



## Role of Saccharomyces Boulardii and Bacillus Clausii in Children with Acute Diarrhea – A Randomized Control Trial

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### Abstract:

**Background:** Probiotics are live microorganisms which when administered confer benefits to host. They are recommended as add on therapy for acute diarrhea.

**Objectives:** To find out the effect of probiotics, Saccharomyces boulardii and Bacillus clausii on the duration of diarrhea in patients with acute diarrhea.

**Material and Methods:** This was a single blinded randomized controlled trial done with one group receiving ORS and zinc as per WHO recommendations and the other two groups along with ORS and zinc were receiving Saccharomyces boulardii and Bacillus Clausii respectively as probiotics.

**Results:** All the characteristics were equally distributed between the groups before intervention. There was significant reduction in the duration of diarrhea in the groups receiving probiotics as an add on therapy than the other group ( $p < 0.05$ ). No significant difference was found between the two groups receiving probiotic add on therapy.

**Conclusion:** Probiotics as an add on therapy would aid in decreasing the duration of diarrhea in acute patients with acute diarrhea.

**Keywords:** Probiotics, Acute diarrhea, Saccharomyces boulardii, Bacillus clausii.

### Introduction

Diarrhea is defined as the passage of three or more loose or liquid stools per day (or more frequent passage than is normal for the individual)<sup>(1)</sup>. Diarrheal disease is considered as major health problem in developing countries<sup>(2)</sup>. Acute diarrheal disease accounts for nearly 1.7 billion cases worldwide every year and 5.25 lakhs children younger than 5 years die from diarrhea annually. The burden is more in developing countries with > 90% occurring in those countries<sup>(1)</sup>.

Reduced osmolarity oral rehydration salt solution (ORS) and zinc supplementation bear a great potential for better management of diarrhea. Severity of diarrhea is linked to etiology, and rotavirus is the most common infectious agent and is frequently associated with dehydration. Investigations are generally not needed. Oral rehydration with hypo-osmolar solution is the major treatment and should start as soon as possible. Routine feeding should continue with no dietary changes including milk. Active therapy may reduce the duration and severity of diarrhea<sup>(3)</sup>.

Probiotics are live microbes which when administered in adequate amounts confer health benefit to the host<sup>(4)</sup>. Recently probiotics therapy, evidenced by numerous randomized clinical trials (RCTs) followed by meta-analyses and Cochrane reviews, has attracted a great deal of renewed interest, due to its significant therapeutic effect on rotavirus-associated diarrhea in children in developed countries. Canani et al illustrated that all probiotics are not equally effective in treating acute diarrhea in children and emphasized that the particular probiotic preparation should be chosen based on solid efficacy data<sup>(5)</sup>. The main objective of the study was to find whether there was any change in diarrheal duration with *Saccharomyces boulardii* (*S.boulardii*) or *Bacillus clausii* (*B.clausii*) as an adjuvant therapy in acute diarrhea.

### Materials and Methods

This was a single blind randomized controlled trial conducted at tertiary care hospital in Chidambaram, Tamilnadu, India from February 2016 to September 2016. The eligible subjects were hospitalized patients of age group 6 months to 36 months who had acute diarrheal disease. Participants with bloody stools, parenteral diarrhea, patients who have taken antibiotic or probiotic 7 days prior to hospital admission and severely malnourished and immunocompromised individuals were excluded from the study.

The study was approved by the Institutional Human Ethical Committee. All participating subjects/guardians signed the informed consent form. Randomization was done according to computer generated random numbers and the participants were allotted into three groups.

Group A being the control group was treated with standard protocol of WHO for acute diarrhea i.e with ORS and zinc at appropriate dosages. Group B was intervened with *Saccharomyces boulardii* at a dose of 250 mg twice daily for 5 days, along with ORS and zinc. Group C was treated with *Bacillus clausii* at a dose of  $2 \times 10^9$  CFU per

mltwice daily for 5 days, along with ORS and zinc.

Due information was given to all parents / care givers before administration of probiotics. Participant demographic data, clinical symptomatology and daily note on frequency of stools was noted and patients were regularly followed up till the diarrheal episode ceases. All the information provided by the care giver starting from day 1 was recorded by the principal investigator.

