European Review for Medical and Pharmacological Sciences 2013; 17: 2481-2485

Effect of microbiological and immunological enteral nutrition on intestinal function and immune status in the patients with long-term use of antibiotics

F. SHAO, X.D. XU[1]

Department of Gastrointestinal Surgery, and [1]Department of Neurology; Liaocheng City Hospital, Liaocheng, Shandong Province, China

Abstract. – BACKGROUND: To investigate the effect of microbiological and immunological enteral nutrition (MEIN composed by probiotics, L-Glutamide, deep-sea fish oil and Nutrison Fibre) on intestinal function and immune status in the patients with long-term use of antibiotics.

PATIENTS AND METHODS: 56 severe apoplexy patients with pulmonary infectious complication were randomly divided into two groups: a microbiological and immunological enteral nutrition group (MEIN group, n=28) and an enteral nutrition group (EN group, n=28). MEIN suspension (Live Combined Bifidobacterium, L-Glutamide, deep-sea fish oil and Nutrison Fibre) and ordinary enteral nutrition liquid (Nutrison Fibre) were given to patients of the MEIN group and EN group respectively for at least for 20 days. Then the trophonemata, incidence rates of abdominal pain, abdominal distention and diarrhea, tolerance and immunologic parameters including CD4+, CD8+ T-lymphocyte percentage, CD4+/CD8+ ratio and NK cells in peripheral blood were estimated and compared between the two groups during the period of nutritional support.

RESULTS: No statistical difference was observed in trophonemata between the two groups ($p > 0.05$). The abdominal pain and abdominal distension incidence rates of the patients in MEIN group were significantly lower than those of patients in EN group. (7.2% vs 32.1%, 14.2% vs 39.3%, 0% vs 10.7%) ($p < 0.05$). There was a significantly better tolerance in MEIN group compared to EN group after treatment ($p < 0.05$). In addition, the levels of immune parameters of the patients in MEIN group were much higher compared to that of those in EN group on the 20th day after grouping ($p < 0.05$).

CONCLUSIONS: Compared with the general formula EN, MEIN is more helpful for the patients with Long-term use of antibiotics in improving intestinal function and cellular immune function.

Key Words:

Probiotics, Glutamine, Enteral nutrition, Fish oil, Antibiotic, Intestinal function.

Introduction

Severe apoplexy is an acute cerebrovascular disease characterized by a sudden onset of headache, visual symptoms, altered mental status, and hormonal dysfunction due to acute hemorrhage or infarction of a pituitary gland. Most patients with severe apoplexy are easy to develop protein-energy malnutrition, decreased immune function in organism, and even sepsis[1]. Sepsis is an independent risk factor of multiple organ dysfunction syndrome after severe apoplexy. Xu et al[2] reported that the complication prevalence rate was 54.76% in apoplexy patients, and the pulmonary infection was 22.62% of the total. The improvement of immune function may improve prognosis and reduce the appearance rate of complication[3,4]. Studies have shown that EN could be helpful in regulation of metabolism and immune function[5]. In general, the patients who suffer from severe apoplexy complicated with pulmonary infection may use one or more kinds of antibiotics for long term because of severe pathogenetic condition. However, intestinal flora balance and intestinal mucosa barrier of the patients might be inevitable destructed as the result of long-term use of antibiotics. And then in the patients, the conditions of abdominal distension and diarrhea would appear while using enteral nutrition. Microbiological and immunological enteral nutrition (MEIN) that we designed refers to addition of some specific nutrients such as probiotics and deep sea fish oil and glutamine into enteral nutrition (EN), which helps to reduce the inflammatory reaction, and increases the immune function and intestinal tolerance[6].

Therefore, this study aimed to investigate the effect of MEIN on intestinal function and immune status in the patients with long-term use of antibiotics.

Corresponding Author: Feng Shao, MD; e-mail: fengshaocn@126.com

Patients and Methods

Patients

56 severe apoplexy patients with pulmonary infectious complication, 32 males and 24 females, aged 62-75 years, median age 69.2, were recruited in this study. Among them, 21 cerebral hemorrhage and 35 cerebral infarction. The selection for these patients is in accordance with the following criteria: (1) without any antibiotic before admission; (2) after the chest X ray and sputum bacterial culture diagnosis of pulmonary infection; (3) with enteral nutrition therapy of Nutrison Fibre (30-35 kcal/kg×d) before admission. The patients were randomly divided into two groups: an MEIN group (therapy group n=28) and an EN group (control group, n=28). This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Liaocheng City Hospital. Written informed consent was obtained from all participants.

