Clinical Efficacy Comparison of *Saccharomyces Boulardii* and Lactic Acid as Probiotics in Acute Pediatric Diarrhea

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**ABSTRACT**

**Objective:** To compare the efficacy of *Saccharomyces boulardii* and lactic acid producing probiotics in addition to usual treatment regimen to cure diarrhea among children (6 months to 5 years of age).

**Study Design:** Randomized controlled trial.

**Place and Duration of Study:** Department of Pediatrics, Sheikh Zayed Hospital, Lahore, from February to July 2015.

**Methodology:** Children suffering from acute diarrhea were orally administered *Saccharomyces boulardii* and lactic acid producing probiotics for 5 days. The efficacy of administered probiotics was monitored. Patients were given *Saccharomyces boulardii* and lactic acid producing probiotics randomly to remove the bias.

**Results:** Two hundred patients randomly selected for trials; out of which, 100 were treated with *Saccharomyces boulardii* while the other 100 were supplemented with lactic acid concomitantly along with conventional diarrhea treatment. Results indicated that *Saccharomyces boulardii* treatment group has significantly higher efficacy rate (45%) compared to lactic acid producing probiotics (26%).

**Conclusion:** This study concluded that *Saccharomyces boulardii* has a better efficacy compared to lactic acid and may be adopted as a probiotic of choice.

**Key Words:** Acute diarrhea. Children. *Saccharomyces boulardii*. Lactic acid producing probiotics. Additive efficacy.

**INTRODUCTION**

Diarrhea is defined as three or more passages of loose or watery stool and frequent defecation in a 24-hour period. Acute diarrhea has been reported as a second leading cause of death (after pneumonia) in children of age less than 5 years. Diarrhea is a worldwide health issue accounting for an estimated 5000 deaths per day and 1.9 million annual losses of lives at childhood. On the basis of clinical and epidemiologic parameters, episodes of diarrhea are classified into three categories: acute diarrhea, dysentery, and persistent diarrhea. Acute diarrhea is defined as the presence of three or more loose, watery stools within a 24-hour period. In under-developed countries, enteric bacteria such as *Escherichia coli*, *Campylobacter*, *Shigella*, *Vibrio cholerae*, *Salmonella*, viruses such as *Rotavirus*, *Human calicivirus*, and parasites like *Cryptosporidium parvum*, *Giardia intestinalis*, *Entamoeba histolytica*, *Cyclosporacayetanensis* are major pathogens to cause diarrhea. Diarrhea results in higher amount of water losses that may lead to death, if left untreated. Oral rehydration solutions (ORS) have been found to decrease the incidence of mortality and morbidity caused by diarrhea; but ORS did not have any effect on the duration of the disease, consistency of the stools, and gastrointestinal flora.

Probiotics are living microorganisms, commensal of intestinal tract, and if required, can be administered orally to change the micro-flora balance in the gut positively. Probiotics are effective in inhibiting the growth of harmful bacteria, promote good digestion, boost immune function, and increase resistance to infections. Most common probiotics include strains of lactic acid bacilli (*Lactobacillus* and *Bifidobacterium*), nonpathogenic strains of *Escherichia coli* (*E. coli*), *Clostridium butyricum*, *Streptococcus salivarius* and *Saccharomyces boulardii*. Also under development are the strains of bacteria that have been genetically engineered to secrete immuno-modulators, such as interleukin-10, trefoil factors, or defensins, or express altered surface proteins such as lipoteichoic acid, which have the potential to modulate the immune system. Lactic Acid Bacteria (LAB) comprise a wide range of genera and include a considerable number of species. These bacteria are able to produce lactic acid as the main end-product of the fermentation of carbohydrates. These acid producing bacteria can also be used as probiotics.

