

A Randomized Open Label Comparative Clinical Study Of A Probiotic Against A Symbiotic In The Treatment Of Acute Diarrhea In Children

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ABSTRACT: Objective: To evaluate the safety, efficacy and tolerability of a probiotic against a symbiotic in reducing the frequency and the duration of acute diarrhea. **Methods:** One hundred children aged 6 months to 6 years, with acute diarrhea, admitted in the Pediatric ward of Pokhara Academy of Health Sciences (PAHS) were recruited in the study. Group A (n=50) received standard therapy plus probiotic 5m (Enterogermina®) twice-daily for 7 days. Group B (n = 50) received standard treatment plus symbiotic 5 mL (Bifilac® dry syrup) twice-daily for 7 days. Patients were assessed for diarrhea and dehydration. **Results:** The frequency of diarrhea was reduced from 9.03 on Day 1 to 0.81 on Day 3 in Group B, compared with 10.1 on Day 1 to 6.24 on Day 3 in Group A. On comparing the two groups on Day 3, Group A produced a statistically significant reduction in the frequency of diarrhea. Similarly, there was a statistically significant reduction in the duration of diarrhea on comparing Group A with Group B. The mean duration of diarrhea was 36.2 hours in Group B, compared with 72.6 hours in Group A. The adverse events were mild and no serious adverse effects were reported. **Conclusion:** From our study, it can be concluded that the symbiotic is more effective in reducing the frequency and duration of diarrhea than the probiotic and is well-tolerated.

Keywords: Probiotic, Symbiotic, diarrhea, children

Diarrheal disease is the second most common cause of death in children less than 5 years of age (0.58 million or 11%).¹ Diarrhea, defined as passage of three or more liquid or watery stools in a day, represents a significant cause of childhood mortality and morbidity affecting nearly 1.7-5 billion of children worldwide.^{2,3} Acute diarrhea refers to diarrhea of less than 14 days duration in a previously normal child and is usually due to infective etiology. The most common age group affected is 6-24 months. Diarrhea is usually a symptom of gastrointestinal (GI) infection that can be caused by a variety of viral, bacterial and parasitic organisms. Infection is spread through contaminated food or drinking water, or from person to person due to poor hygiene. Diarrhea has the potential to cause dehydration, with children, elderly and immunocompromised individuals being at increased risk. Dehydration should thus be treated promptly to avoid complications like organ damage, shock or coma. Fluid replacement is the cornerstone of therapy for diarrhea regardless of etiology. Mild dehydration is treated with oral rehydration therapy (ORT) while severe dehydration is managed with intravenous fluids. Antibiotics and antimotility agents do not seem to be effective in acute diarrhea. Zinc, at a dose of 20 mg, improves absorption of oral rehydration salt (ORS) and facilitates quick recovery.⁴ The current guidelines by the Government of Nepal recommend low osmolarity ORS, zinc and continued feeding of energy dense foods in addition to breastfeeding in the management of diarrhea.⁵

Dysbiosis, i.e., deviations in composition or function from the usual microbiota, has been observed in certain disease states like atopy (allergy) and asthma, celiac disease, colon cancer, type 1 diabetes, inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), GI infections, antibiotic-associated diarrhea (AAD) and probiotics and symbiotic have been tried in these conditions. Probiotics are microorganisms purported to have a health benefit on the host organism. Probiotics activate local macrophages and increase secretory immunoglobulin A (IgA) production both locally and systemically. They modulate cytokine profiles, scavenge superoxide radicals, stimulate epithelial mucin production and enhance intestinal barrier function. Probiotics appear to reduce the duration of diarrhea.⁷ Prebiotics represent non-digestible food ingredients that enhance host immunity by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon and thus improve host health. Symbiotic are preparations in which probiotic organisms and prebiotics are combined, presumably to form a synergistic relationship. There is a scarcity of studies regarding the use of probiotics and symbiotic in diarrhea. The present study has been undertaken to compare the efficacy of symbiotic with probiotics, when administered along with standard therapy, in reducing the frequency and duration of acute diarrhea in children.

