

Efficacy of *Saccharomyces Boulardii* Vs Zinc Supplementation in the Management of Acute Childhood Diarrhoea

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ABSTRACT

The purpose of this trial was to evaluate the clinical efficacy and effectiveness of *Saccharomyces boulardii* compared with zinc supplementation in acute non-bloody diarrhea in children. This randomized, prospective clinical trial included a total of 150 children. Group A (n=75) received *S. boulardii* and group B (n=75) received zinc. The mean age of the patients in group A was 13.0±6.5 months and in group B was 14.0±5.6 months. In group A, at day-3, the mean grade of stool was 2.0±0.9. In group B, at day-3, the mean grade of stool was 2.3±1.1. In group A, at day-3, the mean frequency of stool was 2.8±1.7. In group B, at day-3, the mean frequency of stool was 2.3±1.1. In group A, 60(80%) patients had efficacy of treatment and in group B, 45(60%) patients had efficacy of treatment. It is concluded from this study that *Saccharomyces boulardii* is efficacious in more cases when used for the management of acute childhood diarrhea as compared to zinc supplementation.

Keywords: Acute diarrhoea, efficacy, *Saccharomyces boulardii*, Zinc supplementation, Lahore

INTRODUCTION

Gastroenteritis of infectious origin remains a worldwide problem of healthcare with about four billion diarrheal episodes each year¹. Diarrhea is defined by the World Health Organization (WHO) as 3 or more passages of loose or watery stool and increments in stool frequency in a 24-hour period. The most common cause of diarrhea is a gut infection (viral, bacterial, and parasitic). Other causes include side effects of medicine (especially antibiotics), infections not associated with the gastrointestinal tract, food poisoning, and allergy.² Diarrhea is also categorized into acute (lasts several hours or days) and persistent (continues for 14 days or longer). 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 immediately². Globally, ~1.7 billion cases of diarrheal disease occur every year, resulting in nearly 760 000 deaths in children younger than age 5 years, especially in developing countries³. Acute diarrhoea is a leading cause of child mortality in developing countries, accounting for 1.5–2 million deaths in children under five years. In consequence, the economic impact of the disease and its treatment are of considerable importance³.

Treatment of acute diarrhoea consists of maintenance of rehydration by giving oral rehydrating solution or intravenous fluids as well as zinc supplementation as per the WHO guidelines.

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Treatment with oral rehydration solutions (ORS) has reduced significantly the incidence of mortality and morbidity caused by diarrhea but ORS does not shorten the duration of diarrhea, does not change the consistency of the stools, and it does not normalize gastrointestinal flora³.

Probiotics are living microorganisms that survive in the gastrointestinal tract and, when ingested in sufficient large amount, confer a health benefit on the host. There is evidence that selected strains of probiotics decrease the duration of acute diarrhea.⁴ Kelesidis et al.⁵ showed that *S. boulardii* significantly reduced the duration of diarrhea (mean difference [MD], -19.7 hours; 95% confidence interval [CI]), stool frequency on day 2 (MD, -0.74; 95% CI) and day 3 (MD, -1.24; 95% CI), the risk for diarrhea on day 3 (risk ratio [RR], 0.41; 95% CI) and day 4 (RR, 0.38; 95% CI) after intervention compared with control⁵. The multiple mechanisms of action of *S. boulardii* and its properties may explain its efficacy and beneficial effects in acute and chronic gastrointestinal diseases that have been confirmed by clinical trials⁵.

