(cc) BY

# Clinical study on the improvement in functional constipation for Panax notoginseng stem and leaf tea combine with panaxnotoginseng fruit and vegetable enzyme and probiotic powder

Shuping HAO<sup>1#</sup>, Yongchao ZHANG<sup>2#</sup>, Weiwei MA<sup>3</sup>, Mei LI<sup>1</sup>, Sisi TAN<sup>1</sup>, Jing LI<sup>1</sup>, Jingyun LI<sup>1</sup>, Lan LIU<sup>4\*</sup> 💿

# Abstract

The ingredients in fruit and vegetable enzymes are not only medicine and food for relieving constipation but also rich in dietary fiber. We aimed to investigate the efficacy of panax notoginseng stem, leaf tea combined with panaxnotoginseng fruit, vegetable enzyme, and probiotic powder for functional constipation. Patients with functional constipation had been recruited and been randomly divided into the lactulose intervention group and probiotic intervention group. In the probiotic intervention group, patients received panaxnotoginseng stem and leaf tea + Panaxnotoginseng fruit and vegetable enzyme+probiotic powder, once a day. In the lactulose intervention group, patients received normal drug treatment for 2 weeks. Both probiotics intervention and lactulose intervention can improve the fecal quality of patients with constipation. Probiotics group can lead to an increase the levels of blood SP and GAS and decrease the level of MTL in patients with constipation. Both probiotics intervention and lactulose for functional constipation. Probiotics and lactulose can significantly increase the levels of blood SP and GAS and decrease the level of MTL in patients with constipation. Both probiotics intervention and lactulose intervention can improve the quality of life of patients with constipation and the fecal quality of patients with constipation. Probiotics group can lead to an increase in the proportion of diarrhea in patients with constipation and the fecal quality of patients with constipation.

Keywords: Panax notoginseng stem; leaf tea; probiotic powder; vegetable enzyme; functional constipation.

**Practical Application:** Investigate the efficacy of panax notoginseng stem, leaf tea combined with panaxnotoginseng fruit, vegetable enzyme, and probiotic powder for functional constipation.

#### 1 Introduction

Functional constipation (FC) is the most common form of constipation and can be defined as the difficult or infrequent passage of stool. The prevalence of functional constipation is probably greater than 10% in the general population as a whole, and 20% among elderly people living in the community, and it negatively affects all areas of health-related quality of life (HRQoL). Current guidelines recommend PEG or enemas as a pharmacological treatment for disimpaction (Casias & Newton, 2021). Oral laxatives may also be used in conjunction with PEG to help promote the emptying of stool (Chassagne et al., 2017).

Intake of dietary fiber and bulking agents (psyllium) may be effective in alleviating constipation in patients without slow colonic transit or disordered constipation. Fiber and probiotics are well-known food supplements for improving chronic constipation. Probiotic can be defined as viable or inviable microbial cells (vegetative or spore; intact or ruptured) that are potentially healthful to the host (Zendeboodi et al., 2020). They can be used in daily products such as ice cream, daily drinks, and mango juice to maintain microbiota balance and increase health benefits (Pimentel et al., 2022; Yerlikaya et al., 2020; Ryan et al., 2020). It has been reported that increased dietary fiber intake is more likely beneficial in individuals with fiber deficiency (Rajindrajith et al., 2020; Fernández-Bañares, 2006). The ingredients in fruit and vegetable enzymes are not only medicine and food for relieving constipation but also rich in dietary fiber.

Therefore, we conducted this study to explore the clinical efficacy of panax notoginseng stem, leaf tea combined with panaxnotoginseng fruit, vegetable enzyme, and probiotic powder for functional constipation.

# 2 Materials and methods

#### 2.1 Subjects

In this study, patients with functional constipation had been recruited. These participants were aged between 18 and 65 years and were randomly divided into the lactulose intervention group and probiotic intervention group. Functional constipation was defined based on the Rome criteria III as a stool and clinically diagnosed as slow transit constipation. This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of our hospital. All participants had

Received 03 Feb., 2022

Accepted 11 Apr., 2022

<sup>&</sup>lt;sup>1</sup>Department of Clinical Nutrition, Pinggu Hospital, Beijing Friendship Hospital, Capital Medical University, Beijing, China

<sup>&</sup>lt;sup>2</sup>Department of Gastroenterology-Related Internal Medicine, Pinggu Hospital, Beijing Friendship Hospital, Capital Medical University, Beijing, China <sup>3</sup>School of Public Health, Capital Medical University, Beijing, China

<sup>&</sup>lt;sup>4</sup>Beijing Dietitian Association, Beijing, China

<sup>\*</sup>Corresponding author: Lan Liu, Beijing Dietitian Association, R&F Morgan Center, No. 6 Taiping Street, Xicheng District, Beijing, China. dietetic@163.com #These authors contributed equally to this study

signed the informed consent. The flow diagram of this study is shown in Figure 1.

#### 2.2 Inclusion and exclusion criteria

Inclusion criteria: (1) patients who were diagnosed with functional constipation; (2) age was older than 18 years old; (3) patients who have signed informed consent.

Exclusion criteria: (1) women who are pregnant or lactating; (2) subjects with mental retardation; (3) patients who had any tumor, neurological disease, and intestinal mechanical disorder; (4) complicated with diabetes, tumors, neurological disease, or other severe disease and its complications; (5) patients with the history of gastrointestinal surgery, metabolic diseases, or suspected colorectal cancer; (6) consumed probiotics, prebiotics products more than once a week before screening or during intervention; (7) long-term use of laxatives (more than once per week), having used antibiotics, docusate, anticholinergics, laxatives within 2 weeks of the screen and throughout the trial; (8) patients whose data was incomplete.

