

Anti-Diarrhoeal Effects of Probiotics on Children

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Abstract

Diarrhoeal disease is one of the major problems among under-five year children in Bangladesh. Probiotics have been suggested to be used in acute diarrhoea. Several different probiotics are commercially available in our country. The objective of this experimental study was to assess the effects of probiotics among under-five year children suffering from diarrhoea. This study was conducted using probiotics with oral rehydration solution (ORS) and ORS only which were given to the children for the treatment of acute diarrhoea. It was conducted using three probiotics namely, Probio, Enterogermina, and TS6 with ORS only (control group) among one hundred and sixty under-five children admitted to Chittagong Maa-Shishu General Hospital in Chittagong, Bangladesh. Children were divided into group 1, received ORS only and group 2, group 3, group 4, received Probio, Enterogermina, TS6 probiotics with ORS, respectively. The duration of diarrhoea and daily stool outputs of children was recorded during hospitalization. The study showed that three probiotics had significantly reduced the frequency of diarrhoea of children than ORS only. Three probiotics had significant or positive effect on children with acute diarrhoea resulting in shorter ($P < 0.001$) duration of diarrhoea (hours).

Keywords: Diarrhoeal diseases, children, probiotics, oral rehydration solution (ORS)

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INTRODUCTION

Gastrointestinal (GI) tract contain different normal microbiota which plays a significant role in the maturation and function of the immune system in the gut. The microbiota is continuously interacting with the environment, including other bacteria, the gut epithelium, and the mucosal and endocrine systems. The different microbiota in the GI tract between healthy and diseased individuals was identified during the late 19th century. These types of beneficial microorganisms which are found in the GI tract are named as probiotics. Probiotic therapy is based on the concept of maintaining a healthy and balanced microbiota. Probiotic means “for life”, comes from the Greek. In 1907, the Nobel laureate Metchnikoff is credited with the health benefits of probiotics suggesting that the consumption of living lactic acid bacteria in fermented foods may promote health and longevity by favorably modulating the GI microflora [1]. Consumption of probiotics has health benefit effects in a host of disorders including

diarrhoea, irritable bowel syndrome, inflammatory bowel disease, food allergies, lactose intolerance, urogenital infections, and atopic eczema [2]. The concept of probiotics is characterized as microorganisms that promote growth of other microorganisms [3]. Nowadays, the universal meaning of the term “probiotic” was established by the World Health Organization (WHO) and the Food and Agriculture Organization of the United States. These two organizations defined probiotics as live microorganisms which when administered in adequate amount have a beneficial effect on health of the host organism. A number of studies have found probiotic consumption to be useful in the treatment of many types of diarrhoea, including acute diarrhoea, travelers’ diarrhoea, and diarrhoeal diseases in young children. Probiotic bacteria of *Lactobacillus* and *Bifidobacterium* families are most commonly used in the market. These probiotics may be sold as single components, marketed in combination products with other probiotic ingredients, or added to enriched

fermented foods such as yogurts. The “dosage” of bacteria probiotics is mainly measured in colony-forming units (CFUs). Probiotics are essential in the range 5–10 billion CFUs for a child and 10–20 billion CFUs for an adult dosage daily. Probiotic yogurt products and fermented milks contain varying amounts of bacteria, depending on the brand and ounces consumed. Probiotics are primarily used for GI conditions such as diarrhoea caused by infections, inflammation, or extended use of antibiotics. They increase the amount of healthy microorganisms in the gut, thereby controlling the amount of harmful organisms that cause diarrhoea. Most healthy people open their bowels about three times per day and their normal stools are usually solid. Diarrhoea is defined as more than three times loose and watery stools in a day when stools are passed. The common cause of an attack of acute diarrhoea is an intestinal infection and also food poisoning is a common form of acute diarrhoea, most commonly caused by the bacteria *Salmonella* and *Campylobacter*; these infections are passed on through contaminated food, such as poultry and eggs, or water; and sometimes by a person such as food handler who has the infection, but has no symptoms of that infection that are easily affected to infants and children. In mechanisms of acute diarrhoea, small intestine absorbs nutrients, fluids and salts of food and large intestine absorbs remaining extra fluid, that's way healthy people's stools are solid. But diarrhoea occurs when these processes are impaired when the lining of the gut is damaged by bacteria or viruses and when there is excessive secretion of fluid into the bowel. The aim of treatment is to reduce the period that a person is infectious. Treatment options available are oral rehydration solution (ORS), antibiotics, and gut motility suppressing agents such as loperamide, codeine, and probiotics. This review considers the use of probiotics and ORS [4]. Acute diarrhoea management consists of the replacement of lost fluid with ORS. This solution, however, reduces neither the severity nor the duration of diarrhoea. The search for such agents started over 20 years ago [5]. Several trials with probiotic preparations have been conducted in different settings and with different end points. Few of these studies, however, meet the criteria of

