

Comparison of combination of probiotic and standard therapy compared to standard therapy on eradication of *Helicobacter pylori* infection in children

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Abstract

Background *Helicobacter pylori* (*H. pylori*) infection is thought to be the etiology of chronic gastritis, peptic ulcer, and risk factor for gastric cancer. Management of *H. pylori* infection in children is associated with several problems such as compliance to therapy, intolerated side effects, and antibiotic resistance. Probiotic is reported to give beneficial effect in the management of *H. pylori* infection and there is no study yet on the effect of probiotic in eradication of *H. pylori* infection in Indonesian children.

Objectives To study the effect of additional probiotic in the standard therapy on the rate of *H. pylori* infection eradication in children and its side effect.

Methods This was a double blind randomized controlled trial performed in 23 children with *H. pylori* infection at Kampung Melayu and Rawa Bunga District. The diagnosis was determined based on *Helicobacter pylori* stool antigen test (HpSA). Subjects were randomly assigned to either receive receive amoxycillin, clarithromycin, omeprazole, and probiotic (2 x 10⁹ cfu of *Lactobacillus acidophilus* La5 and *Bifidobacterium lactis* Bb12) or amoxicillin, clarithromycin, omeprazole dan placebo (maltodextrin). HpSA examination was evaluated again after 2 weeks of therapy.

Results Two of 13 subjects in the treatment group and 6 of 10 subjects in the control group experienced side effects. Eradication rate in the treatment group is higher than the control group (13/13 vs 7/10) but the correlation between additional probiotic with the eradication rate of *H. pylori* is not statistically significant.

Conclusions Probiotic can reduce the incidence of side effects due to antibiotic used in *H. pylori* eradication (2/13 vs 6/10, $p < 0.012$). [Paediatr Indones. 2010;50:38-41].

Keywords: eradication, probiotic, *H. pylori* infection, RCT

H. *pylori* infection is a world health problem because it is thought to be the etiology of chronic gastritis, peptic ulcer, and risk factor for gastric cancer with a prevalence of proximately 50%. In children under 10 years old the prevalence is 80%. The management of *H. pylori* infection in children have several problems such as treatment compliance, side effects that are not well-tolerated, and increasing resistance to antibiotic.¹⁻⁵ Probiotic is reported to have beneficial effects on the management of *H. pylori* infection such as increasing the eradication rate by various mechanisms, reducing the side effects of antibiotic used on the management of *H. pylori* infection and suppressing resistance to *H. pylori* to antibiotics.⁷⁻¹¹ The aim of this study was to find the role of probiotic to the eradication rate and the incidence of side effects in the management of *H. pylori* infection in children.

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Methods

A double blind randomized controlled trial was performed at Rawa Bunga and Kampung Melayu District, Jatinegara, East Jakarta from October 2008-June 2009. *H. pylori* stool antigen test (HpSA) was performed in 459 subjects and 23 subjects were infected by *H. pylori*. Subjects were randomly assigned into treatment and control group. Treatment group consisted of 13 subjects who were given amoxicilin 50 mg/kg BW two times daily, clarithromycin 15 mg/kg BW two times daily, omeprazole 1 mg/kg BW/day for 14 day and probiotic (2×10^9 cfu *Lactobacillus acidophilus* La5 and *Bifidobacterium lactis* Bb12) for 28 days. Control group consisted of 10 subjects who were given amoxicilin, clarithromycin, omeprazole, dan placebo (maltodekstrin). Eradication was defined as treatment success based on negative result of the two consecutive HpSA examination performed two weeks after treatment free. Side effect was defined as symptom presence after consuming standard therapy with probiotic or placebo such as headache, nausea, vomit, and diarrhea.

Results

The prevalence of *H. pylori* infection in our study was 5% (23/459). Demographic characteristics recorded were age, sex, social economic status, number of siblings, eating and drinking habit, washing hands, source of water, and incidence of *H. pylori* infection showed equal results and suitable for comparison. Comparison of effectivity of additional probiotic to the eradication of *H. pylori* infection is shown in Table 1.

The success of eradication in both groups was determined by HpSA examination performed two weeks after treatment. In the control group who received standard therapy and placebo, eradication was found in 7 of 10 subjects. Meanwhile in the treatment group, who received standard antibiotics and probiotic, eradication was found in all subjects.

Side effects presence due to treatment were also noted in this study. There were 6 reports and only 2 reports of side effects in the control and treatment group, respectively. Side effects found were nausea, diarrhea, and bloating.

Table 1. Treatment results according to study group

Study Group	HpSA (-)	HpSA (+)	P
Probiotic group	13	-	0.068
Placebo group	7	3	
Total	20	3	

Table 2. Incidence of side effects according to study group

Side effects of therapy	Probiotic group	Placebo group	P
Abdominal pain	-	-	0.012*
Nausea	1	2	
Vomit	-	-	
Bloating	1	1	
Diarrhea	-	2	
Total	2	6	

*Significant with Fisher test if $P < 0.05$

Discussion

There have been many studies, which comparing standard therapy and standard therapy combined with probiotic, in other countries. The majority of those studies were performed in adult subjects and using various diagnostic test, treatment, and type of probiotic. Most of those studies used urea breath test or combination with other modalities such as biopsy or serology.¹²⁻¹⁶ In this study, we used the HpSA diagnostic test because it was a non-invasive modality, had high sensitivity and specificity, and it could be used to evaluate treatment result.¹⁷⁻¹⁹

In this study amoxicillin, clarithromycin, and proton pump inhibitor were used for 14 days and probiotic was given for 28 days. This combination of antibiotic was also used in similar previous studies.¹²⁻¹⁶ In this study, eradication in the placebo group was found in 7 of 10 subjects and in all subjects of the probiotic group (13/13), but this was not statistically significant ($P = 0.068$). Sheu et al¹² in their study involving 160 adult subjects using yoghurt containing *Lactobacillus* and *Bifidobacterium* showed rate of eradication 91% vs 78% ($P < 0.05$). Similar result was also reported by Tursi et al¹⁵ in their study in 70 adult subjects with rate of eradication 94% vs 86%. Wang et al²⁰ in China reported a study in 14 adult subjects using the same type of probiotic as our study but did not report rate of eradication. They found a decreased in *H.pylori* density and severity of the gastritis.

Various type of probiotic has been studied either *in vitro* or *in vivo* in order to find the best strain of probiotic for combination therapy in eradication of *H. pylori* infection. Most reported probiotic giving promising result in *in vitro* studies are *Lactobacillus casei*, *Lactobacillus gasseri* LG21, *Lactobacillus johnsonii* La1, and *Lactobacillus acidophilus* strain LB.²⁰⁻²⁶ In this study, we used *Lactobacillus acidophilus* La 5 dan *Bifidobacterium lactis* Bb 12 due to the availability in Indonesia.

Standard therapy consists of two antibiotic and proton pump inhibitor, usually cause burden to the gastrointestinal tract resulting in unpleasant side effects such as nausea, vomit, bloating, and diarrhea that are pharmacologically predicted. These side effects for children can cause bad compliance, so other solutions are searched to reduce it. Probiotic has been studied and reported that it could reduce side effects of antibiotics by an unknown mechanism. In this study, side effects presence in the probiotic group were less than the placebo group (2/13 vs 6/10, P=0.012).

We conclude that the addition of probiotic to the standard therapy for *H. pylori* infection can increase the rate of eradication and probiotic can also reduce side effects of antibiotics used in the treatment.

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