Paediatrica Indonesiana

VOLUME 52 July • 2012 NUMBER 4

Original Article

# Efficacy of synbiotic and probiotic treatments on acute watery diarrhea in children

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## Abstract

***Background*** In developing countries, acute watery diarrhea is a common cause of morbidity and mortality in children. Giving synbiotics or probiotics may decrease the severity of diarrhea.

***Objective*** To compare the efficacy of synbiotics and probiotics in decreasing the frequency of diarrhea, shortening the duration, and increasing patient body weight.

***Methods*** This was a double-blind, randomized clinical trial to compare the effects of synbiotic vs probiotic treatment in children aged 6-59 months with acute watery diarrhea. This study was performed from October to December 2010 in two hospitals in Central Java. Subjects received either synbiotics or probiotics twice daily for five days. The measured outcomes were duration of diarrhea, daily frequency of diarrhea, and increase in body weight.

***Results*** There was no significant difference in the mean duration of the diarrhea in the synbiotic and probiotic groups, 3.92 days (SD 0.79) vs 3.80 days (SD 0.82),(P=0.35), respectively. Nor did we observe a significant difference in the mean increase in body weight in the synbiotic and probiotic groups, 150 g (SD 49.7) vs 160 g (SD 48.9), (P= 0.67), respectively.

***Conclusion*** We observed no significant differences in efficacy of synbiotic and probiotic treatment for management of acute watery diarrhea. **[Paediatr Indones. 2012;52:209-12]**.

***Keywords***: *Acute watery diarrhea, synbiotic, probiotic*

Acute watery diarrhea is a common cause of morbidity and mortality in children. Dehydration, as its main complication, causes the death of 5 to 10 million children in the world annually.[1] The main treatments for managing acute watery diarrhea are rehydration, prevention of further dehydration, and dietetic treatment. The goal of dietetic treatment is to improve the microbial ecosystem of the gut.[2] Effects of probiotics in the gastrointestinal tract are improvement of lactose absorption, normalization of gut microflora, clearance of pathological microorganisms, and improvement of humoral immunity by increasing IgA secretion.[3,4] Intake of probiotics (living microorganisms), and synbiotics (consisting of a mixture of living microorganisms and oligosaccharides) has been demonstrated to modify the composition of the gut microflora, restore the microbial balance, hence, providing potential health benefits[5,6,7,8].

Previous studies have assessed the efficacy of probiotics compared to placebo, as well as synbiotics compared to placebo, in the management

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of acute watery diarrhea. Both reported significant benefits.[9,10,11] However, there has been little data on which of the two, probiotics or synbiotics, is more effective for treating acute watery diarrhea in children.[5,6,7]

We conducted this study to compare the effects of synbiotics and probiotics in decreasing the frequency of diarrhea, shortening the duration of diarrhea, and increasing body weight during illness.

## Methods

We conducted this study in the pediatric ward of Soeradji Tirtonegoro Hospital, Klaten, and Muntilan Hospital, Magelang, from October to December 2010. The study design was a randomized, double-blind clinical trial. Subjects were children aged 6-59 months with acute watery diarrhea admitted at the two hospitals. Acute watery diarrhea was defined as watery stools occurring more than three times per day and lasting for at least seven days. We excluded subjects with bloody diarrhea and diarrhea with severe complications, such as severe dehydration, metabolic acidosis, or seizures. Parents of subjects provided written informed consent. This study was approved by the Health and Medical Ethics Committee of the Gadjah Mada University Medical Faculty.

The required number of subjects (176) was determined by hypothesis test, based on the means of the two populations. Subjects were consecutively allocated into the two treatment groups using a random number table. Only the appointed pharmacist had access to the subjects' allocated intervention, while subjects and physicians were blinded to the information (see study profile in **Figure 1)**.

Before the study, subjects were examined to determine their level of dehydration, based on WHO guidelines. Subjects suffering from dehydration were rehydrated before weighing. The synbiotic and probiotic sachets were administered twice daily for five days by nurses. Patient compliance was recorded.