properly controlled trials [4]. Probiotic supplements are generally considered safe for most people and rarely cause side effects. Little is known about the long-term effects of regular use of these supplements, however, and they may be less safe for use in people with poor immune systems. The most common side effects reported are temporary bloating, gas, and mild stomach upset. Side effects are rare, primarily because probiotic microorganisms already are found naturally in the GI tracts of healthy people. Probiotic supplements basically restore the body's balance between good and harmful bacteria and yeasts [4]. In recent studies of children with diarrhoea, probiotics were the most commonly prescribed treatment. With the increasing availability and widespread use of probiotics, it is important to identify products which are most effective. We evaluated the efficacy of three probiotic products for the treatment of acute diarrhoea in children.

METHODS

An experimental study was designed to assess the effectiveness of probiotics in children with acute diarrhoea received written instructions to purchase a specific brand of probiotic. Data collection was conducted between 1st April and 31st May 2016. During this period, all the admitted children of the hospital, aged 6–60 months were enrolled in the study. From all children, one hundred and sixty children were purposively studied for the research purposes. The study was performed in collaboration with family members and assigned doctors. It was also collected from doctor's prescriptions at the Chittagong Maa-Shishu General Hospital in Bangladesh for children aged 6–60 months. These children were diagnosed with acute watery diarrhoea of more than three times for more than 24 h and less than 7 days with moderate dehydration by the WHO criteria. All children who were three or more outputs of loose or liquid stools a day were included in the study. Children with visible blood in the stool, history of allergy to cow's milk, severe dehydration, fever of more than 39 °C and severe systemic infections (e.g. pneumonia, sepsis) and other disease requiring additional treatment were excluded from the study. All children were given ORS for three to six hours.

