Paediatrica Indonesiana

VOLUME 51 July • 2011 NUMBER 4

Original Article

Lansoprazole for recurrent abdominal pain in adolescents

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Abstract

Background Recurrent abdominal pain is common among adolescents. School absenteeism and lower quality of life are associated with severity of symptoms. Lansoprazole has been used to treat recurrent abdominal pain.

Objective To investigate the effectiveness of lansoprazole as a treatment for recurrent abdominal pain in adolescents.

Methods We conducted a randomized, double-blind, controlled trial from August 2009 to October 2009. Adolescents suffering recurrent abdominal pain were eligible for the study. Simple randomization was done to divide subjects into two groups. Groups received 30 mg of lansoprazole or placebo, once a day for 14 days. Before treatment, we performed laboratory and physical examinations. Pain frequency was measured in number of abdominal pain episodes per month. Duration was measured in minutes and pain intensity was measured by a pain rating scale. Drug efficacy was measured before, during and after intervention. Data was analyzed using Mann-Whitney U-test and t-test.

Results One hundred sixteen recurrent abdominal pain patients were randomized into two groups of 58 patients. There were no statistically significant differences in pain frequency before and after treatment for either the lansoprazole group or the placebo group (P=0.083, 95%CI, -0.033 to 0.021 and P=0.096, 95%CI -0.376 to 0.031, respectively). In addition, there were no significant differences in frequency, duration, and degree of abdominal pain at baseline and after 1, 2 and 3 months of treatment between the two groups.

Conclusion Lansoprazole was not more effective than the placebo for treatment of recurrent abdominal pain among adolescents. **[Paediatr Indones. 2011;51:234-40]**.

Keywords: *lansoprazole, recurrent abdominal pain, adolescent*

Recurrent abdominal pain (RAP) is defined as abdominal pain attacks occurring at least three times or more within a period of three months with effects on activity.[1] Incidence ranges from 10% to 20% of school-aged children, with a peak incidence at age 10 to 12 years and occurring more often in girls.[2,3] An epidemiological study reported 13% to 17% of teenagers experience abdominal pain weekly, with 20% of the incidents being quite heavy and affecting activity.[4] A study in Malaysia also reported an incidence of 10.2% in school-aged children.[5]

Recurrent abdominal pain is presumably caused by organic or functional disorders. Although organic disorders should be considered, they are found in less than 10% of patients. Functional abdominal pain is characterized by abdominal pain in the umbilicus usually accompanied by symptoms such as nausea, vomiting, dizziness, pallor and headaches.[6,7] Several studies have reported that RAP reduces quality of

This study has been presented at 4th National Congress of Indonesian Pediatric Gastroenterology Coordination Boards, 2010 December 4 – 7, Medan.

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life by causing sleep disorders, more visits to child health services, decline in academic achievement and significantly increased school absences.[8-10]

Clinical trials have suggested H_2-receptor antagonists significantly reduce frequency and severity of RAP when accompanied by symptoms of dyspepsia.[11] The proton pump inhibitor (PPI) lansoprazole reportedly has a better efficacy than H_2-receptor antagonists in reducing gastric acid secretion, treatment of gastrointestinal ulcers and esophagitis in some studies.[12,13] Our study aimed to investigate the effectiveness of lansoprazole as a treatment for recurrent abdominal pain among adolescents.

Methods

We conducted a randomized, double-blind, controlled trial from August to October 2009, at five junior/senior high schools in the Langkat district. Adolescents with a history of abdominal pain and meeting the inclusion criteria were eligible for the study. Inclusion criteria were adolescents aged 12 to 18 years who met the diagnostic criteria for RAP (Apley's criteria),[1] and had good nutritional status. We excluded patients using other drugs for abdominal pain, and those with malnutrition, chronic diarrhea, constipation, bloody stools, urinary tract infection, anemia, parasitic infection and dysmenorrhea.