OBJECTIVE

To compare the safety, efficacy and tolerability of probiotic and symbiotic in reducing the episodes (frequency) and the duration of acute diarrhea.

METHODOLOGY

A randomized, open-label, comparative study was conducted among children, aged 6 months to 6 years, with acute diarrhea admitted in the indoor department of Pediatric ward of Pokhara Academy of Health Science (PAHS) between 15 May 2017 and 15 July 2017. The study duration was of 2 month, with 1 week of treatment and

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every day follow-up till discharge.

Study Population

Children with acute diarrhea (less than 14 days duration).
Parents willing to give written informed consent.

Exclusion Criteria

Children with persistent diarrhea. Children with severe dehydration. Children with severe malnutrition. Children having respiratory/systemic infection. Subjects who participated in any investigational drug within 30 days prior to study screening. Children with known hypersensitivity for symbiotic or probiotics. Children with chronic systemic illness. Parents not willing to give written informed consent. Children were screened by complete medical history, clinical examination and laboratory investigations, and those who fulfilled the inclusion and exclusion criteria were enrolled and randomized to either Group A or Group B.

Treatment

Group A (n = 50) were given standard therapy *plus* probiotic 5 mL (Enterogermina®) twice-daily for 1 week. Group B (n = 50) received standard treatment *plus* symbiotic 5 mL (Bifilac® dry syrup) twice-daily for 1 week.. Standard treatment included ORT and zinc sulfate 20 mg one tablet daily for 2 weeks. Each 5 mL of the Bifilac® dry syrup has: *Streptococcus faecalis* T-110 - 30 million *Clostridium butyricum* TO-A - 2 million *Bacillus mesentericus* TO-A - 1 million *Lactobacillus sporogenes* - 50 million.

Dosage: Dry syrup made up to 6 mL by adding water; Overall, 100 children aged 6 months to 6 years, with acute diarrhea, admitted in Pediatric department of Pokhara Academy of Health Science (PAHS) were screened, of which 4 were excluded from the study as they had severe dehydration. One hundred children were recruited in the study after obtaining written informed consent from the parents. The study was conducted after obtaining the approval from Hospital Developmental Committee. The eligibility criteria were as follows:

Inclusion Criteria

Age - 6 months to 6 years.

Sex - both genders.

5 mL to be taken orally twice a day. Each 5 mL of the probiotic (Enterogermina®) has *Bacillus clausii* - 2 billion spores/vial.

Dosage: One vial twice-daily for 1 week. Each vial contains 5 ml. Contents of the vial to be emptied and taken orally. Patients were assessed for diarrhea and dehydration. Recovery was defined as the passage of first semi-solid stools or no stools in the previous 18 hours. Any adverse event observed or reported by the parent was recorded.

Statistical Analysis

Distribution of age was analyzed using analysis of variance (ANOVA) and sex distribution was analyzed by Chi-square test. Biochemical investigations were performed on Day 1 and Day 7. The difference within the groups before

and after treatment was analyzed using Student's paired *t*-test, whereas the difference between the Groups A and B was analyzed using one way ANOVA. The difference within the groups in diarrhea was analyzed using Student's paired *t*-test, whereas the difference between the Groups A and B in diarrhea assessment was analyzed using one way ANOVA. $P < 0.05$ is considered to be statistically significant.

RESULTS

About 84% children in Group A and 92% in Group B were in the age group of 6 months to 2 years. Also 16% children in Group A and 8% in Group B were in the age group of 2 to 6 years. There was no statistically significant difference in age between Group A and Group B. In Group A, 62% patients were male while in Group B, 64% patients were male. In this study, there was a statistically significant reduction in the frequency of diarrhea within the groups. The frequency of diarrhea was reduced from 9.03 on Day 1 to 0.81 on Day 3 in Group B, compared with 10.1 on Day 1 to 6.24 on Day 3 in Group A (Table 1). This shows that both therapies were effective in reducing the frequency of diarrhea. On comparing the symbiotic with the probiotic on Day 3, there was a statistically significant reduction in the frequency of diarrhea ($p < 0.02$). This may probably be because of symbiotic in reducing the frequency of diarrhea. There was a statistically significant reduction in the duration of diarrhea on comparing the symbiotic with the probiotic ($p < 0.001$). The mean duration of diarrhea was 36.2 hours in Group B, compared with 72.6 hours in Group A (Table 2 and Fig. 1). This shows that the reduction in duration of diarrhea may be due to the

