. Esophagitis levels classified according to the Los Angeles classification were compared. Furthermore, it was questioned whether there was an improvement in the following initial complaints: burning in the stomach, abdominal pain, bloating, belching and flatulence, nausea-vomiting, a bitter or acidic taste in the mouth, and water brash. Headache, abdominal pain, diarrhoea, vomiting, bloating, and upper respiratory tract infections that were not present initially but developed after drug use were considered as side effects.

Outcome Measures

Primary outcome measures were providing a full benefit by resolution of all the complaints of the patient with four weeks of lansoprazole treatment.

Secondary outcome measures are the frequency of side effects such as headache, abdominal pain, diarrhoea, vomiting, bloating and upper respiratory tract infections at the end of four and eight weeks of treatment.

Statistical Analysis

Statistical analyses were performed using SPSS version 15.0 software (SPSS Inc., Chicago, IL, USA) and

Table 1 Patients included and excluded as a result of histopathology

Included patients	Excluded patients
Reflux esophagitis	Crohn's disease
	Eosinophilic esophagitis
	Infectious esophagitis

Microsoft Excel 2010. Chi-Square Test and Fisher's exact test were used to compare the data. In the descriptive statistical analysis of the data, numerical variables were expressed as mean±standard deviation whereas categorical variables were expressed as number and percentage. Calculation result was made with 95% confidence interval and 5% margin of error. Level of significance was accepted as $p<0.05$.

Results

Nine patients diagnosed with eosinophilic esophagitis based on the histopathology result were excluded from the study. Eight of the patients were excluded from the study because they declined participation in the study and 13 patients start the treatment but cannot complete the whole treatment. The remaining 118 patients were consecutively divided into groups; Group 1 consisted of 58 patients and Group 2 consisted of 60 patients. The mean age of the patients was 10.42±1.34 years. The female-to-male ratio was 1.3/1. The demographic characteristics of the groups, symptoms at the time of admission, and comparison results according to esophagitis findings are presented in Table 2. The recovery rate was 89.5% after four weeks in Group 1 while this rate was 91.2% after eight weeks in Group 2. Histopathological improvement is 70% and 74%, respectively, were similar in the two groups. The difference between the groups was not statistically significant ($p>0.05$) (Figure 1). The most common side effects in both groups were abdominal pain, headache, and diarrhoea, which were seen at a rate of 3.4%, 3.7%, and 3.1% in Group 2, respectively. In Group 1, these rates were found to be 1.6%, 2.1%, and 1.9%, respectively. Although the difference between the groups was not statistically significant, the incidence of side effects was low in Group 1 (Figure 2).

Follow-up

At the end of the treatment, the patients were followed for 3 months. In the first group, recurrence of GERD symptoms was observed at a rate of 25%. In the second group, it was observed at a rate of 20%, and no statistical difference was observed between the two groups ($p=0.176$).

Discussion

In a study in the literature, eight-week lansoprazole 15 mg treatment was compared with lansoprazole 30 mg in patients with non-erosive GERD and the recovery rate was found to be similar.[8] In another study, the efficacy of four-week lansoprazole 15 mg, 30 mg, and 60 mg treatment was shown to provide better results compared to placebo and the results were reported to be similar between the groups.[9] In another study, PPI treatment was applied for a total of eight weeks, 15 mg in patients with non-erosive esophagitis and 30 mg in patients with erosive esophagitis, and the rate of improvement in symptoms was reported to be similar in both groups and recovery was reported in patients with erosive esophagitis with eight-week treatment.[10] In a study involving adult patients, similar results were reported to be obtained when the lansoprazole

Table 2 Comparison of the groups according to demographic characteristics, application symptoms and esophagitis findings

Parameters	Group 1	Group 2	p*
n	58	60	
Age (years)	10.12±1.53	10.52±1.21	0.172
Gender	24 Male, 34 Female	22 Male, 38 Female	0.692
Dyspeptic complaints (n, %)	46 (79.3)	45 (75)	0.561
Weight loss-malnutrition (n, %)	4 (6.8)	6 (10)	0.413
Respiratory symptoms (n, %)	8 (13.8)	9 (15)	0.731
Non erosive (n, %)	20 (34.5)	23 (38.3)	0.385
Grade A (n, %)	18 (31.1)	17 (28.3)	0.521
Grade B (n, %)	13 (22.4)	14 (23.3)	0.582
Grade C (n, %)	5 (8.6)	4 (6.7)	0.982
Grade D (n, %)	2 (3.4)	2 (3.3)	0.835

* Chi square

15 mg and 30 mg treatment were compared in patients with GERD.[11] The comparison of placebo and ranitidine with four- and eight-week single dose PPI (15 mg or 30 mg once daily) treatments in patients with non-erosive GERD showed that PPI was significantly superior to ranitidine and placebo and dose-independent side effects and duration of treatment were similar.[12] The results obtained from our study are similar to those in the literature. The efficacy of short-term and long-term treatment has been shown to be similar. In the present study, the majority of the study population were patients with non-erosive and low-grade erosive esophagitis. In a study involving patients with erosive esophagitis due to GER, in which the eight- and 12-week use of lansoprazole were compared, all patients were seen to be recovered at the end of 12 weeks whereas the recovery rate was reported to be 78% in the eight-week treatment and the difference was found to be statistically significant.[10]