We divided patients by simple randomization into two groups of 58 patients each, with patients receiving either lansoprazole or placebo. Group I received 30 mg of lansoprazole once daily in the morning for fourteen days and group II received a placebo. A questionnaire was used to identify adolescents suffering from RAP, as well as to establish the frequency, duration and severity of pain. Pain frequency was measured in number of abdominal pain episodes per month. Duration was measured in minutes and pain severity was measured with a pain rating scale (0= no pain, 10= awful pain). Pain severity was further stratified according to one of three categories (mild 0-3; moderate 4-6; severe 7-10). We collected the frequency, duration and severity of pain from each group in a daily diary provided monthly for 3 months.

We measured anthropometric values of patients at the beginning of the study. Weight was measured with Camry® scales (sensitivity 0.1 kg) and height was measured with a 2M stature meter (sensitivity 0.5 cm). Nutritional stage was calculated as body weight (BW) per body height (BH), with the value then plotted on the Centers for Disease Control and Prevention (CDC) growth chart, 2000. Obesity was noted if the BMI was $\geq 95^{th}$, overweight if the BMI was 85^{th} to $< 95^{th}$, good nutritional status if the BMI was 5^{th} to $< 85^{th}$, and poor nutritional status if the BMI was $< 5^{th}$. We performed physical and laboratory examinations. Blood tests were performed using Sahli's hemoglobin method, urine tests using *Verify* dipstick test, and stool examination using Kato Katz method.

Both lansoprazole and placebo were packed in similarly colored and shaped capsules. If abdominal pain continued at dosing, patients were allowed to take paracetamol (500 mg) every 8 hours. Patients provided written, informed consent. This study was approved by the Research Ethics Committee, University of North Sumatera Medical School.

Data was processed, analyzed and presented using the Statistical Package for the Social Sciences (Windows version 15.0; SPSS Inc, Chicago). T test was used to statistically analyze frequency of pain. Mann-Whitney U-test was used to analyze pain severity and duration. We used a 95% confidence interval and $P<0.05$ level of significance in this intention-to-treat analysis.

Results

Of 820 students, we found 228 students with RAP, 66 of which did not meet the inclusion criteria and 46 of which refused to participate in the study. The remaining 116 children were included in our study and divided into two groups of 58 students each, who received either lansoprazole or placebo. After three months follow-up, no subjects had dropped out of the study. (**Figure 1**)

Average age in the lansoprazole group was 13.2 years, while in the placebo group it was 13.8 years. Females made up the majority in both groups. Nutritional status based on the mean BW/BH for both groups was within the normal range. Mean hemoglobin concentration was ≥ 12 g/dL. Most common parental income category was between Rp 500,000 to 1,000,000 per month and the most common parental educational level was high school.

