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Effect of Ecological Immune-Enhanced Enteral Nutrition on the Gastrointestinal Fistula Patients

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Abstract

Objective: To study the effect of early ecological immune-enhanced enteral nutrition on nutritional status and immune function and intestinal mucosal barrier of the gastrointestinal fistula patients.

Methods: The 54 patients with gastrointestinal fistula were randomized to ecological immune-enhanced enteral nutrition (EIEN group) 28 and parenteral nutrition (PN group) 26 respectively. The changes of immunity index and nutrition index and the index of intestinal mucosal barrier before ecological immune-enhanced enteral nutrition support and post ecological immunity enteral nutrition support in 7 days and 14days was determined.

Results: Compared with the PN group, at the 7th days after EIEN nutritional support, the number of CD3 and CD4 positive cell and CD4/CD8 value and the plasma level of IgA and IgM and nutrition index such as plasma ALB, PA and TFN and intestinal mucosal barrier index（plasma D-lactate levels and endotoxin levels）in EIEN group recovered gradually to the normal level and were higher than those of the PN group ($P<0.05$).

Conclusion: Ecological immune-enhanced enteral nutrition can improve cellular immunity function and humoral immunity and nutritional status and enhanced intestinal mucosal barrier in the gastrointestinal fistula patients.

Keywords: Ecological immune-enhanced enteral nutrition; Gastrointestinal fistula; Nutrition status; Immunity; Intestinal mucosal barrier

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Introduction

Gastrointestinal（GI）fistula is an abnormal opening that allows the contents of the stomach or intestines to leak. GI fistula may occur either postoperatively or other reasons. Approximately 15% to 25% of fistulas are associated with inflammatory processes (diverticulitis, inflammatory bowel disease), cancer, or radiation treatment. The remaining 75% to 85% of GI fistulas are related to postoperative surgical procedures (anastomotic dehiscence, erosion by anadjacent drain, unrecognizes diatrogenic injury) [1]. Other medical factors contributing to the development of GI fistulas are malnutrition, inadequate blood supply to the anastomosis site, sepsis, shock/hypotension, steroid therapy or inflammatory processes, such as infection or inflammatory bowel disease (most often Crohn's disease or ulcerative colitis), Trauma, especially penetrating wounds such as those due to a stabbing or traffic accidents and so on. GI

fistula may result in malnutrition and dehydration, depending on their location in the intestine. Malnutrition has been associated with complications such as higher rates of infection, increased Length Of Stay (LOS), and increased morbidity and mortality [2]. The increased energy requirements because of disease-associated stress produce a negative energy balance, which also has a role in malnutrition. Immunonutrition has become associated most closely with attempts to improve the clinical course of critically ill and surgical patients, who will often require an exogenous supply of nutrients through the parenteral or enteral routes. Improving immune function may reduce complications due to infection or stress. In these GI fistulas patients complex variable immune and inflammatory changes occur that are only now being well defined. A biphasic response with an early hyper-inflammatory response followed by an excessive compensatory response associated with immunosuppression is seen in many patients. Ecological immunonutrition is based on immune-enhanced treatment, add probiotic bacteria as probiotics in order to enhance the effect of nutrition support and suppressed overgrowth of pathogenic bacteria of the gut and protect intestinal microecology and function of the intestinal mucosal barrier [3]. Here, early ecological immune-enhanced enteral nutrition is aimed at decreasing the inflammatory response rather than enhancing it, to abrogate the process of hyper-inflammation and prevent the compensatory immunosuppression of the gastrointestinal fistula patients.Initiation and maintenance of nutrition are essential for treating patients with GI fistulas. Bowel rest by keeping the patient NPO is recommended for at least 2 to3 weeks. When indicated; enteral nutrition is preferred to avoid atrophy of the mucosal villi and allows for normal bowel function. As it is reasonable to assume that immune-enhanced enteral nutrition should reach suitable tissue and plasma concentrations to exert their maximum effects.

