

THERAPEUTIC EVALUATION OF *SACCHAROMYCES BOULARDII* IN CHILDREN WITH ACUTE DIARRHEA

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SUMMARY

A double-blind placebo-controlled study was designed to evaluate the efficacy and tolerability of the yeast *Saccharomyces boulardii* as an anti-diarrheal in 130 children aged 3 months to 3 years. Evaluation of the results after 24 h showed a reduction in the number of stools and an improvement in their consistency in the group treated with *S. boulardii*. Evaluation of the percentage clinical cure after 48 and 96 h showed significant differences from the control group. It is concluded that more cures were obtained in the group treated with *S. boulardii* than in the placebo group, without adverse reactions, and that this yeast can be used as an adjunct to oral rehydration in treating acute diarrhea in infants.

Keywords: *Saccharomyces boulardii*, therapeutic applications, acute diarrhea, treatment.

INTRODUCTION

Various studies show that acute diarrhea, particularly if not sanguinolent, is self-limiting in 90% of cases in the first week, and that basic management consists in preventing dehydration by administration of electrolyte solutions and maintaining nutrition, restricting the use of antimicrobials to specific cases (1-3).

Of the various drugs that have been used in the control of acute diarrhea, anticholinergics possess known side effects and are even contraindicated in the treatment of diarrhea (4). Others such as astringents have more of a placebo than a curative effect (5).

The use of yeasts in the treatment of acute diarrhea has yielded encouraging results as regards their anti-diarrheal activity and safety (6-9). *S. boulardii* (*Saccharomyces cerevisiae* Hansen CBS 5926) has functional properties similar to those of the normal intestinal flora and natural resistance to antibacterial agents, with the exception of antimycotics (10).

PATIENTS AND METHOD

A study was conducted from 1st April 1988 to 15th March 1989 of 130 patients of both sexes, aged 3 months to 3 years, with acute, non-sanguinolent diarrhea who were able to receive oral medication. They had no concomitant illnesses, were receiving no other medication, had not previously received antimicrobials antidiarrheals or other drugs which influence intestinal motility, and did not have severe electrolyte imbalance or dehydration. Patients who exhibited a deterioration or any concomitant illness during the study and required other drugs, or those whose parents wished to withdraw them from the study were excluded. The patients were divided into 2 groups according to a random table to set up a double-blind study. The patients in group I received 200 mg *S. boulardii* every 8h, diluted in 5 ml of cold liquid. Those in group II received 200 mg placebo (glucose) diluted in 5 ml of cold liquid every 8 h. All the patients were given WHO oral electrolytes and normal food for their age. The number of stools daily, the first day on which a formed stool was obtained after beginning treatment, and the occurrence of side effects were recorded on a form. The calculation of the size of the sample for 97% efficacy with an error of 5% was approximately 50 patients per group. Statistical analysis was carried out using the chi-square test and Student's t-test for two independent samples (11). The criterion of efficacy considered was fewer than 4 stools in 24 h and absence of liquid stools. The treatment was regarded as ineffective if the above requirements were not met or if the symptoms worsened during the study.

RESULTS

130 patients completed the study. Group I (65 patients): 36 boys and 29 girls with a mean age of 11.6 months, SD 7.5 months, and a mean weight of 8.540 kg, SD 2.240 kg. Group II (65 patients): 26 boys and 39 girls with a mean age of 10.7 months, SD 5.6 months, and a mean weight of 8.550 kg, SD 1.820 kg. There were no significant differences between the two groups. There were no significant differences between the groups in the number of stools in the 24 h preceding the beginning of the treatment. Table 1 and Fig.1 show the course in the two groups, with an initial progressive reduction and with statistically significant differences ($p < 0.05$) in favour of the group treated with *S. boulardii* from 48 h to the end of the treatment.

Table 1: Number of stools and days of treatment

| Day | Group I (<i>S. boulardii</i>) | | Group II (Placebo) | |
|---------|------------------------------------|------|-----------------------|------|
| | Mean | SD | Mean | SD |
| Initial | 7.5 | 2.15 | 6.66 | 2.26 |
| 1 | 5.15 | 1.93 | 5.47 | 2.40 |
| 2 | 3.76 | 2.31 | 4.38 | 2.73 |
| 3 | 2.53 | 1.78 | 3.63 | 2.53 |
| 4 | 2.00 | 1.94 | 3.29 | 2.19 |

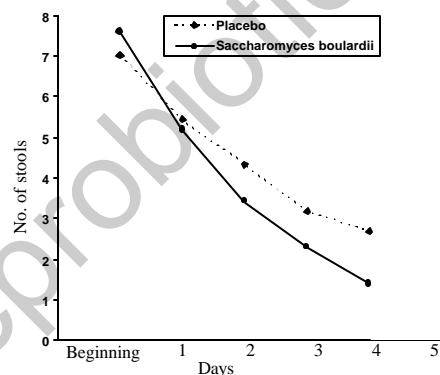


Figure 1: Number of stools and days of treatment.

