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*Original Article*

# The influence of the intestinal microecological preparation bifido on the nutritional status, gastrointestinal function, adverse reactions, and other indicators of peritoneal dialysis patients

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**Abstract:** Objective: This study aimed to analyze the therapeutic effect of bifido, an intestinal microecological preparation (IMP), on patients treated with peritoneal dialysis (PD). Methods: 89 patients who received PD in our hospital from July 2018 to June 2019 were selected as the study cohort and divided into a control group (CG), which included 44 patients treated routinely, and an observation group (OG), which included 45 patients treated with bifido on the basis of routine treatment, according to the sequence of admission. A retrospective analysis was performed based on the clinical data of both groups to compare the nutritional statuses, gastrointestinal functions, adverse reactions, immune functions, and biochemical statuses in the two groups. Results: (1) The nutrition risk screening (NRS) scores of the OG were lower than the scores of the CG 2 weeks after treatment ($P<0.05$). (2) The hemoglobin levels and albumin levels of the OG were higher than the corresponding levels of the CG 2 weeks after treatment ($P<0.05$). (3) The abdominal distension remission time, the borborygmus disappearance time, the intestinal exhaust recovery time, and the defecation recovery time in the OG were shorter than they were in the CG ($P<0.05$). (4) The incidence of adverse reactions was 8.89% in the OG and 13.64% in the CG ($P>0.05$). (5) The CD4+, CD4+/CD8+, natural killer cells (NK) and the CD8+ levels of the OG were better than those of the CG 2 weeks after treatment ($P<0.05$). (6) There were no significant differences in the serum creatinine (SC), urea nitrogen (UN), total cholesterol (TC), or triacylglycerol (TG) levels in the two groups 2 weeks after treatment ($P>0.05$). Conclusion: The application of bifido, an IMP, to the treatment of PD patients could significantly improve their nutritional statuses and gastrointestinal functions, without increasing adverse reactions. In addition, it can improve patients' immune function without significantly affecting their biochemical statuses, so it is worthy of promotion.

**Keywords:** Intestinal microecological preparation, bifido peritoneal dialysis, nutritional status, gastrointestinal function, adverse reactions, immune function, biochemical status

## Introduction

Peritoneal dialysis (PD) is an important renal replacement therapy used for patients with kidney diseases in the terminal stage. PD, which is simple, can protect the residual renal function, and the patients can receive the dialysis treatment at home, so this therapy is highly accepted [1, 2].

With the progress of medical technology, PD has been improved accordingly and the patients' survival time has been prolonged gradually after the treatment of PD, but the overall survival is not significantly enhanced [3]. In addition, long-term PD has a significant impact on the nutritional status of patients and a lot of patients suffer from malnutrition which further affects patients' tolerance to PD, and which may increase the toxic and side effects of the dialysis treatment and influence the safety of the treatment [4, 5]. Hence, it is very important to improve the nutritional status of PD patients, an improvement that will play a crucial role in ensuring the effect of PD and improving the prognoses of the patients [6].

To be specific, microecological preparation (MP) is a nutritional preparation made by using normal microbes, metabolites, and growth pro-

moting substances which are beneficial to the host, based on the principle of microecology, with the aim to improve the health of the host by regulating the micro dysbiosis and maintaining the microecological balance [7, 8]. IMP is a kind of MP that mainly acts on the intestinal tract, including many kinds in this regard [9]. In this study, the application value of bifido in the treatment of PD patients was analyzed in detail, and 89 patients who were admitted to our hospital from July 2018 to June 2019 were selected as the study cohort, with a summary shown below.