Patients

The data of 54 patients with gastrointestinal fistula in the department of General Surgery, Binzhou Hospital of Binzhou medical University（Binzhou, China）from March 2010 to August 2014 were collected. Inclusion criteria were: (1) The fistulography confirmed intestinal fistula; (2) Through adequate drainage and anti-infective therapy, the patents can tolerance the enteral nutritional support. Patients will undergo a fistulogram to assist in determining the treatment regimen. The fistulogram is performed by inserting a soft catheter into the fistula and then instilling the contrast dye. A series of radiographic studies of the GI tract are performed to identify the site of the fistula in the GI tract, the tract between the GI tract and the skin (simple vs. complex), and the patency of the GI tract distal to the fistula. Other tests such as a barium enema may be performed; upper gastrointestinal X-rays with small bowel follow-through may also be performed. Exclusion criteria were: endocrine or metabolic disorders, immune insufficiency, cardiac, hepatic, renal or respiratory dysfunction, history of radiotherapy or treatment with immunosuppressive drugs and terminal state. Finally, 54 patients（29 males and 26 females）with a mean age of 48.5 years（range 23-69 years）were included in the study. Gastric or esophageal fistula 19 cases, pancreatic fistula 21cases, duodenal fistula 14 cases, all the patients were intestinal fistula. At the early stage of intestinal fistula, comprehensive therapy was used such as somatostatin continuous intravenous pumping, NPO（nothing by mouth）5-18 days, antibiotics and continuous drainage of intestinal fistula. The patients were randomized to two groups: ecological immune-enhanced enteral nutrition (EIEN group) （n=28）, and Parenteral Nutrition (PN group) （n=26）, according to the random number table. There were no significant difference among the two groups in terms of age, gender, immunity and nutrition status and staging and location of fistula and the severity of the disease (P>0.05).

Nutritional support

Ecological Immune-enhanced Enteral Nutrition (EIEN) group

Nutritional support was administered through endoscopic assisted to the distal to the fistula and inserted nutritional catheter to administer the EIEN, enteral formulas was Nutrison（Intacted Protein Enteral Nutrition Powder）, according to 35kcal/Kg.d calculation of total

energy, NPC（kcal）: N（g）130 : 1. And adding polymeric diets, particularly those containing glutamine such as Glutamine Granules and Bifidobiogen to have immunologic facilitation. A stepwise increase of intake calories from enteral nutrition was scheduled and started. On the first day, around 250 ml of 5% fluid of enteral formula (20–30 ml/hr) was infused, the temperature of the nutrient fluid was set as 38–42°C while the speed of input was modulated to 3–4 mL/min using enteral feeding pump（Foulke800）, which controlled the speed, time and usage. From the second day, enteral nutrients were given at a rate of about 25 ml/hr and increased by about 25 ml/hr each day until the target rate (maximum 100–120 ml/hr, 20% Nutrison 1500-2000 ml/d, 6225-8300 kJ/d) was achieved, with a goal of 20–25 kcal/kg per day, as tolerated by the patient. The patient's ability to tolerate this enteral formula feeding was recorded daily, noting symptom and sign such as cramping, distention, nausea, and diarrhea and other complications. Before and after every infusion the enteral formula and every 3-4hrs, using normal saline 20ml with a syringe wash the feeding tube, keep the tube unobstructed.

Parenteral nutrition (PN) group

The patients in the PN group received normal infusion and after vital signs stable, then used the PN through Peripherally Inserted Central Catheter（PICC）, Parenteral formula choose standard system nutritional preparation made from Huarui Science & Technology CO.LTD. PN formulation contains amino acids, glucose and fat emulsion, plus electrolytes, trace elements, vitamins, and additives. Caloric distribution is 50–60% glucose and 40–50% fat. All patients in two groups were received antibiotics 10-14 days and other treatment and nursing care was alike.