#### 2.3 Intervention substance

In this study, the Youbanotoginseng flower fruit and vegetable enzyme, Youbanotoginseng probiotic powder, Youbanotoginseng flower stem, and leaves tea are provided by Beijing Jinsanqi Technology Co., Ltd. The main ingredients of fermented fruit and

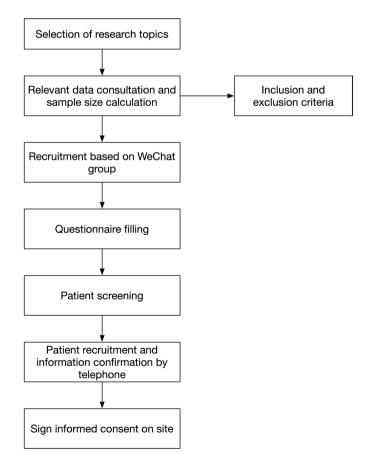


Figure 1. The flow diagram of this study.

vegetable powder: pomegranate powder, Lemon powder, apple powder, spinach powder, papaya powder, mushroom powder, orange powder, passion fruit powder, kiwi powder, broccoli powder, celery powder, cherry powder, white radish powder, cucumber powder, loofah powder, banana powder, Pineapple powder, cantaloupe), oligofructose, inulin, aloe powder, cassia seed, lotus leaf, hemp seed, barley seedlings, panaxnotoginseng. Probiotics include Lactobacillus casei, Lactobacillus acidophilus, Bifidobacteriumlactis, Lactobacillus rhamnosus. Lactulose is the production of Beijing Hanmi Pharmaceutical Company.

#### 2.4 Intervention methods

In this study, patients had been randomly divided into the lactulose intervention group and probiotic intervention group. In the probiotic intervention group, patients received panaxnotoginseng stem and leaf tea + Panaxnotoginseng fruit and vegetable enzyme + probiotic powder, once a day. In the lactulose intervention group, patients received normal drug treatment for 2 weeks.

# 2.5 Indicator detection

# *Investment of diet and bowel movement in constipation patients*

The study employed a case-control study followed by a randomized controlled study. Before the trial, a detailed medical history should be asked, after meeting the criteria for enrollment, the defecation situation of the constipated patients in the past week should be investigated.

#### Life quality investment in constipation patients

Investigation tools PAC-QOL including 28 questions was used to investigate the life quality of patients with constipation in the two groups.

#### Anthropometric indicators investment in constipation patients

Height and weight of the subjects were measured using standardized procedures. The body fat content and other indexes of the subjects were measured by the body fat analyzer.

#### Fecal improvement investment in constipation patients

The subjects were asked to record the stool frequency per day on the diary card (two bowel movements with an interval of less than 10 min were counted as one) and the stool traits were recorded according to the Bristol stool scale. The stools were divided into 7 grades from the hardest type to the water sample type, and the stools from type 1 to type 7 were rated as 1 to 7 respectively

# *Changes of the gastrointestinal hormone in constipation patients*

The plasma levels of gastrin, motilin, and substance P were measured by ELISA.

# 2.6 Statistical analysis

We used SPSS software (version 22.0; IBM Corp., Armonk, NY, USA) for the statistical analysis. The continuous variables of normal distribution were expressed as mean  $\pm$  standard deviation, the continuous variables of non-normal distribution were expressed as median (interquartile range [IQR]), the categorical variables were expressed as frequency (percentage [%]). For two comparisons, each value was compared by t-test when each datum conformed to a normal distribution, while the non-normally distributed continuous data were compared using non-parametric tests. The counting data were tested by the chi-square test. A value of P < 0.05 was considered statistically significant.

# **3 Results**

#### 3.1 Baseline characteristics in two groups

A total of 111 subjects had been recruited in the study and been randomized divided into the probiotic group (n = 57) and lactulose group (n = 54). The baseline characteristics of the two groups, including age, sex, education level, and anthropometric indicators index were well-balanced with no significant differences. The details had been presented in Table 1.

#### 3.2 Comparison of the disease conditions in two groups

The results showed that no significant difference was found between the two study groups in Gastrointestinal disorders, Thyroid problems, Cerebrovascular disease, and Myopathy (P > 0.05). The details had been listed in Table 2.

#### 3.3 Defecation symptom in two groups

The results showed that the rate of fixed defecation in the probiotic group was significantly higher than the lactulose group

| Table 1. Baseline | characteristics | of two | groups. |
|-------------------|-----------------|--------|---------|
|-------------------|-----------------|--------|---------|

(38.6% vs. 20.4, P = 0.041). The bowel movement frequency, difficult defecation, stool traits, sensation of incomplete evacuation, the sensation of blockage, manual support for evacuation, duration of defecation, defecation concomitant behavior, bleeding with defecation and scrubbing mode in the probiotic group did not improve significantly when compared with the lactulose group. The details had been listed in Table 3.

#### 3.4 Dietary and exercise behaviors for two groups

The results showed that the two groups revealed a significant improvement in physical activity intensity (P = 0.023). There was no significant difference in diet behavior or exercise behavior between the two groups. The details had been listed in Table 4.

#### 3.5 PAC-QOL scores for two groups

Compared with baseline, the total PAC-QOL scores of the two study groups reduced significantly after intervention, which indicated that the two kinds of intervention could improve the quality of life of the subjects in both groups, but there was no statistical difference between the two groups. The details had been listed in Table 5.

#### 3.6 Changes of constipation in two groups

Figure 2 presented the changes in stool frequency in two groups which were decreased under the intervention of probiotics and lactulose.

With the increase of intervention time, in the probiotics group, the proportion of constipated stool in patients with constipation gradually decreased, the proportion of ideal feces of patients with constipation tended to be smooth, while the proportion of lactulose to ideal feces showed a slow upward trend. The proportion of diarrhea feces in the probiotics group tends to increase. (Figures 3-5).

| Index                    | Probiotic group $(n = 57)$ | Lactulose group $(n = 54)$ | P value |
|--------------------------|----------------------------|----------------------------|---------|
| Age (years)              | $48.07 \pm 6.23$           | $45.67 \pm 9.24$           | > 0.05  |
| Female [N, (%)]          | 94.7                       | 88.9                       | > 0.05  |
| Education level          |                            |                            | > 0.05  |
| ≤ Secondary school       | 36.8                       | 29.6                       |         |
| Academic education       | 63.2                       | 70.4                       |         |
| BMI (kg/m <sup>2</sup> ) | $24.37 \pm 2.58$           | $24.88 \pm 3.71$           | > 0.05  |
| Body fat (kg)            | $21.29\pm5.30$             | $21.65 \pm 6.92$           | > 0.05  |
| Lean body weight (kg)    | $40.09\pm7.09$             | $42.05 \pm 5.17$           | > 0.05  |
| Body muscle (kg)         | $38.56 \pm 4.83$           | $39.69 \pm 4.92$           | > 0.05  |
| Body fat percentage (%)  | $34.09 \pm 6.49$           | $33.38 \pm 6.40$           | > 0.05  |