## Material and methods

### *Material*

The retrospective analysis was performed based on the clinical data of 89 patients who were treated with PD from July 2018 to June 2019 in our hospital. The basic diseases included polycystic kidney disease (PKD), chronic glomerulonephritis (CGN), ischemic renal disease (IRD), diabetic nephropathy (DN), hyperuricemic nephropathy (HN), drug induced kidney disease (DIKD), systemic lupus erythenlatosus nephritis (SLEN) and hypertensive kidney lesions (HKL). These patients were divided into a control group (CG) (n=44), aged 45-67 years old with a PD duration of 4-11 months, and an observation group (OG) (n=45) aged 43-66 years old with a PD duration of 4-12 months, according to the admission sequence. (1) Inclusion criteria: this study included patients with a definite history of kidney diseases; those treated with PD for at least 3 months; those in a stable condition; and those who signed the informed consent form after learning about and agreeing to the contents of this study. This study was approved by the Ethics Committee of the First Affiliated Hospital of Hebei North University. (2) Exclusion criteria: this study excluded patients in significantly deteriorated conditions or critical conditions during treatment; those with low compliance; those with mental or cognitive disorders; those with neoplastic diseases; and those who could not complete all the follow-up visits.

### *Methods*

Routine diet therapy was provided for the CG on the basis of PD, and the patients were informed of the influence of PD on nutritional status, the impact of nutritional status on prognosis, and the significance of alimentary control. The diet plan was determined based on the specific nutritional statuses and food preferences of the patients and the suggestions of dieticians. A manual for nutrient contents in food was issued to the patients to instruct them to master bromatometry and select the correct cooking methods. The patients' dietary statuses were evaluated regularly and any dietary problems faced by patients were quickly solved. Reasonable guidance was provided to the patients to guarantee a reasonable diet to the greatest extent.

The OG was treated with bifido, an IMP, in combination with the diet therapy. The patients took bifido (Bifid Triple Viable Capsules Dissolving at Intestines; specification: 0.21 g*36 capsules; registered number of approval: SFDA approval number S19993065; manufacturing enterprise: Jincheng Health Pharmaceutical Co., Ltd.) orally, 2-3 capsules each time and 2-3 times per day.

### *Observation targets*

(1) Nutrition risk: the NRS scale (NRS2002) [10] was used to evaluate the nutritional statuses of both groups respectively before treatment and at 2 weeks after treatment, using a 0-3 scoring system. 0 refers to normal; 1 refers to mild, which meant that the body weight loss was 5% within 3 months or the food intake dose was 50%-75% of the normal requirement; 2 refers to moderate, which meant that the body weight loss was 5% within 2 months or the food intake dose of the last week was 25%-50% of the normal requirement; and 3 refers to severe, which meant that the body weight loss normal requirement.

(2) Nutrient level: the indices of albumin and hemoglobin in the serum were measured respectively before the treatment and at 2 weeks after treatment. 5 ml fasting venous blood was collected before and after the treatment and centrifuged for 10 minutes at a temperature of 4°C, with the speed controlled at 3,000 rpm. The serum was kept at a temperature of -80°C for later measurement. All the indices were measured using the enzymatic

**Table 1.** Comparison of the clinicopathological data in the two groups ($\bar{x}$ ± s)/[n (%)]

| Data | | OG (n=45) | CG (n=44) | $t/X^2$ | *P* |
|---|---|---|---|---|---|
| Gender | Male | 24 (53.33) | 25 (56.82) | 0.109 | 0.741 |
| | Female | 21 (46.67) | 19 (43.18) | | |
| Age (years old) | | 53.29±5.19 | 53.15±5.13 | 0.128 | 0.899 |
| PD duration (month) | | 7.95±2.16 | 7.99±2.18 | 0.087 | 0.931 |
| Weight (kg) | | 62.85±10.43 | 63.38±11.45 | 0.228 | 0.820 |
| Basic kidney diseases | PKD | 2 (4.44) | 1 (2.27) | 1.524 | 0.361 |
| | CGN | 9 (20.00) | 9 (20.45) | | |
| | IRD | 3 (6.67) | 4 (9.09) | | |
| | DN | 8 (17.78) | 10 (22.73) | | |
| | HN | 8 (17.78) | 8 (18.18) | | |
| | DIKD | 5 (11.11) | 4 (9.09) | | |
| | SLEN | 7 (15.56) | 6 (13.64) | | |
| | HKL | 3 (6.67) | 2 (4.55) | | |

method, and the operation was carried out in strict accordance with the instructions.