In addition, in response to mounting evidence supporting the efficacy and effectiveness of therapeutic zinc supplementation for diarrhea among children under five years of age, the World Health Organization (WHO) and the United Nation's Children Fund (UNICEF) issued a global recommendation in 2004, which advised zinc supplementation in addition to oral rehydration solution (ORS) for the treatment of all diarrhea episodes among children <5 years of age⁶. Chinese and Indian studies reported the effect of therapeutic zinc supplementation on decreased episode duration, stool output, stool frequency,

hospitalization duration and proportion of episodes lasting beyond three and seven days. Those studies yielded an overall 26% (95% CI: 20%–32%) reduction in the estimated relative risk of diarrhea lasting beyond three days among zinc-treated children⁶. Studies conducted in and outside China also report reductions in morbidity as a result of oral therapeutic zinc supplementation for acute diarrhea among children less than five years of age⁶.

There are different treatment modalities available in Pakistani market including probiotics (*Saccharomyces boulardii*) and zinc supplementation, but the efficacy & superiority over each other is not established with certainty. At the same time whatever information is available none is conducted over Pakistani children so far. Hence, there is a need to study the efficacy of *Saccharomyces boulardii* versus zinc supplementation in the management of acute childhood diarrhoea in Pakistani children.

MATERIALS AND METHODS

This randomized, prospective clinical trial over 6 months (from 01-11-2010 to 30-04-2011) period was conducted in children who were admitted with acute diarrhea in the Department of Pediatrics Sir Ganga Ram Hospital, Lahore. Acute diarrhea was defined as the presence of 3 or more liquid or loose stools per day lasting for less than 14 days. Sample of 150 cases, 75 cases in each group was calculated with 80% power of test, 2.5% margin of error and taken expected percentage of efficacy i.e. 76% in patients treated with *S. boulardii* and 53.8% of patients treated with zinc supplementation in addition to ORS presenting with acute watery diarrhoea.

Inclusion criteria:

Patients with diarrhea (as per definition) admitted in pediatric ward.

Patients of either sex and are between six months to two years of age.

Only patients with no dehydration and some dehydration according to WHO criteria were selected.

Exclusion criteria:

Patients with history of post diarrheal abdominal distention (assessed clinically).

Patients having serious co-morbid conditions like cardiac (history examination, CXR, ECG), renal (serum creatinine >1mg/dl, BUN) or respiratory disease (assessed clinically and by taking history, CXR).

Patients with diarrhea who have blood in their stool

After approval from Hospital Ethical Committee, a total of 150 admitted patients of acute watery diarrhoea (fulfilling the inclusion criteria) were selected from Department of Paediatrics, Sir Ganga

Ram Hospital Lahore. Informed consent was obtained from parents of all the patients. The diagnosis was confirmed on the basis of history, duration and frequency of diarrhoea. The patient's age, sex and address were obtained. The patients were randomly divided into two groups (A & B) by lottery method. Both groups were managed with oral rehydration therapy as per WHO criteria. Group A received *saccharomyces boulardii* (250mg BID for five days) diluted in 10ml ORS while patients in group B were given 20mg of zinc once daily for three days. The patients were assessed daily from 1 to 3 days for effectiveness of treatment. The reduction of diarrhoea of 2 or less stools of grade two or less per days was considered as effectiveness of treatment.

Statistical analyses: The descriptive statistical analysis included examinations of means, standard deviations, frequencies, ranges, and percentages. Chi Square test was applied to compare efficacy of treatment between the two groups. A p-value of 0.05 or less was taken as significant. The statistical packages SPSS (Version 20) and MS Excel (MS Office 2010) were used.

RESULTS

This study comprised of a total of 150 patients, 75 patients in each group. The mean age of the patients in group A was 13.0±6.5 months and in group B was 14.0±5.6 months. In group A, there were 46 (61.3%) male and 29 (38.7%) female patients with male to female ratio of 1:1.6. In group B, there were 42 (56%) male and 33 (44%) female patients with male to female ratio of 1:1.3 (Table 1).

