

# A Comparative Study of Probiotic Lactic Acid Bacilli alone and in Combination with Bifidobacterium and Saccharomyces as Adjuvants to ORS and Zinc in the Management of Acute Pediatric Diarrhoea

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## ABSTRACT

**Introduction:** Pediatric diarrhoea is the second leading cause of childhood mortality. It is a major global health problem, particularly affecting children under the age of 5 years. It is managed with oral rehydration salt, and zinc supplements. Recently, there has been a trend of prescribing probiotics which help in reducing the frequency and duration of diarrhoea. As India is fast emerging as a potential market for probiotics, scientific studies are required to ensure their efficacy. With this background, this study was undertaken to evaluate the role of probiotics in the treatment of acute onset mild and moderate pediatric diarrhea.

**Materials and Methods:** This was an observational, prospective, open label, comparative study. It was conducted on 90 children after obtaining informed consent from their guardian. The participants were allocated to one of three study groups as follows; Group A: ORS & zinc Group, B: ORS, Zinc and lactic acid bacilli; Group C: ORS, Zinc and combination of lactic acid bacilli acidophilus, Bifidobacterium lactis and Saccharomyces boulardii. They were followed up for 72 hours after receiving the treatment and after 7 days. The outcome measures were reduction in mean duration and mean frequency of diarrhea. Data was collected in case report forms. Statistical analysis was done using ANOVA followed by Dunnet's test.


**Results:** The mean frequency of diarrhea on day 1 in Group A, B and C were 5.87±1.23; 6.5±1.15 and 6.63±1.42 respectively. On day 2, in Group A it was 2.93±0.82; Group B, 3.23±0.99 and in Group C, 2.73±0.89 respectively. On day 3, in Group A it was 1.33±0.47; Group B, 0.86±0.5 and in Group C, 0.53±0.5 respectively. The mean duration of diarrhea in Group A, B and C were 4.5±0.76, 3.47±0.5 and 3.17±0.37 days respectively. There was significant reduction in mean frequency and duration of diarrhea in Group B and C compared to Group A (p<0.05).

**Conclusion:** Probiotics when used alone or in combination as adjuvant to ORS and Zinc in the treatment of acute pediatric diarrhea results in significant reduction in mean frequency and mean duration of diarrhea.

**Key words:** Bifidobacterium, Diarrhea, ORS

## INTRODUCTION

Pediatric diarrhoea is the second leading cause of childhood

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mortality after pneumonia. It is a major global health problem, particularly affecting children under the age of 5 years. The overall prevalence of pediatric diarrhea under 5 years was 37.6% in India in the year 2011.<sup>[1,2]</sup> Out of those cases, acute watery diarrhea was most common (58.9%) followed by dysentery (24.2%) and persistent diarrhea (16.9%). The prevalence of acute pediatric diarrhea was found to be highest in the lower socio-economic class (41%). Pediatric diarrhea is classified into acute, persistent and chronic diarrhea. Acute diarrhea is defined as the passage of liquid or watery stool more than three times a day. Persistent diarrhea is defined as diarrhea of presumed infectious origin that begins acutely and lasts for 14 days or more. Diarrhoea that lasts for 2-4 weeks is termed as chronic diarrhoea. Based on the severity and frequency,

diarrhoea is divided into mild, moderate and severe types.<sup>[2,3]</sup> The main therapy for mild to moderate pediatric diarrhea consists of ORS and zinc. The WHO guidelines for treatment of acute diarrhea in children recommend rehydration comprising corrective electrolyte therapy, maintenance of breast feeding or early feeding during diarrheal episode. Although rehydration can be achieved by ORS, it has no effect on the frequency of bowel movements and duration of diarrhea. Adjuvant therapy to rehydration such as micronutrient supplementation (zinc) and probiotics may offer a safe complement to ORS in acute mild-moderate diarrhea in reducing duration and severity of symptoms.<sup>[4,5]</sup>

Now-a-days, probiotics are commonly prescribed for the treatment of pediatric diarrhea.<sup>[6,7]</sup> They are effective in acute diarrhea of mild to moderate intensity by oral route.<sup>[8]</sup> The rationale for the use of probiotics in acute diarrhea is based on one or more of their postulated effects. These include competition for nutrients with pathogenic microorganisms, inhibition of adhesion of pathogens to intestinal epithelial cells, production of antimicrobial substances, modification of toxins or toxin receptors and enhanced immune responses to pathogens.<sup>[5]</sup> Even though probiotics are prescribed by pediatricians and are readily available, their use has not been yet standardized and the most effective and safe organism has not been yet identified.<sup>[4]</sup> Also, there is limited data available about their therapeutic efficacy. In most countries, probiotics are considered to be food additives rather than drugs.<sup>[9]</sup> Therefore, they do not need proof of efficacy for marketing. India has fast emerged as a potential market for probiotics and scientific studies are required to ensure their standardization.<sup>[4]</sup> Lactobacillus sporogenes is one of the most commonly available and marketed probiotic preparations in many European and Asian countries, including India.<sup>[5]</sup> Efficacy of this preparation has not been evaluated by a controlled clinical study. This is also available in combination with Bifidobacterium and Sacharrhomyces. With this background, this study was undertaken to evaluate the role of probiotics in the treatment of acute onset mild and moderate pediatric diarrhea.

