Original Article

Effects of enteral immunonutrition on immune function in patients with multiple trauma

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BACKGROUND: Enteral immunonutrition (EIN) refers to addition of some specific nutrients in enteral nutrition (EN), which can help to increase the immune function, and reduce the inflammatory reaction and septic complications. This study aimed to determine whether EIN can improve the immune function in multiple trauma patients.

METHODS: Thirty-two patients with multiple trauma who had been admitted to the general ICU of Changzheng Hospital, Shanghai, from March 2007 to May 2008, were randomly divided into two groups: an enteral immunonutrition group (EIN group, $n=16$) and an enteral nutrition group (EN group, $n=16$). EIN suspension (RuiNeng produced by Sino-Swed Co., Ltd) and ordinary nutrition liquid (RuiSu produced by Sino-Swed Co., Ltd) were given to patients of the EIN group and EN group respectively for at least for 14 days. Peripheral blood lymphocyte count (TLC), immunoglobulin (IgG, IgM, IgA), and T-lymphocyte subsets (CD3, CD4, CD8, CD4 / CD8) were detected on the 1st day after grouping, and the 7th day and 14th day after nutritional support.

RESULTS: TLC, IgG, IgM, IgA, CD4 and CD4/CD8 ratio were significantly higher in the EIN group on the 7th and 14th day than that on the 1st day ($P<0.05$), and continually increased with a prolonged time of EIN. The parameters of immune function in the EN group on the 7th day didn't change significantly compared with those on the 1st day after grouping; on the 14th day, TLC, IgG, IgM, IgA, CD4 and CD4/CD8 ratio were significantly higher than those on the 1st day after grouping ($P<0.05$), but were significantly lower than those in the EIN group on the 14th day ($P<0.05$).

CONCLUSION: Compared with the general formula EN, EIN is more helpful for the recovery of humoral and cellular immune function in the early post-multitraumatic phase.

KEY WORDS: Multiple trauma; Enteral immune nutrition; Immune function

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INTRODUCTION

Most patients with multiple trauma are easy to develop protein-energy malnutrition, decreased immune function in organism, and even sepsis. Sepsis is an independent risk factor of multiple organ dysfunction syndrome after multiple trauma. The improvement of immune function may improve prognosis and reduce the incidence rate of sepsis.^[1] Enteral immunonutrition (EIN) refers to addition of some specific nutrients into enteral nutrition (EN),

which helps to increase the immune function, and reduces the inflammatory reaction and septic complications.^[2] This study aimed to determine whether EIN can improve the immune function in patients with multiple trauma.

METHODS

General data

From March 2007 to May 2008, 32 patients with

multiple trauma, 19 males and 13 females, aged 23-68 years, were admitted to ICU of Changzheng Hospital, Shanghai, China. Among them, 19 patients had moderate or severe craniocerebral injury with stupor, 22 had closed thoracic injury and acute lung contusion with respiratory failure, 12 had closed abdominal injury, 26 had injury of the vertebrarium, limbs and pelvis, and 6 had injury of the urinary system. The tube-feeding was given to the patients if they were unable to eat because of stupor or mechanical breathing. The hemodynamics of all patients was steady at 48-72 hours after admission. They didn't have EN contraindications or history of metabolic and immune diseases. Within 6 months before admission, they didn't take any glucocorticoids or other immunosuppressive agents. The patients were randomly divided into two groups: an EIN group ($n=16$) and an EN group (control group, $n=16$).

Nutritional support

For all patients, nutrient canals were established via the nose-stomach or the nose-jejunum approach. On the 3rd day after injury, the patients were administered with enteral nutrition without any other food (including water). EIN suspension (RuiNeng produced by Sino-Swed Co., Ltd) and ordinary nutrition liquid (RuiSu produced by Sino-Swed Co., Ltd) were administered in the EIN group and EN group, respectively, for at least for 14 days. The quantity standard of heat was all 25 kcal/ (kg/d). The patients were administered with 1/3 dose, 1/2 dose, and full dose on the 1st day, 2nd day, and 3rd day respectively; the nutrient fluid was pumped or dropped into the patients for 24 hours. The prescription of RuiNeng and RuiSu is shown in Table 1.

Measurement of indexes

Safety and tolerance

During the period of nutritional support, vital signs

were monitored and symptoms like nausea, emesis, abdominal distention, and diarrhea were recorded. Liver function, kidney function, blood fat and electrolyte were detected on the first day after grouping and the 7th day and 14th day after nutritional support.

