

# Study of *Saccharomyces boularii* in acute watery diarrhea in children between 2 months to 5 years of age at a tertiary hospital

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## Abstract

**Background:** Diarrhea with any cause and any period of time may lead to dehydration and even may be lethal in infants, children, and the elderly if not corrected immediately. Probiotics secrete antimicrobial products, intestinal mucin, and bacteriocins which inhibit pathogens and help to produce immunomodulation at the gut level to decrease duration of diarrheal symptoms. In present study we compared role of *Saccharomyces boularii* in acute watery diarrhea in children between 2 months to 5 years of age at tertiary hospital. **Material and Methods:** Present study was single-center, prospective, comparative, interventional study, conducted in children Hospitalized due to diarrhea, aged from 2 month to 5 years of age, clinical suspicion of rotavirus infection, with mild to moderate dehydration and no prior probiotic administration. 80 children were randomly divided into 2 groups. children received oral rehydration therapy, Zinc and *Saccharomyces boulardii* (Group 1) versus children received ORT+ Zinc (Group 2). **Results:** During study period, 80 children were equally divided into 2 groups. General characteristics such as age, gender, average weight, dehydration status were comparable in both groups and difference was not statistically significant ( $p > 0.05$ ). Total duration of diarrhea in group I was  $58.96 \pm 11.53$  Hours as compared to  $92.8 \pm 13.07$  Hours in group 2, difference was statistically significant ( $p = 0.032$ ). Mean number of stools per day was  $4.12 \pm 3.64$ /day in group I and  $6.05 \pm 3.20$ /day in group II, difference was statistically significant ( $p = 0.007$ ). Mean duration of Fever after the Treatment in group I was  $45.96 \pm 1.53$  Hours as compared to  $45.84 \pm 0.81$  Hours in group 2, difference was statistically not significant ( $p = 0.062$ ). While Mean duration of Vomiting after the Treatment in group I was,  $52.8 \pm 1.07$  hours while  $69.6 \pm 0.69$  hours in group II, difference was statistically significant ( $p = 0.046$ ). **Conclusion:** *Saccharomyces boulardii* is effective in reducing the duration of diarrhea and hospital stay in children with acute gastroenteritis.

**Keywords:** *Saccharomyces boulardii*, diarrhea, acute gastroenteritis, frequency of stools,

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## INTRODUCTION

Diarrhea with any cause and any period of time may lead to dehydration and even may be lethal in infants, children, and the elderly if not corrected immediately.<sup>1</sup> Rotaviral

gastroenteritis is associated with a substantial clinical and economic burden in both developed and developing countries. Vaccination is the primary public health intervention for prevention of rotavirus infection.<sup>2</sup> The mainstay of treatment of an acute rotavirus diarrhea episode includes oral rehydration therapy (ORT) and zinc. ORT aims to prevent or reverse dehydration, and has no effect either on the duration of diarrhea or on the stool output. Zinc is not universally effective in the treatment of acute diarrhea, and has been used mainly in developing country settings.<sup>3</sup> Bacterio-therapy is known to play an important role in intestinal dysbiosis and judicious use of probiotics could reduce the duration and frequency of diarrhoea. Probiotics secrete antimicrobial products, intestinal mucin, and bacteriocins which inhibit pathogens and help to produce immunomodulation at the gut level to

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decrease duration of diarrheal symptoms. *Saccharomyces boulardii* (SB) is a nonpathogenic yeast that have demonstrated an antiinflammatory, anti-microbial, enzymatic, metabolic and anti-toxin activity including trophic effect by enhancing the metabolic function of the gut mucosa. In present study we compared role of *Saccharomyces boularii* in acute watery diarrhea in children between 2 months to 5 years of age at tertiary hospital.

**MATERIAL AND METHODS**

Present study was single-center, prospective, comparative, interventional study, conducted in Department of Pediatrics, BKL Walalwalkar Trust Rural, Medical Collage, Sawarde, India. Study duration was of 1 year (January 2020 to December 2020). Study was approved by institutional ethical committee.

**Inclusion criteria:** Children Hospitalized due to diarrhea, aged from 2 month to 5 years of age, clinical suspicion of rotavirus infection, with mild to moderate dehydration and no prior probiotic administration. Parents willing to participate in study.