Checking blood parameters

Collecting the blood parameters of patients before nutritional support and after 7 days and 14 days respectively, using Hitachi 7080 automatic biochemical analyzer checking serum Albumin (ALB), Proalbumin (PA) and transferrin levels in the two groups. And using flow cytometer checking CD3+, CD4+, CD8+and CD4+/CD8+ and the plasma level of IgA and IgM with immunofluorescent stained mouse anti-human monoclonal anti-bodies. Spectrophotometric Determination of blood lactic acid D level; the level of serum endotoxin limulus test application, all the specimen were finished in the central-lab of the hospital.

Data analysis

The Statistical Package for the Social Science (SPSS, version 19.0) was used for all analyses. The data were expressed as mean ± Standard deviation（SD）and analyzed using ANOVA test. All significant levels were two-tailed and set at a 0.05 significance level. $P<0.05$ was considered statistically significant.

Ethical considerations

This study received approval from the ethics committee of Binzhou medical University. Informed consent was obtained according to procedures approved by both the University of Research Board and the Human Volunteers Protection Committee. All participants gave their written informed consents for take part in the study. We kept the information of the participants' confidentiality and anonymity.

Results

A total of 54 patients were enrolled in this study. The median age of the subjects was 48.5 years (range 23–69years). The formulas were tolerated well in all the patients. The baseline characteristics in terms of age, gender, biochemical parameters and staging and location of fistula and the severity of the disease was no differences between the EIEN groups and the PN groups ($P>0.05$).With respect to the comparison of the immune function and nutrition index and the index of intestinal mucosal barrier before nutritional support（D-1）and post nutritional support day7（D7）and day14（D14）, there were a significant differences between the 2 groups ($P<0.05$) (Tables 1, 2, 3). There was no significant difference in the incidence of complications including anastomosis leakage and pulmonary infection between the EIEN groups and the PN group.

Table 1. Comparison of immune function before nutritional support（D-1）and post nutritional support day7（D7）and day14（D14）among the two groups ($\bar{x}$ ± s)

Index	EIEN group	PN group	P value
CD3+			
D-1	60.63 ± 5.48	60.17 ± 5.66	>0.05
D7	68.73 ± 4.76	64.85 ± 7.28 *	<0.05
D14	69.34 ± 5.38	65.24 ± 8.27*	<0.05
CD4+			
D-1	34.76 ± 5.65	35.07 ± 6.37	>0.05
D7	44.65 ± 6.39	40.94 ± 7.76*	<0.05
D14	47.49 ± 5.48	42.66 ± 6.25 *	<0.05
CD8+			
D-1	24.16 ± 6.95	23.92 ± 6.85	>0.05
D7	27.59 ± 6.72	24.37 ± 7.48*	<0.05
D14	31.37 ± 5.84	27.89 ± 6.25*	<0.05
CD4+/CD8			
D-1	1.24 ± 0.79	1.26 ± 0.75	>0.05
D7	1.61 ± 0.67	1.32 ± 0.59*	<0.05
D14	1.87 ± 0.53	1.42 ± 0.67*	<0.05
Ig M (g/L)			
D-1	0.61 ± 0.29	0.65 ± 0.25	>0.05
D7	1.53 ± 0.63	1.07 ± 0.59*	<0.05
D14	1.78 ± 0.83	1.32 ± 0.97*	<0.05
Ig G (g/L)			
D-1	10.24 ± 3.79	10.26 ± 3.75	>0.05
D7	15.69 ± 4.64	12.37 ± 4.59*	<0.05
D14	18.87 ± 3.58	15.42 ± 5.61*	<0.05

* P<0.05 compared the serum CD3+, CD4+, CD8+and CD4+/CD8+ and the plasma level of IgA and IgM with EIEN group and PN group on D-1 and D7 and D14 respectively.

Table 2. Comparison of nutrition index before nutrition support（D-1）and post nutrition support day 7（D7）and day14（D14）among the two groups ($\bar{x}$ ± s).