(3) Gastrointestinal function: the two groups were compared in terms of abdominal distension remission times, borborygmus disappearance times, intestinal exhaust recovery times, and defecation recovery times after treatment.

(4) Adverse reactions: the two groups were compared in their incidences of abdominal distension, constipation, nausea and vomiting, and anorexia during the treatment.

(5) Immune function: the cellular immune function indexes were measured before the treatment and at two weeks after the treatment in the two groups, including their CD4+, CD8+, CD4+/CD8+ and natural killer cell (NK) levels. Before and after the treatment, 5 ml of fasting venous blood was collected and analyzed using a FACS-420 flow cytometer manufactured by BD of America.

(6) Biochemical index: the of serum creatinine (SC), urea nitrogen (UN), total cholesterol (TC), and triacylglycerol (TG) levels were measured before the treatment and at two weeks after the treatment in the two groups. 5 ml of fasting venous blood was collected before and after the treatment centrifuged for 10 minutes at a temperature of 4°C, with the speed set at 3,000 rpm. The serum was kept at a temperature of -80°C for later measurement. All the indices were measured using the enzymatic method, and the operation was carried out in strict accordance with the instructions.

*Statistical methods*

SPSS 22.0 was used for the statistical analysis. The measurement data were represented by the means ± standard deviations, and the results between groups were compared using independent-samples *t* tests. The enumeration data were represented by [n (%)], and the results between groups were compared using $X^2$ tests. The multipoint group comparisons were performed using ANVOA and F tests. $P<0.05$ meant that the difference had statistical significance.

## Results

*Comparison of the clinicopathological data in the two groups*

There were no obvious difference in terms of gender ratio, average age, average PD duration, average weight, or proportion of basic kidney diseases between the two groups ($P>0.05$) (**Table 1**).

*Comparison of the nutrition risk in the two groups*

There was little difference in the NRS scores in the two groups before treatment ($P>0.05$). The two groups' scores were significantly reduced 2 weeks after treatment and those of the OG were much lower than those of the CG at 2 weeks after treatment ($P<0.05$) (**Table 2** and **Figure 1**).

*Comparison of the nutrient levels in the two groups*

Before treatment, the hemoglobin and albumin levels were (10.15±1.34) g/L and (32.16±1.19) g/L in the OG and (10.16±1.35) g/L and (32.19±1.21) g/L in the CG. At two weeks after treatment, the hemoglobin and albumin levels were (12.34±1.38) g/L and (37.21±1.85) g/L

**Table 2.** Comparison of the NRS scores in the two groups ($\bar{x}$ ± s, scores)

| Group | Number of cases | Before treatment | 2 weeks after treatment |
|---|---|---|---|
| OG | 45 | 2.31±0.39 | 0.86±0.43* |
| CG | 44 | 2.29±0.38 | 1.83±0.35* |
| *t* | | 0.322 | 5.725 |
| *P* | | 0.749 | 0.000 |

Notes: *$P$<0.05 refers to the comparison before treatment and 2 weeks after treatment in each group.

