Comparison of efficacy of *Saccharomyces boulardii* strain in the treatment of acute diarrhea in children: A prospective, single-blind, randomized controlled clinical trial

Sir,

Probiotics are defined as "live microorganisms which when

administered in adequate amounts confer a health benefit on the host"[1] and used as an adjunctive in diarrhea. They are gaining popularity without established efficacy[2] or with mild benefit regardless of strain[3] or depending on strain.[4]

There are different probiotics available in the Indian market, but the efficacy and superiority over each other is not established with certainty.

The sample size was calculated from the data shown in previous studies.[5] Accordingly with predictive power of 90%, an alpha error of 5, in each group 35 patients were included.

After approval from Institutional Ethical Committee, the study was conducted from July 2009 to July 2011 as a prospective, parallel, single-blind, randomized controlled clinical trial with allocation ratio 1:1, in a tertiary care hospital attached with Medical College, including the children who were diagnosed as acute diarrhea [child having ≥3 unformed stool in last 24 h with a duration of <48 h] with no dehydration or some dehydration as per the WHO criteria by experts in pediatrics. Children with any concurrent chronic illness, severe, and very severe under nutrition (weight for age <60% of 50th percentile of CDC 2000 Standards), severe dehydration (as per WHO criteria) allergy or history of use of probiotic, antibiotic, or antidiarrheal in last 24 h were excluded. Non-infective cases were defined as acute diarrhea negative for *Vibrio cholarae* by a hanging drop method, *Entamoeba histolytica* and *Giarrdea lamblia* by stool microscopy examination. Children found positive for above organisms were excluded from the study. The study protocol was explained in detail to the parent and informed written consent was obtained.

Patients were assigned a study number corresponding to their entry in the trial. They were randomized by simple randomization with the help of computer-generated random numbers. As per the allocation, drugs were prescribed to the patients by the pediatrician. All children included in the study received oral rehydration solution (ORS) *ad libitum* (as much as required after passing of each stool or vomiting or both and whenever child demand for it) till resolution of diarrhea and zinc 10 mg/day in a child of <6 months and 20 mg/day for a child >6 months a day for 14 days.

Children in the study arm also received *Saccharomyces boulardii* 250 mg orally twice a day for 5 days as lyophilized

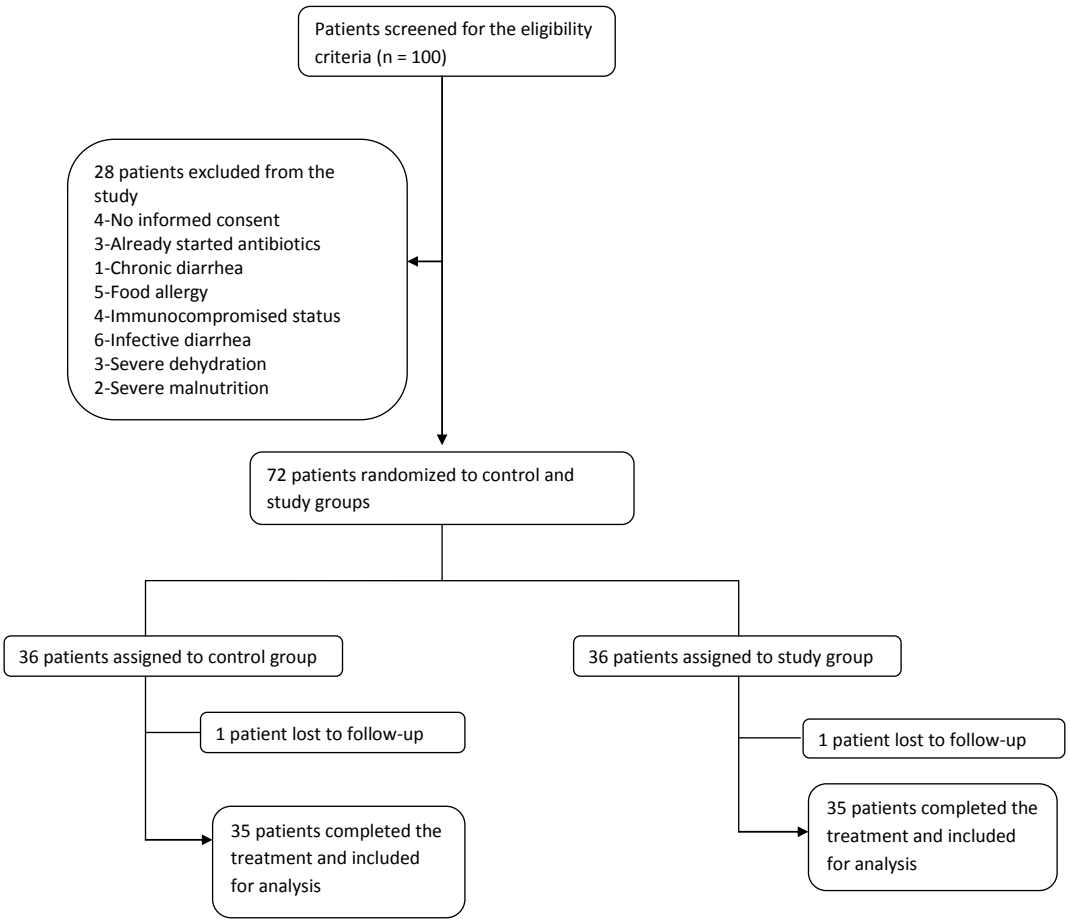

Figure 1: Patient flow through the trial

Table 1: Demographic characteristics and associated symptoms

Characteristic	Study group, *n*=35	Control group, *n*=35
Mean age±SD (months)	11.46±8.64	13.55±12.84
Mean weight±SD (kg)	7.98±3.21	8.51±3.81
Male	17 (48.6)	14 (40)
Female	18 (51.4)	21 (60)
Cold	2 (5.7)	1 (2.9)
Sneezing	0 (0)	1 (2.9)
Fever	16 (45.7)	13 (37.1)
Cough	2 (5.7)	2 (5.7)
Irritability	1 (2.9)	1 (2.9)
Pain in abdomen	5 (14.3)	7 (20)
Weakness	3 (8.6)	2 (5.7)
Some dehydration	3 (8.6)	4 (11.4)
No dehydration	32 (91.4)	31 (88.6)