Index	EIEN group	PN group	P value
ALB (g/L)			
D-1	22.91 ± 1.71	22.87 ± 1.23	>0.05
D7	27.29 ± 2.57	24.53 ± 3.36*	<0.05
D14	31.65 ± 2.39	28.49 ± 2.77*	<0.05
PA (mg/L)			
D-1	204.79 ± 2.58	204.76 ± 2 .77	>0.05
D7	212.56 ± 3.75	207.86 ± 4.73*	<0.05
D14	215.89 ± 4.72	210.29 ± 5.81*	<0.05
TFN (g/L)			
D-1	1.67 ± 0.57	1.76 ± 0.49	>0.05
D7	2.35 ± 1.42	2.06 ± 1.73*	<0.05
D14	2.74 ± 1.91	2.49 ± 1.48*	<0.05

* P<0.05 compared the plasma ALB, PA and TFN with EIEN group and PN group on D-1 and D7 and D14 respectively.

Table 3. Comparison the index of intestinal mucosal barrier before nutrition support（D-1）and post nutrition support day7（D7）and day14（D14）among the two groups ($\bar{x}$ ± s)

Index	EIEN group	PN group	P value
Endotoxin（pg/ml）			
D-1	27.97 ± 0.78	27.86 ± 0.72	>0.05
D7	21.23 ± 0.92	24.54 ± 0.96*	<0.05
D14	9.63 ± 4.38	12.45 ± 4.57*	<0.05
D-Lactic acid（ug/ml）			
D-1	16.71 ± 1.59	16.76 ± 1 .51	>0.05
D7	11.59 ± 3.24	13.85 ± 4.73*	<0.05
D14	8.54 ± 3.75	10.25 ± 5.46*	<0.05

* P<0.05 compared the serum level of Endotoxin and D-Lactic acid with EIEN group and PN group on D-1 and D7 and D14 respectively.

Discussion

GastroIntestinal（GI） fistula is a complication because of accident, operation or other reasons, lots of digestive liquid flows from the fistula, and the body lost amount of fluids, electrolyte, extremely easy to cause the imbalance and systemic pathological changes [4]. Treating patients with a GI fistula requires a comprehensive team approach. These patients will most likely have a prolonged hospitalization as conservative medical management is generally considered rather than surgery. Medical management with GI fistula should include maintaining fluid and electrolyte balance, providing bowel rest and nutrition support, initiating medication treatment, ensuring skin protection, and containing the fistula effluent [5]. With progressing of nutritional support and treatment technology, and combination of somatostatin and growth hormone, the mortality was decreased, but the mortality rate was 20-30% in the GI fistula patients. Octreotide (Sandostatin) can decrease fistula output by inhibiting the release of gastrin and other GI hormones [6]. This decreases secretions of bicarbonate, water, and pancreatic enzymes into the intestine, thus decreasing intestinal volume. Octreotide also releases intestinal smooth muscle, allowing more intestinal capacity, and increases intestinal water and electrolyte absorption [7]. Ecological immune-enhanced enteral nutrition could improve the nutritional status and immune function recovery and stimulation of proliferation and repair of intestinal mucosa cells, avoid of intestinal mucosa atrophy thinning because of long time using PN, enhanced the immunity and the intestinal mucosal barrier function of the patients [8]. The plan of care should include treating sepsis, initiating nutritional support, maintaining fluid and electrolyte balances, and providing patient education and care. We divided the 54 patients into 2 groups according to the mode of postoperative nutritional support: Although the routes of administration of the diet were different, the patients in both groups had a similar total caloric intake, but there was a significant difference between the immunological function and nutritional status and the index of intestinal mucosal barrier analyses in the 2 groups ($P<0.05$).