Detection of immune function

On the 1st day after grouping, and the 7th day and 14th day after nutritional support, blood was collected from each patient to detect the periphery blood-lymphocyte count (TLC), immunoglobulins (IgG, IgM, IgA) by ELISA, and T lymphocyte subsets (CD3, CD4, CD8, and CD4/CD8) by flow cytometry.

Statistical analysis

All data were analyzed by the SPSS11.5 statistical software. The data were examined using the intergroup non-pairing t test, and enumeration data using the chi-square test. $P \leq 0.05$ was considered statistically significant.

RESULTS

General information

Between the two groups, there was no significant difference in age, gender, weight (Wt), mean arterial pressure (MAP), heart rate (HR), respiratory rate (RR), injury seriousness grade (ISS), hemaglobin (Hb) content, and serum albumin (Alb) concentration (Table 2). During the nutritional support, vital signs were steady in all patients; their liver function and kidney function, and blood fat and electrolyte were normal. During the EN fluid infusion through the nose-stomach or nose-jejunum approaches, most patients had good tolerance, except for those who developed slight abdominal distention.

Table 1. Main components of EIN and EN (per 100 mL)

Ingredients	Content	
	EIN	EN
Energy (KJ)	543.4	418
Protein (g)	5.85	3.8
Fat (g)	7.2	3.4
Carbohydrate (g)	10.4	13.8
ω -3 fatty acid (g)	0.3	0.17
ω -3: ω -6	1:2.5	1:6.5
Dietary fiber (g)	1.3	
Vitamin A (mg)	0.2	0.06
Vitamin C (mg)	8.0	4.5
Vitamin E (mg)	2.7	0.75
Osmotic concentration (mmol/L)	350	250

Table 2. General information about patients

Patient information	EIN group ($n=16$)	EN group ($n=16$)
Age (yr)	53.2 $\pm$ 10.1	54.9 $\pm$ 8.7
Sex (M/F)	10/6	9/7
Wt (kg)	61.8 $\pm$ 9.6	63.1 $\pm$ 10.2
MAP (mmHg)	88.4 $\pm$ 11.5	84.6 $\pm$ 10.6
HR (times/min)	96.8 $\pm$ 21.1	94.6 $\pm$ 16.3
RR (times/min)	24.2 $\pm$ 6.5	22.8 $\pm$ 5.4
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<20 (no.)	4	6
$\geq$ 20 (no.)	12	10
Hb (g/L)	103 $\pm$ 20	110 $\pm$ 16
Alb (g/L)	29.6 $\pm$ 4.8	28.7 $\pm$ 4.2

Table 3. Comparison of immune function indices on the 1st day after grouping, and on the 7th day and 14th day after nutritional support between the two groups

Immune indices	EIN group (n=16)			EN group (n=16)		
	1st day	7th day	14th day	1st day	7th day	14th day
TLC ($\times 10^9/L$)	1.21 $\pm$ 0.25	1.46 $\pm$ 0.20	1.62 $\pm$ 0.19 [#]	1.24 $\pm$ 0.22	1.31 $\pm$ 0.26	1.42 $\pm$ 0.30
IgG (g/L)	10.12 $\pm$ 2.06	12.20 $\pm$ 1.83	13.08 $\pm$ 1.94 [#]	9.81 $\pm$ 2.11	10.03 $\pm$ 2.08	11.18 $\pm$ 2.14
IgM (g/L)	1.26 $\pm$ 2.34	1.92 $\pm$ 3.06	2.14 $\pm$ 3.26 [#]	1.30 $\pm$ 2.18	1.58 $\pm$ 1.99	1.87 $\pm$ 2.60
IgA (g/L)	2.20 $\pm$ 1.91	2.58 $\pm$ 2.15	2.66 $\pm$ 1.80 [#]	2.25 $\pm$ 1.12	2.23 $\pm$ 2.09	2.41 $\pm$ 1.76
CD3 (%)	49.70 $\pm$ 3.25	50.48 $\pm$ 4.17	49.66 $\pm$ 6.25	48.96 $\pm$ 4.22	48.05 $\pm$ 3.45	49.02 $\pm$ 5.72
CD4 (%)	32.14 $\pm$ 3.60	37.22 $\pm$ 5.35	42.63 $\pm$ 3.86 [#]	33.85 $\pm$ 4.01	32.64 $\pm$ 4.58	36.06 $\pm$ 3.21
CD8 (%)	21.30 $\pm$ 2.40	20.04 $\pm$ 2.60	19.98 $\pm$ 2.33	21.06 $\pm$ 1.99	22.14 $\pm$ 2.83	21.86 $\pm$ 2.90
CD4/CD8	1.70 $\pm$ 0.31	1.90 $\pm$ 0.40	2.20 $\pm$ 0.63 [#]	1.68 $\pm$ 0.42	1.70 $\pm$ 0.44	1.94 $\pm$ 0.52