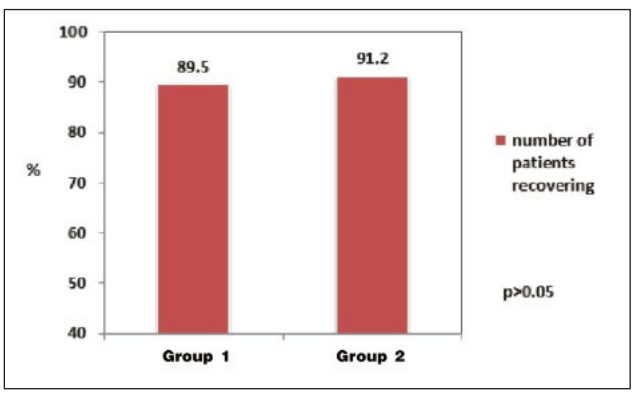

Figure 1 Comparison of groups according to the response to treatment.

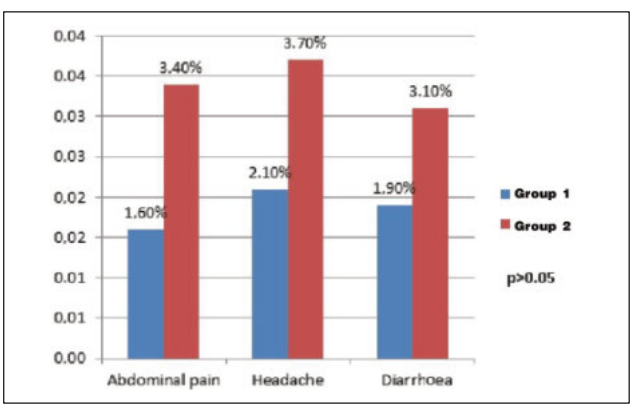

Figure 2 Comparison of groups in terms of side effects.

With clinical significance of 0.05, and a power of 80% to detect an absolute difference of 20% we needed a sample size of 60 patients for Group 1 and 60 patients for Group 2. In our study, the first group consisted of 58 patients, and the second group consisted of 60 patients. This is the limitation of the study.

Limitations of this study the impedance-pH monitoring could not be performed in patients for diagnostic purposes. Since the majority of the study population consisted of patients with non-erosive esophagitis and those with grade A and B esophagitis according to the Los Angeles classification and a sufficient number of patients with severe esophagitis could not be reached, treatment response could not be compared in these patients.

Discussion

In conclusion, in children who develop reflux esophagitis due to gastroesophageal disease, four-week lansoprazole treatment has been found to be as effective as the eight-week treatment. However, further randomised controlled trails are needed to confirm the finding of this study.

Declaration of Interest

None

References

1. Lightdale JR, Gremse DA; Section on Gastroenterology, Hepatology, and Nutrition. Gastroesophageal reflux: management guidance for the pediatrician. Pediatrics 2013;131:1684-95.
2. Rosen R, Vandenplas Y, Singendonk M, et al. Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. J Pediatr Gastroenterol Nutr 2018;66:516-54.
3. Hassall E. Over-prescription of acid-suppressing medications in infants: how it came about, why it's wrong, and what to do about it. J Pediatr 2012;160:193-8.
4. Canani RB, Cirillo P, Roggero P, et al; Working Group on Intestinal Infections of the Italian Society of Pediatric Gastroenterology, Hepatology and Nutrition (SIGENP). Therapy with gastric acidity inhibitors increases the risk of acute gastroenteritis and community-acquired pneumonia in children. Pediatrics 2006;117:817-20.

5. Freedberg DE, Lamousé-Smith ES, Lightdale JR, Jin Z, Yang YX, Abrams JA. Use of acid suppression medication is associated with risk for C. difficile infection in infants and children: a population-based study. Clin Infect Dis 2015;61:912-7.
6. Lundell LR, Dent J, Bennett JR, et al. Endoscopic assessment of oesophagitis: clinical and functional correlates and further validation of the Los Angeles classification. Gut 1999;45:172-80.
7. Repchinsky C, ed. Compendium of pharmaceuticals and specialties. Ottawa, Ontario: Canadian Pharmacists Association, 2006
8. Richter JE, Kovacs TO, Greski-Rose PA, Huang B, Fisher R. Lansoprazol in the treatment of heartburn in patients without erosive oesophagitis. Aliment Pharmacol Ther 1999;13:795-804.
9. Dorsch E, Jones J, Rose P, Jennings D. Lansoprazole provides superior symptom relief for patients with non-erosive reflux esophagitis. Gastroenterology 1996;110:987.
10. Tolia V, Ferry G, Gunasekaran T, Huang B, Keith R, Book L. Efficacy of lansoprazole in the treatment of gastroesophageal reflux disease in children. J Pediatr Gastroenterol Nutr 2002;35:308-18.
11. Gunasekaran T, Gupta S, Gremse D, et al. Lansoprazole in adolescents with gastroesophageal reflux disease: pharmacokinetics, pharmacodynamics, symptom relief efficacy, and tolerability. J Pediatr Gastroenterol Nutr 2002;35:327-35.
12. Richter JE, Campbell DR, Kahrilas PJ, Huang B, Fludas C. Lansoprazole compared with ranitidine for the treatment of nonerosive gastroesophageal reflux disease. Arch Intern Med 2000;160:1803-9.