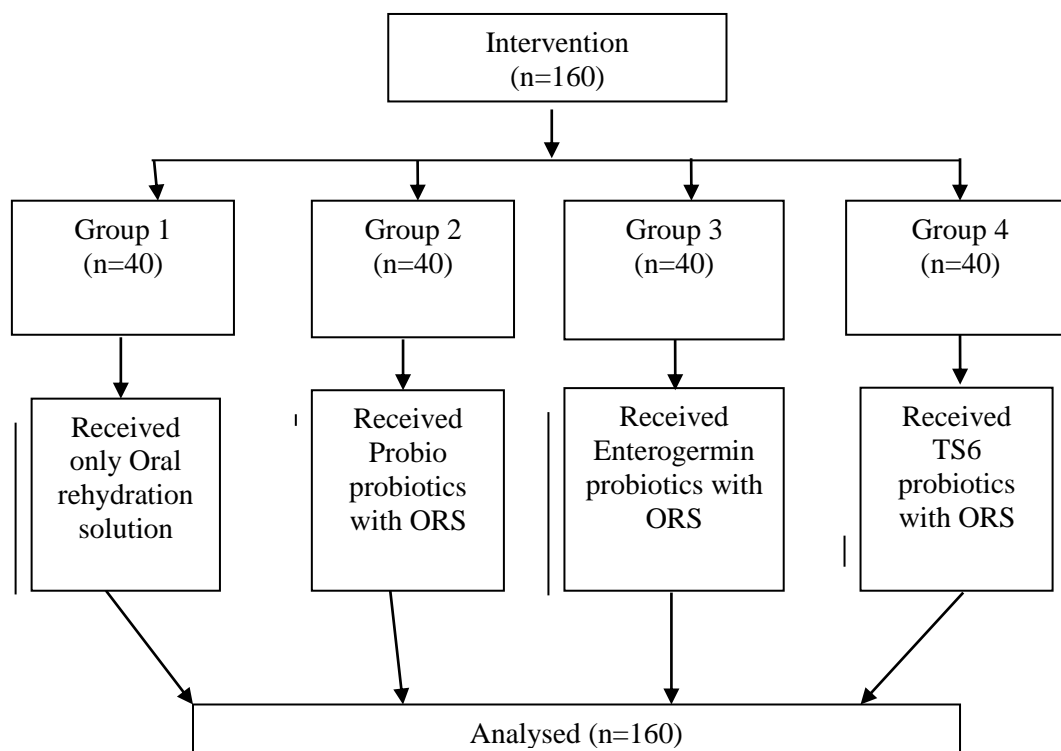


Fig. 1: Flow Diagram of the Uses of Probiotics for the Treatment of Children Suffering from Acute Diarrhoea.

Children also received ORS only; probiotics with ORS such as Probio (*Lactobacillus acidophilus*, *L. bulgaricus*, *Bifidobacterium bifidum*); Enterogermina (*Bacillus clausii* having poly-antibiotic resistant); TS6 (*L. acidophilus*, *L. casei*, *B. bifidum*, *L. rhamnosus* GG, *B. longum*, *B. infantis*, *L. lactis*, *L. paracasei*). One hundred and sixty children were divided into four groups: Group 1, Group 2, Group 3 and Group 4, respectively. Group 1 (control group) received ORS; Group (2 to 4) received probiotics with ORS (Figure 1).

Probiotics were prescribed for seven days and administered orally according to the manufacturers' instructions. All the probiotics used in this study were available only in pharmacies and had a similar brand image. The group of children who received only ORS served as controls.

The total duration of diarrhoea and daily stool outputs was recorded during hospitalization. Duration of diarrhoea was the time in hours from the first to the last abnormal (loose or liquid) stools preceding a normal stool output. Stool consistency was evaluated through a

score system [6] and faeces were graded as 1 (normal), 2 (loose), 3 (semi-liquid), and 4 (liquid).

Data Analysis

Duration of diarrhoea (hours) or recovery from diarrhoea (hours) of one hundred and sixty studied children were entered into the SPSS for statistical analysis.

Statistical Analysis

Statistical analysis was performed by using SPSS for Windows versions 16.0 (SPSS Inc, Chicago, IL). Duration of diarrhoea (hours) or recovery from diarrhoea (hours) outcomes were presented as mean difference between the probiotic treatment and controls (ORS) with 95% confidence intervals. Two-tailed P values < 0.001 were considered significant.

RESULTS AND DISCUSSION

The anthropometric measurements (age and weight) of one hundred and sixty studied children were shown in Table 1.

Table 1 depicts that anthropometric measurements, the mean of age (months) of study group 1, group 2, group 3 and group 4

were 27.80, 21.30, 15.68 and 22.43, respectively and the mean of weight (kg) of study group 1, group 2, group 3 and group 4 were 9.57, 8.33, 7.93 and 8.61, respectively.

Table 2 shows that duration of diarrhoea (hour) or recovery from diarrhoea (hour) was significantly lower ($P < 0.001$) in children receiving Probio probiotic (group 2) with ORS than in patients receiving ORS only (group 1).

Table 3 shows that duration of diarrhoea (hour) or recovery from diarrhoea (hour) was significantly lower ($P < 0.001$) in children receiving Enterogermina probiotic (group 3)

with ORS than in patients receiving ORS only (group 1).

Table 4 depicts that duration of diarrhoea (hour) or recovery from diarrhoea (hour) was significantly lower ($P < 0.001$) in children receiving TS6 probiotic (group 4) with ORS than in patients receiving ORS only (group 1).

Table 5 shows that Enterogermina probiotic had relatively lower effect in the recovery from diarrhoea (83.5 h) than Probio (76.1 h) and TS6 probiotics (75.8 h) (mean).

Table 1: Anthropometric Measurements of the Studied Under-5 Children.

	Group 1 (ORS)	Group 2 (probio)	Group 3 (Enterogermina)	Group 4 (TS6)
Age (months) Mean (range)	27.80 (6–60)	21.30 (6–54)	15.68 (6–30)	22.43 (6–54)
Weight (kg) Mean (range)	9.57 (5–16)	8.33 (4–12.50)	7.93 (4.50–9.50)	8.61 (4.90–13.20)

Table 2: Association Between ORS (Group 1) and Probio Probiotic (Group 2) for Reducing Duration of Diarrhoea (h).

