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Effect of microecological regulator combined with enteral nutrition on immune and coagulation function in patients with chronic critical illness

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ABSTRACT

This study was to investigate the effect of microecological regulators combined with enteral nutrition on immune and coagulation function in patients with a chronic critical illness. For this purpose, 78 patients with chronic critical illness in our hospital from January 2020 to January 2022 were divided into study and control groups according to a simple random number table, with 39 cases in each group. The control group was given enteral nutrition support, and the study group was given a microecological regulator. The variables of the study were the intervention effects [albumin (ALB), prealbumin (PA), serum total protein (TP)], immune function ($CD3^+$, $CD4^+$, $CD4^+/CD8^+$), coagulation function [platelet count (PLT), Fibrinogen (FIB), prothrombin time (PT) and the incidence of complications. Results showed that Before the intervention, ALB (30.69 ± 3.66) G/L, PA (132.91 ± 18.04) mg/L, TP (55.65 ± 5.42) G/L in the study group and ALB (31.78 ± 4.24) TP (57.01 ± 5.13) G/L had no significant difference (P>0.05). After the intervention, the levels of ALB, PA and TP in the two groups were higher than those before the intervention. ALB (38.91 ± 3.54) G/L, PA (204.24 ± 28.80) mg/L and TP (69.75 ± 7.48) G/L in the study group were higher than those in the control group (ALB 34.83 ± 3.82) TP (62.70 ± 6.33) g/L (P<0.05). There was no significant difference between $CD4^+/CD8^+$ (1.31 ± 0.39) (P>0.05). After the intervention, the levels of $CD3^+$, $CD4^+$, CD4 and CD8 in the two groups were higher than those before the intervention. $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ were higher than that of the control group. in the study group PLT (226.57 ± 41.15) × 10^9/L, FIB (3.58 ± 1.09) G/L, PT (9.41 ± 0.82) s were recoeded. There was no significant difference between FIB (3.71 ± 1.13) G/L and PT (9.24 ± 0.77) s (P>0.05). After the intervention, PLT and FIB decreased and PT increased in both groups. PLT (177.15 ± 12.51) × 10^9/L and FIB (2.57 ± 0.39) G/L in the study group were lower than PLT (198.54 ± 10.77) × 10^9/L and FIB (3.04 ± 0.54) PT (15.79 ± 1.21) s was higher than PT (13.13 ± 1.33) s in the control group (P<0.05). The incidence of complications in the study group (5.13%) was lower than that in the control group (20.51%) (P<0.05). The conclusion was that the intervention effect of microecological regulators combined with enteral nutrition on patients with chronic critical illness is significant, which can improve their nutritional status and immune function, improve coagulation function, and reduce the incidence of complications.

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Introduction

Chronic critically ill patients are mainly those who survive the acute stage in ICU, but still have persistent organ dysfunction, enter the chronic stage of continuous dependence on a life support system, and still need to stay in ICU. Chronic critical illness is often accompanied by immunosuppression, excessive inflammatory response, multiple organ dysfunction, etc. (1,2). Long-term internal environment disorder and persistent dysfunction can cause immunosuppression (3). Therefore, it is of great significance to intervene in patients with chronic critical illness in the early stage.

The clinical treatment of chronic critical illness involves multidisciplinary collaboration, in which nutritional support is an important link. Because it is difficult for critically ill patients to eat by mouth, enteral nutrition is usually chosen, which can improve nutrition and general condition, protect intestinal mucosa, reduce the inflammatory response and strengthen immune function. It is conducive to reducing the risk of complications such as enterogenic infection and ventilator-associated pneumonia and has a positive effect on ensuring a good outcome of the disease (4-6). However, chronically critically ill patients are often accompanied by nutritional absorption disorders, and it is difficult to completely absorb intestinal nutrients. Microecological regulators can repair the intestinal mucosal barrier, enhance immunity, and correct intestinal flora disorders (7,8).

Based on this, 78 patients with chronic critical illness in our hospital were selected to explore the clinical value of microecological regulators combined with enteral nutri-

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tion. The report is as follows.