Table 1: Distribution of patients by gender

Gender	Group A	Group B
Male	46(61.3%)	42(56%)
Female	29(38.7%)	33(44%)
Male to female ratio	1:1.6	1.13

In the distribution of patients by stool grades, in group A, at day-1, the mean grade of stool was 4.4±0.7, at day-2 the mean grade of stool was 3.2±0.8 and at day-3, the mean grade of stool was 2.0±0.9. In group B, at day-1, the mean grade of stool was 4.3±0.7, at day-2 the mean grade of stool was 3.6±0.7 and at day-3, the mean grade of stool was 2.3±1.1 (Fig. 1).

Fig. 2 shows the distribution of patients by stool frequency. In group A, at day-1, the mean frequency of stool was 7.9±2.2, at day-2 the mean frequency of stool was 5.0±1.8 and at day-3, the mean frequency of stool was 2.8±1.7. In group B, at day-1, the mean frequency of stool was 8.3±2.4, at day-2 the mean frequency of stool was 5.9±2.1 and at day-3, the mean frequency of stool was 2.3±1.1 (Fig. 2).

Fig. 1. Frequency of Meningitis in neonatal patients with late-onset sepsis.

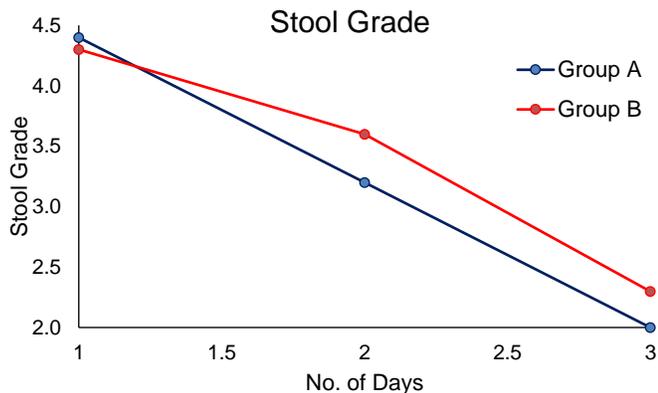


Fig.2:

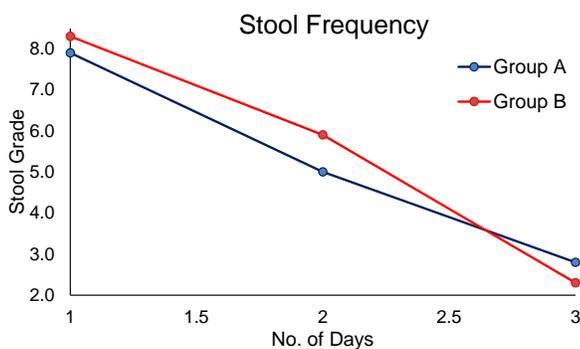
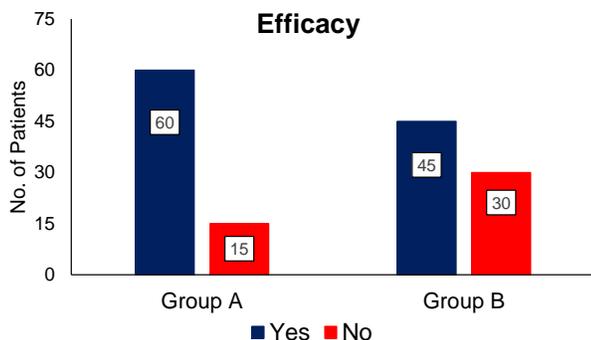


Fig. 3 indicates the distribution of patients by efficacy of treatment. Our results indicate that in group A, a total of 60(80%) patients had efficacy of treatment whereas 15(20%) patients had not efficacy of treatment. In group B, there were 45(60%) patients had efficacy of treatment and 30(40%) patients had not efficacy of treatment (Fig. 3).