Nutrition Protocols

The patients were underwent the conventional therapy for cerebrovascular disease and were administered with Cephalosporin antibiotics for pulmonary infection before the bacterial drug sensitive test of sputum. Then, they were given some targeted antibiotics according to the result of drug sensitive test. For all patients, nutrient canals were established via the nose-stomach or the nose-jejunum approach. Patients in MEIN group obtained MEIN suspension, while the patients in EN group received Nutrison Fibre alone. Each 500 ml MEIN suspension were composed by 500ml Nutrison Fibre (Nutricia Ltd, Zoetermeer, Netherland), 4 pieces Live Combined Bifidobacterium (0.5 g/piece, LiZhu Ltd, Zhuhai, China), 6 pills L-Glutamide (0.25 g/pill, Lukang Ltd, Jining, China) and 3 pills deep-sea fish oil (Nunet Ltd, Chengdu, China). If the patients were intolerant due to abdominal distension and so on, we would slow down the feeding rate, dilute the feedings concentration, give the albumin, and use total parenteral nutrition to improve the intestinal motility.

Data Collection

During the period of nutritional support, vital signs were monitored and symptoms like abdominal pain, abdominal distention, and diarrhea were recorded. Arm muscle circumference and triceps skinfold thickness were detected. The serum albumin and prealbumin levels, and the immunologic parameters including CD4+, CD8+ T-lymphocyte percentage, $CD4^+/CD8^+$ ratio and NK cells in peripheral blood were collected on the first day after grouping and the 10^{th} day and 20th day after nutritional support.

Statistical Analysis

Statistical analysis was performed using SPSS13.0 (SPSS Inc., Chicago, IL, USA). All values were expressed as x±s. The data were examined using the intergroup non-paring *t* test, and enumeration data using the Fisher's exact probability. $p < 0.05$ was considered statistically significant.

Results

Comparison of Trophonemata of the Two Groups

No statistical difference was observed in trophonemata between the two groups on the first day after grouping and the 10^{th} day and 20^{th} day after nutritional support ($p > 0.05$, Table I).

Comparison of Abdominal Pain and Abdominal Distension Incidence Rates and ReCovery Rates of the two Groups

Fisher's exact probability demonstrated that the abdominal pain and abdominal distension percentage rates of the patients in MEIN group were significantly lower than those of patients in EN group (7.2% vs 32.1%, 14.2% vs 39.3%, 0% vs 10.7%) ($p < 0.05$). However, there was no difference of recovery rates between the two groups ($p > 0.05$) (Table II).

Comparison of Tolerance of the Two Groups

During the MEIN fluid infusion through the nose-stomach or nose-jejunum approaches, most patients had good tolerance, except for those who developed slight abdominal distention. As shown in Table III, the tolerance of the patients in MEIN group were better than that of those in EN group after treatment ($p < 0.05$).

Comparison of Immune Parameters of the Two Groups

On the 1^{st} day after grouping, there was no significant difference in the parameters of immune function between the two groups. CD3+, CD4+, CD8+, $CD4^+/CD8^+$ ratio and the NK cells were

Table I. Comparison of trophonemata of the two groups.

	Albumin (g/l)		Prealbumin (mg/l)		Arm muscle circumference (cm)		Triceps skinfold thickness (mm)	
	EN group	MEIN group	EN group	MEIN group	EN group	MEIN group	EN group	MEIN group
1d	34.32 ± 3.6	35.12 ± 2.7	206 ± 23.7	199 ± 18.9	27.26 ± 2.37	27.09 ± 3.11	9.67 ± 2.11	9.32 ± 2.35
I value		0.4066		0.352		0.383		0.424
p value		0.661		0.736		0.692		0.601
10d	36.62 ± 4.6	36.86 ± 3.9	186 ± 27.9	203 ± 28.1	26.56 ± 3.82	26.62 ± 3.65	9.13 ± 2.68	9.25 ± 2.76
t value		0.369		0.735		0.376		0.411
p value		0.712		0.367		0.703		0.632
20d	37.12 ± 5.9	39.02 ± 4.6	192 ± 28.7	212 ± 31.4	26.86 ± 3.42	26.92 ± 3.97	9.02 ± 2.57	9.37 ± 2.22
t value		1.086		1.396		0.350		0.826
p value		0.262		0.189		0.737		0.311

Note: $p > 0.05$ vs. EN group.