#### Table 2. Basic disease of the two groups.

| Index  | Probiotic group $(n = 57)$ | Lactulose group ( $n = 54$ ). | P value |
|--|----------------------------|-------------------------------|---------|
| Gastrointestinal disorders (Hemorrhoids, anal fissure, etc.) | 45.6                       | 33.3                          | > 0.05  |
| Thyroid problems   | 14.0                       | 5.6                           | > 0.05  |
| Cerebrovascular disease                                      | 1.8                        | 5.6                           | > 0.05  |
| Myopathy   | 0                          | 3.7                           | > 0.05  |

#### Table 3. Defecation symptom in two groups.

| Index   | Probiotic group $(n = 57)$ | Lactulose group $(n = 54)$ | <i>P</i> value |
|---|----------------------------|----------------------------|----------------|
| Bowel movement frequency/Stool frequency/The frequency of spontaneous bowel movements |                            |                            | > 0.05         |
| > twice a day   | 10.5                       | 3.7                        |                |
| Once a day  | 24.6                       | 25.9                       |                |
| 2-3 times a week  | 61.4                       | 66.7                       |                |
| Once a week   | 1.8                        | 1.9                        |                |
| < Once a week   | 1.8                        | 1.9                        |                |
| Difficult defecation/Straining with defecation  |                            |                            | > 0.05         |
| Everytime   | 50.9                       | 46.3                       |                |
| At least one of the four times  | 47.4                       | 44.4                       |                |
| Never   | 1.8                        | 9.3                        |                |
| Stool traits/Stool Form Scale   |                            |                            | > 0.05         |
| Always soft and not forming/Fluffy pieces with ragged edges, a mushy stool            | 17.5                       | 16.7                       |                |
| Banana poop   | 14.0                       | 11.1                       |                |
| Soft and hard alternate   | 49.1                       | 51.9                       |                |
| Always hard   | 19.3                       | 20.4                       |                |
| Sensation of incomplete evacuation  |                            | *                          |                |
| Never   | 10.5                       | 11.1                       | > 0.05         |
| Sometimes   | 42.1                       | 42.6                       | 2 0.00         |
| Always  | 47.4                       | 46.3                       |                |
| Sensation of Blockage   | 17.1                       | 40.5                       | > 0.05         |
| Never   | 7.0                        | 11.1                       | 2 0.05         |
| Occasionally  | 47.4                       | 53.7                       |                |
|   | 45.6                       | 35.2                       |                |
| Always<br>Manual support for avacuation   | 45.0                       | 55.2                       |                |
| Manual support for evacuation<br>Never  | 43.9                       | 57.4                       |                |
|   |                            |                            |                |
| Occasionally<br>Often   | 40.4<br>15.8               | 25.9<br>16.7               |                |
|   | 15.0                       | 10.7                       | 0.041          |
| Fixed defecation time   | 20 (                       | 20.4                       | 0.041          |
| Yes<br>No   | 38.6                       | 20.4                       |                |
|   | 61.4                       | 77.8                       |                |
| Duration of defecation  | 21.1                       | 22.2                       | > 0.05         |
| ≤ 5 min   | 21.1                       | 22.2                       |                |
| 5-10 min  | 45.6                       | 40.7                       |                |
| 0-20 min  | 24.6                       | 29.6                       |                |
| > 20 min  | 8.8                        | 7.4                        | 0.07           |
| Defecation concomitant behavior   |                            | 10 -                       | > 0.05         |
| Check the phone   | 56.1                       | 40.7                       |                |
| Reading a book or newspaper   | 0                          | 1.9                        |                |
| None  | 43.9                       | 57.4                       |                |
| Bleeding with defecation  |                            |                            |                |
| Yes   | 35.1                       | 27.8                       |                |
| No  | 64.9                       | 72.2                       |                |
| Scrubbing mode  |                            |                            | > 0.05         |
| Using toilet paper  | 93.0                       | 88.9                       |                |
| Intelligent toilet flushing   | 7.0                        | 7.4                        |                |
| Both  | 0                          | 3.7                        |                |

The results showed that there was no difference in overall product satisfaction from day 1 to day 13. The details were listed in Table 6.

No significant difference was found in blood levels of three hormones between the probiotics group and lactulose group before and after the intervention. The results of self-control showed that the levels of blood SP and GAS increased significantly, while the level of MTL decreased significantly in patients with constipation in the probiotics group and lactulose group. The details were listed in Table 7.

### Hao et al.

 Table 4. Dietary and exercise behavior for two groups.