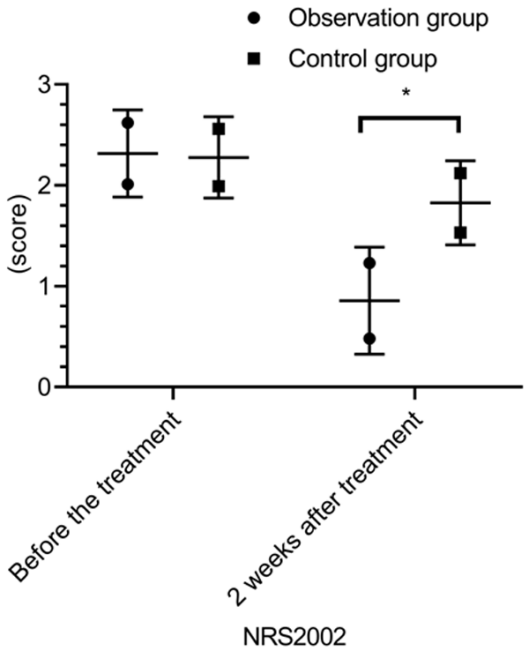


**Figure 1.** Comparison of the nutrition risk between two groups. There were little differences in the NRS scores in the two groups before treatment ($P$>0.05). The NRS scores of the OG were much lower than those of the CG at two weeks after treatment ($P$<0.05). * means $P$<0.05 when the two groups were compared at the same time point.

in the OG and (10.86±1.26) g/L and (33.46±1.52) g/L in the CG. There were no significant differences in the hemoglobin and albumin levels in the two groups before treatment ($P$>0.05). The hemoglobin and albumin levels in the two groups increased to some extent 2 weeks after treatment, and the levels in the OG were much higher than those in the CG at two weeks after treatment ($P$<0.05) (**Figure 2**).

*Comparison of the gastrointestinal function in the two groups*

The abdominal distension remission times, the borborygmus disappearance times, the intestinal exhaust recovery times, and the defecation recovery times in the OG were much shorter than they were in the CG, which indicated that the differences had statistical significance ($P$< 0.05) (**Table 3**).

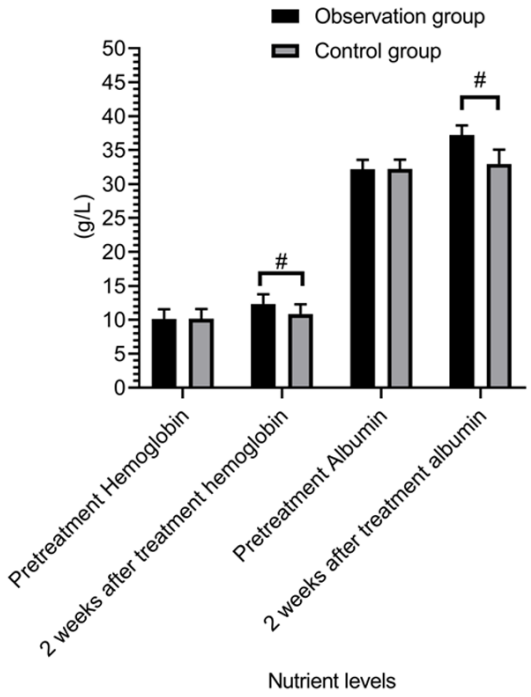


**Figure 2.** Comparison of the nutrient levels in the two groups. There was little difference in the hemoglobin and albumin levels between the two groups before treatment ($P$>0.05). The hemoglobin and albumin levels of the OG were much higher than those of the CG at two weeks after treatment ($P$<0.05). # means $P$<0.05 when the two groups were compared at the same time point.

*Comparison of adverse reactions in the two groups*

The incidence of adverse reactions was 8.89% in the OG and 13.64% in the CG, showing no statistical difference ($P$>0.05) (**Table 4**).

*Comparison of the immune function in the two groups*

There was no significant difference in the immune indices in the two groups before treatment, including the CD4+, CD8+, CD4+/CD8+, and NK levels ($P$>0.05). In both groups, the CD4+, CD4+/CD8+ and NK levels increased, and the CD8+ level decreased at two weeks after treatment. The CD4+, CD4+/CD8+, and NK levels in the OG were much higher than they were in the CG and CD8+ of the OG was much

