Efficacy of Probiotic *Saccharomyces boulardii* as an Adjuvant Therapy in Acute Childhood Diarrhoea

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Abstract

**Introduction:** Administration of *S. boulardii* in addition to rehydration therapy in diarrhea found to be beneficial in many aspects owing to a variety of causes and importantly it is was not associated with any adverse effects.

**Material and Methods:**
We conducted a prospective study of children suffering from acute diarrhoea, at a private tertiary care hospital. Children were divided into 2 groups randomly as per odd (Group 1) and even (Group 2) bed allotted in indoor at the time of admission: Group 1 included children on oral rehydration therapy (ORT) + Zinc + *Saccharomyces boulardii* (Probiotic 5 billion CFU twice daily) and Group 2 comprised of children on ORT+ Zinc. Our objective was to systematically review data on the effect of *S. boulardii* on acute childhood diarrhoea.

**Results:**
Out of a total of 126 children less than 2 years, 2-6 years and 6-14 years were 72 (57.14%), 42(33.33%) and 12(09.52%) respectively. 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.

**Conclusion:** This study shows that *S. boulardii* reduced the duration, frequency and hospital stay of diarrhoea thereby reducing the treatment and social costs.

**Key words:** Childhood diarrhoea, *Saccharomyces boulardii*, therapy.

Introduction

Diarrhoea is defined by the World Health Organization (WHO) as 3 or more passage of loose or watery stool and increments in stool frequency in a 24-hour period. Diarrhoea 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 ¹. 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 ²,³. The most common cause of diarrhoea is a gut infection (viral, bacterial, and parasitic). Other causes include...
adverse effects of medicine (especially antibiotics), infections not associated with the gastrointestinal tract, food poisoning, and allergy4. Diarrhoea is also categorized into acute (lasts several hours or days) and persistent (continues for 14 days or longer). Globally, ~1.7 billion cases of diarrheal disease occur every year, resulting in nearly 760,000 deaths in children younger than age five years, especially in developing countries5. In many clinical trials, S. boulardii has been shown to be effective in prevention and management of diarrhoea, especially antibiotic-associated diarrhea. S. boulardii can be administered simultaneously to prevent antibiotic-associated diarrhea owing to its resistance to most antibiotics6. The Cochrane review of meta-analysis has shown a decrease in duration and frequency of acute diarrhoea within 24 hours6,7. The efficacy of S. boulardii has been documented in various types of diarrhoea such as the prevention of antibiotic-associated diarrhoea8.

Aims and Objectives: To evaluate the role of S. boulardii related to: Duration of diarrhoea, frequency of diarrhoea, complications, hospital stay the direct and indirect costs involved.

Material and Methods

We studied 126 children admitted to the paediatric ward of a private tertiary care hospital. Cases were divided into two groups: Group 1 comprised of children who were administered oral rehydration therapy (ORT) with Zinc and S. boulardii (5 billion CFU in each sachet twice daily) and Group 2 was treated with ORT and Zinc. ORS and diet was given to both groups with no difference. It was a prospective, randomized, open label, comparative study. Data was filled in a pre-designed preform and statistical analysis was done using the Chi-square test and sample t test of proportion.

Children were administered 5 billion sachetS. boulardii/12 hourly for 5 days. They were followed up at 6 hours, 12 hours, 24, 36, 48, 60 and 72 hours.

Institutional Ethics Committee approval was taken and an informed consent with assent was obtained before enrolling the subjects in the study.

Inclusion Criteria included: Age between 6 months to 14 years, children with mild to moderate dehydration and no prior probiotic administration.

Exclusion Criteria included: Age < 6 months, cases with chronic and severe diarrhoea, children transferred to PICU and parents refusal to participate in the study.

Safety was evaluated by assessing the incidence and type of adverse effects such as increase in blood pressure, Electrolyte imbalance and pulse rate, physical examination and clinical laboratory tests, i.e. complete blood count, serum creatinine, and stool examination both microscopy and routine, on day 1 and day 3.

Results

We studied 126 cases of which Group 1 and Group 2 comprised of 64 cases and 62 cases respectively of whom 88 (63.4%) were males and 38 (36.6%) were females Table1. Children less than 2 years were 72 (57.14%); 2-6 years were 42 (33.33%) and 6-14 years were 12 (9.52%) Table1. The duration of diarrhoea in Group 1 was 26.31 hours and Group 2 was 48.71 hours (p<0.01) Fig-1. The frequency of stool in Group 1 and Group 2 reduced within 24 and 60 hours respectively (p<0.01) Fig-2. The mean duration of hospital stay was 2.68 days when compared to 4.8 days in Group 1 and Group 2 reduced within 24 and 60 hours respectively (p<0.01) Fig-4. The cost of treatment was INR 850 in Group 1 and INR 1680 in Group 2 (Fig 3). The indirect and social cost was INR 1250 and INR 2600 in the above groups respectively (Fig5). Cost of each sachet of S. boulardii was rupees 35 INR and was purchased by parents from pharmacy.