Compared with the grouping day, $P < 0.05$; compared with the EN group, [#] $P < 0.05$

Immune function

On the 1st day after grouping, there was no significant difference in the parameters of immune function between the two groups. TLC, IgG, IgM, IgA, and CD4 and the CD4/CD8 ratio were significantly higher on the 7th day and 14th day after nutritional support than on the 1st day after grouping ($t = 6.788-9.023$, $P < 0.05$). They were increased by a prolonged time of EIN, but CD3 and CD8 didn't change significantly ($t = 0.276, 1.034$, all $P > 0.05$). Parameters of immune function in the EN group on the 7th day didn't change significantly compared with those on the 1st day after grouping ($t = 0.464-2.199$, all $P > 0.05$); on the 14th day, they were higher than those on the 1st day after grouping ($t = 0.464-2.199$, all $P > 0.05$), but lower than those on the 14th day in the EN group ($t = 7.206-12.553$, all $P < 0.05$) (Table 3).

DISCUSSION

In multiple trauma patients, severe traumatic stress, high inflammatory response, high catabolism, fasting at early stage after injury, surgery and other intervention treatments often lead to protein-energy malnutrition, and further consumption of fat deposit and lean tissue. This can cause the decrease of immune function, the structural and functional impairment of the intestinal barrier, the translocation of bacteria and endotoxin. Therefore the resultant systemic inflammatory response and infectious complications affect the prognosis of patients.^[3]

Traditional enteral nutrition is not effective to improve immune function and intestinal barrier function. Studies^[4,5] have shown that EIN could be helpful in regulation of metabolism and immune function, i.e. EIN can reduce the high metabolism caused by operation and trauma, maintain the function of the mucosal barrier, and reduce the occurrence rate of enterogenic infection.

The specific nutrients include glutamine, arginine, -3 fatty acids, nucleotides, dietary fiber, and so on. In this study, the EIN suspension RuiNeng is characterized by high energy density, high-fat, high protein, low carbohydrate; the prescription is rich in high-proportional immunopotentiator (w-3 polyunsaturated fatty acid) and antioxidation vitamin A, C, and E.^[6-8] The fatty acid contains w-3, w-6 and linoleate. Among them, w-6 fatty acid and linoleate can promote the release of inflammatory response factor, while w-3 fatty acid can inhibit the linoleate transition into arachidonic acid, reduce the formation of prostaglandin and leukotrienes, and thus decrease the production of inflammatory response factor and the hypersensitivity reaction, enhance immunologic competence, and decrease the translocation of endotoxin.^[9] Therefore, the w-3 fatty acid is the key component of immunity nutrient.

Nathens et al^[10] reported that early administration of antioxidant supplementation using alpha-tocopherol and ascorbic acid reduces the incidence of organ failure and shortens ICU stay in a cohort of critically ill surgical patients. The use of high dose vitamin C is helpful to improve anti-oxidative damage, and is safe for the organism.^[11] The extra-dose of vitamin A, E, and C after infection can correct the vitamin dysbolism, improve the oxidation resistance of tissue, and alleviate the over-oxidation injury of lipid after infection.^[12]

In this study, we observed the effect of early administration of RuiNeng EIN and RuiSu EN on the immune function of trauma patients. The results showed that RuiNeng through nasogastric gavage has good tolerance and safety; on the 7th day after using RuiNeng EIN, parameters of immune function, such as TLC, IgG, IgM, IgA, CD4 and the CD4/CD8 ratio were significantly increased, and continued to increase with a prolonged time of EIN; whereas in the RuiSu EN group, parameters of immune function were not increased until

the 14th day, indicating that compared with the ordinary prescription of EN and early EIN after multiple trauma, EIN is more conducive to the recovery of early humoral and cellular immune function. Daly et al^[13] reported that the beneficial effect of arginine on the immune system appeared to be distinct from its more moderate effect on nitrogen metabolism. As a nutrient substrate, arginine is nontoxic and beneficial to surgical patients who are at increased risk of infection. But further study is needed to investigate whether EIN can reduce the incidence rate of sepsis and MODS.

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