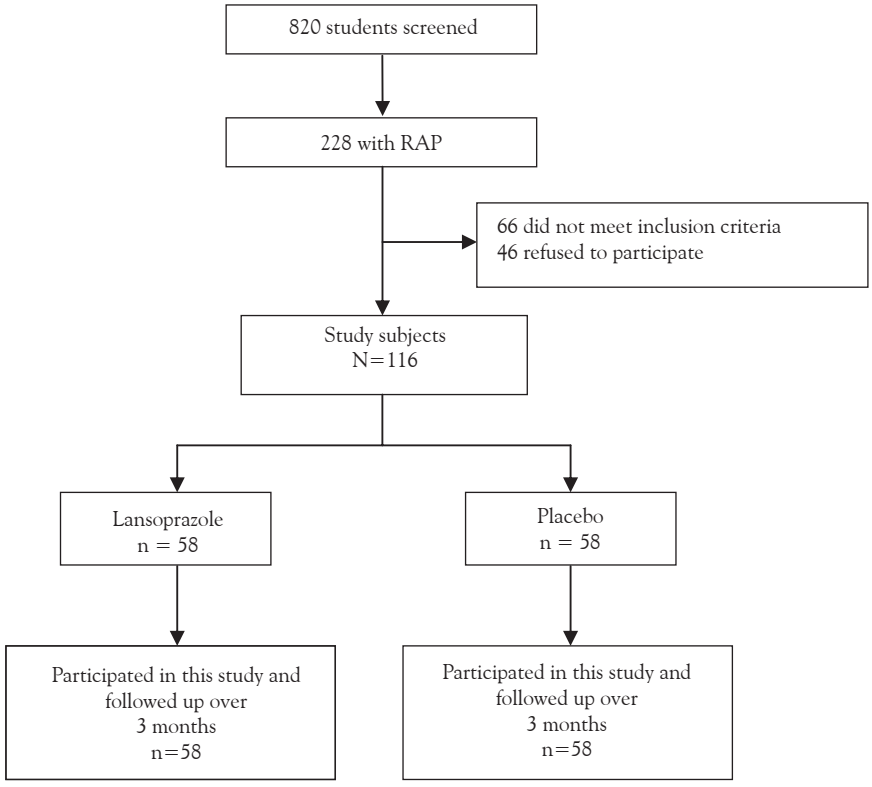

Figure 1. Study profile

Table 1. Baseline characteristics

Characteristic	Lansoprazole n=58	Placebo n=58
Mean age, years (SD)	13.2 (0.85)	13.8 (1.63)
Sex, n		
Male	23	25
Female	35	33
Mean body weight, kg (SD)	36.7 (4.50)	40.5 (7.60)
Mean body height, cm, (SD)	145.1 (5.80)	147.0 (8.10)
Mean BW/BH, % (SD)	97.6 (8.31)	99.3 (13.08)
Mean hemoglobin, g/dL (SD)	12.4(0.87)	12.5 (0.76)
Parental income, n		
< Rp. 500.000	15	8
Rp. 500.000 – 1.000.000	37	42
> Rp. 1.000.000	6	8
Parents' education, n		
Primary school	3	3
Junior high school	13	10
Senior high school	32	36
University	10	9
Associated symptoms, n		
Headache	7	9
Nausea and vomiting	10	13
Joint pain	2	3
Location of pain, n		
Periumbilicus	33	37
Upper abdomen	13	25
Lower abdomen	3	5
Visited physicians, n	4	3

The most commonly associated symptoms were nausea and vomiting, reported in both groups. Periumbilical abdominal pain was reported by 33 (28.44%) and 37 (31.89%) subjects in the lansoprazole and placebo groups, respectively. Only 6% of all subjects reported visits to health services.

In **Table 2**, decreased frequency of RAP in adolescents was not significantly different before and after treatment in either the lansoprazole group or the placebo group during the 3 months of observation.

We also found no statistically significant differences in the mean frequency of RAP in adolescents between the lansoprazole and placebo groups at baseline. Similarly, the average frequency of RAP during months 1, 2 and 3 of treatment with lansoprazole was comparable to that of the placebo. **(Table 3)**

Pain duration (minutes) in the lansoprazole and placebo groups at baseline was not significantly different. Similarly, pain duration after 1 month, 2 months and 3 months of treatment was not significantly different between the two groups. **(Table 4)**

There were also no reductions in degree of pain in both groups at the end of the study. Similarly, there were no statistically significant differences between the two groups at each time interval of the study. **(Table 5)**

Table 2. Frequency of pain before and after treatment

	Before	After	95% CI	P
Lansoprazole	5.9 (1.17)	5.8 (1.11)	-0.331 to 0.021	0.083
Placebo	5.4 (1.31)	5.2 (1.48)	-0.376 to 0.031	0.096

Mean value (SD)

Table 3. Frequency of pain per month in the lansoprazole and placebo groups

	Lansoprazole	Placebo	95% CI	P
At baseline	5.9 (1.17)	5.4 (1.31)	0.113 to 1.025	0.081
After 3 months	5.8 (1.109)	5.2 (1.48)	0.105 to 1.068	0.064
1 month	2.0 (0.65)	1.8 (0.53)	-0.028 to 0.408	0.087
2 months	1.9 (0.51)	1.7 (0.60)	-0.016 to 0.395	0.071
3 months	1.9 (0.539)	1.7 (0.59)	-0.017 to 0.397	0.072

Value in mean (SD)

Table 4. Duration of pain before and after receiving treatment

	Duration of pain (minutes)	Lansoprazole n=58	Placebo n=58	P
At baseline	< 10	20	33	
	10-30	33	17	0.076
	30-60	4	8	
	> 60	1	0	
1 month	< 10	15	31	0.065
	10-30	39	17	
	30-60	4	10	
	> 60	0	0	
2 months	< 10	23	37	0.067
	10-30	32	13	
	30-60	3	8	
	> 60	0	0	
3 months	< 10	32	44	0.060
	10-30	22	7	
	30-60	4	7	
	> 60	0	0	