Immunological function of the gastrointestinal fistula patients

In the subanalysis of immunological function, there were significant differences in the parameters indicating cellular immunity, i.e. the T cell subpopulation and serum immunoglobulin plays an important role in humoral immunity ($P<0.05$). Although the serum levels of IgA and IgM dropped remarkably in all the patients after the nutritional support, they recovered quickly in the EIEN group and were significantly higher than those in the PN group ($P<0.05$). However, because of the small number of patients in the present study, it is unclear whether this findings suggests and improvement in the GI fistula immunological status. One reason lies in the fact that the gut plays an increasingly central role in maintaining nutritional status and regulating the immune system [9]. Table 1 shown, post-EIEN nutritional support compare with before EIEN, plasma positive cell counts of CD3, CD4 and CD4/CD8 ratio gradually returned to normal level, and higher than PN group ($P<0.05$). EIEN nutritional support could enhance immune function and reducing the excessive inflammatory response. The gastrointestinal tract is the largest immune organ; it is mainly composed of Gut Associated Lymphatic Tissue (GALT), the overall solution about 80 % of human body immunity and cellular immunity about 50 %. Glutamine (Gln), as a substance for the synthesis of arginine, purine, pyrimidines and glutathione, is essential for rapid cell proliferation [10]. It is also protect the intestinal mucosal barrier, capable of preventing intestinal mucosal atrophy, reduce the intestinal mucosal permeability, to prevent the shift of intestinal flora in intestinal mucosa and promote the secretion of IgA, enhanced intestinal lymphoid tissue (GALT) function, improve the immune function of intestinal tract and shift reduce intestinal bacteria and endotoxin. Micro-ecological preparation (Jin Shuangqi) can improve the intestinal microflora and intestinal

function, often combined with immune nutrition, so called ecological immunonutrition [11]. It can make use of probiotics biological antagonism, inhibition of pathogenic bacteria overgrowth and it can improve the immune function of organism immune nutrients.

Nutritional status of the gastrointestinal fistula patients

Table 2 shown, post-EIEN nutrition support 7 days (D7), it was recovered slowly of ALB and PA levels. After 14days (D14), it was recovered to normal level of PA and TNF in the EIEN group and were significantly higher than those in the PN group ($P<0.05$). The plasma level of ALB and PA and TNF, reflected nutrition status and was visceral protein synthesis effective and objective indexes. The main cause of malnutrition in the GI fistula patient's maybe: a lot of digestive fluid loss, nutrients is lost and intestinal fistula causes intestinal integrity failure, infection and stress status, lead to catabolism hyperthyroidism [12]. Choosing to support the patient with enteral or parenteral nutrition is based upon the anatomical location of the fistula. Enteral nutrition is beneficial with low-output fistulas and fistulas located in the most proximal portion of the small bowel (feeding provided distally). The implementation of EIEN has many advantages in GI fistula patients, can directly supply to the intestinal energy and nutrients, maintain the structure and function of intestinal mucosa cells of intact, improve the function of intestinal mucosal immunity, and reduce the inflammatory reaction, shorten the duration of systemic inflammatory response syndrome, lower the body protein consumption, and increase the rate of protein synthesis.

The function of intestinal mucosal barrier of the gastrointestinal fistula patients

Table 3 shown, post-EIEN nutritional support compare with PN group, the level of Endotoxin and D-Lactic acid is lower ($P<0.05$). Increased endotoxin and intestinal mucosal atrophy and intestinal permeability were closely related to each other. Reduce intestinal mucosal barrier function can lead to translocation of bacteria and endotoxin and the final result of bacteria and endotoxin in blood circulation of enterogenous infection [13]. Application of the whole protein enteral nutrition (Nutrison) add An Kaishu, Containing glutamine (Gin) and micro ecological preparation (Jin Shuangqi) has on the intestinal mucosal barrier protection, especially under stress condition of intestinal mucosal growth and differentiation of cells conditionally essential amino acid, it is important to maintain and improve the structure and function of intestinal mucosa [14]. Nutritional factors specific tissue with small intestinal mucosa and intestinal mucosal immune tissue specific glutamine, There are special in colonic mucosa of Short chain Fatty Acids (SFA). To improve the nutritional status of patients, and prevent the intestinal bacteria translocation and contribute to the prevention of enterogenic infection and multiple organ dysfunction syndrome