| Index                                     | Probiotic group $(n = 57)$ | Lactulose group $(n = 54)$ | P value |
|---|----------------------------|----------------------------|---------|
| Frequency of spicy                        |                            |                            | > 0.05  |
| 3 times a week                            | 45.6                       | 42.6                       |         |
| -5 times a week                           | 12.3                       | 16.7                       |         |
| Once a day                                | 3.5                        | 5.6                        |         |
| very meal                                 | 0                          | 3.7                        |         |
| 5 times a month                           | 38.6                       | 31.5                       |         |
| requency of vegetables                    |                            |                            | > 0.05  |
| Dnce a day                                | 45.6                       | 40.7                       |         |
| -3 times a day                            | 49.1                       | 51.9                       |         |
| -5 times a week                           | 3.5                        | 7.4                        |         |
| lmost not                                 | 1.8                        | 0                          |         |
| Consumption of vegetables                 |                            |                            | > 0.05  |
| 300 g                                     | 35.1                       | 29.6                       |         |
| 00 g-500 g                                | 59.6                       | 50.0                       |         |
| 500 g                                     | 5.3                        | 20.4                       |         |
| requency of fruit                         | 0.0                        | 20.1                       | > 0.05  |
| 3 times a week                            | 15.8                       | 16.7                       | 2 0.00  |
| -5 times a week                           | 17.5                       | 25.9                       |         |
| Dice a day                                | 45.6                       | 40.7                       |         |
| -3times a day                             | 17.5                       | 16.7                       |         |
| 5 times a month                           | 1.8                        | 0                          |         |
|   |                            |                            |         |
| lever                                     | 1.8                        | 0                          | . 0.05  |
| Consumption of fruit                      | 50.4                       | 16.2                       | > 0.05  |
| 250 g                                     | 59.6                       | 46.3                       |         |
| 50 g-500 g                                | 35.1                       | 46.3                       |         |
| 500 g                                     | 5.3                        | 7.4                        |         |
| Consumption of water                      |                            |                            | > 0.05  |
| 1200 mL                                   | 57.9                       | 59.3                       |         |
| 200 mL-1500 mL                            | 28.1                       | 29.6                       |         |
| 500 mL-1700 mL                            | 8.8                        | 5.6                        |         |
| 2000 mL                                   | 5.3                        | 5.6                        |         |
| lea                                       |                            |                            | > 0.05  |
| es  | 49.1                       | 55.6                       |         |
| lo  | 49.1                       | 44.4                       |         |
| 1idnight snack                            |                            |                            | > 0.05  |
| lever                                     | 70.2                       | 66.7                       |         |
| Occasionally                              | 24.6                       | 25.9                       |         |
| -3 times a week                           | 3.5                        | 1.9                        |         |
| veryday                                   | 1.8                        | 3.7                        |         |
| requency of grains, mixed beans, potatoes |                            |                            | > 0.05  |
| lever                                     | 1.8                        | 9.3                        |         |
| Occasionally (2-3 times a month)          | 35.1                       | 31.5                       |         |
| Often (twice a week)                      | 59.6                       | 59.3                       |         |
| veryday                                   | 3.5                        | 0                          |         |
| hysical activity intensity                |                            |                            | 0.023   |
| ight activity                             | 61.4                       | 37.0                       |         |
| Ioderate activity                         | 35.1                       | 61.1                       |         |
| /igorous activity                         | 3.5                        | 1.9                        |         |
| Vork hours                                | 5.5                        | 1.7                        | > 0.05  |
| h   | 56.1                       | 62.3                       |         |
| -10 h                                     | 36.8                       | 24.5                       |         |
| 10 h                                      | 5.3                        | 11.3                       |         |
| Exercise frequency                        | 5.5                        | 11.5                       | > 0.05  |

#### Table 4. Continued...

| Index                | Probiotic group $(n = 57)$ | Lactulose group $(n = 54)$ | P value |
|----------------------|----------------------------|----------------------------|---------|
| Everyday             | 29.8                       | 25.9                       |         |
| < 3 times a week     | 19.3                       | 14.8                       |         |
| > 3 times a week     | 19.3                       | 18.6                       |         |
| Occasionally         | 26.3                       | 35.2                       |         |
| Never                | 5.3                        | 5.6                        |         |
| Sleeping time        |                            |                            | > 0.05  |
| < 5 h                | 3.5                        | 11.1                       |         |
| 5-8 h                | 86.0                       | 79.6                       |         |
| > 8 h                | 10.5                       | 9.3                        |         |
| Sleep quality        |                            |                            | > 0.05  |
| Getting enough sleep | 19.3                       | 24.1                       |         |
| Moderate quality     | 42.1                       | 42.6                       |         |
| Poor sleep quality   | 38.6                       | 33.3                       |         |

Table 5. Changes in PAC-QOL scores before and after intervention for two groups.

| Index                       | Probiotic group $(n = 57)$ | Lactulose group $(n = 54)$ | <i>P</i> value (baseline) |
|-----------------------------|----------------------------|----------------------------|---------------------------|
| PAC-QOL (pre-intervention)  | $39.25 \pm 2.46$           | $37.50 \pm 2.38$           | < 0.05                    |
| PAC-QOL (post-intervention) | $25.39 \pm 2.75^*$         | $23.13 \pm 14.27^{*}$      | < 0.05                    |

\*Compared with before self-intervention, p < 0.05. PAC-QOL refers to "Patient Assessment of Constipation quality of life"

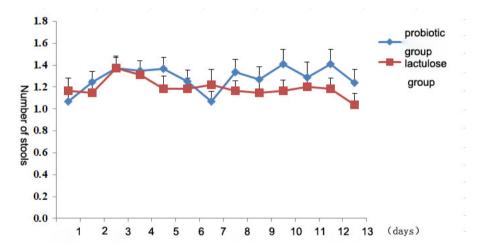


Figure 2. The effect of probiotics and lactulose on stool frequency in patients with constipation.

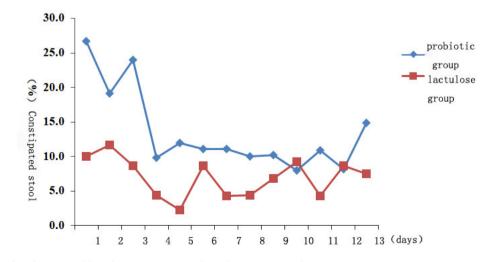


Figure 3. The effect of probiotics and lactulose on constipated stool in patients with constipation.

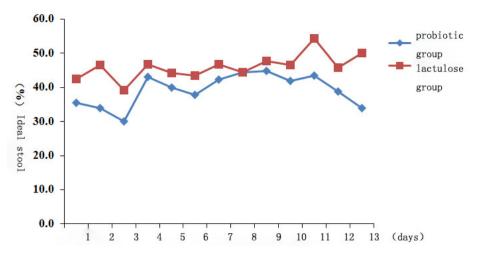


Figure 4. The effect of probiotics and lactulose on ideal feces in patients with constipation.

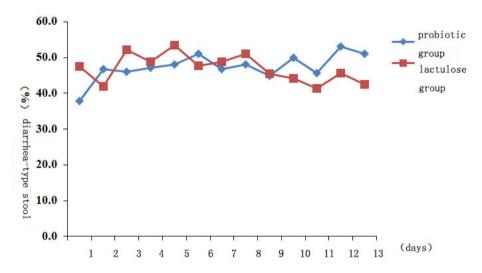


Figure 5. The effect of probiotics and lactulose on diarrhea-type stool in patients with constipation.

