

Original Research Article

Role of *Saccharomyces boulardii* and *Bacillus clausii* in reducing the duration of diarrhea: a three-armed randomised controlled trial

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ABSTRACT

Background: Diarrhea is a major public health problem. Probiotics have been recommended as an add-on therapy for the treatment of diarrhea. Recently *Saccharomyces boulardii* and *Bacillus clausii*, yeast and spore forming bacilli are among the probiotics in use for diarrheal disorder.

Methods: This was a three armed randomised controlled trial conducted in pediatrics department, in a tertiary level care at Chidambaram. The randomisation was done using permuted blocks method. Of the three groups, Group A received ORS and zinc; Group B ORS, zinc and *S. boulardii* and Group C ORS, zinc and *B. clausii*. The outcome variables included duration of diarrhea and duration of stay in hospital.

Results: The duration of diarrhea decreased significantly in Group B and C than Group A. Both the probiotics had similar effect in reducing the duration of diarrhea. There was no significant difference in duration of stay at hospital between the groups.

Conclusions: Addition of probiotics as an add-on therapy would aid in decreasing the duration of diarrhea rather than giving ORS and zinc alone. The duration of stay in hospital was unaffected by the change in regimen of treatment.

Keywords: *B. clausii*, Probiotics, *S. boulardii*, Three armed randomised controlled trial

INTRODUCTION

Diarrhea is a major public health problem and continues to be a major cause of morbidity and mortality in developing countries.¹ Diarrhea kills 300,000 children in India each year.² Though the overall incidence of diarrhea declined from 3.4 to 2.9 episodes per child-year, the burden of the disease remains unacceptably high.³

The recent declining trends in total deaths were driven by various universal programs like expanded programme on immunization, program for the control of diarrheal diseases and acute respiratory infection.⁴ Oral rehydration therapy along with continued feeding and zinc supplementation were used for the treatment of diarrhea.⁵ Microorganisms that colonise the bowel and exert

beneficial effect on human health were called as probiotics.⁶ They have been found to be efficacious for the treatment of diarrhea of suspected viral origin as well as antibiotic associated diarrhea.⁷ They have been documented to reduce both the frequency and duration of diarrhea.⁸ Canani et al reported that the effect of probiotics varies with the type of preparation and a particular probiotic preparation have to be chosen based on solid efficacy data.⁹

Bacillus clausii is a spore forming probiotic, stable at room temperature and resistant to low pH. It can reach the small intestine, colonise it and exerts beneficial effect.⁶ *Saccharomyces boulardii*, a yeast is capable of acting as probiotic organism.¹⁰ *B. clausii* colonise the free ecological niche, compete for epithelial cell adhesion and

enhance enzyme secretion into intestinal environment.⁶ The mechanism of action for *S. boulardii* were inhibition of some bacterial toxin, anti-inflammatory effects and by stimulatory effects on intestinal mucosa.¹⁰

This three-armed randomised controlled trial was performed with the objective to find out the effect of *Saccharomyces boulardii* and *Bacillus clausii* on the mean number of diarrheal episodes and duration of hospital stay.

METHODS

This was a single blinded three-armed prospective Randomized Controlled Trial conducted between February 2017 and September 2017 in pediatric department, Rajah Muthiah Medical College and hospital, Chidambaram. Ethical committee approval was obtained from the institute’s human ethical committee.

Study participants included all the children aged 6 months and 36 months admitted in the pediatric department with acute diarrhea irrespective of the hydration status. The exclusion criteria included cases with blood in stools, clinical signs of a coexisting acute systemic illness like meningitis, sepsis, pneumonia, severely malnourished and immunocompromised children, and children with prior probiotic or antibiotic drug administration, known hypersensitivity to probiotics. Written consent was obtained from all the study participants.

The sample size was calculated and was found to be 30 participants per arm. The study participants were randomized using permuted random blocks into three groups A, B, C. Group A received ORS and zinc as intervention. Group B and C received *Saccharomyces boulardii* and *Bacillus clausii*, respectively along with ORS and zinc. Authors recruited 35 participants for each group. During the course of study 6 participants were dropped out from the study, 3 from group A, 1 from group B and 2 from group C respectively (Figure 1). The study participants were blinded in order to prevent information bias.