Group A 10.1 4.42 6.24 3.32 0.006
Group B 9.03 3.41 0.81 1.01 <0.0001
P value 0.42 0.02

Table 1. Frequency of Diarrhea

Groups	Day 1		Day 3		P value
	Mean	SD	Mean	SD	
Group A	10.1	4.42	6.24	3.32	0.006
Group B	9.03	3.41	0.81	1.01	<0.0001
P value	0.42		0.02		

Table 2. Duration of Diarrhea

Groups	Duration in hours	
	Mean	SD
Group A	72.6	31.2
Group B	36.2	12.3
P value	0.001	

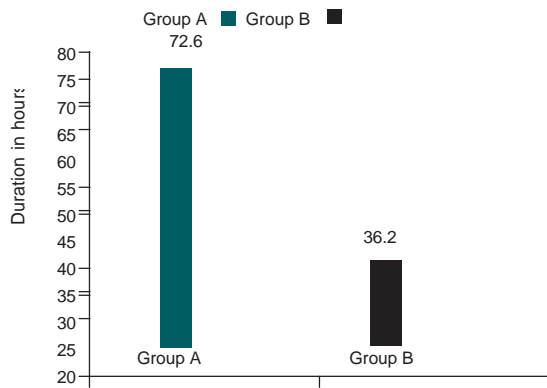


Figure 1. Duration of diarrhea among Groups A and B.

effect of symbiotic. On Day 1, 21 (42%) children had some dehydration and 29 (58%) had no dehydration in Group A. Twenty-four (48%) children had some dehydration and 26 (52%) had no dehydration in Group B. None of the children had dehydration on Day 3 in both the groups.

DISCUSSION

Acute diarrhea commonly affects children in the 6-72 months age-group. If left untreated, diarrhea can lead to dehydration, acidosis and electrolyte imbalance. Replacing fluid loss and electrolytes to correct dehydration is the principal treatment required. Fluid replacement is done by administration of oral rehydration solution and intravenous fluids if necessary. Probiotics and symbiotic may help in reducing the frequency and duration of the diarrhea. This study assessed the safety and efficacy of a probiotic and a symbiotic in acute diarrhea in children. One hundred children, equally distributed in two groups, received either a probiotic or a symbiotic along with standard therapy. The age distribution was similar in both the groups. In this study, there was a statistically significant reduction in the frequency of diarrhea within the groups. The frequency of diarrhea was reduced from 9.03 on Day 1 to 0.81 on Day 3 in Group B, compared with 10.1 on Day 1 to 6.24 on Day 3 in Group A (Table 1). This shows that both therapies were effective in reducing the frequency of diarrhea. On comparing the symbiotic with the probiotic on Day 3, there was a statistically significant reduction in the frequency of diarrhea ($p < 0.02$). This may probably be because of symbiotic in reducing the frequency of diarrhea. There was a statistically significant reduction in the duration of diarrhea on comparing the symbiotic with the probiotic ($p < 0.001$). The mean duration of diarrhea was 36.2 hours in Group B, compared with 72.6 hours in Group A (Table 2 and Fig. 1). This shows that the reduction in duration of diarrhea may be because of symbiotic. This is in correlation with the studies conducted by Allen SJ (2004), Dhingra U, Malik (2006) and Szajewska (2007), which also showed similar reduction of frequency and duration by adding symbiotic.⁸⁻¹⁰

CONCLUSION

It can be concluded from the study that the symbiotic is effective in reducing the frequency and duration of diarrhea, when administered along with standard therapy in children

with acute diarrhea, and is well-tolerated.

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