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A retrospective study of probiotics for the treatment of children with antibiotic-associated diarrhea

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Abstract

This retrospective study aimed to explore the benefits and safety of probiotics (live combined *Bacillus subtilis* and *Enterococcus faecium* granules with multivitamines) for the treatment of children with antibiotic-associated diarrhea (AAD).

A total of 72 children with AAD were analyzed in this study. Of these, 36 children received routine treatment plus probiotics, and were assigned to a treatment group. The other 36 children underwent routine treatment alone, and were assigned to a control group. Patients in both groups were treated for a total of 7 days. The efficacy and safety were evaluated by duration of diarrhea (days), number of dressings needed daily, abdominal pain intensity, stool consistency (as assessed by Bristol Stool Scale (BSS)), and any adverse events.

After treatment, probiotics showed encouraging benefits in decreasing duration of diarrhea (days) ($P < .01$), number of dressings needed every day ($P < .01$), abdominal pain intensity ($P < .01$), and stool consistency (BSS (3–5), $P < .01$; BSS (6–7), $P < .01$). In addition, no adverse events were documented in this study.

The findings of this study demonstrated that probiotics may provide promising benefit for children with AAD. Further studies are still needed to warrant theses findings.

Abbreviations: AAD = antibiotic-associated diarrhea, BSS = Bristol stool scale.

Keywords: antibiotic-associated diarrhea, efficacy, probiotics, safety

1. Introduction

Antibiotic-associated diarrhea (AAD) is a very common disorder that is associated with utilization of many antibiotics.[1–4] Such antibiotics disrupt the colonization resistance of gastrointestinal flora and related overgrowth of bacteria.[5–6] It is defined as diarrhea of at least 3 times loose stools each day up to 2 weeks after the first treatment of antibiotics.[7–9] It has been estimated that about 11% to 40% children who underwent broad spectrum antibiotics experience AAD.[9–13] Several factors are responsible for such condition, including nearly all antibiotics and C. difficile infection.[14–16]

Several studies have reported to use probiotics for the treatment of children with AAD.[17–24] However, there are insufficient data to support probiotics (live combined *Bacillus subtilis* and *Enterococcus faecium* granules with multivitamines) for the treatment of ADD, although several similar studies reported such intervention may benefit children with diarrhea.[25–30] Therefore, more studies are still needed to further explore the efficacy of probiotics for the treatment of children with AAD. The present study investigated the efficacy and safety of probiotics for the treatment of children with AAD.

2. Patients and methods

2.1. Ethical consideration

This study was approved by the ethics medical committee of First Affiliated Hospital of Jiamusi University. All included subjects provided written informed consent by their guardians.

2.2. Design

This retrospective study included 72 children with AAD from First Affiliated Hospital of Jiamusi University between December 2017 and November 2019. All 72 children were equally assigned to the treatment group (n = 36) and the control group (n = 36) according to the different treatment schedules they received. All children in both groups received routine treatment. In addition, children in the treatment group also received probiotics.

2.3. Patients

All eligible participants aged between 5 and 11 years old were diagnosed as AAD.[31] Patients were excluded if they had other gastrointestinal pathologies, allergy to the study medication,

Editor: Undurti N. Das.

The authors have no funding and conflicts of interest to disclose.

The data that support the findings of this study are available from a third party, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are available from the authors upon reasonable request and with permission of the third party.

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How to cite this article: Rui X, Ma Sx. A retrospective study of probiotics for the treatment of children with antibiotic-associated diarrhea. Medicine 2020;99:23 (e20631).

Received: 8 March 2020 / Received in final form: 23 April 2020 / Accepted: 8 May 2020

http://dx.doi.org/10.1097/MD.0000000000020631

other medications that could affect the results of this study, and took laxatives. There were no limitations to the race, country and gender in this study.

2.4. Treatment schedule

All 72 patients in both groups received routine treatment, including fluids replenishment to prevent dehydration and to balance water and electrolyte disorders.

In addition, 36 patients in the treatment group received probiotics (live combined *Bacillus subtilis* and *Enterococcus faecium* granules with multivitamines, Beijing Hanmei Pharmaceutical Co., Ltd (S20020037)),[32–33] 1 g/pack, 1 pack each time, twice daily for a total of 7 days.

2.5. Outcome measurements

The primary outcomes were duration of diarrhea (days), and number of dressings needed every day.

The secondary outcomes were abdominal pain intensity (as measured by visual analog scale, varies from 0 (no pain), to 10 (the worst pain)),[34–35] stool consistency (as assessed by Bristol Stool Scale (BSS), including 7 types as follows: type 1 to 2 indicates constipation; type 3 to 5 suggests normal stools; and type 6 to 7 means liquid stool[36–37]), and any adverse events.

2.6. Statistical analysis

This study utilized SAS package (Version 9.1; SAS Institute Inc., Cary, North Carolina) to analyze all baseline and outcome data. We used *t* test or Wilcoxon test to analyze continuous data, and applied Pearson chi-square test or Fisher exact test to analyze discontinuous data. The value of $P < .05$ was defined as having statistical significance.