Treatment	Mean (SD) (h)	Median (Range) (h)	P value	Mean difference (95%CI)
Group 1	117.5 (18.02418)	114.00 (96–168)	$P < 0.001$	(33.37–49.43) 41.400
Group 2	76.1 (18.07277)	72.00 (48–120)		

Table 3: Association Between ORS (Group 1) and Enterogermina Probiotic (Group 3) for Reducing Duration of Diarrhoea (h).

Treatment	Mean (SD) (h)	Median (Range) (h)	P value	Mean difference (95%CI)
Group 1	117.5 (18.02418)	114.00 (96–168)	$P < 0.001$	(24.01–43.94) 33.98
Group 3	83.6 (26.03444)	84 (48–144)		

Table 4: Association Between ORS (Group 1) and TS6 Probiotic (Group 4) for Reducing Duration of Diarrhoea (h).

Treatment	Mean (SD) (h)	Median (Range) (h)	P value	Mean difference (95%CI)
Group 1	117.5 (18.02418)	114.00 (96–168)	$P < 0.001$	(32.81–50.59) 41.70
Group 4	75.8 (21.75020)	75 (48–144)		

Table 5: Duration of Diarrhoea (h) or Recovery from Diarrhoea by Using Three Probiotics in Study Groups of Children.

Group	Treatment	Number of Children	Age (years)	Mean	Median Range) (h)	SD
2	Probio probiotic	40	6–60 months	76.1	72 (48–120)	18.07277
3	Enterogermina probiotic	40	6–60 months	83.5	84 (48–144)	26.03444
4	TS6 probiotic	40	6–60 months	75.8	75 (48–144)	21.75020

Table 6: Daily Stool Outputs of Under-Five Children from the First Day (24 h) of Probiotic Application.

Group	Treatment	Hour						
		24	48	72	75	84	96	114
1	Oral rehydration solution	>15	10–12	8	6	5–6	4–5	3
2	Probio probiotic	>20	8–10	2	-	-	-	-
3	Enterogermina probiotic	>20	10	5–6	4	2–3	-	-
4	TS6 probiotic	>20	8–10	4–5	3	-	-	-

Table 6 shows that daily stool output was shorten in group 2, group 3 and group 4 than group 1 starting the day after the first probiotic application.

DISCUSSION

Diarrhoea in most of the developing countries including Bangladesh is usually self-limiting and does not require active treatment except replacement of fluids and electrolytes for prevention or correction of dehydration. Many probiotics are prescribed by the doctors and some probiotics have proven efficacy in children in developing countries but not all. Acute infectious diarrhoea is still a major cause of childhood morbidity. It is also a source of worry to families of affected children and represents a heavy economic burden for families and society [7]. Most of the children are spontaneously affected by diarrhoea during April and May in Bangladesh. In the previous study, the peak value of diarrhoea occurs during the winter, between January and April [8]. Family members are worried about this problem and most of the family members purchase drugs but they do not know about probiotics. These drugs that affect intestinal motility, ion transport and adsorptive moieties, and living bacteria have been used to reduce the duration of diarrhoea [7]. Probiotics have gained incredibility for the treatment of diarrhoeal diseases. Probiotics have properties which are considered to be food additives rather than drugs. Therefore, only safety features of

probiotics and not proof of efficacy are required for marketing [9]. We did not conduct a qualitative and quantitative study of the microbial content of the probiotics in this trial because we wanted to carry out a field trial of the clinical effectiveness of commercially available probiotics that had been prescribed by the doctors. But in the recent study, commercially available three probiotics have shown clinical effectiveness for treating diarrhoeal disease.

We conducted this clinical trial to evaluate the clinical efficacy of three probiotics (Probio, Enterogermina and TS6), which are most commonly marketed probiotics in Bangladesh and are prescribed frequently by doctors for treatment of diarrhoea in children. These probiotics has been marketed in many countries, because it is cheap to produce, easy to prepare, robust to production process and has a long shelf life over wide range of temperatures. It is quite stable in formulation of powder, granules, dry syrup, tablets, capsule, resistant to high moisture and oxygen, and compatible with pharmaceutical ingredients such as vitamins, minerals, amino acids [10] easily received by parents because it is easy to prepare and they can feed their child easily. In hospital, parents can easily prepare probiotics with water or ORS before feeding their child because of these existing properties.

