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A Randomized Open Label Comparative Clinical Study of a Probiotic against a Symbiotic in the Treatment of Acute Diarrhoea 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 diarrhoea.* ***Methods:*** *One hundred children aged 6 months to 6 years, with acute diarrhoea, admitted in the paediatric ward of Pokhara Academy of Health Sciences (PAHS) were recruited in the study. Group A (n=50) received standard therapy plus probiotic 5 mL (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 diarrhoea and dehydration.* ***Results:*** *The frequency of diarrhoea 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 diarrhoea. Similarly, there was a statistically significant reduction in the duration of diarrhoea on comparing Group A with Group B. The mean duration of diarrhoea 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 diarrhoea then the probiotic and is well-tolerated.*

Keywords: Probiotic, Symbiotic, Diarrhoea, Children

INTRODUCTION

Diarrheal disease is the second most common cause of death in children less than 5 years of age (0.58 million or 11%) [1]. Diarrhoea, 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 to 5 billion of children worldwide [2,3]. Acute diarrhoea refers to diarrhoea of less than 14 days duration in a previously normal child and is usually due to infective aetiology.

The most common age group affected is 6-24 months. Diarrhoea 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. Diarrhoea has the potential to cause dehydration, with children, elderly and immuno-compromised 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 diarrhoea regardless of aetiology. Mild dehydration is treated with oral rehydration therapy (ORT) while severe dehydration is managed with intravenous fluids. Antibiotics and anti-motility agents do not seem to be effective in acute diarrhoea. 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 diarrhoea [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 diarrhoea (AAD) and probiotics and symbiotic have been tried in these conditions [6].

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 diarrhoea [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 diarrhoea. 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 diarrhoea in children.

OBJECTIVE

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

METHODOLOGY

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

Study population

Overall, 100 children aged 6 months to 6 years, with acute diarrhoea, admitted in Paediatric 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
- Children with acute diarrhoea (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 5 mL by adding water; 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 volume. Contents of the vial to be emptied and taken orally.

Patients were assessed for diarrhoea 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 diarrhoea was analyzed using Student's paired t-test, whereas the difference between the Groups A and B in diarrhoea 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 diarrhoea within the groups. The frequency of diarrhoea 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 diarrhoea. On comparing the symbiotic with the probiotic on Day 3, there was a statistically significant reduction in the frequency of diarrhoea ($p<0.02$). This may probably be because of symbiotic in reducing the frequency of diarrhoea.

Table 1 Frequency of diarrhoea

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	-	-	-

There was a statistically significant reduction in the duration of diarrhoea on comparing the symbiotic with the probiotic ($p<0.001$). The mean duration of diarrhoea was 36.2 hours in Group B, compared with 72.6 hours in Group A (Table 2 and Figure 1). This shows that the reduction in duration of diarrhoea may be due to the 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.

Table 2 Duration of diarrhoea

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

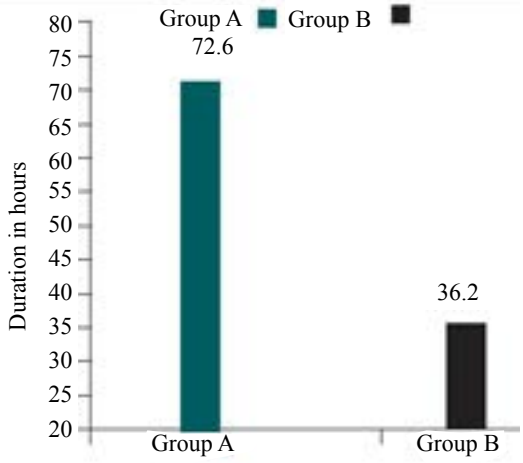

Figure 1 Duration of diarrhoea among Groups A and B

DISCUSSION

Acute diarrhoea commonly affects children in the 6-72 months age group. If left untreated, diarrhoea 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 diarrhoea.

This study assessed the safety and efficacy of a probiotic and a symbiotic in acute diarrhoea 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 diarrhoea within the groups. The frequency of diarrhoea 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 diarrhoea. On comparing the symbiotic with the probiotic on Day 3, there was a statistically significant reduction in the frequency of diarrhoea ($p<0.02$). This may probably be because of symbiotic in reducing the frequency of diarrhoea. There was a statistically significant reduction in the duration of diarrhoea on comparing the symbiotic with the probiotic ($p<0.001$). The mean duration of diarrhoea was 36.2 hours in Group B, compared with 72.6 hours in Group A (Table 2 and Figure 1). This shows that the reduction in duration of diarrhoea may be because of symbiotic. This is in correlation with the studies conducted by Allen, Dhingra, Malik and Szajewska, 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 diarrhoea, when administered along with standard therapy in children with acute diarrhoea, and is well- tolerated.

REFERENCES

[1] Black, Robert E., Saul S. Morris, and Jennifer Bryce. "Where and why are 10 million children dying every year?" *The Lancet* Vol. 361, No. 9376, 2003, pp. 2226-34.

[2] Liu, Li, et al. "Child Health Epidemiology Reference Group of WHO and UNICEF Global, regional, and national causes of child mortality: An updated systematic analysis for 2010 with time trends since 2000." *Lancet* Vol. 379, No. 9832, 2012, pp. 2151-61.

[3] WHO/UNICEF. Joint Statement: Clinical management of acute diarrhoea. Geneva/New York: World Health Organization, Department of Child and Adolescent Health and Development, and United Nations Children's Fund, Programme Division; 2004. (WHO/FCH/CAH/04.07).

[4] Hoque, Kazi Mirajul, and Henry J. Binder. "Zinc in the treatment of acute diarrhea: current status and assessment." *Gastroenterology* Vol. 130, No. 7, 2006, pp. 2201-05.

[5] World Health Organization. "Reduced osmolarity: Oral rehydration salts (ORS) formulation: a report from a meeting of experts jointly organised by UNICEF and WHO: UNICEF house, New York, USA, 18 July 2001." 2002.

[6] Szajewska, Hania, et al. "Probiotics in gastrointestinal diseases in children: Hard and not-so-hard evidence of efficacy." *Journal of Pediatric Gastroenterology and Nutrition* 42.5 (2006): 454-75.

[7] Sanders, Mary Ellen. "Impact of probiotics on colonizing microbiota of the gut." *Journal of Clinical Gastroenterology* Vol. 45, 2011, pp. S115-S119.

[8] Allen, Stephen J., et al. "Probiotics for treating infectious diarrhoea." *The Cochrane Database of Systematic Reviews* Vol. 4, 2003.

[9] Sazawal, Sunil, et al. "Efficacy of probiotics in prevention of acute diarrhoea: a meta-analysis of masked, randomised, placebo-controlled trials." *The Lancet Infectious Diseases* Vol. 6, No. 6, 2006, pp. 374-82.

[10] Szajewska, Hania, et al. "Meta-analysis: *Lactobacillus* GG for treating acute diarrhoea in children." *Alimentary Pharmacology & Therapeutics* Vol. 25, No. 8, 2007, pp. 871-81.