3. Results

The comparison of baseline characteristics of patients in both groups is shown in Table 1. There are not significant differences regarding the baseline characteristics between two groups.

Table 1

Comparison of baseline characteristics between 2 groups.

Characteristics	Treatment group (n = 36)	Control group (n = 36)	*P* value
Mean age (yr)	7.5 (2.1)	7.3 (2.4)	.71
Gender			
Boy	20 (55.6)	17 (47.2)	.48
Girl	16 (44.4)	19 (52.8)	.48
Ethnicity (China)	36 (100.0)	36 (100.0)	–
Number of patients with AAD	36 (100.0)	36 (100.0)	–
Duration of diarrhea (d)	3.1 (1.1)	2.9 (1.4)	.50
Number of dressings needed daily	4.4 (1.3)	4.2 (1.5)	.55
Pain intensity (VAS)	6.8 (2.2)	6.6 (2.5)	.28
Stool consistency (BSS scale)			
BSS (1–2)	0 (0)	0 (0)	–
BSS (3–5)	1 (2.8)	0 (0)	.49
BSS (6–7)	35 (97.2)	36 (100.0)	.49
Causes			
Amoxicillin	16 (44.4)	13 (36.1)	.47
Ampicillin	13 (36.1)	14 (38.9)	.81
Cephalosporins	7 (19.5)	9 (25.0)	.57

Data are present as mean±standard deviation or number (%); AAD = antibiotic-associated diarrhea; BSS = Bristol Stool Form; VAS = Visual Analog Scale.

Table 2

Comparison of duration of diarrhea between 2 groups.

Outcomes	Treatment group (n = 36)	Control group (n = 36)	*P* value
Duration of diarrhea (d)	1.3 (0.5)	1.9 (0.8)	
Difference between groups		−0.7 (−1.3, −0.2)	<.01

Data are present as mean±standard deviation (range).

Table 3

Comparison of number of dressings needed daily between 2 groups.

Outcomes	Treatment group (n = 36)	Control group (n = 36)	*P* value
Number of dressings needed daily	0.9 (0.4)	2.1 (0.9)	
Difference between groups		−1.2 (−1.9, −0.3)	<.01

Data are present as mean±standard deviation (range).

The results exerted that patients in the treatment group achieved more benefit in duration of diarrhea (days) ($P < .01$, Table 2), number of dressings needed every day ($P < .01$, Table 3), abdominal pain intensity ($P < .01$, Table 4), and stool consistency (BSS (3–5), $P < .01$; BSS (6–7), $P < .01$, Table 5), than patients in the control group.

In addition, no expected or unexpected adverse events were recorded in both groups in this study.

4. Discussion

Although several studies have investigated the efficacy and safety of probiotics for the treatment of children with AAD,[17–24] few data are available to specifically support the efficacy and safety of probiotics for the treatment of Chinese children with AAD. This retrospective study explored the benefits and safety of probiotics for the treatment of Chinese children with AAD. Its results exerted promising benefits in Chinese children with AAD.

The findings of this study are partly consistent with previous studies.[25–30] In this study, our results found that probiotics

Table 4

Comparison of abdominal pain intensity between two groups.

Outcomes	Treatment group (n = 36)	Control group (n = 36)	*P* value
Visual Analogue Scale	1.0 (0.4)	2.3 (1.1)	
Difference between groups		−1.3 (−2.1, −0.5)	<.01

Data are present as mean±standard deviation (range).

Table 5

Comparison of stool consistency between two groups.

Bristol Stool Scale (BSS)	Treatment group (n = 36)	Control group (n = 36)	*P* value
BSS (1–2)	1 (2.8)	0 (0)	.49
BSS (3–5)	33 (91.7)	22 (61.1)	<.0.1
BSS (6–7)	2 (5.5)	14 (38.9)	<.0.1

Data are present as number (%); BSS = Bristol stool scale.

showed promising benefits in children with AAD in reducing duration of diarrhea, number of dressings needed daily, abdominal pain intensity, and enhancing stool consistency. In addition, this study did not identify any adverse events after treatment. The results of this study indicated that probiotics may benefit Chinese children with AAD.

There are several limitations in this study. First, this retrospective study did not apply randomization procedure to assign patients to the treatment and control groups, because this study only collected data from previously completed patient case records. Second, all patient cases were collected from 1 center of First Affiliated Hospital of Jiamusi University, which may affect its generalization to the other hospitals in China. Third, this study evaluated the efficacy and safety of probiotics for the treatment of children with AAD within 7-day treatment period, and no follow-up measurement was assessed. Fourth, the sample size was quite small in this study, which may impact our findings. Finally, this study is a retrospective study, so it has an intrinsic limitation. Therefore, further studies should avoid above limitations.

5. Conclusion

The findings of this study found that probiotics may benefit children with AAD. However, future studies are still needed to verify the results of this study.

Author contributions

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