Table 6. Comparison of product satisfaction between the two groups.

| Index                | Probiotic group $(n = 57)$ | Lactulose group $(n = 54)$ | P value |
|----------------------|----------------------------|----------------------------|---------|
| Day 1                |                            |                            | 0.560   |
| Very satisfied       | 0                          | 2                          |         |
| Quite satisfied      | 19                         | 13                         |         |
| Moderately satisfied | 12                         | 9                          |         |
| A little satisfied   | 8                          | 8                          |         |
| Not at all satisfied | 6                          | 6                          |         |
| Day 2                |                            |                            | 0.913   |
| Very satisfied       | 2                          | 3                          |         |
| Quite satisfied      | 22                         | 16                         |         |
| Moderately satisfied | 9                          | 8                          |         |
| A little satisfied   | 11                         | 12                         |         |
| Not at all satisfied | 4                          | 4                          |         |
| Day 3                |                            |                            | 0.606   |
| Very satisfied       | 6                          | 3                          |         |
| Quite satisfied      | 22                         | 18                         |         |
| Moderately satisfied | 10                         | 10                         |         |
| A little satisfied   | 7                          | 12                         |         |
| Not at all satisfied | 6                          | 5                          |         |

# Table 6. Continued...

| Index                                      | Probiotic group ( $n = 57$ )          | Lactulose group $(n = 54)$ | P value |
|--|---------------------------------------|----------------------------|---------|
| Day 4                                      |                                       |                            | 0.189   |
| Very satisfied                             | 10                                    | 2                          |         |
| Quite satisfied                            | 20                                    | 20                         |         |
| Moderately satisfied                       | 12                                    | 9                          |         |
| A little satisfied                         | 7                                     | 7                          |         |
| Not at all satisfied                       | 3                                     | 6                          |         |
| Day 5                                      |                                       |                            | 0.085   |
| Very satisfied                             | 6                                     | 2                          |         |
| Quite satisfied                            | 27                                    | 18                         |         |
| Moderately satisfied                       | 12                                    | 12                         |         |
| A little satisfied                         | 6                                     | 6                          |         |
| Not at all satisfied                       | 0                                     | 5                          |         |
| Day 6                                      |                                       |                            | 0.166   |
| Very satisfied                             | 3                                     | 1                          |         |
| Quite satisfied                            | 24                                    | 18                         |         |
| Moderately satisfied                       | 11                                    | 12                         |         |
| A little satisfied                         | 6                                     | 7                          |         |
| Not at all satisfied                       | 1                                     | 7                          |         |
| Day 7                                      |                                       |                            | 0.285   |
| Very satisfied                             | 3                                     | 3                          |         |
| Quite satisfied                            | 26                                    | 18                         |         |
| Moderately satisfied                       | 8                                     | 12                         |         |
| A little satisfied                         | 6                                     | 6                          |         |
| Not at all satisfied                       | 2                                     | 7                          |         |
| Day 8                                      |                                       |                            | 0.406   |
| Very satisfied                             | 3                                     | 1                          |         |
| Quite satisfied                            | 28                                    | 19                         |         |
| Moderately satisfied                       | 9                                     | 11                         |         |
| A little satisfied                         | 4                                     | 8                          |         |
| Not at all satisfied                       | 5                                     | 5                          |         |
| Day 9                                      | u u u u u u u u u u u u u u u u u u u | U U                        | 0.222   |
| Very satisfied                             | 9                                     | 2                          | 0.222   |
| Quite satisfied                            | 22                                    | 21                         |         |
| Moderately satisfied                       | 8                                     | 10                         |         |
| A little satisfied                         | 6                                     | 9                          |         |
| Not at all satisfied                       | 4                                     | 2                          |         |
| Day 10                                     | T                                     | 2                          | 0.472   |
| Very satisfied                             | 6                                     | 1                          | 0.172   |
| Quite satisfied                            | 28                                    | 23                         |         |
| Moderately satisfied                       | 9                                     | 10                         |         |
| A little satisfied                         | 6                                     | 7                          |         |
| Not at all satisfied                       | 2                                     | 2                          |         |
| Day 11                                     | ۷                                     | 2                          | 0.595   |
| Very satisfied                             | 5                                     | 5                          | 0.393   |
| Quite satisfied                            | 5<br>25                               | 5<br>19                    |         |
|  |                                       |                            |         |
| Moderately satisfied<br>A little satisfied | 8                                     | 13                         |         |
|  | 4                                     | 7                          |         |
| Not at all satisfied                       | 2                                     | 2                          |         |
| Day 12                                     | -                                     | -                          | 0 500   |
| Very satisfied                             | 5                                     | 5                          | 0.589   |
| Quite satisfied                            | 25                                    | 17                         |         |
| Moderately satisfied                       | 7                                     | 12                         |         |
| A little satisfied                         | 7                                     | 7                          |         |
| Not at all satisfied                       | 4                                     | 3                          |         |

| Index                | Probiotic group $(n = 57)$ | Lactulose group $(n = 54)$ | P value |
|----------------------|----------------------------|----------------------------|---------|
| Day 13               |                            |                            | 0.498   |
| Very satisfied       | 5                          | 2                          |         |
| Quite satisfied      | 23                         | 20                         |         |
| Moderately satisfied | 6                          | 11                         |         |
| A little satisfied   | 7                          | 6                          |         |
| Not at all satisfied | 5                          | 3                          |         |

Table 6. Continued...

Table 7. Changes in hormone before and after intervention for two groups.

| Index | Probioticgroup $(n = 57)$ | Lactulose group $(n = 54)$ | P vaule (Baseline) | P vaule (Intergroup) |
|-------|---------------------------|----------------------------|--------------------|----------------------|
| SP1   | $10.02\pm4.40$            | $10.88 \pm 4.05$           |                    |                      |
| SP1   | $12.81 \pm 4.45^{*}$      | $13.05 \pm 4.69^{*}$       | P < 0.05           | 0.895                |
| GAS1  | $30.50 \pm 12.04$         | $32.75 \pm 13.17$          |                    |                      |
| GAS2  | $39.37 \pm 14.83^{*}$     | $39.80 \pm 16.21^{*}$      | P < 0.05           | 0.140                |
| MTL1  | $92.80 \pm 40.44$         | 96.70 ± 38.67              |                    |                      |
| MTL2  | $66.31 \pm 24.31^{*}$     | $67.25 \pm 29.27^{*}$      | P < 0.05           | 0.593                |

\*Compared with before self-intervention, P < 0.05.