Table II. Comparison of abdominal pain and abdominal distension incidence rates and recovery rates of the two groups.

	MEIN group (n=28)	EN group (n=28)	*p*-value
Abdominal pain	2	9	0.040
Abdominal distention	4	11	0.029
Diarrhea	0	3	0.031
Death toll	2	3	0.901

Note: Abdominal pain and abdominal distension incidence rates: $p < 0.05$ vs. EN group; recovery rates: $p > 0.05$ vs. EN group.

significantly higher on the 10th day and 20th day after nutritional support than on the 1st day after grouping ($p < 0.05$). They were increased by a prolonged time of MEIN. Therefore, the levels of immune parameters of the patients in MEIN group were much higher compared to that of those in EN group on the 20th day after grouping ($p < 0.05$) (Table IV).

Discussion

In severe apoplexy patients, surgery and other intervention treatments often lead to protein-energy malnutrition, and further infectious complication. This can cause the decrease of immune function, the structural and functional impairment of the intestinal barrier, the translocation of bacteria and endotoxin[7]. The patients of severe apoplexy complicated with pulmonary infection usually should use antibiotics for a long time. The resultant of using antibiotics can affect the intestinal function, and even the tolerance of patients during the phase of enteral nutrition. Traditional enteral nutrition is not effective to improve immune function and intestinal barrier function.

Ecoalimental that Bengmark[8] suggested in 1996 refers to addition of some probiotics into traditional enteral nutrition (EN), which helps to

Table III. Comparison of tolerance of the two groups.

	Wholly tolerance	Partly tolerance	Inability tolerance
MEIN group (n=28)	26	2	0
EN group (n=28)	18	8	2

Note: $p < 0.05$ vs. EN group.

Table IV. Comparison of immune parameters of the two groups.

		CD3+/%	CD4+/%	CD8+/%	CD4+/CD8+	NK/%
EN group (n=28)	1d	51.25 ± 4.65	31.35 ± 3.42	23.35 ± 3.29	1.34 ± 0.17	13.57 ± 4.83
	10d	52.66 ± 5.23	33.65 ± 2.72	24.55 ± 2.73	1.36 ± 0.23	14.23 ± 4.55
	20d	55.93 ± 4.25	32.80 ± 2.13$^{\#}$	25.29 ± 3.36	1.30 ± 0.19†	14.02 ± 4.58*
MEIN group (n=28)	1d	53.52 ± 4.55	30.23 ± 4.10	22.63 ± 3.53	1.33 ± 0.20	13.66 ± 5.18
	10d	57.35 ± 6.15	35.53 ± 4.26	24.18 ± 2.88	1.47 ± 0.31	15.35 ± 4.63
	20d	58.28 ± 5.68	40.38 ± 5.68$^{\#}$	22.81 ± 2.90	1.77 ± 0.23†	18.65 ± 4.51*

Note: $^{\#}p < 0.05$, $^{\dagger}p < 0.05$, $^{*}p < 0.05$ vs. EN group, $p < 0.05$ vs grouping day.

increase the enteric bacteria glycolysis, reduces the pathogenic bacterium hypertrophy, and then maintains the intestinal microecology. In this study, the MEIN suspension (probiotics, L-Glutamide, deep-sea fish oil, Nutrison Fibre) is characterized by high energy density, high-fat, high protein, low carbohydrate. Among them, L-Glutamide can heighten intestinal mucous membrane, probiotics can inhibit the growth of enteropathogenic bacteria, decrease the translocation of endotoxin, repair the intestinal mucosa barricade and, thus, recover intestinal microecology balance and enhance immune function[9-11]. In this study, we found that the patients in MEIN group had good tolerance except for those who developed slight abdominal distention. But the tolerance of the patients in EN group were much lower after using antibiotic as the results showed. In addition, Fisher's exact probability demonstrated that the abdominal pain and abdominal distension percentage rates of the patients in MEIN group were significantly lower than those of patients in EN group. So, we suggested that the MEIN composed by probiotics and L-Glutamide may paly an important role in protecting intestinal microecology and elevating tolerance of patients.

Some study had indicated that ω-3 fatty acids had beneficial effects on immune function and inflammatory reaction[12-15]. EPA and DHA, the essential components of ω-3 fatty acids which extracted from deep-sea fish oil, can affect T-lymphocyte function, increase stability stability, and thus enhance cellular immune function[16-18].