## MATERIALS AND METHODS

This was a randomized, open labelled, comparative, observational study. It was undertaken in the Department of Pediatrics, Vydehi Institute of Medical Sciences and Research Center, Whitefield, Bangalore. The study was commenced after obtaining approval from the Institutional Ethical Committee. The duration of the study was one year from January 2012 to December 2012. The study was undertaken in 90 children suffering from acute non-infective diarrhea of mild to moderate intensity, of age between 6 months to 6 years, after taking informed consent from their guardian. Children suffering from malnutrition, severe dehydration, or if immunocompromised or on any probiotic supplementation were excluded from the study. The participants were allocated one of the three study

groups. Each study group included 30 participants. The groups envisaged received treatment as follows

1. ORS and Zinc
2. ORS, zinc and Lactic acid bacilli acidophilus and
3. ORS, zinc and combination of Lactic acid bacilli acidophilus with Bifidobacterium lactis and Sacharromyces boulardii.

They were given the study drugs after screening the inclusion and exclusion criteria. They were followed up for a period of 72 hours. A detailed history of all children particularly with respect to demographics was recorded. A thorough clinical examination was done for all children including weight, height, body mass index (BMI), pulse rate, respiratory rate and signs of dehydration. They were given a diary and advised to come for follow up. In case they fail to return they were contacted over telephone. Investigations like complete blood count, serum electrolytes, stool routine and stool culture were done and recorded for all children during the study. Statistical analysis was performed using ANOVA followed by Dunnet's t test.

## RESULTS

A total of 112 subjects were approached to take part in the study. However, a total of 22 children could not be included due to unwillingness of their guardian to sign the informed consent form. The demographic details are shown in Table 1

**Table 1: Baseline demographic features of study participants**

	GROUP A	GROUP B	GROUP C
Mean Age (months)	14±6.38	11±5.19	13±4.91
Gender distribution			
Male children:	18 (60%)	22 (79.33%)	19 (63.33%)
Female children:	12 (40%)	08 (26.67%)	11 (36.67%)
Mean height (centimeter)	84±10.36	85±9.81	88±22.16
Mean weight (kilogram)	10.3±1.78	9.9±1.95	10.7±1.66
Mean BMI	14.6±2.09	13.9±1.62	14.3±2.59

The mean duration of diarrhea in group A was found to be 4.5±0.76; group B, 3.47±0.5; and group C, 3.17±0.37 respectively. The reduction in mean duration of diarrhea in group B and C were found to be statistically significant when compared to group A (p<0.05). The mean frequency of diarrhea on day 1 in Group A was 5.87±1.23, Group B; 6.5±1.15 and Group C, 6.63±1.42 respectively. There was no significant difference between the mean frequency of diarrhea on day 1 in the three groups (p>0.05). In group A, the mean frequency of diarrhea on day 1 was 5.87±1.23, day 2 was 2.93±0.82 and day 3; 1.33±0.47 respectively. In group B, the mean frequency of diarrhea on day 1 was 6.5±1.15, day 2 was 3.93±0.99 and day 3; 0.86±0.5 respectively. In group C, the mean frequency of diarrhea on day 1 was 6.63±1.42, day 2 was 2.73±0.79 and on day 3 was 0.53±0.5 respectively. It was found that combination of probiotics (group C) significantly reduced the mean frequency of diarrhea when compared to group A and B

respectively ( $p < 0.05$ ). The results are shown in Table 2 and 3.

**Table 2: Mean Duration of diarrhoea in various groups(days)**

Group A	Group B	Group C
4.5±0.76	3.47±0.5*	3.17±0.37*

n=30 in each group, df(2,87), F= 44.47,  $p < 0.05$

**Table 3: Mean Frequency of diarrhoea in the various groups**

Mean frequency of diarrhea	Group A	Group B	Group C
Day 1	5.87±1.23	6.5±1.15 <sup>†</sup>	6.63±1.42 <sup>†</sup>
Day 2	2.93±0.82	3.93±0.99*	2.73±0.79*
Day 3	1.33±0.47	0.86±0.5*	0.53±0.5*

n=30 in each group, df(2,87), F= 2.30, 2.25 & 19.52 respectively,  $p < 0.05$

\*' significant reduction in the frequency of diarrhoea

<sup>†</sup>' no significant difference in the reduction of diarrhoeal frequency

The study medications were well received and tolerated by all children. No adverse reaction was observed during hospital stay or the follow up period. No study subject discontinued the treatment due to compliance issues.