All the data thus collected were entered into MS excel spread sheet 2013 and then analysed using SPSS version 21. For quantitative variables ANOVA was employed as statistical test and for Qualitative variables Chi square test was applied.

### Results

Table 1 shows the baseline characteristics of the study population. Mean age of the study participants in Group A, B, C was found to be  $18.22 \pm 9.10$  months,  $16.67 \pm 8.61$  months and  $17.57 \pm 9.39$  months, respectively. After applying ANOVA the p-value was found to be more than 0.05, which indicated that there was no significant difference between the groups according to age. significant difference were also not found between other variables like weight(kg), sex, dehydration status, nutritional status, breast feeding, exclusive breast feeding and Rotavirus vaccination status. The above indicated that all the three groups were similar in characteristics.

About 58% of the study participants had no diarrhea after 72 hours in Group B while in Group C it was 45% and in Group A it was only 15% (Fig 1). The mean diarrheal duration for group A was  $107.25 \pm 24.37$  hours and that of Group B and Group C were  $84.7 \pm 21.49$  hours and  $89.4 \pm 24.2$  hours, respectively. After doing the post HOC test, it was found out that Group B and Group C were statistically similar ( $p > 0.05$ ), but when Group A was compared with Group B and Group C respectively, significant difference were found between the groups ( $p < 0.05$ ).

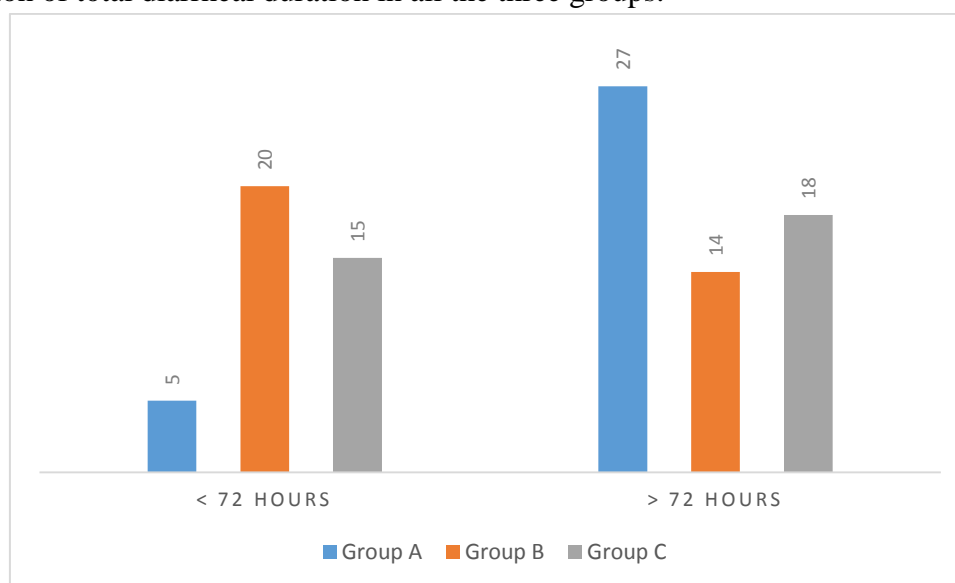
**Table 1:** Baseline characteristics of the study participants

Variable		Group A No (%)	Group B No (%)	Group C No (%)	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 <sup>§</sup>	Boys	17(49%)	19(54%)	20(57%)	>0.05
	Girls	18(51%)	16(46%)	15(43%)	
Dehydration status <sup>§</sup> (as per WHO classification)	No dehydration	18(51%)	17(49%)	19(54%)	>0.05
	Some dehydration	17(49%)	15(43%)	16(46%)	
	Severe dehydration	0	3(8%)	0 (4%)	
Nutritional status <sup>§</sup> (as per IAP grading)	Normal	26(74%)	28(80%)	28(80%)	>0.05
	Grade I malnutrition	6(17%)	5 (14%)	6(17%)	
	Grade II malnutrition	3(9%)	2(6%)	1(3%)	
On Breast feeding <sup>§</sup>	Yes	22(63%)	15(57%)	23(66%)	>0.05
	No	13(37%)	20(43%)	12(34%)	
On Exclusive Breast feeding <sup>§</sup>	Yes	26(74%)	26(74%)	30(86%)	>0.05
	No	9(26%)	9(26%)	5(14%)	
Rotavirus vaccination status <sup>§</sup>	Given	1(3%)	2(6%)	2(6%)	>0.05
	Not given	34(97%)	33(94%)	33(94%)	

\*The variables were expressed in mean ± standard deviation and ANOVA was applied.