#### **4** Discussion

In this study, we compared the efficacy of probiotic intervention (panax notoginseng stem, leaf tea combined with panaxnotoginseng fruit, vegetable enzyme, and probiotic powder) versus lactulose intervention for functional constipation. The main findings were as follows: (1) both probiotics intervention and lactulose intervention can improve the quality of life of patients with constipation; (2) both probiotics intervention and lactulose intervention can improve the fecal quality of patients with constipation but probiotics could lead to an increase in the proportion of diarrhea in patients with constipation due to the long intervention time of probiotics, leading to the improvement of constipation and the occurrence of diarrhea; (3) both probiotics and lactulose can significantly increase the levels of blood SP and GAS and decrease the level of MTL in patients with constipation. For clinical practice, the current study suggested that both probiotics and lactulose have a certain therapeutic effect on functional constipation. On the basis of probiotics, we added dietary fiber and other intestinal beneficial ingredients. Dietary fiber is a healthy way to stimulate intestinal peristalsis. At the same time, it can absorb water in feces, soften feces and help defecate smoothly. Therefore, the compound of probiotics can be a feasible and effective method in daily treatment of constipation, which is also easy to be accepted by patients.

Constipation is one of the most common digestive system diseases. With the change of people's lifestyle and environment, the incidence rate of patients has been increasing gradually. The epidemiological survey showed that the incidence rate of constipation was 27%, and the prevalence rate of males and females was about 1 : 1.5 (Tian et al., 2019; Guo et al., 2002). At present, the studies have found that people in economically underdeveloped areas and those with low education levels are more likely to have constipation (Ebling et al., 2014), which is related to race and region (Roque & Bouras, 2015; Chu et al., 2014; Singh et al., 2018). Chronic constipation is closely related to multiple system diseases, such as cardiovascular and cerebrovascular diseases, colorectal tumors, and so on (Singh et al., 2018; Dehghani et al., 2013).

At present, the common treatments for functional constipation mainly include lifestyle intervention, biofeedback therapy, sacral nerve stimulation, fecal microbial transplantation, psychological and spiritual intervention, etc. (Zhang et al., 2014). However, it is not clear whether the above treatments have a definite effect on functional constipation, and there is a lack of clinical evidence. If the patient cannot be symptomatic for a long time, and the symptoms gradually worsen, it will develop into intractable constipation in severe cases (Clemens et al., 2013). Therefore, it is very important to find a safe and effective treatment.

Our study aims to investigate the efficacy of panax notoginseng stem, leaf tea combined with panaxnotoginseng fruit, vegetable enzyme, and probiotic powder for functional constipation. By observing 118 patients with functional constipation, the following results were demonstrated: (1) The lactulose intervention group could significantly improve the physical strength of patients; (2) The lactulose intervention group improved the quality of life of patients; (3) The lactulose intervention group ameliorated fecal quality of constipation patients without increasing the number of diarrhea.

The main components of the probiotics intervention group were panax notoginseng stem, leaf tea combined with panaxnotoginseng fruit, vegetable enzyme, and probiotic powder. The patients with constipation have dysbacteriosis and disorder, a decrease of intestinal specific anaerobes, an increase of intestinal pH, intestinal dysfunction, and slow intestinal peristalsis (Zhang & Xia, 2020). Fruit and vegetable enzymes are rich in bifdobacteria, lactobacillus acidophilus, lactobacillus, and other living bacteria, which can form biofilm in the intestine after reaching the intestine (Pan et al., 2019), increase the proliferation of beneficial bacteria and fermentation bacteria in the intestine, and promote the secretion of lactic acid and short-chain fatty acids by intestinal flora. It can reduce the pH of feces, increase the acidity of feces, stimulate intestinal peristalsis, increase the frequency of defecation, soften the stool and facilitate excretion (Escribano et al., 2018; Yu et al., 2017; Barichella et al., 2016).

The intestinal flora of patients with constipation was significantly unbalanced. In recent years, due to the function of probiotics in correcting intestinal disorders, the therapeutic effect of probiotics on constipation has gradually attracted attention (Zhao & Yu, 2016). According to a randomized controlled trial (RCT) conducted in South Korea (Yoon et al., 2018), probiotics supplementation is beneficial to change fecal characteristics, defecation frequency, and intestinal microecology of patients with constipation. It is helpful to maintain fecal stability even if it is stopped for a period of time.

In addition, the stems and leaves of Panax notoginseng are rich in vitamin C (Yang et al., 2014) and crude fiber (Qu et al., 2014). Among them, vitamin C can form soluble sodium salt with alkaline intestinal juice in the human body. Soluble sodium salt can increase the fluid in the intestinal cavity to promote the movement of the intestine and achieve the final effect of defecation.

At the same time, Dietary fiber can be decomposed by bacterial polysaccharide enzymes in the large intestine to produce short-chain fatty acids. Short-chain fatty acids can stimulate mucosal cell proliferation and mucosal blood supply, promote the release of gastrointestinal hormones, and improve intestinal peristalsis (Ebrahimi et al., 2016). A foreign RCT showed that soluble dietary fiber mixed with insoluble dietary fiber can improve the intestinal flatulence of patients with constipation, significantly improve the symptoms of constipation, and improve the quality of life of patients (Erdogan et al., 2016).

Changes in diet and behavior are still the first-line treatment for constipation. Dietary fiber supplementation can improve fecal properties and increase defecation frequency (Fathallah et al., 2017). At present, the guidelines recommend that the basic treatment of constipation include eating more high dietary fiber food, drinking more water, forming the habit of regular defecation, and relieving psychological tension (Hayat et al., 2017; Rao et al., 2016). The single-use of dietary fiber and probiotics has a positive effect on constipation, and the combination of them may promote each other. Sheep dairy products containing prebiotics and probiotics may not only have health-promoting properties, but also reduce chemically induced colon cancer in mice (Balthazar et al., 2021). In the future, further studies are still warranted to explore the effect of this combination in other models such as postmenopausal osteoporosis (Eor et al., 2020; Lee et al., 2020).