This clinical trial showed that probiotics has a beneficial effect in reducing diarrhoea of 6

months to 60 months of children which was close to previous studies that found beneficial effects on diarrhoea among children of 4 months to 2 years of age [11–13]; also this trial was statistically significant. Three probiotics early reduced the duration of diarrhoea than ORS only. A recent Cochrane meta-analysis of 23 randomised controlled trials found mild therapeutic benefit from probiotics that was generally reproducible regardless of organism for treating infectious diarrhoea [4].

Oral administration of *Lactobacillus* GG is effective in rotavirus-positive and rotavirus-negative ambulatory children with diarrhoea. Furthermore, it reduces the duration of rotavirus excretion [6].

Addition of *L. acidophilus* LB to oral rehydration therapy was found to be effective in the treatment of children aged 3–24 months with acute diarrhoea and mild or moderate dehydration by decreasing the duration of diarrhoea [14].

Probio probiotic contains bacterial strains such as *Lactobacillus acidophilus*, *L. bulgaricus*, *Bifidobacterium bifidum*; Enterogermina probiotic contains bacterial strains such as *Bacillus clausii* having poly-antibiotic resistant; and TS6 probiotic contains bacterial strains such as *L. acidophilus*, *L. casei*, *B. bifidum*, *L. rhamnosus* GG, *B. longum*, *B. infantis*, *L. lactis*, *L. paracasei*. These probiotics were associated with shorter duration of diarrhoea and two among three probiotics contained *Lactobacillus* strains. In previous study, *Lactobacillus* GG was associated with a shorter duration of diarrhoea, which was expected because proof of efficacy of this strain has been obtained in children in hospitals and outpatients in both industrialised and developing countries [15]. The probiotic effects are also known to be strain and species dependent. Mixing two or more probiotic strains/species has been marginally more effective than using single strains in preventing diarrhoea [16]. Probio probiotics and TS6 probiotics were mix of three strains and eight stains, respectively whereas Enterogermina probiotic was *Bacillus clausii* stain which was relatively lower than mixture of stains probiotic. *Bacillus* species, except

Bacillus cereus and *Bacillus anthracis*, are generally regarded as nonpathogenic but it was felt that the safety of *B. coagulans* as probiotics should be evaluated by experts [10]. *Bacillus clausii* existing in Enterogermina probiotics has beneficial effect in children.

In the recent study, uses of probiotics reduced the duration of diarrhoea which was 117.5 h in group 1 as compared to 76.1 h in group 2, 83.6 h in group 3 and 75.8 h in group 4 (mean value) with ORS. Three probiotics had positive ($P < 0.001$) effect on children for reducing acute diarrhoea that was close to a clinical trial, which was conducted with 287 hospitalised children suffering from acute diarrhoea, *Lactobacillus* GG administered with an ORS reduced the duration of diarrhoea from 71 to 58 h, and in rotavirus-positive patients even more markedly, from 77 to 56 h [17]. Among the three probiotics, Probio and TS6 probiotics worked the best than Enterogermina probiotics among studied children.

CONCLUSION

The current study concluded that acute diarrhoeal disease of children who received probiotics such as Probio, Enterogermina and TS6 with ORS had a shorter duration of diarrhoea (hour) or recovery from diarrhoea than frequency of diarrhoea with ORS only. These three probiotics with ORS receiving children demonstrated significant efficacy ($p < 0.001$) towards the treatment of acute diarrhoeal disease when compared to ORS receiving children. Among the three probiotics, Enterogermina probiotic had relatively lower effect than Probio and TS6 probiotics on studied children. Probiotics had a beneficial effect in reducing diarrhoea of 6 months to 60 months children and these probiotics are included in the everyday diet for reducing acute diarrhoea during their hospital stay or the follow up period. They can be considered as a suitable, easy and safe method for balancing the body's natural defenses against infections.

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Cite this Article

Akter S, Aziz MA, Sharmin KN *et al*. Anti-Diarrhoeal Effects of Probiotics on Children. *Research & Reviews: A Journal of Microbiology and Virology*. 2018; 8(1): 15–21p.