In conclusion, immune-enhanced EN can improve the nutritional status and immune function for patients with GI fistula, which can enable the faster recovery of the bowel and immune function and the synthesis of proteins. It is safe and clinically feasible, and is therefore recommended to be used in GI fistula [15]. The management of GI fistulas can be very challenging for the health care team and the patients. The treatment goals are to provide bowel rest, prevent fluid and electrolyte imbalances, protect perifistula skin, and contain the effluent and nutritional support. Thus, this study allows a more precise estimated direction of the effect of EIEN on GI fistula patients.

References

1. Chander J, Lal P, Ramteke VK (2004) Rectus abdominis muscle flap for high-output duodenal fistula: novel technique. World J Surg 28: 179-182.
2. Huang CS, Hess DT, Lichtenstein DR (2004) Successful endoscopic management of postoperative GI fi stula with fibrin glue injection: report of two cases. Gastronintest Endosc 60: 460-462.
3. Kudsk KA (2006) Immunonutrition in surgery and critical care. Annu Rev Nutr 26: 463 -479.
4. Mazaki T, Ebisawa K (2008) Enteral versus parenteral

nutrition after gastrointestinal surgery: a systematic review and meta-analysis of randomized controlled trials in the English literature. J Gastrointest Surg 12: 739-755.

5. Shingeyuki Nagata, Kengo Fukuzawa, Yukio lwashita, Akira Kabashima, Tadahiko, et al. (2009) Comparison of enteral nutrition with combined enteral and parenteral nutrition in post pancreaticoduodenectomy patients：A pilot study. Nutr J 8：24-31.
6. Derikx JP, Vreuqdenhil AC, Van den Neucker AM, Grootjans J, Van Bijnen AA, et al. (2009) A pilot study on the noninvasive evaluation of intestinal damage in celiac disease using I-FABP and L-FABP. J Clin Gastroenterol 43:727-733.
7. Lobo Tamer G, Ruiz Lopez MD, Pe´rez de la Cruz AJ (2009) Hospital malnutrition:relation between the hospital length of stay and the rate of early readmissions. Med Clin 132: 377-384.
8. Hendry PO, Hausel J, Nygren J,Lassen K, Dejong CH, et al. (2009) Determinants of outcome after colorectal resection within an enhanced recovery programme. Br J Surg 96: 197 - 205.
9. Meijers JM, van Bokhorst-de van der Schueren MA, Schols JM, Soeters PB, Halfens RJ (2010) Defining malnutrition: mission or mission impossible? Nutrition 26: 432-440.
10. Heyland DK, Heyland J, Dhaliwal R, Madden S, Cook D (2010) Randomized trials in critical care nutrition: look how far we've come! (and where do we go from here?). JPEN J Parenter Enteral Nutr 34: 697-706.
11. Yaqoob P (2010) Mechanisms underlying the immunomodulatory effects of n-3 PUFA. Proc Nutr Soc 69: 311-315.
12. Marik PE, Zaloga GP (2010) Immunonutrition in high-risk surgical patients: a systematic review and analysis of the literature. JPEN J Parenter Enteral Nutr 34: 378-386.
13. Rasmussen HH, Holst M, Kondrup J (2010) Measuring nutritional risk in hospitals. Clin Epidemiol 2: 209-216.
14. Cerantola Y, Hubner M, Grass F, Demartines N, Schafer M (2011) Immunonutrition in gastrointestinal surgery. Br J Surg 98: 37-48.
15. Cahill NE, Murch L, Cook D, Heyland DK (2014) Improving the provision of enteral nutrition in the intensive care unit: a description of a multifaceted intervention tailored to overcome local barriers. Nutr Clin Pract 29: 110-117.