Source data was collected by the investigator from day 1 and daily till diarrhea stopped completely as mentioned in the case proforma and filled into master chart after the study. The data on the master chart were entered into the computer database. Data was coded, cleaned, verified and analyzed using SPSS (Statistical Package for Social Sciences) computer version 21.0 and Microsoft Excel 2013.

To assess the difference between the two groups, ANOVA test was used to analyze categorical variables and Chi square test for qualitative variables. Post HOC test, Mann Whitney U test, Kruskal Wallis test were applied to test the significance between the groups. Data is presented using bar graphs and tables and Whisker box plot.

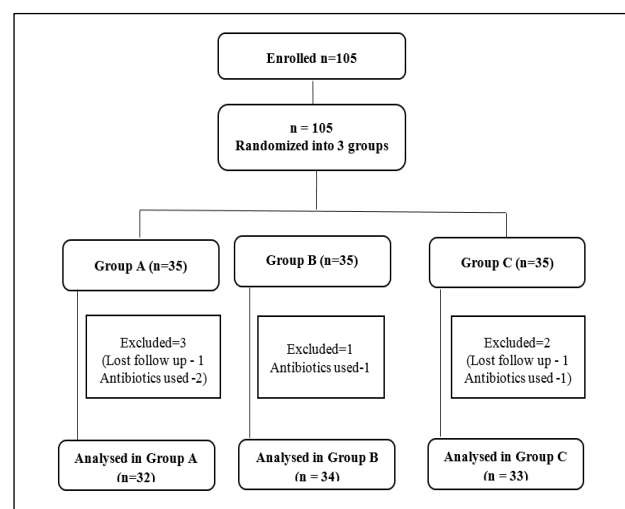


Figure 1: Flow diagram of the subjects’ progression through the study.

RESULTS

The baseline characteristics of the study participants were described below (Table 1). All the three groups were similar in characteristics with p value >0.05.

Table 1: Baseline characteristics of the study participants.

Variable	Group A	Group B	Group C	P-value
Age in months*	18.22±9.10	16.67±8.61	17.57±9.39	>0.05
Weight in kg*	9.18±1.98	9.00±1.53	9.2±1.75	>0.05
Sex [§]				
Boys	17 (49%)	19 (54%)	20 (57%)	>0.05
Girls	18 (51%)	16 (46%)	15 (43%)	

* The variables were expressed in mean±standard deviation and ANOVA was applied; § Chi-square test was applied.

In Group A (n=32), only 5 participants had diarrhea settled within 72 hours after standard therapy of ORS with zinc

while in Group B (n=34), 20 participants had diarrhea settled within 72 hours following *S. boulardii* administration and in Group C (n=33), 15 participants had

diarrhea settled within 72 hours following *B. clausii* administration (Figure 2). None had diarrhea in Group B and Group C by 120 hours but for Group A it took 144 hours.

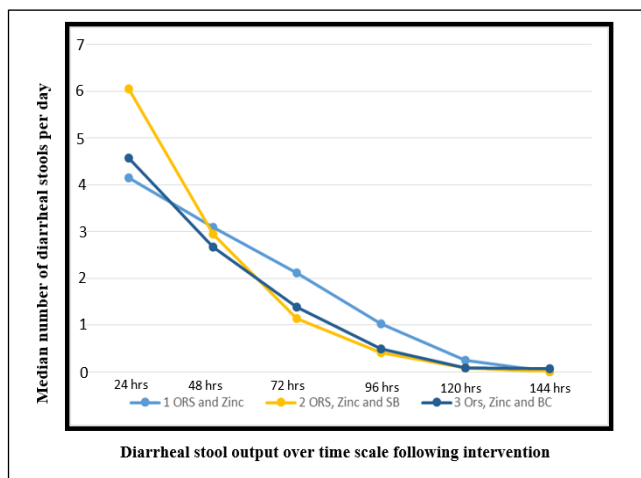


Figure 2: Diarrheal episodes per day with relation to time of starting the intervention.