Fig.3:



DISCUSSION

Probiotics are live microorganisms that survive in the gastrointestinal tract and have a health benefit on the host. *S. boulardii* is a non-pathogenic probiotic yeast,

which is naturally resistant to gastric acidity and antibiotics. Extensive research has shown a significant reduction of the duration of acute watery diarrhea of infectious origin¹. Also bloody diarrhea due to amebiasis in children is shortened in comparison to placebo when *S. boulardii* is added to metronidazole¹. Similarly, the findings of previous studies confirm and highlight the benefits of therapeutic zinc supplementation for diarrhea among children under five years of age in low- and middle-income countries. The effects of zinc treatment, which include reductions in episode duration, stool output, stool frequency and length of hospitalization, were consistent across many Asian studies⁶.

The aim of this prospective clinical trial was to investigate the therapeutic efficacy and safety of *S. boulardii* versus zinc supplementation in treating acute diarrhea in children. The results showed that *S. boulardii* showed improvement in terms of both time to response and response rate. Acute diarrhea in children is very often self-limiting within few days. However, children are in danger of developing dehydration and a deteriorating general health. Therefore, an effective antidiarrheal treatment would be beneficial. Several investigations have been carried out with probiotics for the treatment of acute gastroenteritis, and different meta-analyses and systematic reviews have been published in this field. All of these have demonstrated the efficacy of probiotics in treating or preventing diarrhea. On an average, the treatment of diarrhea with lactobacilli, bifidobacteria and/or *S. boulardii* shortened the duration of diarrhea by 0.5-1.5 days^{5,7}.

Szajewska and Mrukowicz reviewed ten randomized, double-blind, placebo-controlled studies and concluded that the administration of probiotics led to a substantial reduction in the duration of acute diarrheal symptoms, an average of 20 h.⁸ In the present trial, 150 patients were enrolled, and who completed the trial successfully. Primary outcome analyzed in this study is duration of diarrhea, frequency and consistency of stools.

Zinc is a trace element essential for growth and development, cellular immunity, metalloenzymes and stabilizes cell membrane. Zinc deficiency is more common in malnourished and immunocompromised children and causes sever and prolonged diarrhea, dry scaly skin and hair loss. Lambertis et al⁶ evaluated that zinc supplementation reduces the duration and severity of diarrhea and found that 53.8% children were found effective with the treatment of zinc supplementation.⁶ *Saccharomyces boulardii* shortens the duration of diarrhea and normalizes stool consistency and frequency. The efficacy of *S. boulardii* was found in 76% children on day^{3,9}.

Acute diarrhoea is a major problem of Pakistani children and is associated with poor hygiene and sanitation. Immuno-compromised and malnourished children are at highest risk. Lack of breast feeding, unhygienic bottle-feeding practices, and uneducated mothers put infants at risks. In our study in group A, the efficacy of treatment was found in 80% patients. As compared with the study of Htwe et al.¹⁰ the efficacy of treatment *S. boulardii* group was found in 76% patients, which is comparable with our study. In group B, the efficacy of treatment was found in 60% patients. As compared with the study of Shimelis et al.⁹ zinc supplementation reduces the duration and severity of diarrhea and found that 53.8% children were found effective with the treatment of zinc supplementation, which is comparable with our study⁹.

On the above discussion, it is concluded both the treatment modalities are effective in the management of acute watery diarrhoea, but *saccharomyces boulardii* is significantly more effective than zinc supplementation in the treatment of acute watery diarrhoea.

CONCLUSION

In conclusion, the effect of *Saccharomyces boulardii* was comparable to zinc supplementation in the treatment of acute non-bloody diarrhea in children. Although the overall duration of diarrhea in both groups was slightly different, normalization of stool composition and frequency was more rapid in the *S. boulardii* group. On day 3, significantly more patients were cured in the *S. boulardii* group than in the zinc supplementation group. It is concluded that *Saccharomyces boulardii* is efficacious in more cases when used for the management of acute childhood diarrhea as compared to zinc supplementation. However, these results should be confirmed with a large scale controlled clinical trial evaluating the efficacy of commercialized formulation of *Saccharomyces boulardii*.

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