# **5** Conclusions

In conclusion, both probiotics intervention and lactulose intervention can improve the quality of life of patients with constipation and the fecal quality of patients with constipation. Probiotics group can lead to an increase in the proportion of diarrhea in patients with constipation.

# **Ethical approval**

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of our hospital. All participants had signed the informed consent.

# **Conflict of interest**

All of the authors had no any personal, financial, commercial, or academic conflicts of interest separately.

# Availability of data and material

All data generated or analyzed during this study are included in this published article.

# Funding

Not applicable.

# Author contributions

Conceptualization: HSP and ZYC; Investigation: LM and LL; Supervision: MWW, LM and LL; data analyses, interpreted the data: TSS and LL; Writing–original draft: HSP and ZYC; Writing–review and editing: LJ, LJY and LL; Approval of the final manuscript: all authors.

# Acknowledgements

Not applicable.

#### References

- Balthazar, C. F., Moura, N. A., Romualdo, G. R., Rocha, R. S., Pimentel, T. C., Esmerino, E. A., Freitas, M. Q., Santillo, A., Silva, M. C., Barbisan, L. F., Cruz, A. G., & Albenzio, M. (2021). Synbiotic sheep milk ice cream reduces chemically induced mouse colon carcinogenesis. *Journal of Dairy Science*, 104(7), 7406-7414. http:// dx.doi.org/10.3168/jds.2020-19979. PMid:33934866.
- Barichella, M., Pacchetti, C., Bolliri, C., Cassani, E., Iorio, L., Pusani, C., Pinelli, G., Privitera, G., Cesari, I., Faierman, S. A., Caccialanza, R., Pezzoli, G., & Cereda, E. (2016). Probiotics and prebiotic fiber for constipation associated with Parkinson disease: an RCT. *Neurology*, 87(12), 1274-1280. http://dx.doi.org/10.1212/WNL.000000000003127. PMid:27543643.
- Casias, A., & Newton, L. (2021). Functional constipation: a case report. *Journal of Pediatric Health Care*, 35(1), 99-103. http://dx.doi. org/10.1016/j.pedhc.2020.07.014. PMid:33046326.
- Chassagne, P., Ducrotte, P., Garnier, P., & Mathiex-Fortunet, H. (2017). Tolerance and long-term efficacy of polyethylene glycol 4000 (Forlax\*) compared to lactulose in elderly patients with chronic constipation. *The Journal of Nutrition, Health & Aging*, 21(4), 429-439. http:// dx.doi.org/10.1007/s12603-016-0762-6. PMid:28346570.
- Chu, H., Zhong, L., Li, H., Zhang, X., Zhang, J., & Hou, X. (2014). Epidemiology characteristics of constipation for general population, pediatric population, and elderly population in China. *Gastroenterology Research and Practice*, 2014, 532734. http://dx.doi. org/10.1155/2014/532734. PMid:25386187.
- Clemens, K. E., Faust, M., Jaspers, B., & Mikus, G. (2013). Pharmacological treatment of constipation in palliative care. *Current Opinion in Supportive and Palliative Care*, 7(2), 183-191. http://dx.doi.org/10.1097/ SPC.0b013e32835f1e17. PMid:23478431.
- Dehghani, S. M., Basiratnia, M., Matin, M., Hamidpour, L., Haghighat, M., & Imanieh, M. H. (2013). Urinary tract infection and enuresis in children with chronic functional constipation. *Iranian Journal* of Kidney Diseases, 7(5), 363-366. PMid:24072148.

- Ebling, B., Gulić, S., Jurcić, D., Martinac, M., Gmajnić, R., Bilić, A., Pribić, S., & Levak, M. T. (2014). Demographic, anthropometric and socioeconomic charateristics of functional constipation in eastern Croatia. *Collegium Antropologicum*, 38(2), 539-546. PMid:25144985.
- Ebrahimi, H., Sadeghi, M., Amanpour, F., & Dadgari, A. (2016). Influence of nutritional education on hemodialysis patients knowl-edge and quality of life. *Saudi Journal of Kidney Diseases and Transplantation*, 27(2), 250-255. http://dx.doi.org/10.4103/1319-2442.178253. PMid:26997377.
- Eor, J. Y., Tan, P. L., Son, Y. J., Lee, C. S., & Kim, S. H. (2020). Milk products fermented by Lactobacillus strains modulate the gut–bone axis in an ovariectomised murine model. *International Journal of Dairy Technology*, 73(4), 743-756. http://dx.doi.org/10.1111/1471-0307.12708.
- Erdogan, A., Rao, S. S. C., Thiruvaiyaru, D., Lee, Y. Y., Adame, E. C., Valestin, J., & O'Banion, M. (2016). Randomised clinical trial: mixed soluble/insoluble fibre vs. psyllium for chronic constipation. *Alimentary Pharmacology & Therapeutics*, 44(1), 35-44. http://dx.doi. org/10.1111/apt.13647. PMid:27125883.
- Escribano, J., Ferré, N., Gispert-llaurado, M., Luque, V., Rubio-Torrents, C., Zaragoza-Jordana, M., Polanco, I., Codoñer, F. M., Chenoll, E., Morera, M., Moreno-Muñoz, J. A., Rivero, M., & Closa-Monasterolo, R. (2018). Bifidobacterium longum subsp infantis CECT7210supplemented formula reduces diarrhea in healthy infants: a randomized controlled trial. *Pediatric Research*, 83(6), 1120-1128. http://dx.doi.org/10.1038/pr.2018.34. PMid:29538368.
- Fathallah, N., Bouchard, D., & Parades, V. (2017). Diet and lifestyle rules in chronic constipation in adults: from fantasy to reality.... *La Presse Médicale*, 46(1), 23-30. http://dx.doi.org/10.1016/j.lpm.2016.03.019. PMid:28065611.
- Fernández-Bañares, F. (2006). Nutritional care of the patient with constipation. Best Practice & Research Clinical Gastroenterology, 20(3), 575-587. http://dx.doi.org/10.1016/j.bpg.2005.11.002. PMid:16782530.
- Guo, X., Ke, M., Pan, G., Han, S., Fang, X., Lu, S., & Guo, H. (2002). Chronic constipation among adults in Beijing area, stratified, randomized epidemiological investigation and analysis of related factors. *Chinese Journal of Digestion*, 22(10), 637-638.
- Hayat, U., Dugum, M., & Garg, S. (2017). Chronic constipation: update on management. *Cleveland Clinic Journal of Medicine*, 84(5), 397-408. http://dx.doi.org/10.3949/ccjm.84a.15141. PMid:28530898.
- Lee, C. S., Lee, S. H., & Kim, S. H. (2020). Bone-protective effects of *Lactobacillus plantarum* B719-fermented milk product. *International Journal of Dairy Technology*, 73(4), 706-717. http://dx.doi. org/10.1111/1471-0307.12701.
- Pan, D. D., Shen, T. Y., & Qin, H. L. (2019). Probiotic preparation in treatment of chronic constipation: its clinic regimen and strategy. *Shanghai Journal of Preventive Medicine*, 31(10), 794-798.
- Pimentel, T. C., Oliveira, L. L. G., Souza, R. C., & Magnani, M. (2022). Probiotic ice cream: a literature overview of the technological and sensory aspects and health properties. *International Journal of Dairy Technology*, 75(1), 59-76. http://dx.doi.org/10.1111/1471-0307.12821.
- Qu, Y., Liu, Y., Huang, Q. L., Guo, L. P., & Cui, X. M. (2014). Analysis and evaluation of nutritive elements in aerial part of Panax notoginseng. *Zhongguo Zhongyao Zazhi*, 39(4), 601-605. PMid:25204129.
- Rajindrajith, S., Ranathunga, N., Jayawickrama, N., van Dijk, M., Benninga, M. A., & Devanarayana, N. M. (2020). Behavioral and emotional problems in adolescents with constipation and their