<sup>§</sup>Chi-square test was applied.

**Fig 1:** Distribution of total diarrheal duration in all the three groups.



**Table 2:** Diarrheal duration between the three groups

Group	Mean (hours)	Standard deviation	F value	p value
Group A	107.250	24.3721	8.444	<0.05
Group B	84.706	21.4949		
Group C	89.455	24.2037		

**Table 3:** Post hoc analysis

Group comparison	Mean difference (hours)	p-value
Group A VS Group B	22.54	< 0.05
Group A VS Group C	17.79	<0.05
Group B VS Group C	4.74	>0.05

## Discussion

This was a randomized controlled trial with the objective to find out whether any change occurred in the diarrheal duration with *Saccharomyces boulardii* or *Bacillus clausii* as adjuvant therapy in acute diarrhea. The study consisted of three groups A, B and C receiving ORS and zinc, ORS, zinc and *S.boulardii* and ORS, Zinc and *B.clausii*, respectively. All the three groups were characteristically similar pertaining to age, sex, weight, nutritional status, hydration status, breast feeding and rotavirus vaccination status with  $p$  value  $> 0.05$ .

After applying the intervention, the median diarrheal duration for group A, B (*S.boulardii*) and C (*B.clausii*) were  $107.25 \pm 24.37$  hours,  $84.7 \pm 21.49$  hours and  $89.4 \pm 24.2$  hours, respectively. The median duration was found to be 105(90-104.5) and 118 (95.2-12.7) hours for *S.boulardii* and *B.clausii*, respectively in a study by Canani et al<sup>(5)</sup>.

Significant difference in diarrheal duration were found between the group A receiving ORS and zinc and group B, C receiving probiotics. On the other hand no significant difference were found between Group B (*S.boulardii*) and Group C (*B.clausii*). A systematic review by Dinleyici et al reported that *S.boulardii* reduced diarrheal duration considerably when compared to the controls<sup>(6)</sup>. Similar observation was reported by Susrut et al where the mean duration of diarrhea reduced by about 29 hours in the group receiving *S.boulardii* than the control group<sup>(7)</sup>.

Vandenplas et al in a review reported that *boulardii* could be used in treatment of acute diarrhea and also reduced prolonged diarrheal episodes<sup>(8)</sup>. Another Randomised controlled trial by Htwe et al reported that the mean duration of diarrhea was 3.08 days for group receiving probiotics and 4.68 days in the control group<sup>(9)</sup>. Similar results on the efficacy of *S.boulardii* was reported by systematic review<sup>(6)</sup>.

Vineeth et al in their study reported that *S.boulardii* significantly decreased the duration of diarrhea than *B.clausii*<sup>(10)</sup>. In contrast to present

study, Canani et al reported no significant difference in diarrheal duration due to probiotics *S.boulardii* or *B.clausii* when compared with other group receiving ORS only<sup>(5)</sup>.

The use of probiotics along with ORS and zinc decreased the duration of diarrhea rather than intervening with ORS and zinc alone. The present study showed no difference in clinical effects between *S.boulardii* and *B.clausii*. The strength of the present study is that this is a randomized controlled trial and the evaluation was done in Indian setting as there are very few studies done on the effect of probiotics on Indian population. The limitations were the etiological factors of diarrhea were not explored and we could not measure the volume of the stools.

## Conclusion

Probiotics are microorganisms that benefits the human health when they colonise the gut. When given as an add on therapy along with ORS and Zinc they help in reducing the duration of diarrhea. The same effect was demonstrated in the present study population.

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