Statistically significant differences in the first day of formed stools were found between the groups in favour of the one receiving *S. boulardii* (Fig. 2). Efficacy, evaluated according to the criterion of clinical cure, was assessed after 48 h (Fig. 3) and at the end of the treatment (Fig. 3 and Table 2).

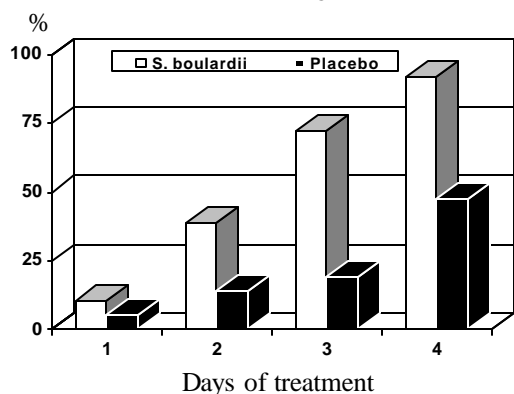


Figure 2 Treatment days and percentage of cases in the two groups with formed stools.

DISCUSSION

The use of antimicrobials in diarrhea is restricted and has very specific indications. Antimicrobials are, for example, administered to patients with shigellosis to reduce the level of contagion and the duration of the enteric process, to patients whose nutritional state merits it, or to prevent complications such as dehydration or death (12). Apart from these indications, it must be kept in mind that antimicrobials used in diarrhea have toxic side effects and disrupt the equilibrium of the intestinal ecosystem, and can even prolong diarrhea which is normally self-limiting (15).

Table 2: Number and percentage of cures in the two groups

| Effectiveness | Group I (<i>S. boulardii</i>) | | Group II (Placebo) | |
|---------------|------------------------------------|-----|-----------------------|-----|
| | No. of cases | % | No. of cases | % |
| Effective | 55 | 85 | 26 | 40 |
| Ineffective | 10 | 15 | 39 | 60 |
| Total | 65 | 100 | 65 | 100 |

Chi-square was 25.67 with $p < 0.01$, which is a statistically significant difference

Torres (16) and Manzano (17) obtained an effective response in 90 and 97%, respectively, of adults and children over 12 years on the third day of treatment with *S. boulardii*. Experience with children has been variable, since Chapoy (18) obtained 80% efficacy in a controlled study while Sánchez (19) obtained 60%; however, the patients in the last study had already received various treatments. Neither of these studies was double-blind.

The present study yields satisfactory results with *S. boulardii*, a yeast which survives at all levels of the digestive tract, including the stomach (20). Its efficacy is attributed to an inhibitory effect on the growth of pathogenic strains (21), to stimulation of non-specific anti-infectious mechanisms, to activation of complement, and to acceleration of the migration of polymorphonuclear cells and monocytes (18-20).

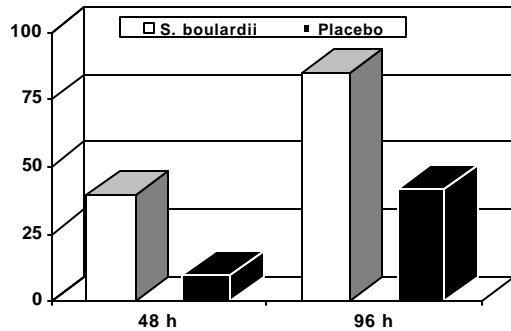


Figure 3 Percentage of cases cured after 48 and 96 h of treatment. There was a statistically significant difference at both times. Chi-square was 11.9 ($p < 0.01$) after 48 h and 25.67 ($p < 0.01$) after 96 h.

The fact that normal milk feeding could be continued without side effects due to intolerance of disaccharides could be due to the fact the *S. boulardii* increases the specific activity of lactase and sucrase (21).

In the present study of *S. boulardii* versus placebo the number of stools was lower in the active treatment group from 24 h after the start of the study onwards. The number of clinical cures was larger than in the placebo group, formed stools were obtained earlier, and there were no side effects. In the light of these results and the previously documented safety of *S. boulardii* (6), its use can be recommended together with oral rehydration in the treatment of acute non-specific diarrhea.

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