Table 5. Degree of pain before and after receiving treatment

	Degree of pain	Lansoprazole n=58	Placebo n=58	P
At baseline	Mild	28	39	0.060
	Moderate	26	15	
	Severe	4	4	
1 month	Mild	23	36	0.051
	Moderate	31	16	
	Severe	4	6	
2 months	Mild	29	39	0.070
	Moderate	25	16	
	Severe	4	3	
3 months	Mild	29	40	0.058
	Moderate	25	14	
	Severe	4	4	

Discussion

Our study was conducted in rural areas in the Langkat district. We surveyed the average income of parents, with most subjects surveyed coming from low-income groups. Most parents had received a high school education. The study also indicated that the prevalence of RAP was high, amounting to 27.8%, with an average age of 13.2 years in the lansoprazole group and 13.8 years in the placebo group. Lower prevalence of 0.3 - 19% was described by a systematic review in Western countries,[14] but a Malaysian study reported the prevalence of RAP in a rural school to be 41.2%, with lower parents' education level.[15] An American study involving 507 adolescents, with an average age of 12.6 years for junior high and 15.6 years for high school students, found 13 - 17% experienced abdominal pain and 21% reported interference with their activities.[16]

We found RAP to be more frequent in adolescent females (58.6%) than in adolescent males (41.4%). Similarly, a cohort study in Sri Lanka reported a higher incidence in girls.[17] RAP incidence is similar in girls and boys up to the age of 9 years. After age 9 years, incidence in girls increases, with a male: female ratio of 1:1.5.[3]

More than half of the subjects (60%) in this study, reported pain locations in the periumbilical region, similar to previous studies in Australia and Bangladesh.[18,19] RAP may be accompanied by symptoms such as headache, nausea, vomiting and joint pain.[19,20] Similar symptoms were reported by our subjects.

Visits to a physician or to seek medication vary from study to study. Only 6% of our subjects reported medical visits seeking medication in the previous 3 months. A higher numbers of visits (8%) was reported in the United States.[16] However, a study in Australia reported 34% of subjects visited a physician,[18] while Malaysian studies reported 45% and 48%.[20,21]

Malnutrition and anemia associated with RAP would necessitate ruling out an organic disorder as the underlying cause.[3,22,23] For our purposes, we included patients with good nutritional status and not suffering from anemia. Both groups show a BW/BH in the 90% to < 110% range, and a hemoglobin level of ≥ 12 g / dL.

Lansoprazole is a proton pump inhibitor (PPI) with substituted benzimidazole, a lipophilic weak base, that crosses membranes to enter canaliculus parietal cells. In this acidic environment, PPIs are activated to a sulphenamide form that binds covalently with H^+, K^+-adenosine triphosphatase enzyme to inhibit acid secretion by proton pumps.[24,25] One study reported lansoprazole to be effective and safe in children with reflux oesophagitis, with an optimal starting dosage of 30 mg/m^2 or 1.4 mg/kg.[26] However, the use of lansoprazole for RAP treatment has not been previously reported.

The baseline reports of frequency, duration and level of abdominal pain in adolescents was not significantly different between the two groups. Similarly, there were no significant differences in the groups after 1 month, 2 months, and 3 months of treatment. Our results contrasted to those of previous studies using famotidine, though we

made no assessment of dyspepsia symptoms in our study.

A limitation in our study was in the use of Apley's criteria for diagnosis of RAP. Its use has been considered to be too broad in assessing specific disorders of RAP, whereas the Rome criteria may provide clearer operational limits. However, there have been few studies using the Rome criteria. Another limitation was the lack of supervision to assess patient compliance in taking the medication. Monitoring was based on counting the number of leftover capsules returned by patients at follow-up visits. Furthermore, patient assessment of pain duration and degree of severity may be subjective.

We found that RAP treatment with lansoprazole at a dose of 30 mg once a day for 14 days in adolescents, did not significantly improve pain frequency after treatment. Also, treatment with lansoprazole was not significantly different from placebo in changing frequency, duration and degree of abdominal pain in adolescents.

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