Table 1: Age and sex distribution of 126 patients in the study

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Sex</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2 year</td>
<td>52</td>
<td>20</td>
<td>72</td>
</tr>
<tr>
<td>2-6 year</td>
<td>28</td>
<td>14</td>
<td>42</td>
</tr>
<tr>
<td>6-14 year</td>
<td>08</td>
<td>04</td>
<td>12</td>
</tr>
</tbody>
</table>
**Fig 1:** Hours required improving the consistency of stool or duration of diarrhoea

**Fig 2:** Comparison of frequency of stool in patient with and without probiotics

**Fig 3:** Treatment cost (Rupees)
Discussion

Saccharomyces boulardii is beneficial yeast that was first isolated from lychee and mangosteen fruit. In many clinical trials, *S. boulardii* has been shown to be effective in prevention and management of diarrhea, especially antibiotic-associated diarrhea. *S. boulardii* can be administered simultaneously to prevent antibiotic-associated diarrhea owing to its resistance to most antibiotics. *Clostridium difficile*–associated enteropathies, chronic diarrhea caused by *Giardia* and amebiasis, prevention of traveler’s diarrhea, prevention of diarrhea in critically ill tube-fed patients and treatment of human immunodeficiency virus–associated diarrhea. However, the major indication is acute diarrhea in children and adults. An increasing number of potential health benefits are being attributed to probiotic treatments. *S. boulardii* is a live yeast used extensively as a probiotic and often marketed as a dietary supplement. Several mechanisms of action have been identified directed against the host as well as pathogenic microorganisms and include regulation of intestinal microbial homeostasis, interference with the ability of pathogens to colonize and infect the mucosa, modulation of local and systemic immune responses, stabilization of the gastrointestinal barrier function and induction of enzymatic activity favoring absorption and nutrition. The normal gut micro biota in acute diarrhea is disrupted in children and in the present study; we have tried to highlight the therapeutic efficacy of *S. boulardii*. The duration of diarrhoea was significantly altered in Group 1: 26.31 hours when compared to Group 2: 48.71 hours (*p*<0.001, *t* test= 16.014) (Fig 1). The result of *t* test revealed that the mean frequency of stool in Group 1 was significantly less as compared to Group 2 (*p*<0.001) and improved within 24–36 hours, (Fig 2) thus preventing fluid loss and electrolyte imbalance. The patients in Group 1 were discharged within 3 to 4 days while Group 2 had a longer stay of 6 to 8 days (*p*<0.001). *S. boulardii* has been tested for clinical efficacy in several types of acute gastrointestinal conditions, including antibiotic-associated diarrhea (*AAD*), *Clostridium difficile* infection (*CDI*), acute diarrhea, enteral nutrition-related diarrhoea, traveller’s diarrhoea and Helicobacter pylori infection. *S. boulardii* has been tested for clinical efficacy in several types of chronic diseases including Crohn’s disease.
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ulcerative colitis, irritable bowel syndrome (IBS), parasitic infections and human immunodeficiency virus (HIV)-related diarrhea. Interleukin (IL-8) is a pro-inflammatory cytokine secreted during an E. coli infection in the gut. S. boulardii has been shown to decrease the secretion of IL-8 during an E. coli infection; S. boulardii could have a protective effect in inflammatory bowel disease. The trophic effect on enterocytes has been shown to increase levels of disaccharidases such as lactase, sucrase, maltase, glucoamylase, and N-aminopeptidase in the intestinal mucosa of humans and rats. This can lead to the increased breakdown of disaccharides into monosaccharides that can then be absorbed into the bloodstream via enterocytes. This can help in the treatment of diarrhea, as the level of enzymatic activity has diminished and carbohydrate cannot be degraded and absorbed. S. boulardii induces the secretion of immunoglobulin A in the small intestine of the rat. Previous reports reveal the cost of treatment was INR 779 in probiotic group (Bacillus clausii) and INR 944 in without probiotic group. Similarly the indirect and social cost was INR 937 and INR 1409 in the above groups respectively. In our present study treatment and indirect social cost closely matching the previous study.

Conclusions

Administration of S. boulardii in addition to rehydration therapy in diarrhea found to be beneficial in many aspects owing to a variety of causes and importantly it was not associated with any adverse effects as shown in our present study.

Recommendation: Further clinical studies are needed to identify different causes of diarrhea for each participant, and especially more studies should be performed in children who have bacterial and parasitic diarrhea and efficacy of S. boulardii in each group. Limitation of this study was, it was a hospital based study, and needs large population based study to get more convincing results.

References

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