Materials and Methods

General information

78 patients with chronic critical illness in our hospital from January 2020 to January 2022 were selected and divided into a study group and control group according to a simple random number table, with 39 cases in each group. In the control group, there were 23 males and 16 females, aged 34-79 years, with an average of (56.41 ± 10.78) years; body mass index was 17.4-27.3 kg/m^2, with an average of (22.35 ± 3.18) kg/m^2; Disease distribution: 9 cases of craniocerebral injury, 6 cases of sepsis, 6 cases of tracheotomy, 16 cases of prolonged mechanical ventilation, 2 cases of other. There were 25 males and 14 females in the study group, with an average age of (55.93 ± 12.02) years and a body mass index of (22.54 ± 3.32) kg/m^2(17.2 ~ 27.6 kg/m^2); Disease distribution: 11 cases of craniocerebral injury, 4 cases of sepsis, 4 cases of tracheotomy, 17 cases of prolonged mechanical ventilation, 3 cases of other. The clinical data of the two groups were balanced and comparable (P>0.05), and the study was approved by the ethics committee of our hospital.

Selection criteria

Inclusion criteria

(I) ICU stay ≥ 7 days; (II) Nutritional risk screening score (NRS2002) > 3; (III) Inability to eat by mouth; (IV) Informed consent of the patient's family.

Exclusion criteria

(I) Patients with contraindication of enteral nutrition; (II) Brain death; (III) Patients with digestive tract malignant tumor and digestive tract ulcer; (IV) Patients with immune system disease; (V) Patients who have sinusitis and other diseases that may affect the support of enteral nutrition; (VI) Women in lactation and pregnancy; (VII) Allergic constitution.

Method

Control group

Enteral nutrition support was adopted, and Ruisu (Huarui Pharmaceutical Co., Ltd., GYZZ H20020588) was selected, including carbohydrate 1.2 G/100 ml, fat 13.8 G/100 ml, protein 3.4 G/100ml, and energy density 1 kcal/100ml. The daily calorie requirement [25 (kcal/kg) × ideal body weight × (1 ± 5%)] was calculated according to the ideal body weight [(height-100) × 0.9]. The initial infusion rate was 20 ml/H, and the infusion rate was increased by 10 ml/H every other day to the target energy of 30-35 kcal (kg · d).

Study group

On the basis of the control group, the microecological regulator Tafecan was used, 420 mg/time, diluted with 20 ml water and then injected into the nose, twice a day.

Observation index

(I) The levels of albumin (ALB), prealbumin (PA) and serum total protein (TP) were measured by an automatic biochemical analyzer (Hitachi 7600-110) before and after the intervention. (II) The immune function of the two groups before and after intervention (CD3 $^+$, CD4$^+$, CD4 <lt R="39">/CD8) was measured by FACS Caliber flow cytometry. (III) Coagulation function [platelet count (PLT), fibrinogen (FIB), prothrombin time (PT)] was measured before and after intervention in the two groups and was measured by automatic coagulation analyzer. (IV) The incidence of complications in the two groups was analyzed.

Statistical methods

The data were analyzed by SPSS22.0, and the measurement data ($\bar{x} \pm s$) was expressed by t-test, the enumeration data n (%) was expressed by χ^2test, and P< 0.05 indicated that the difference was statistically significant.

Results

Intervention effect

Before the intervention, ALB (30.69 ± 3.66) G/L, PA (132.91 ± 18.04) mg/L, TP (55.65 ± 5.42) G/L in the study group and ALB (31.78 ± 4.24) mg/L, PA (135.64 ± 15.82) TP (57.01 ± 5.13) G/L had no significant difference (P>0.05). After the intervention, the levels of ALB, PA and TP in the two groups were higher than those before the intervention. ALB (38.91 ± 3.54) G/L, PA (204.24 ± 28.80) mg/L, and TP (69.75 ± 7.48) G/L in the study group were higher than those in the control group (ALB 34.83 ± 3.82) TP (62.70 ± 6.33) g/L (P<0.05). (Table 1).

Immune function

CD3$^+$(50.42 ± 5.13)%, CD4$^+$(27.54 ± 3.08)%, CD4$^+$/CD8$^+$(1.27 +/- 0.42) vs control CD3 <lt R="48"/> (49.79 +/- 5.34)%, CD4 <lt R="49"/> There was no significant

Table 1. Comparison of intervention effects between the two groups ($\bar{x} \pm s$).