**Exclusion criteria:** Children with Chronic diarrhea (more than two weeks), infections caused by other bacteria, patients treated with antimotility agents for diarrhea, patient who were taken antibiotic/probiotic 7 days prior to hospital admission, ICU admitted patients.

80 children were randomly divided into 2 groups: Group 1 - children received oral rehydration therapy (ORT) +Zinc + *Saccharomyces boulardii* (500 mg/day, contains 2.5 million colony forming units -CFU). It was diluted in 20 ml of water according to the manufacturers’ instructions, and given in two divided doses particularly

morning and evening, and minimum duration of administration was 5 days.

Group 2 - children received ORT+ Zinc (Group 2).

All the patients received the same diet; those below 6 months of age maintained breast feeding.

On admission, study patient demographic data, type of treatment given, and daily note on frequency of stools, consistency of stools, vomiting, fever and also blood count values were noted and patients were regularly followed up to the hospital discharge. All the information was provided by the mother or attendant every morning starting from day 1 to date of discharge.

The primary outcome measures were the total duration of diarrhea (Duration from the first to the last abnormal loose/liquid stools preceding a normal stool output) and the number of stools per day and their consistency. Secondary outcome measures were the incidence and mean duration of vomiting, fever. Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi- square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

**RESULTS**

During study period, 80 children were equally divided into 2 groups. Majority of children were from 6-12 months age group followed by 1-2 years age group. General characteristics such as age, gender, average weight, dehydration status were comparable in both groups and difference was not statistically significant (p>0.05).

**Table 1: Demographic Characteristics of the Subjects**

Characteristics	Group I	Group II	p-value
Age			0.62
2–6 months	5 (12.5 %)	3 (7.5 %)	
6–12 months	18 (45 %)	19 (47.5 %)	
1–2 years	11 (27.5 %)	12 (30 %)	
2–3 years	3 (7.5 %)	4 (10 %)	
3–5 years	3 (7.5 %)	2 (5 %)	
Gender			0.71
Male	23 (57.5 %)	22 (55 %)	
Female	17 (42.5 %)	18 (55 %)	
Average weight	9.1 ± 3.6 kg	9.6 ± 4.2 kg	0.80
Dehydration status			0.82
Mild	24 (60 %)	26 (65 %)	
Moderate	16 (40 %)	14 (35 %)	

Total duration of diarrhea in group I was 58.96 ± 11.53 Hours as compared to 92.8 ± 13.07 Hours in group 2, difference was statistically significant (p- 0.032). Mean number of stools per day was 4.12 ± 3.64/day in group I and 6.05 ± 3.20/day in group II, difference was statistically significant (p-0.007). Mean duration of Fever after the Treatment in group I was 45.96 ± 1.53 Hours as compared to 45.84 ± 0.81 Hours in group 2, difference was statistically not significant (p-0.062). While Mean duration of Vomiting after the Treatment in group I was, 52.8 ± 1.07 hours while 69.6 ± 0.69 hours in group II, difference was statistically significant (p- 0.046).

Table 2: Study outcome

Outcome	Group I	Group II	*p-value
total duration of diarrhea (Hours)	58.96 ± 11.53	92.8 ± 13.07	0.032
number of stools per day			
Day 1	11.2 ± 3.89	11.1 ± 4.10	
Day 2	6.1 ± 3.14	7.5 ± 2.18	
Day 3	2.9 ± 2.25	5.2 ± 2.64	
Day 4	0.5 ± 1.46	2.3 ± 1.02	
Day 5	0.5 ± 1.02	1.8 ± 0.9	
Mean	4.12 ± 3.64	6.05 ± 3.20	0.007
Duration after Treatment (Hours)			
Fever	45.96 ± 1.53	45.84 ± 0.81	0.062
Vomiting	52.8 ± 1.07	69.6 ± 0.69	0.046