The physician evaluated the level of dehydration and frequency of diarrhea every two hours in the first six hours after admission, followed by evaluation every twelve hours. We evaluated the duration of diarrhea from acute watery diarrhea, as well as the increase in body weight during illness. Duration of diarrhea was defined as the time taken for diarrheal frequency to decrease to less than three times per day. If subjects were discharged in less than five days, we asked parents to have their children weighed at the outpatient clinic on day five after admission.

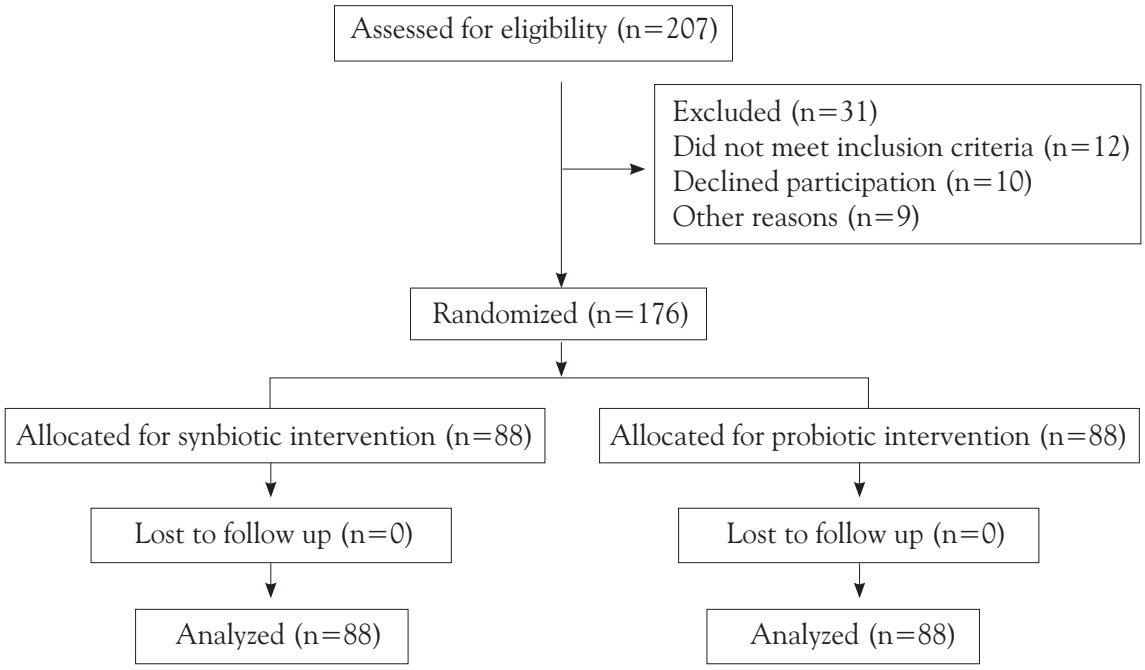


**Figure 1.** Study profile

## Results

Of the 207 children recruited, 176 subjects completed the study. There were 88 subjects in each of the two groups. Baseline characteristics of subjects are shown in **Table 1**. The results of this study are shown in **Table 2**. There was no significant difference in the duration of the diarrhea (P=0.35), the daily frequency of diarrhea, or the increase in body weight (P=0.67). We observed potential side effects of giving synbiotics and probiotics, like bloating and flatulence. Three patients suffered from bloating in synbiotic group. No other gastrointestinal adverse effects were observed during the study.

## Discussion

We conducted this study to compare the effects of synbiotics and probiotics in decreasing the frequency of diarrhea, shortening the duration of diarrhea, and increasing body weight during illness. We found no significant differences between the two groups for mean daily frequency of diarrhea, mean duration of diarrhea or mean increase in body weight.