The results showed that MEIN through nasogastric gavage has good tolerance and safety; on the 10th day after using MEIN, parameters of immune function, such as CD3+, CD4+, CD8+, CD4^{+}/CD8^{+} ratio and the NK cells were significantly increased, and continued to increase with a prolonged time of MEIN; whereas in the EN group, parameters of immune function were not significantly increased until the 20th day, indicating that compared with the ordinary prescription of EN, MEIN is more conducive to the recovery of intestinal barrier function and immune status.

Conclusions

It can be concluded that MEIN has great benefits for patients with long-term use of antibiotics, compared to EN alone. The detailed mechanisms of action require further investigation.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

1) Su YY, Lin PX, Wang JY, Ding Y. Severe brain impairment complicated by multiple organ dysfunction syndrome and prognosis. Chin Crit Care Med 2002; 14: 684-691.
2) Xu SC, Liu M, Li B, Wang YH, Quan Y, Zhang JY. Analysis of complication of apoplexy patients. Chinese J Geriatr Heart Brain Vessel Dis 2003; 5: 111.
3) Zhang SW, Wang H, Su Q, Wang BE, Wang C, Yin CH. Clinical epidemiolog of 1,087 patients with multiple organ dysfunction syndrome. Chin Crit Care Med 2007; 19: 2-6.
4) Chandra RK. Nutrition and the immune system: an introduction. Am J Clin Nutr 1997; 66: S460-463.
5) Menges T, Engel J, Welters I, Wagner RM, Little S, Ruwoldt R, Wollbrueck M, Hempelmann G. Changes in blood lymphocyte populations after multiple trauma: association with posttraumatic complications. Crit Care Med 1999; 27: 733-740.
6) Bertolini G, Iapichino G, Radrizzani D, Facchini R, Simini B, Bruzzone P, Zanforlin G, Tognoni G. Early enteral immunonutrition in patients with severe sepsis: results of an interim analysis of a randomized multicentre clinical trial. Intensive Care Med 2003; 29: 834-840.

7) Descotes J. Immunotoxicity of monoclonal antibodies. MAbs 2009; 1: 104-111.
8) Bengmark S. Ecological control of the gastrointestinal tract. The role of probiotic flora. Gut 1998; 42: 2-7.
9) Kung SP, Wu CW, Lui WY. Arginine modulated cyclosporine-induced immune suppression in rats transplanted with gastric cancer cells. In Vivo 2001; 15: 39-44.
10) Xia Q, Chen P, Liu J, Zhong FQ. Effects of perioperative glutamine-supplemented total parenteral nutrition support on nutritional status of patients with gastrointestinal cancer. Parenter Enter Nutr 2006; 13: 148-151.
11) Bai LZ, Kang LM, Lu XG, Kang X, Fan ZW, Ji CY. Enteral ecoimmunonutrition support alleviates hepatic injury in patients with severe acute pancreatitis. World Chin J Digestol 2010; 18: 616-620.
12) Liu X, Xin FZ, Zhang YB, Mi YT, Guo Z, Shao F, Xu CY, Yang DG. The effect of ω-3 fish oil on immunologic function and inflammatory reaction of patients with gastrointestinal tumor after operation. Parenter Enter Nutr 2009; 16: 280-285.
13) Grimm H, Mayer K, Mayser P, Eigenbrodt E. Regulatory potential of n-3 fatty acids in immunological and inflammatory processes. Br J Nutr 2002; 87: S59-67.
14) Zararsiz I, Sonmez MF, Yilmaz HR, Tas U, Kus I, Kavakli A, Sarsilmaz M. Effects of omega-3 essential fatty acids against formaldehyde-induced nephropathy in rats. Toxicol Ind Health 2006; 22: 223-229.
15) Al-Khalifa H, Givens DI, Rymer C, Yaqoob P. Effect of n-3 fatty acids on immune function in broiler chickens. Poult Sci 2012; 91: 74-88.
16) Wang H, Li JS. Effects of ω-3 polyunsaturated fatty acids on immune cell. Parenter Enter Nutr 2004; 11: 304-308.
17) Swanson D, Block R, Mousa SA. Omega-3 fatty acids EPA and DHA: health benefits throughout life. Adv Nutr 2012; 3: 1-7.
18) Koletzko B, Uauy R, Palou A, Kok F, Hornstra G, Eilander A, Moretti D, Osendarp S, Zock P, Innis S. Dietary intake of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in children–a workshop report. Br J Nutr 2010; 103: 923-928.