

Original Research Article

Efficacy of probiotics in acute diarrhoea in children

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Received: 14 May 2018

Accepted: 06 June 2018

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ABSTRACT

Background: Gastroenteritis is a major public health problem worldwide and remains the second leading cause of death among children under five globally. Objective of this study was to investigate and compare the efficacy of commonly available probiotics in the treatment of acute watery diarrhoea (AWD) in children.

Methods: This was an open label randomised controlled trial conducted in a tertiary care hospital in Bangalore for 2 years. 120 children aged 6 months to 5 years admitted with AWD of less than or equal to 48 hours duration were randomized into three groups – Group I (control) received oral rehydration therapy and zinc, Group II received *Bacillus clausii* in a dose of 2 billion spores twice a day and Group III received *Saccharomyces boulardii* as 250 mg twice a day. The primary outcome measures were total duration of diarrhoea, mean number of stools per day, consistency of stools and secondary outcome measures were duration of vomiting, fever and hospital stay. ANOVA, Student t test, Mann Whitney U test and Chi square test were used for analysis.

Results: The duration of diarrhoea and hospital stay significantly reduced (41.68 hrs) in Group III compared to Group I (57.65 hrs) and Group II (53.33 hrs). ($p < 0.05$). The frequency of stools reduced significantly on Day 4 and the consistency of stools improved significantly on Day 3 in both the probiotic groups ($p < 0.05$). Both the probiotics reduced the duration of fever significantly but had no effect on the duration of vomiting.

Conclusions: *Saccharomyces boulardii* is effective in reducing the duration of diarrhea and hospital stay in children with acute gastroenteritis.

Keywords: *Bacillus clausii*, Children, Diarrhoea, Efficacy, *Saccharomyces boulardii*

INTRODUCTION

Gastroenteritis is a major public health problem worldwide and remains the second leading cause of death among children under five globally.¹ About 10% of infants and 14% of 0-4 years children die due to diarrhea in India.² Incidence of gastroenteritis is highest in the first two years of life.

Rotavirus is the most common pathogen causing diarrhoea in children below 5 years of age. Dehydration, hypokalemia and acidosis are the main life-threatening complications of AWD.³ Low osmolarity oral rehydration

solution (ORS) and zinc are the two effective interventions introduced in the last two decades for diarrhoea management.⁴ With this treatment, the complications of diarrhea could be effectively treated or prevented. However, its use neither shortens the duration of the illness nor reduces the stool loss.⁵ Several trials on probiotics, as an adjuvant to oral rehydration therapy (ORT) have been conducted in the recent years in different settings and with different end points and have been found to reduce the duration of illness. *Saccharomyces boulardii*, a non-pathogenic yeast has been proven to be efficacious in many studies in AWD in children.⁶ *Bacillus clausii* has been proven to be

efficacious in phase III trial but further studies are required. Both the probiotics are commonly being prescribed by the pediatricians.

Unfortunately, data comparing probiotic species in a systematic manner have been scant and mostly derived from animal and laboratory studies.⁷ Most of the studies till date are from developed countries. It is not possible to extrapolate the findings of these studies to present settings since the microbial colonization of the gut is different.⁴ The effect of probiotics is strain related.³ With the increasing availability and widespread use of probiotics randomized controlled trials in Indian children are required before a particular strain is recommended to the patients. There is scanty data to establish the efficacy of the probiotics available in the Indian market.⁴ Hence the need for this study.

METHODS

This was an open label randomised controlled trial conducted in a tertiary care hospital in Bangalore for two years (2010-2012). Children belonging to different socioeconomic strata and from different parts of the city visit the hospital for its pediatric services.

Children between the age of 6 months to 5 years admitted to the hospital with AWD of less than or equal to 48 hours duration were included in the study. An informed written consent was taken from their parents. Diarrhoea was defined as passage of three or more liquid or watery stools occurring in a 24-hour period.

Exclusion criteria

- History of presence of blood or pus in stools
- severe dehydration (WHO criteria)
- severely malnourished patients (grade III and IV according to IAP classification)
- treatment with antibiotics, probiotics, or prebiotics within a period of two weeks before enrolment
- history of conditions known to producing immunodeficiency (AIDS, other congenital immunodeficiency syndrome, drug therapy with steroids, anticancer drugs etc.)
- presence of acute systemic illness (meningitis, pneumonia, sepsis)
- chronic diarrhea
- known hypersensitivity to *Bacillus clausii* and *Saccharomyces boulardii* or other probiotics.