The median duration of diarrhea after intervention for group A was 108 hours while median duration of diarrhea for Group B and Group C were 72 and 96 hours, respectively. The median duration was found to be highest in group A followed by group C and Group B. The above difference in diarrheal duration was found to be statistically significant with p-value of < 0.05 after the application of ANOVA test.

The post hoc tests reported that the diarrheal duration was significantly reduced for the groups that received probiotics (Group B and C) than the non-probiotic group that received only ORS and zinc with p value < 0.05. When the probiotics group were compared between themselves, the difference was not found to be statistically significant i.e. the reduction in diarrheal duration was similar between groups B and C (Table 2).

Table 2: Comparison of diarrheal duration between the three groups.

Groups	Median (hours±IQR)	P-value
Group A	108 (96-120)	< 0.05
Group B	72 (72-96)	
Group C	96 (72-96)	
Group A versus Group B	108 (96-120) / 72 (72-96)	< 0.05
Group A versus Group C	108 (96-120) / 96 (72-96)	< 0.05
Group B versus Group C	72 (72-96) / 96 (72-96)	> 0.05

The mean duration of hospital stay for the groups A, B and C was found to be 3.34±1.06 days, 3.41±1.04 days and 3.06±0.86 days, respectively and no significant difference

were found between the three groups with p value > 0.05 (Table 3).

Table 3: Mean duration of stay (in days) at hospital.

Group	Mean±SD	P-value
A	3.34±1.06	>0.05
B	3.41±1.04	
C	3.06±0.86	
Total	3.27±0.99	

DISCUSSION

The outcome variables studied were the duration of diarrhea and the mean duration of hospital stay in each group. Randomisation was done using permuted random blocks and the study participants were allotted to three groups. All the groups were found to be similar with respect to various characteristics. This indicated that the interventions were the only factors that could change the above outcomes.

Total drop outs in the study were 6; 3 from group A, 1 from group B and 2 from group C. Though at the end, all the three groups had more than 30 participants which was the sample size calculated. The study participants were unaware of the type of intervention that they had received, and it would have helped in decreasing the role of information bias as some of the variables were subjective.

The study reported that the duration of diarrhea had reduced significantly in the groups that received probiotics than the other group that received only ORS and zinc, proving that the probiotics were effective in reducing the duration of diarrhea. The effectiveness of both the probiotics used in the study *S. boulardii* and *B. clausii* was similar with respect to the duration of diarrhea. Feizizadeh et al in his study reported that *S. boulardii* reduced the duration of diarrhea considerably and he also reported that various doses of *boulardii* to be compared against each other.¹¹ In contrast to present study Vineeth et al reported that *S. boulardii* was more effective in reducing the duration of diarrhea than *B. clausii*.¹² Another study reported both *S. boulardii* and *B. clausii* had no effect in reducing the duration of diarrhea.⁹

The present study proved that addition of probiotic definitely had beneficial effect by decreasing the duration of diarrhea. This could help to increase the quality of treatment. The present study also reported that there is no difference between the two probiotics in question. Similar comparisons between the probiotics could be done in similar genetic with different environmental circumstance, in order to get more valid evidence on effectiveness between them. Similarity in efficacy of probiotics could help physicians to take decisions that could help influence the cost-effectiveness of the treatment.

When mean duration of stay was taken into account, there was found to be no difference between the groups A, B and

C. Irrespective of the use of probiotics in the present study, the duration of stay was found to be similar. This may be due to influence by various other managerial factors than the duration required for the recovery from diarrhea. Similar findings were also reported by Canani et al.⁹

CONCLUSION

Authors came to a conclusion that addition of probiotics as an add-on therapy would aid in decreasing the duration of diarrhea rather than giving ORS and zinc alone from this study. The choice of probiotic can also be subjective. More studies have to be carried to prove the efficacy of probiotics in reducing the duration of diarrhea.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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