## DISCUSSION

The aetiology of acute diarrhoea in children includes infections of the gastrointestinal tract (i.e. bacteria, viruses, protozoa), intoxications, systemic infections, malabsorption disorders, nutritional deficiency and allergy or intolerance to food or drugs (i.e. antibiotics, laxatives).<sup>5</sup> Probiotics (multiple single strains) with potentially multiple mechanisms of action were found to reduce the associated risk of acute GE (AGE) in children, with the effect dependent on the age of the host and the genera of the strain used.<sup>6</sup> The mechanisms of action of *S. boulardii*, depend mainly on the inhibition of some bacterial toxins, anti-inflammatory effects, and on stimulating effects on the intestinal mucosa such as trophic effects on the brush border enzymes and immunostimulatory effects.<sup>7</sup> Importantly, *S. boulardii* might interfere with cellular signalling pathways common in many inflammatory conditions and show antimicrobial activity, prevent apoptosis and Tumour Necrotic Factor (TNF) Synthesis, increase immunity.<sup>8</sup> Das S *et al.*,<sup>9</sup> studied 60 Children with WHO-defined acute watery diarrhea and stool rotavirus positive and were randomized into intervention (n-30) and control (n- 30) groups. The intervention group received SB (500 mg/day) for 5 days. The median duration (hours) of diarrhea was significantly shorter in the intervention group. A significantly shorter duration of hospitalization was also seen in the intervention group, but no significant difference was seen for fever and vomiting. There was also no difference between the two groups in the proportion of children requiring parenteral rehydration and persistence of diarrhea lasting beyond day 7. Similar findings were noted in present study. Feizizadeh S *et al.*,<sup>10</sup> studied 22 articles, and noted that *S. boulardii* significantly reduced the duration of diarrhea (mean difference [MD], 219.7 hours; 95% confidence interval [CI], 226.05 to 213.34), stool frequency on day 2 (MD, 20.74; 95% CI, 21.38 to 20.10) and day 3 (MD, 21.24; 95% CI, 22.13 to 20.35), the risk for diarrhea on day 3 (risk ratio [RR], 0.41; 95% CI, 0.27 to 0.60) and day 4 (RR, 0.38; 95% CI, 0.24 to 0.59) after intervention compared with control. This review and

meta-analysis show that *S. boulardii* was safe and has clear beneficial effects in children who have acute diarrhea. Dash DK *et al.*,<sup>11</sup> conducted a comparative study between children on oral rehydration therapy (ORT) +Zinc + *Saccharomyces boulardii*(Probiotic 5 billion CFU twicedaily) ((Group 1)) and children on ORT+ Zinc (Group 2). The duration of diarrhoea in Group 1 was 26.31 hours and Group 2 was 47.81 hours (p<0.01). The frequency of diarrhoea showed improvement within 24 and 72 hours in Group 1 and Group 2 respectively (p<0.01). Similarly, the mean duration of hospital stay was 2.68 days in Group 1 and 4.8 days in Group 2. The treatment cost was INR 850 and INR 1650 while social cost was INR 1250 and 2600 in Group 1 and 2 respectively. They noted that *S. boulardii* reduced the duration, frequency and hospital stay of diarrhoea thereby reducing the treatment and social costs. Morgambal P. *et al.*,<sup>12</sup> conducted a systematic review and noted that *Saccharomyces boulardii* showed a potential benefit in treating acute GE in the paediatric patient. A dose of 250 mg 1–2 times per day for up to 5 days showed some benefit and appears safe. Larger, rigorous RCTs are needed to investigate the efficacy and safety of *Saccharomyces boulardii* in order to offer specific treatment guidelines. *S. boulardii* can be administered simultaneously to prevent antibiotic-associated diarrhea owing to its resistance to most antibiotics. However, a recent randomized controlled trial reported *S. boulardii* was not effective in preventing the development of antibiotic-associated diarrhea in elderly hospitalized patients.<sup>13</sup> Certain probiotics have demonstrated efficacy and are widely used for preventing and treating medical conditions involving the gastrointestinal tract in children. *Lactobacillus rhamnosus* GG (LGG), *L. reuteri* and *Saccharomyces boulardii* are the best studied probiotics and have been shown to be most effective as treatment if introduced early in the course of the disease.

## CONCLUSION

*Saccharomyces boulardii* is effective in reducing the duration of diarrhea and hospital stay in children with acute gastroenteritis. We noted reduced duration of diarrhoea, less mean frequency of stools, improved consistency of stools in the *Saccharomyces boulardii* group. Children treated with *Saccharomyces boulardii* had a significantly shorter duration of hospital stay as compared to the children from other group.

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