Sample size estimation

Based on previous literature for effect size of 0.34, type I error of 5% level, the sample size of 120 was decided to meet the statistical power of at least 90%.

Interventions

They underwent a thorough physical examination, assessment of vital signs, assessment of hydration, frequency and severity of diarrhoea, and nutritional status. The first group served as the control group and they were given ORT and zinc supplement as per the WHO management protocol.⁸

Primary outcome measures

Total duration of diarrhoea after admission: time calculated in hours from the time of admission to the time the child passed the last abnormal (loose or liquid) stools. Mean number of stools per day (Frequency of abnormal stools and Consistency of stools: evaluated through a score system.⁹ Faeces were graded as: 1= Normal 2= Loose 3= Semiliquid 4= Liquid.

Secondary outcome measures

Duration of vomiting, duration of fever (>37.5 degree), duration of hospital stays in hours.

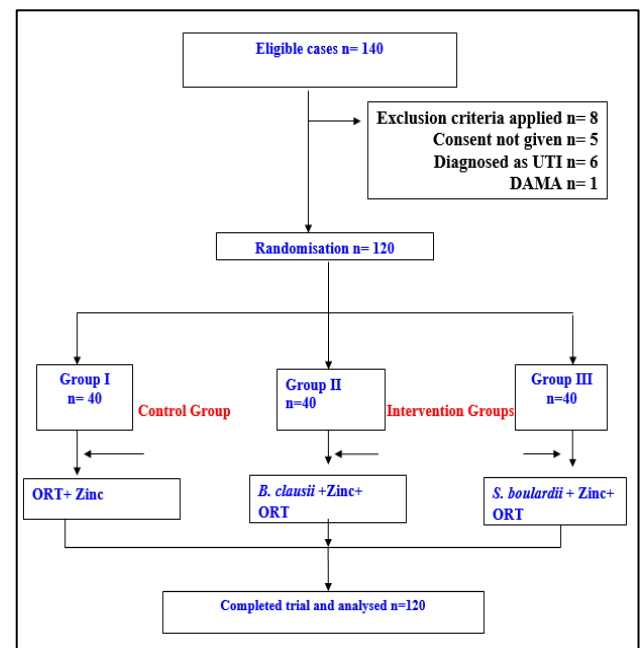


Figure 1: Study flow chart.

RESULTS

The mean age of the children included in the study was 15 months. The gender distribution was comparable in all the groups. The nutritional status and the feeding pattern of the study groups and the control group was similar. There was no significant difference in the degree of dehydration in all the three groups. None of the patients had severe dehydration.

The mean duration of diarrhoea, vomiting and fever before admission was comparable in the study groups and

the control group. ($p < 0.05$) All the patients had diarrhoea for around 30 hours prior to admission. The duration of diarrhoea, duration of hospital stays, and duration of fever was significantly lesser in Group III

(*Saccharomyces boulardii* group) when compared with the control group. ($P = 0.001^{**}$, $P = 0.001^{**}$, $P < 0.001$ respectively).

Table 1: Baseline characteristics of the study group.

Parameter	Group I	Group II	Group III	p value
Mean age of the child months	15.40±7.00	14.98±6.98	15.70±7.61	0.903
Gender				
Males No: (%)	22 (55%)	21 (52.5%)	26 (65%)	0.489
Females No: (%)	18 (45%)	19 (47.5%)	14 (35%)	
Nutritional status				
No malnutrition	24 (60.0%)	21 (52.5%)	19 (47.5%)	0.849
Grade 1	14 (35.0%)	17 (42.5%)	18 (45%)	
Grade 2	2 (5%)	2 (5%)	3 (7.5%)	
Degree of dehydration				
No dehydration	18 (45.0%)	11 (27.5%)	16 (40%)	0.250
Some dehydration	22 (55.0%)	29 (72.5%)	24 (60%)	
Feeding pattern				
Breast feeds	5 (12.5%)	3 (7.5%)	6 (15%)	
Mixed feeds	31 (77.5%)	34 (85%)	29 (72.5%)	0.756
Formula milk	4 (10%)	3 (7.5%)	5 (12.5%)	

Table 2: Comparison of duration of symptoms prior to admission.