Time	Group	Number of cases	ALB (g/L)	PA (mg/L)	TP (g/L)
Before the intervention	Study Group	39	30.69±3.66	132.91±18.04	55.65±5.42
	Control group	39	31.78±4.24	135.64±15.82	57.01±5.13
	T-value		1.215	0.711	1.138
	P value		0.228	0.480	0.259
After the intervention	Study Group	39	38.91±3.54	204.24±28.80	69.75±7.48
	Control group	39	34.83±3.82	187.64±23.73	62.70±6.33
	T-value		4.892	2.778	4.493
	P value		0.000	0.007	0.000

Table 2. Comparison of immune function between the two groups ($\bar{x} \pm s$).

Time	Group	Number of cases	$CD3^+$ (%)	$CD4^+$ (%)	$CD4^+/CD8^+$
Before the intervention	Study Group	39	50.42±5.13	27.54±3.08	1.27±0.42
	Control group	39	49.79±5.34	28.26±3.33	1.31±0.39
	T-value		0.531	0.991	0.436
	P value		0.597	0.325	0.664
After the intervention	Study Group	39	63.24±5.51	44.03±4.53	1.77±0.35
	Control group	39	59.86±5.45	40.51±4.07	1.61±0.33
	T-value		2.724	3.610	2.077
	P value		0.008	0.001	0.041

difference between $CD4^+/CD8^+$(1.31 ± 0.39) (P>0.05). After the intervention, the levels of $CD3^+$, $CD4^+$, CD4 <> R="54"/> and CD8 <> R=("55")/> in the two groups were higher than those before the intervention. $CD3^+$(63.24 ± 5.51)%, $CD4^+$(44.03 ± 4.53)%, $CD4^+/CD8^+$(1.77 +-0.35) was higher than that of the control group CD3 <lt R="60"/> (59.86 +-5.45)%, $CD4^+/CD8^+$ (1.61 ± 0.33) (P<0.05). (Table 2).

Coagulation function

PLT (226.57 ± 41.15) × 10^9/L, FIB (3.58 ± 1.09) G/L, PT (9.41 ± 0.82) s in the study group and PLT (228.71 ± 36.96) × 10^9/L in the control group before intervention There was no significant difference between FIB (3.71 ± 1.13) G/L and PT (9.24 ± 0.77) s (P>0.05). After the intervention, PLT and FIB decreased and PT increased in both groups. PLT (177.15 ± 12.51) × 10^9/L and FIB (2.57 ± 0.39) G/L in the study group were lower than PLT (198.54 ± 10.77) × 10^9/L and FIB (3.04 ± 0.54) PT (15.79 ± 1.21) s was higher than PT (13.13±1.33) s in the control group (P<0.05). (Table 3).

Complications

The incidence of complications in the study group (5.13%) was lower than that in the control group (20.51%) (P<0.05). (Table 4).

Discussion

Chronic critically ill patients have different degrees of stress response in the body, the intestine is the initial and central organ of the stress response, and intestinal mucosal injury is an important link in the onset and progress of multiple organ dysfunction syndrome, chronic critically ill patients with malnutrition, poor immune function, poor basic state, coupled with shock, trauma and so on can cause intestinal mucosa. Irrational use of antibiotics can also cause intestinal flora disorder, intestinal flora translocation, endotoxemia, and aggravate intestinal injury (9-11). Therefore, how to effectively intervene in patients with chronic critical illness is still a research hotspot.

Nutritional support plays an important role in critically ill patients, including enteral nutrition and parenteral nutrition, which mainly include trace elements, vitamins, medium-chain and long-chain fats, amino acids, etc. Enteral nutrition can directly contact intestinal mucosa through food, provide nutrients, strengthen the intestinal immune defense, and increase portal and intestinal blood flow. It protects the integrity of intestinal mucosa and maintains the intestinal barrier function. Compared with parenteral nutrition support, it is more in line with the physiological needs of the human body (12,13). However, when enteral nutrition support is taken in chronic critical patients, it is very easy to cause intestinal intolerance, which has a ne-

Table 3. Comparison of coagulation function between the two groups ($\bar{x} \pm s$).

