Comparison of safety, effectiveness and serum inflammatory factor indexes of *Saccharomyces boulardii* versus Bifidobacterium triple viable in treating children with chronic diarrhea

1. Source of study population

Children aged 2–8 years hospitalized with chronic diarrhea been admitted to our hospital

2. Criteria for selection of clinical cases

2.1 Inclusion criteria:

(I) defecation frequency ≥3 times/day and fecal characteristics in accordance with Bristol fecal characteristics types 6 and 7;

(II) duration of diarrhea symptoms ≥2 weeks;

(III) age 2–8 years;

(IV) routine fecal examination without white or red blood cell counts.

2.2 Exclusion criteria:

(I) mucus stool or pyorrhea;

(II) had taken other probiotics, antidiarrheal drugs or drugs affecting gastrointestinal motility within 2 weeks before inclusion in this study;

(III) history of allergic reaction to probiotics.

3. Grouping situation

Divided into *S. boulardii* group, Bifidobacterium triple viable group and control group according to the random number table method.

4. Inform the subjects of the grouping situation

Before signing the informed consent form, please explain the grouping of this study to the subjects.

5. Treatments

The control group was given routine treatments such as oral montmorillonite

powder, rehydration salt and intravenous rehydration, while the S. boulardii group was given routine treatment and oral S. boulardii [Biocodex (France) 0.25 g ×6 bags, batch number: s20150051], and the dosage was selected according to the age of the children as follows. Children >3 years old: one bag twice daily; children <3 years old: one bag once daily. The Bifidobacterium triple viable group was given conventional treatment and oral Bifidobacterium triple viable capsules (Shanghai Xinyi Pharmaceutical Co., Ltd. specification: each capsule contains 210 mg powder, batch No. Guoyao Zhunzi s10950032). The dosage was selected according to age: children >3 years old, 2 capsules each time, twice daily; children <3 years old, 1–2 capsules each time, twice daily. The powder in the capsule could be administered in warm boiled water. The course of each treatment was 14 days.

6. Evaluation indexes

6.1 Serum inflammatory factors

Before treatment and 14 days after treatment, 5 mL sample of peripheral venous blood from the forearm of each child was drawn, centrifuged at 1000g for 15 min, removal of the supernatant for storage at −80 ℃ before testing for changes in serum IL-6, IL-17, and TNF-α levels using a double antibody sandwich enzyme-linked immunosorbent assay [Elabscience (catalog Nos. E-ELN-H0102c, E-EL-H0105c, E- EL-H0109c]. All tests were performed in strict accordance with the manufacturers' instructions.

6.2 Efficacy evaluation

According to the Chinese Diarrhea Disease Diagnosis and Treatment Program (16) , the curative effect of CD is divided into three types: markedly effective [number of stools returned to normal (≤2 times/day) and stool characteristics returned to normal (Bristol types 3, 4, 5)]; effective [defecation frequency returned to normal after treatment (≤2 times/day) or stool characteristics returned to normal (Bristol types 3, 4, 5]; ineffective, defecation frequency still ≥3 times/day after treatment, and stool characteristics still Bristol classification 6 and 7. The total effective rate (%) = (number of markedly effective cases + number of effective cases)/total number of people ×100%. The recovery time was recorded, and the final evaluation of efficacy

was performed on the 14th day of treatment.

6.3 Adverse reaction registration

Any adverse reactions during the treatment of all patients were recorded and compared with the blood routine and liver and kidney function tests before treatment.

7. Statistical analysis

SPSS 22.0 software was used for statistical analysis. The measurement data with a normal distribution was expressed by $\bar{x}\pm s$. The paired *t*-test was used for comparison before and after treatment in the same group, and the *t*-test of independent samples was used for comparison between groups. Chi-square test was used for comparison of count data between groups. $P<0.05$ indicated a statistically significant difference.

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