**Table 3.** Comparison of the gastrointestinal functions in the two groups after treatment ($\bar{x} \pm s$)

| Group | Number of cases | Defecation recovery time (h) | Intestinal exhaust recovery time (h) | Abdominal distension recovery time (d) | Borborygmus disappearance time (d) |
|---|---|---|---|---|---|
| OG | 45 | 32.16±5.82 | 11.35±2.28 | 4.12±1.16 | 4.84±1.42 |
| CG | 44 | 60.38±8.49 | 18.64±4.16 | 7.84±1.49 | 7.98±1.68 |
| *t* | | 18.326 | 10.282 | 13.159 | 9.531 |
| *P* | | 0.000 | 0.000 | 0.000 | 0.000 |

**Table 4.** Comparison of the incidences of adverse reactions in the two groups [n (%)]

| Group | Abdominal distension | Constipation | Nausea and vomiting | Anorexia | Incidences |
|---|---|---|---|---|---|
| OG (n=45) | 1 (2.22) | 1 (2.22) | 2 (4.44) | 0 (0.00) | 4 (8.89) |
| CG (n=44) | 2 (4.55) | 2 (4.55) | 1 (2.27) | 1 (2.27) | 6 (13.64) |
| $X^2$ | | | | | 0.503 |
| *P* | | | | | 0.478 |

lower than that of the CG 2 weeks after treatment ($P<0.05$) (**Table 5** and **Figure 3**).

*Comparison of the biochemical indices in the two groups*

There were no significant differences in the SC, UN, TC, or TG levels between the two groups before treatment and at two weeks after treatment ($P>0.05$). There were little differences in the SC, UN, TC and TG levels before treatment and at two weeks after treatment in both groups ($P>0.05$) (**Table 6** and **Figure 4**).

## Discussion

Actually, the gastrointestinal tract is a huge bank of bacteria. Normally, there are about 450 types of flora in the gastrointestinal tract, including viruses, bacteria, and fungi. Different flora synergistically maintain the microecological balance of the human body through mutual restriction, correlative dependence, and common growth. But an unbalance of these flora will lead to dysbacteriosis and thus cause a variety of diseases [11]. The immunity of PD patients is much poorer than that of healthy people, so these patients are affected to different degrees while taking food, and their gastrointestinal floras are easily disturbed, which will lead to malnutrition [12]. So for PD patients, it must be emphasized that the balance of floras and the stability of the body environment should be maintained to avoid all kinds of complications [13].

In this study, the OG was treated with bifido, an IMP, on the basis of PD. Bifido refers to Bifid Triple Viable, which includes more than 50 million viable bacteria. Clinically, it has been widely used for many diseases with a good effect, including diarrhea, irritable bowel syndrome, inflammatory bowel disease, HP infection, bacterial vaginosis, cirrhosis, and colon cancer [14, 15]. As shown in this study, there was little difference in the SC, UN, TC and TG levels in the two groups after treatment, and there was little difference before and after treatment. Besides, there was little difference in the incidences of adverse reactions in the two groups ($P>0.05$), which implies that IMP had no impact on the safety of the treatment and could not affect the body's biochemical status, so it was highly accepted by the patients.

The specific mechanisms of action of IMP on PD patients are analyzed and summarized as follows. First, the neuromuscular active enzyme can be regulated. Bifido, with a good regulating effect on intestinal neuromuscular activity, can promote intestinal peristalsis and improve intestinal function [16]. The metabolites of bifido mainly include formic acid, lactic acid, and acetic acid. These metabolites can regulate intestinal neuromuscular activity, accelerate intestinal peristalsis, relieve abdominal distension, and reduce the incidence of constipation [17]. This study showed that the abdominal distension remission time, the borborygmus disappearance time, the intestinal exhaust recovery time, and the defecation recovery time in the OG were shorter than they were in the CG after treatment ($P<0.05$). This indicates that the application of IMP can help PD patients improve their gastrointestinal function rapidly, which could promote the improvement of their