association with quality of life. *PLoS One*, 15(10), e0239092. http://dx.doi.org/10.1371/journal.pone.0239092. PMid:33044960.

- Rao, S. S. C., Rattanakovit, K., & Patcharatrakul, T. (2016). Diagnosis and management of chronic constipation in adults. *Nature Reviews Gastroenterology & Hepatology*, 13(5), 295-305. http://dx.doi. org/10.1038/nrgastro.2016.53. PMid:27033126.
- Roque, M. V., & Bouras, E. P. (2015). Epidemiology and management of chronic constipation in elderly patients. *Clinical Interventions in Aging*, 10(6), 919-930. PMid:26082622.
- Ryan, J., Hutchings, S. C., Fang, Z., Bandara, N., Gamlath, S., Ajlouni, S., & Ranadheera, C. S. (2020). Microbial, physico-chemical and sensory characteristics of mango juice-enriched probiotic dairy drinks. *International Journal of Dairy Technology*, 73(1), 182-190. http://dx.doi.org/10.1111/1471-0307.12630.
- Singh, P., Surana, R., Soni, S., Agnihotri, A., Ahuja, V., Makharia, G. K., Staller, K., & Kuo, B. (2018). Cross cultural comparison of constipation profiles at tertiary care centers between India and USA. *Neurogastroenterology and Motility*, 30(8), e13324. http://dx.doi. org/10.1111/nmo.13324. PMid:29521026.
- Tian, X. T., Liang, C. L., Yu, H. F., & Bu, S. R. (2019). Correlation between anorectal manomentry techniques and defecation disorders symptoms and classification in patients with constipation. *Journal* of *Clinical Internal Medicine*, 36(3), 178-181.
- Yang, J. J., Liu, Y., Qu, Y., Cui, X. M., Huang, L. Q., & Guo, L. P. (2014). Content determination of vitamin C in aerial part of Panax notoginseng by three methods. *Science and Technology of Food Industry*, 35(24), 53-56.
- Yerlikaya, O., Akpinar, A., Saygili, D., & Karagozlu, N. (2020). Incorporation of *Propionibacterium shermanii* subsp. *freudenreichii* in probiotic dairy drink production: physicochemical, rheological, microbiological and sensorial properties. *International Journal of Dairy Technology*, 73(2), 392-402. http://dx.doi.org/10.1111/1471-0307.12666.
- Yoon, J. Y., Cha, J. M., Oh, J. K., Tan, P. L., Kim, S. H., Kwak, M. S., Jeon, J. W., & Shin, H. P. (2018). Probiotics ameliorate stool consistency in patients with chronic constipation: a randomized, double-blind, placebo-controlled study. *Digestive Diseases and Sciences*, 63(10), 2754-2764. http://dx.doi.org/10.1007/s10620-018-5139-8. PMid:29876777.
- Yu, T., Zheng, Y. P., Tan, J. C., Xiong, W. J., Wang, Y., & Lin, L. (2017). Effects of prebiotics and synbiotics on functional constipation. *The American Journal of the Medical Sciences*, 353(3), 282-292. http:// dx.doi.org/10.1016/j.amjms.2016.09.014. PMid:28262216.
- Zendeboodi, F., Khorshidian, N., Mortazavian, A. M., & Cruz, A. G. (2020). Probiotic: conceptualization from a new approach. *Current Opinion in Food Science*, 32, 103-123. http://dx.doi.org/10.1016/j. cofs.2020.03.009.
- Zhang, G. P., & Xia, H. P. (2020). Changes of intestinal flora and its correlation with intestinal motility before and after fecal microbiota transplantation in patients with intractable constipation. *Modern Digestion & Intervention*, 25(1), 5-10.
- Zhang, N., Huang, Z., Xu, F., Xu, Y., Chen, J., Yin, J., Lin, L., & Chen, J. D. Z. (2014). Transcutaneous neueomodulation at posterior tibial nerve and ST36 for chronic constipation. *Evidence-Based Complementary and Alternative Medicine*, 2014, 560802. http:// dx.doi.org/10.1155/2014/560802. PMid:25431612.
- Zhao, Y., & Yu, Y. B. (2016). Intestinal microbiota and chronic constipation. *SpringerPlus*, 5(1), 1130. http://dx.doi.org/10.1186/ s40064-016-2821-1. PMid:27478747.