Time	Group	Number of cases	PLT (×10^9/L)	FIB (g/L)	PT (s)
Before the intervention	Study Group	39	226.57±41.15	3.58±1.09	9.41±0.82
	Control group	39	228.71±36.96	3.71±1.13	9.24±0.77
	T-value		0.242	0.517	0.944
	P value		0.810	0.607	0.348
After the intervention	Study Group	39	177.15±12.51	2.57±0.39	15.79±1.21
	Control group	39	198.54±10.77	3.04±0.54	13.13±1.33
	T-value		8.092	4.406	9.239
	P value		0.000	0.000	0.000

Table 4. Comparison of complications between the two groups [n (%)].

Group	Number of cases	Diarrhea	Vomit	Constipation	Gastrointestinal bleeding	Total incidence
Study Group	39	0 (0.00)	1 (2.56)	1 (2.56)	0 (0.00)	2 (5.13)
Control group	39	2 (5.13)	3 (7.69)	2 (5.13)	1 (2.56)	8 (20.51)
χ^2values						4.129
P value						0.042

gative impact on the nutritional supply and the treatment of primary diseases, and chronic critical patients usually need large doses of glucocorticoids or antibiotics to inhibit the inflammatory response, which can inhibit the body's bactericidal and bacteriostatic ability, leading to intestinal and mesenteric lymph nodes. Cause intestinal micro-ecological environment disorder, and cause intestinal absorption disorders, infection, etc. (14,15). Microecological regulators can regulate immune dysfunction, strengthen local immune function, avoid intestinal mucosal barrier damage, maintain the balance of intestinal flora, and promote digestive tract peristalsis and absorption. Studies have pointed out that after taking microecological agents, Enterococcus faecalis, Bifidobacterium and Lactobacillus acidophilus can be planted in various parts of the intestinal tract and form a biological barrier on the surface of the intestinal mucosa. Avoid the invasion of pathogenic microorganisms, supplement dominant bacteria, assist in the synthesis of vitamins, clean up oxygen free radicals, regulate intestinal microenvironment and circulation, and promote nutrient absorption (16-18).

The results of this study showed that after the intervention, the nutritional status and immune function-related indicators of the study group were better than those of the control group, and the incidence of complications (5.13%) was lower than that of the control group (20.51%) ($P<0.05$), which confirmed that the combined intervention program of microecological regulators and enteral nutrition had high application value in patients with chronic critical illness and could regulate the body. Enhance immune function, minimize the occurrence of complications, and ensure the effectiveness and safety of disease intervention. The main reason is that microecological regulators can form a biological barrier in the intestinal tract, inhibit harmful bacteria, add probiotics, accelerate the production of lactic acid, promote intestinal peristalsis, rebuild intestinal microecological balance, so as to regulate the nutritional status and immune function of the body.

In addition, normal flora adheres, reproduces and colonizes at specific locations to form a bacterial membrane barrier, which can resist the colonization of passing bacteria and prevent the body from being attacked by foreign pathogenic bacteria. Enzyme substances, metabolites and bacterial cell walls generated by probiotics are important antidotes. Intestinal flora disorders can cause intestinal barrier dysfunction. Inflammatory reactions mediated by pathogenic microorganisms and toxins can cause or aggravate coagulation dysfunction, and intestinal microorganisms can synthesize vitamin K. If the intestinal microecological environment is abnormal, it can affect the synthesis of vitamin K, and then cause coagulation dysfunction (19). The results of this study showed that PLT and FIB in the study group were lower than those in the control group, and PT was higher than that in the control group ($P<0.05$), which further confirmed that the intervention of enteral nutrition combined with microecological regulators in chronic critically ill patients was also helpful to regulate coagulation function. Mainly because the microecological regulator can supplement probiotic flora and form a biological barrier with other anaerobic bacteria adhered to the surface of intestinal mucosa to inhibit the growth of pathogenic microorganisms, reduce the generation of endotoxin and regulate the intestinal micro-ecological environment, at the same time, intestinal harmful bacteria are sensitive to pH and are not easy to survive in an acidic state, and the microecological regulator can accelerate the decomposition and fermentation of lactic acid in the intestinal tract. A large number of acidic substances are formed to prevent the growth of harmful flora, inhibit the inflammatory reaction caused by toxins and pathogenic microorganisms, and beneficial bacteria can synthesize vitamin K, which is conducive to alleviating abnormal coagulation function.

To sum up, the intervention effect of microecological regulators combined with enteral nutrition on patients with chronic critical illness is significant, which can improve their nutritional status and immune function, improve coagulation function and reduce the incidence of complications.

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