Symptoms (hours) (Mean ±SD)	Group I	Group II	Group III	p value
Duration of diarrhoea	29.15±13.49	30.85±14.80	30.95±12.13	0.800
Duration of vomiting	18.85±13.95	22.33±8.77	23.02±7.63	0.167
Duration of fever	22.65±10.56	22.77±8.85	23.23±10.54	0.978

Table 3: Comparison of outcome variables between the three groups.

Outcome in hour (Mean±SD)	Group I	Group II	Group III	Significance		
				Group I vs Group II	Group I vs Group III	Group II vs Group III
Duration of diarrhoea	57.65±26.31	53.33±16.78	41.68±10.84	0.570	0.001**	0.020*
Duration of stay in the hospital	80.85±26.42	78.15±16.58	65.23±10.17	0.800	0.001**	0.008**
Duration of fever	23.30±23.14	12.15±8.09	10.45±7.18	0.003**	<0.001**	0.864
Frequency of stools						
Day 1	6.30±2.77 (6.0)	6.90±2.16 (7.0)	6.9±2.83 (7.0)	0.559	0.559	1.000
Day 2	4.18±2.63 (4.0)	3.98±1.40 (4.0)	4.48±1.77 (4.0)	0.896	0.781	0.505
Day 3	3.00±2.50 (3.0)	2.28±1.09 (2.0)	2.60±1.28 (3.0)	0.153	0.560	0.681
Day 4	1.28±2.09 (0.0)	0.35±0.66 (0.0)	0.30±0.85 (0.0)	0.008**	0.005**	0.985
Day 5	0.28±0.75 (0.0)	0.08±0.35 (0.0)	0.00±0.00 (0.0)	0.163	0.031*	0.757
Day 6	0.00±0.00 (0.0)	0.03±0.16 (0.0)	0.00±0.00 (0.0)	0.441	1.000	0.441

The duration of diarrhoea, duration of hospital stay and duration of fever was significantly lesser in Group III (*Saccharomyces boulardii* group) when compared with the control group. ($P = 0.001^{**}$, $P = 0.001^{**}$, $P < 0.001$ respectively).

In Group II (*Bacillus clausii*) there was a significant reduction in the duration of fever when compared to the control group with $P = 0.003^{**}$. The duration of diarrhea and hospital stay did not reduce significantly in Group II ($p > 0.05$).

The frequency of stools reduced significantly on Day 4 in both the probiotic groups when compared treatment group. The patients in study and control group had grade 3-4 consistency of stools during admission. The change in consistency of stools to grade 2 was significant on Day 3 in both the treatment groups with ($P < 0.05$). On Day 4 of admission, the stools became normal in all the groups.

Table 4: Median consistency stools in three groups studied.

	Group I	Group II	Group III	P value
Day 1	3 (3-4)	3 (3-4)	3 (3-4)	0.835
Day 2	3 (2-3)	3 (3-3)	3 (3-3)	0.299
Day 3	3 (2-3)	2 (2-2)	2 (2-3)	0.029*
Day 4	1 (1-1)	1 (1-1.75)	1 (1-1)	0.625
Day 5	1 (1-1)	1 (1-1)	1 (1-1)	0.141
Day 6	1 (1-1)	1 (1-1)	1 (1-1)	1.000

DISCUSSION

The primary outcome measure was the duration of diarrhoea. The present study shows that the group which received *Saccharomyces boulardii* had a significantly lesser duration of diarrhea compared to the control group and the *Bacillus clausii* group. The duration of diarrhoea was 15.97 hours lesser in the *Saccharomyces boulardii* group than the control group. The difference in the duration of diarrhea between the *Bacillus clausii* group and the control group was only 4.32 hours. On comparing both the probiotics, *Saccharomyces boulardii* had a better outcome than *Bacillus clausii*. This was consistent with the results of a study done by Billoo et al from Pakistan which showed that duration of diarrhea was lesser by 1.3 days in children who were treated with *Saccharomyces boulardii* for AWD.¹⁰ A double blinded randomized controlled trial done by Grandy et al on Bolivian children also showed that the duration of diarrhea was significantly lower by 26.5 hours in the group treated with *Saccharomyces boulardii* (58 hours in cases vs 84.5 hours in controls).¹¹ Guandalini et al also reported in their review on probiotics that the difference in the mean duration of diarrhea between the interventional group and the control group was 24 hours and it was consistent in most of the trials which used different probiotic strains.¹² Probiotics also reduced the risk of diarrhea lasting for more than 4 days.