Values in parentheses are percentages

powder in a sachet weighing 282.5 mg equivalent to 250 mg of yeast.

Each study day was defined as 24 h counted from the administration of drugs. Patient was monitored till recovery from diarrhea (passage of two consecutive formed stools as per the Kings scoring system[5] or having no stool till 12 h) and vomiting (duration in days in till the last episode of vomiting) or up to 14 days whichever occurred later. We also noted for any possible adverse events like hypersensitivity reactions.

A total of 100 patients were screened and 28 were excluded due to various reasons and one patient in each group lost follow-up [Figure 1], so 35 patients from each group were included in the analysis. The demographic statistics were described in Table 1. Difference between these parameters was nonsignificant between the study and control group and equally distributed. Associated symptoms such as cold, sneezing, cough, and irritability were treated by steam inhalation in both groups at home while fever was treated by paracetamol 5 mg/kg three times a day till temperature come to normal. For weakness, pain in abdomen and dehydration, ORS was given as per protocol. Gripe water was not given to any of the children. All these symptoms were reduced to nil by the end of 3 days in both groups.

Average time for recovery from loose motions, for the study group was 3.4 days ± 1.4 days and for the control group was 5.5 days ± 2.1 days (Z value = 4.9). Eleven patients in the study group and eight patients in the control group were also having the vomiting. Average time of recovery for the study group was 2.5 ± 1.2 days and for the control group was 3.3 ± 1.2 days (a value of two-tailed unpaired Student t-test at the degree of freedom of 7 was3.3, $P < 0.01$).

Reduction in duration of diarrhea by *S.boulardii* was found significant by some authors[6] while nonsignificant by others.[7] Grandy *et al*.[8] showed significant reduction in duration of vomiting by *S.boulardii*. In our study, the *S.boulardii* group have the significantly early recovery from diarrhea and vomiting and may have indirect benefits such as decrease absenteeism and less risk of postdiarrheal consequences like malnutrition.

The beneficial effects of *S.boulardii* may be due to antitoxin effect, antibacterial activity, modulation of intestinal flora, increasing the short chain fatty acids in lumen, increased enzymes against viral infection, increased IgA activity, and decreased synthesis of inflammatory cytokines.[9]

The strength of our study is to see the effect of probiotic in the Indian perspective as we may not extrapolate the results of western population in Indian children due to the higher breast feeding rate and different microbiological colonization.[10]

We conclude that addition of *S.boulardii* in treatment of acute diarrhea significantly reduce the duration of diarrhea as well as vomiting.

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REFERENCES

1. Joint FAO/WHO Working Group Report on Drafting Guidelines for the Evaluation of Probiotics in Food. London, Ontario, Canada: 2002. Available fromttp://www.who.int/foodsafety/fs_management/en/probiotic_guidelines.pdf. [Last accessed on 2012 Jun 16].
2. Reid G, Jass J, Sebulsky MT, McCormick JK. Potential uses of probiotics in clinical practice. Clin Microbiol Rev 2003;16:658-72.
3. Allen SJ, Okoko B, Martinez E, Gregorio G, Dans LF. Probiotics for treating infectious diarrhoea. Cochrane Database Syst Rev 2004;2:CD003048.
4. Canani RB, Cirillo P, Terrin G, Cesarano L, Spagnuolo MI, De Vincenzo A, *et al*. Probiotics for treatment of acute diarrhoea in children: Randomised clinical trial of five different preparations. BMJ 2007;335:340.
5. Kurugöl Z, Koturoğlu G. Effects of *saccharomyces boulardii* in children with acute diarrhoea. Acta Paediatr 2005;94:44-7.
6. Whelan K, Judd PA, Preedy VR, Taylor MA. Covert assessment of concurrent and construct validity of a chart to characterize fecal output and diarrhea in patients receiving enteral nutrition. JPEN J Parenter Enteral Nutr 2008;32:160-8.
7. Htwe K, Yee KS, Tin M, Vandenplas Y. Effect of *saccharomyces boulardii* in the treatment of acute watery diarrhoea in Myanmar children: A randomized

controlled study. Am J Trop Med Hyg 2008;78:214-6.
8. Grandy G, Medina M, Soria R, Terán CG, Araya M. Probiotics in the treatment of acute rotavirus diarrhoea. A randomized, double-blind, controlled trial using two different probiotic preparations in Bolivian children. BMC Infect Dis 2010;10:253.
9. McFarland LV. Systematic review and meta-analysis of *saccharomyces boulardii* in adult patients. World J Gastroenterol 2010;16:2202-22.
10. Shinjini B, Seema A, Piyush G. Management of acute diarrhoea: From evidence to policy. Indian Pediatr 2010;47:215-7.

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