We observed side effects, such as bloating and flatulence, from both synbiotic and probiotic treatment. Three patients in the synbiotic group suffered from bloating. Fermentation of the substrate (prebiotics) produces hydrogen, which may cause

**Table 1.** Baseline characteristics of subjects

| Characteristics | Synbiotic group (n=88) | Probiotic group (n=88) |
|---|---|---|
| Mean age, months ± SD | 27.69 ± 13.73 | 23.69 ± 14.74 |
| Gender | | |
| Males, n (%) | 51 (58) | 41 (47) |
| Females, n (%) | 37 (42) | 47 (53) |
| Socio-economic status[1] | | |
| Low, n (%) | 21 (24) | 41 (76) |
| High, n (%) | 67 (76) | 47 (34) |
| Nutritional status[2] | | |
| Undernourished, n (%) | 31 (35) | 34 (38) |
| Well-nourished, n (%) | 57 (65) | 54 (62) |

[1] Determination of socio-economic status was based on the ratio of meal expenditure to monthly family income. In Central Java in 2009, high socio-economic status was defined as a ratio of ≤ 51.8%, while low socio-economic status was defined as a ratio of > 51.8%.[9]

[2] Nutritional status was categorized by body weight for height z-score, based on the WHO 2006 growth standard. Obesity was defined as a z-score of ≥ 2 SD; well-nourished was defined as a z-score of -2 SD to +2 SD; wasting was defined as a z-score of -2 SD to -3 SD; while severe wasting was defined as a z score of ≤ -3 SD. These four categories were combined into 2 groups: well-nourished for obesity and well-nourished combined, and under-nourished for wasting and severe wasting combined.

**Table 2.** Results of the study

| Variables | Synbiotic group (n=88) | Probiotic group (n=88) | Mean Difference | 95% CI | P value |
|---|---|---|---|---|---|
| Mean duration of diarrhea, days ± SD | 3.92 ± 0.79 | 3.80 ± 0.82 | - 0.11 | -0.35 to 0.12 | 0.35 |
| Mean frequency of diarrhea, per day ± SD | | | | | |
| day 1 | 6.87±1.62 | 6.67±1.52 | - 0.20 | -0.67 to 0.26 | 0.39 |
| day 2 | 4.47±1.82 | 4.28±1.78 | -0.19 | -0.72 to 0.34 | 0.47 |
| day 3 | 2.57±1.52 | 2.52±1.56 | -0.05 | -0.51 to 0.4 | 0.80 |
| day 4 | 0.94±1.09 | 1.13±1.50 | 0.19 | -0.19 to 0.58 | 0.33 |
| day 5 | 0.23±0.47 | 0.20±0.45 | -0.03 | -0.17 to 0.10 | 0.63 |
| Mean increase in body weight, grams ± SD | 150± 49.7 | 165± 48.9 | 15.0 | -1.01 to 29.9 | 0.67 |

bloating, flatulence, and diarrhea. But it is difficult to differentiate if these effects are due the diarrhea itself or due to the additional substrates (prebiotics).

Previous in vitro studies reported that synbiotics decreased the frequency of diarrhea, shortened the duration of diarrhea, and increased body weight better than probiotics.[10] The addition of substrate for bacterial growth to the live microbes increases bacterial survival. Galactooligosaccharides were not only beneficial for the administered bacteria, but also for the residing bifidobacteria and lactobacilli in the intestines. Many species of bifidobacteria and lactobacilli other than the administered probiotics were observed in the feces after synbiotic treatment.[7,8]

Previous studies assessing the efficacy of probiotics compared to placebo, as well as synbiotics compared to placebo, in the management of acute watery diarrhea, reported significant benefits.[11-13] This study is the first to compare administered synbiotics and probiotics in the management of acute watery diarrhea in children. However, we observed no beneficial effect of adding prebiotics into the probiotics, i.e the synbiotics, compared to the probiotics alone. If the substrate for bacterial growth was already present in the intestines, adding additional substrate might be useless.

A limitation of our study was that we did not analyze food intake from daily diet. Food intake would affect the increase in body weight. Also, we assessed the degree of dehydration based on clinical findings alone, not by checking urine specific gravity.

In conclusion, we found no significant differences in daily frequency and duration of diarrhea, or increase in body weight between synbiotic and probiotic treatment in children with acute watery diarrhea.

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