*Saccharomyces boulardii* is a non-pathogenic probiotic yeast and has the ability to tolerate gastric acidity and antibiotics. Previously, it has been reported that *Saccharomyces boulardii* and lactic acid producing bacteria have effectiveness of 46.4% and 22.2%, respectively. In Pakistan, both probiotics are used to treat the acute diarrhea, but the scientific studies and numerical data is still lacking about the comparative effectiveness of these probiotics in Pakistan as well as in international studies. Therefore, a prospective study was designed to compare the efficacy of *Saccharomyces*...
**boulardii** and lactic acid producing bacterial probiotics in the current regimens, so that a better choice can be made to treat acute diarrhea in children.

**METHODOLOGY**

This randomized controlled trial was carried out using non-probability consecutive sampling method and it was adapted to all subjects (200) included in this study; and the patients were divided equally to *Saccharomyces boulardii* (group A) and lactic acid administered groups (group B). Children of both genders from 6 months to 5 years of age, suffering from diarrhea (less than 14 days), were included in this study. Children with severe dehydration, malnutrition, immunodeficient or already treated with anti-diarrheal antibiotics or probiotics were excluded from the study.

After prior approval from hospital ethical committee, children from 6 months to 5 years of age were admitted to the ward via OPD and emergency. A written informed consent was obtained from the patients’ parents/guardian. Baseline tests like CBC, urine routine examination was done. The patients fulfilling the inclusion criteria were included in the study. Patients’ comfort and temperature maintenance were kept in consideration. Patients were given *Saccharomyces boulardii* and lactic acid producing probiotics randomly to eliminate the personal bias. Those patients receiving *Saccharomyces boulardii* were named as group 'A' and those receiving lactic acid producing probiotics were labeled as group 'B'. The dose for probiotics was administered orally twice a day in 20 ml of water for 5 days. Dosage for less than one year of age was 150 mg, and 250 mg for children older than two years, divided into two doses for each of *Saccharomyces boulardii* and lactic acid producing probiotics groups. The subjects were kept on same doses for 5 days. Efficacy of both probiotics was assessed as per operational definition (frequency and consistency of stools/day). In addition to probiotics, all patients were treated with intravenous antibiotics (ceftrioxne) and oral rehydration therapy as per hospital protocol.

Statistical analysis was done using SPSS version 16. Frequencies and percentages were calculated for gender and efficacy of administered probiotics. Chi-square test was applied to compare the efficacy of both groups. Data was stratified for age, gender, gestational, weight, duration of diarrhea and socioeconomic status to deal with effect of modifiers. Post-stratification Chi-square test was applied. P-value of <0.05 was considered as significant.

**RESULTS**

A total of 200 cases (100 in each group), fulfilling the inclusion criteria, were enrolled to compare the efficacy of *Saccharomyces boulardii* and lactic acid producing probiotics in addition to usual treatment to treat acute diarrhea in children of age 6 months to 5 years.

Age distribution of the patients demonstrated that 61% (n=61) in group A and 62% (n=62) in group B were between 6m-3years of age; while 39% (n=39) in group A and 38% (n=38) in group B were between 4-5 years of age. Similarly, gender-based distribution of patients treated with *Saccharomyces boulardii* (group A) and lactic acid (group B) showed that 48% (n=48) in group A and 57% (n=57) in group B were males; while 52% (n=52) in group A and 43% (n=43) in group B were females.

Comparison and efficacy of *Saccharomyces boulardii* (group A) with lactic acid probiotics (group B) to treat diarrhea in children is shown in Table I. Results demonstrated that 45% (n=45) in group A and 26% (n=26) in group B were treated effectively. The results demonstrated a significant effect of treatment (p=0.004) as shown in Table I.

To evaluate the treatment efficacy in relation to age, subjects were further divided into two age groups (6 months to 3 years and 4-5 years of age). Results demonstrate that *Saccharomyces boulardii* efficacy was significantly higher (p=0.01 and p=0.001, respectively, for these two age groups) compared to lactic acid treated patients. Furthermore, *Saccharomyces boulardii* was more effective when administered in 4-5 years age group of patients, as shown in Table II. No significant effects

**Table I:** Comparison of *Saccharomyces boulardii* (Group-A) and lactic acid (Group-B) efficacy to treat the diarrhea patients.