**Table 5.** Comparison of the immune function in the two groups ($\bar{x} \pm s$)

| Group | Time | CD4+ (%) | CD8+ (%) | CD4+/CD8+ | NK (%) |
|---|---|---|---|---|---|
| OG (n=45) | Before treatment | 24.23±2.16 | 31.16±1.38 | 1.13±0.25 | 19.28±2.51 |
| | 2 weeks after treatment | 38.54±3.19 | 22.84±1.24 | 1.53±0.32 | 42.83±3.06 |
| CG (n=44) | Before treatment | 23.89±2.11 | 30.52±1.52 | 1.15±0.26 | 20.20±2.31 |
| | 2 weeks after treatment | 32.16±2.95 | 27.46±1.45 | 1.31±0.28 | 34.19±3.02 |
| *t* | | 9.790 | 16.167 | 3.449 | 13.404 |
| *P* | | 0.000 | 0.000 | 0.001 | 0.000 |

Notes: *t* and *p* refer to the statistical values of comparison between the two groups at two weeks after treatment.

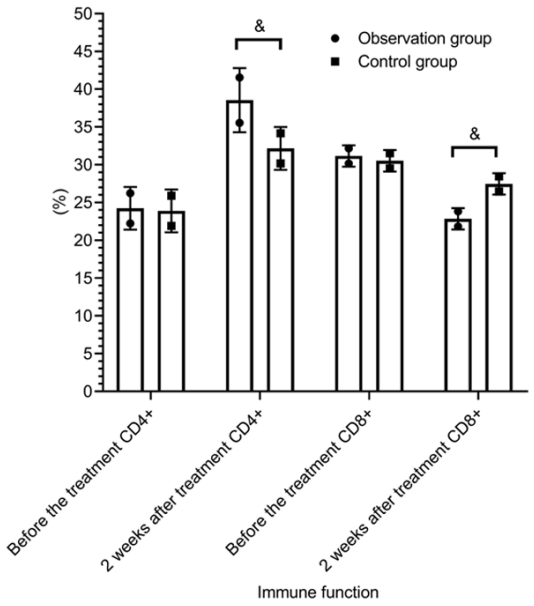


**Figure 3.** Comparison of the immune function in the two groups. There was little difference in the CD4+ and CD8+ levels in the two groups before treatment (*P*>0.05). The CD4+ of the OG was much higher than that of the CG at two weeks after treatment and the CD8+ of the OG was much lower than that of the CG at two weeks after treatment (*P*<0.05). & means *P*<0.05 when the two groups were compared at the same time point.

immune function. Second, the nutrition can be improved. The beneficial bacteria in bifido will become participate in the metabolism of pantothenic acid, vitamin B, folic acid, biotin, and niacin, etc. through in vivo biochemistry, thus providing nutrients for the human body [18]. Bifido can reduce the pH level in the intestinal tract and accelerate the absorption of vitamin D and other microelements [19]. The lactobacilli can reduce the pH level in the intestinal tract and promote the absorption of calcium phosphate, vitamin D, and iron. In addition, they are also the participants in the synthesis and absorption of vitamins and folic acid [20]. This study showed through treatment that the NRS scores of the OG were much lower than those of the CG 2 weeks after treatment, and the hemoglobin and albumin levels of the OG were much higher than those of the CG at two weeks after treatment, which indicates that compared with the routine diet guidance, the treatment combined with IMP can more significantly reduce the nutrition risk of PD patients and enhance the patients' nutrient levels more effectively. Bifido can stimulate the immune response in the host, strengthen cellular and humoral immunity, and greatly improve the phagocytic and complementary activities of macrophages [21]. The lactobacilli can significantly stimulate the activity of NK in the spleen [22]. Lahner et al. [23] indicated that dead lactobacilli accelerated the proliferation of T-helper 1 after medication and thus promoted the generation of IgE antibodies. In this study, the indices of immune function in the OG were better than those in the CG at two weeks after treatment, including the CD4+, CD4+/CD8+, NK, and CD8+ levels (*P*<0.05), which indicates that IMP has a good effect on the promotion of immune function in PD patients. Fourth, it has the functions of adhesion, colonization, and a biological barrier. MP, characterized by reproductivity, excludability and colonization, can be closely bound to occupy the surface of intestinal mucosa with other anaerobic bacteria through the interaction of teichoic acids with intestinal epithelial cells, which will further form a biological barrier and thus enhance the defense capability of epithelial cells [24]. What's more, the metabolites of MP, such as bacteriocin, hydrogen peroxide, acid with low molecular weight and other active substances, will form a chemical barrier to prevent pathogenic bacteria and conditioned pathogens from contacting the intestinal epi-