However, the study done by Canani et al in 2007 showed that both *Saccharomyces boulardii* and *Bacillus clausii* didn't have any significant effect on the duration of diarrhoea.¹³ One of the possibilities for the duration of diarrhoea being more in our study could be that most of the children who were included had diarrhoea >15 hours prior to admission.

Frequency of stools

The present study shows that probiotics show a change in the frequency of stools only on day 4 of admission.

($p < 0.05$). This is similar to that found in a study done by Villarruel G et al on 100 Argentinian children with mild to moderate acute watery diarrhea.¹⁴

Consistency of stools

In the present study the probiotics showed a significant effect on the consistency of stools on Day 3 of admission when compared to the control group. ($p < 0.05$). However, there was no difference when both the probiotics were compared to each other. ($p > 0.05$)

Eren et al did a study in Turkey where they compared *Saccharomyces boulardii* and yoghurt fluid in the treatment of acute diarrhea in children.¹⁵ They found that the consistency of stools improved in both the groups on Day 3 and the difference was not statistically significant.

Vomiting

In the present study observed that both *Saccharomyces boulardii* and *Bacillus clausii* did not significantly reduce the duration of vomiting after treatment when compared to the control group ($p > 0.05$). Among the two probiotics, *Saccharomyces boulardii* had a statistically significant better outcome in terms of vomiting.

This is similar to the observation made by Canani et al in 2007 which compared *Saccharomyces boulardii* with other commonly available probiotics.

The study done by Grandy et al also showed that there was no significant effect on vomiting in the *Saccharomyces boulardii* treated group.¹¹ A RCT done by Kurugol et al in 2005 reported no difference in vomiting in the group intervened with *Saccharomyces boulardii*.¹⁶

Fever

In the present study both the probiotics reduced the fever duration significantly when compared with the control group but when they were compared with each other both were equally effective. This is similar to the observation done by Grandy et al in their study which showed that *Saccharomyces boulardii* significantly reduced the median duration of fever.¹¹

The possible reason for this effect could be that probiotics decrease the production of pro inflammatory cytokines which cause fever.

Duration of hospital stay

This was also significantly less in the *Saccharomyces boulardii* treated group. It was 15 hours lesser compared to the control group and 13 hours lesser compared to the *Bacillus clausii* group. *Bacillus clausii* did not have a significant outcome in this aspect. This is consistent with

the results of the study done by Kurugol et al in which *Saccharomyces boulardii* reduced the duration of hospital stay by 1 day.¹⁶ The present study had a few limitations, but every effort was made to minimize their effects on the study outcome. The study was not blinded as the appearance of both the probiotics was different. Many studies have isolated rotavirus from the stool samples. Probiotics were proven to be most effective in rotaviral diarrhea. In present study authors did not isolate the offending organism. Authors included children with duration of diarrhea of around 30 hours prior to admission. Mean age of the children included in this study was 15 months. The mortality in diarrhea is highest before 24 months of age. This study was done on hospitalized patients and hence the observations were done by a single observer which increases the reliability of present study.

CONCLUSION

The duration of diarrhoea was the least in the *Saccharomyces boulardii* group. The mean frequency of stools was lesser in both the probiotic groups on Day 4 of treatment. The consistency of stools in both *Saccharomyces boulardii* and *Bacillus clausii* group improved on Day 3 of treatment. There was no difference observed in the duration of vomiting between the control group and the probiotic groups. *Saccharomyces boulardii* was better than *B. clausii* in reducing the duration of vomiting. Both *Saccharomyces boulardii* and *Bacillus clausii* reduced the duration of fever but when the probiotics were compared to each other for this outcome there was no significant difference. Children treated with *Saccharomyces boulardii* had a significantly shorter duration of hospital stay when compared to the children who received *Bacillus clausii* and no probiotic.

Funding: No funding sources

Conflict of interest: None declared

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

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Cite this article as: Bhat S, Shreekrishna GN, Savio CD. Efficacy of probiotics in acute diarrhoea in children. Int J Contemp Pediatr 2018;5:1646-50.