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>Group-A (n=100)</th>
<th>Group-B (n=100)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>%</td>
<td>No. of patients</td>
<td>%</td>
</tr>
<tr>
<td>Yes</td>
<td>45</td>
<td>45</td>
<td>26</td>
</tr>
<tr>
<td>No</td>
<td>55</td>
<td>55</td>
<td>74</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

**Table II:** Age-based stratification for efficacy of *Saccharomyces boulardii* (Group-A) and lactic acid (Group-B).

<table>
<thead>
<tr>
<th>Group</th>
<th>Age group</th>
<th>Efficacy</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>6 m - 3 year</td>
<td>Yes</td>
<td>31</td>
</tr>
<tr>
<td>B</td>
<td>6 m - 3 year</td>
<td>No</td>
<td>18</td>
</tr>
<tr>
<td>A</td>
<td>4 - 5 years</td>
<td>Yes</td>
<td>14</td>
</tr>
<tr>
<td>B</td>
<td>4 - 5 years</td>
<td>No</td>
<td>27</td>
</tr>
</tbody>
</table>

**Table III:** Stratification for efficacy with regard to duration of diarrhea.

<table>
<thead>
<tr>
<th>Group</th>
<th>Duration 1-7 days</th>
<th>Efficacy</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Yes</td>
<td>21</td>
<td>32</td>
</tr>
<tr>
<td>B</td>
<td>No</td>
<td>15</td>
<td>34</td>
</tr>
<tr>
<td>Duration 7-13 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>Yes</td>
<td>24</td>
<td>23</td>
</tr>
<tr>
<td>B</td>
<td>No</td>
<td>11</td>
<td>40</td>
</tr>
</tbody>
</table>
Therefore, this study was planned to compare the efficacy of Saccharomyces boulardii with routinely used lactic acid producing probiotic in children suffering from diarrhea. Saccharomyces boulardii is a 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.12

Sahar Feizizadeh and others have systematically reviewed the effect of S. boulardii on acute childhood diarrhea.13-15 Pooling data from trials showed that S. boulardii significantly reduced the duration of diarrhea, stool frequency on day two after intervention compared with control.16 S. boulardii is safe and has clear beneficial effects in children who have acute diarrhea,17-20 and the present results are in agreement with this study. In Pakistan, both probiotics are used to treat the acute diarrhea, but evidence was lacking about the comparative effectiveness of these probiotics in Pakistan as well as in international studies. In this regard, these results suggest that S. boulardii is significantly more effective than lactic acid producing bacteria. Previously, it has been reported that Saccharomyces boulardii and yogurt fluid have effectiveness of 46.4% and 22.2%, respectively,10 but the authors concluded that the duration of diarrhea was much shorter in the S. boulardii-treated group compared to yogurt fluid group. Importantly, majority of patients defecated normal stools on day 3 and our findings are in accordance with these results. Therefore, this prospective study compared the efficacy of Saccharomyces boulardii with lactic acid producing bacterial probiotics and recorded a better choice, which the physicians may make to treat the acute diarrhea.

DISCUSSION

Diarrhea is defined as loose or watery stools with frequent bowel movements (BMs) which may lead to dehydration and ultimately to death, if left untreated. Diarrhea may also contain blood or mucus, depending on severity and etiology. Identifying mild diarrhea may be difficult because in healthy children, the number and consistency of BMs vary with age and diet. Besides conventional and known methods to treat diarrhea, pediatricians and scientists are interested to explore the new horizons to treat the same more effectively and efficiently.11 Therefore, this study was planned to compare the efficacy of Saccharomyces boulardii with routinely used lactic acid producing probiotic in children suffering from diarrhea.

CONCLUSION

This study concludes that Saccharomyces boulardii is more effective than lactic acid producing probiotics when given along with usual treatment to treat acute diarrhea in children of age 6 months to 5 years. These results should be further confirmed with a large scale placebo controlled clinical trials evaluating the efficacy of Saccharomyces boulardii and other routinely used probiotics.

Disclosure: The manuscript is the original study of the corresponding author for FCPS dissertation.

REFERENCES

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