**Table 6.** Comparison of the biochemical indices in the two groups ($\overline{x} \pm s$)

| Group | Time | SC (μmol/L) | UN (mmol/L) | TC (mmol/L) | TG (mmol/L) |
|---|---|---|---|---|---|
| OG (n=45) | Before treatment | 922.13±310.28 | 18.16±6.38 | 4.16±1.15 | 1.45±0.50 |
| | 2 weeks after treatment | 945.16±351.16 | 19.13±6.81 | 4.42±1.32 | 1.51±0.56 |
| CG (n=44) | Before treatment | 920.53±305.46 | 18.32±5.96 | 4.18±1.17 | 1.46±0.52 |
| | 2 weeks after treatment | 937.41±316.52 | 18.79±4.61 | 4.31±1.21 | 1.49±0.54 |
| *t* | | 0.109 | 0.275 | 0.410 | 0.171 |
| *P* | | 0.913 | 0.784 | 0.683 | 0.864 |

Notes: *t* and *p* refer to the statistical values of comparison between two groups at two weeks after treatment.

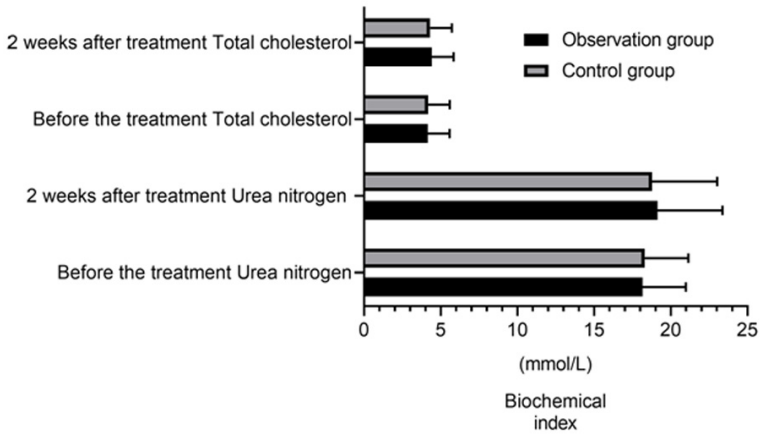


**Figure 4.** Comparison of biochemical indices in the two groups. There was little difference in the TC and UN values in the two groups before treatment and at two weeks after treatment ($P>0.05$).

thelium or avoiding the adhesion or colonization above it. Bifido bacteria can be closely bound to achieve occupation through the metaplasia of phosphates and intestinal epithelial cells, which will form a biological barrier to maintain normal intestinal peristalsis, avoid the colonization of pathogenic bacteria, reduce the pH value in the intestinal tract through the lactic and acetic acids that have has generated, and finally, inhibit the growth of pathogenic bacteria [25].

In conclusion, bifido, an IMP, can rapidly improve the nutritional statuses and gastrointestinal functions of PD patients without increasing adverse reactions, so it is worthy of promotion. But this was a retrospective study with a small cohort and a short follow-up period, so the analysis and its results were not comprehensive, and the results were biased to a certain extent. More intensive studies with larger samples in more aspects should be conducted in the future, and prospective studies should be emphasized to obtain more scientific and representative conclusions and thus provide more references for the treatment of patients.

## Disclosure of conflict of interest

None.

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