## DISCUSSION

The present study was carried out to compare the probiotic lactic acid bacilli acidophilus alone and in combination with Bifidobacterium lactis and Sacharhomyces boulardii as an adjuvant to ORS and zinc in the management of acute pediatric diarrhea. In the present study, it was observed that the recovery was facilitated by the Lactobacilli, and it was more when given in combination with Bifidobacterium and Sacharhomyces. Sharma A K., et al also proved that probiotics reduce the incidence of diarrheal episodes and facilitate the recovery when used as an adjunct to oral rehydration therapy for acute diarrhea. Lactobacilli GG, Bifidobacterium and Sacharhomyces reduced the incidence of diarrhea as compared to control groups. The recovery in terms of reduction in duration of diarrhea was shown to be facilitated by Lactobacilli GG, L. reuteri, L. casei and S. boulardii<sup>[10]</sup>

The study demonstrated that probiotics are efficacious in reducing both frequency and the duration of diarrhea. Applegate et al., conducted a systematic review of probiotic for the treatment of acute diarrhea in children aged less than 5 years. They compared the drugs with control group (ORS & zinc). They concluded that probiotics reduced the diarrhea duration by 14% (95% CI: 3.8-24.2%) and stool frequency on the second day of treatment by 13.1% (95% CI: 0.8 – 25.3%). The authors inferred that probiotics were efficacious in reducing diarrhea duration and stool frequency during a diarrhea episode.<sup>[11]</sup>

In the present study, administration of Lactobacill, Bifidobacterium and Sacharhomyces were found to be safe in pediatric population. Guandalini et al., conducted a randomized, double-blind, placebo-controlled trial among 287 children with acute onset of diarrhea. They were randomized into Group A with 140 children receiving ORS with placebo and group B with 147 children receiving ORS with lactobacillus acidophilus of 1010 CFU/250ml. The

study concluded that administering ORS with lactobacillus to children with acute diarrhea is safe and results in shorter duration of diarrhea, less chance of a protracted course, and faster discharge from the hospital.<sup>[12]</sup>

In this study, combination therapy was found to be more efficacious than Lactobacill alone. Khanna et al., conducted a double-blind randomized controlled-trial among 98 children aged between 6 months to 12 years with acute diarrhea. Lactobacillus or placebo was given to the children for 3 days with ORS and feeding. Out of the 98 children, 48 received lactobacillus and 50 received placebo. The study concluded that children with lactobacillus group showed improvement in acute diarrhea as compared with placebo group.<sup>[13]</sup> Grandy et al., conducted a randomized double-blind controlled clinical trial in children of age group 1-23 months with acute diarrhea. Children were randomly assigned to receive one of three treatments. First group received ORT with placebo. Second group received ORT with Saccharomyces boulardii and third group received compound containing Lactobacillus acidophilus, Lactobacillus rhamnosus, Bifidobacterium longum and Saccharomyces boulardii. In each group 20 children were assigned and outcomes were duration of diarrhea, duration of fever, duration of vomiting and duration of hospitalization. The study concluded that both second and third group decreased the duration of diarrhea compared to first group.<sup>[14]</sup>

In this study, 95.56% subjects were below 2 years of age (mean age: 1.1±0.5). This is consistent with the finding of other researchers that acute diarrhea is more common in children less than 2 years of age<sup>3</sup>. Also, there was male child preponderance in the study. Other researchers also mentioned that number of male children were more in their study even though the gender difference was not statistically significant.<sup>[15]</sup> It was also found out that the children belonged to low socioeconomic status without proper education background. This is again consistent with the finding of other researchers that acute diarrhea is more common in children belonging to low socioeconomic status.<sup>[3]</sup>

The present study thus states that probiotics have an adjuvant role in the treatment of acute pediatric diarrhoea along with ORS and Zinc. The small sample size is a limitation of the present study. There is thus further need of such studies with more number of children and in different settings. Further studies can also be planned to address the pharmacoeconomics and nutrition economic benefits of probiotics in acute pediatric diarrhea.

## CONCLUSION

In this study, it was observed that probiotics reduced the mean duration and mean frequency of acute pediatric diarrhea.

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