Effect of Glutamine's nutrition support on the postoperative nutrition and immune function in malignant tumor of gynecology patients

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Abstract: This paper is mainly to study the influence of Glutamine's reinforcing role in enteral nutrition on postoperative nutrition and immune function of patients with gynecologic malignant tumor. The adopted method is through selecting 60 patients with gynecological malignant tumor, they are randomly divided into groups of enteral immune nutrition (EIN group) and conventional enteral nutrition (EN group), which are given enteral nutrition of equal nitrogen and heat respectively in postoperative 24 hours, the total period of nutritional support are 7 days. The research results represent that nutrition and immunity index in both groups on the first day after operation is lower than the day before operation, and all indicators have picked up on the ninth day after operation.

Keywords: Glutamine, gynecological malignant tumor, enteral nutrition, immune nutrition, immune function.

INTRODUCTOIN

Gynecology tumor is one of the common malignant tumor in our country, the surgical treatment is an important method of combination therapy for tumors, but the tumor surgery often results into big trauma and blood loss, most postoperative body is in a more severe stress and negative nitrogen balance, and the body's function of taking advantage of exogenous nutrients is limited, postoperative nutritional support is particularly important. Protein is major nutrient of cancer patients, which is also the material basis of immune function. If the protein and calorie is in deficit, it will reduce white blood cells, antigen, antibody, immune globulin in the body and causes low immune function and forms vicious circle. PAB and agency is the synthesis of body's functional protein such as albumin and antibody etc and the precusor substance of the important factors in immune cell, its level indicates the body's nutritional status and immune level (Kai *et al.,* 2011; Afolabi *et al.,* 2012). In recent years, research has shown that glutamine is one of the important regulating substances of protein biosynthesis, as the main vehicle of nitrogen source in the human body, by generating ornithine, proline and arginine, precursor, thus it becomes the synthesis precursor of nucleic acids and proteins, which can promote protein synthesis, accelerate the growth of intestinal mucosa, maintain complete intestinal mucosa, prevent bacterial translocation and intestinal toxins into the blood circulation, strengthen the intestinal immune system and systemic immune function. So, combing routine TPN with Gln treatment not only complements the loss of Gln, but also provides sufficient raw material for protein synthesis because of the nitrogen source in amino acid of parenteral nutrition and Gln.

In recent years, the study has found that the immune nutrition not only can effectively improve the metabolism of the patients, but also can improve the immune status of cancer patients, inhibit the proliferation of tumor cell, produce certain anti-tumor treatment effects (Xinhuan, 2010; Aixue and Jun, 2012; Huhmann and August, 2011).

Glutamine is a kind of main immune nutritional elements. Clinical studies have found that adding plenty of glutamine is beneficial to improve the immune response under the stress state and shorten the healing time, reduce the fatality rate (Lixin *et al* 2013; XiChun, 2011). This study is to explore the improvement effect of glutamine's nutrition support on the postoperative immune function of patients with gynecological malignant tumor, in order to be able to provide the reference direction and basis for developing new cancer drugs for the recovery of postoperative tumour.

MATERIAL AND METHODS

Experimental subjects

Selected conditions of cases: (1) Perform radical surgery to patients. (2) Before the surgery, all patients are examined whether they have endocrine and metabolic diseases, the function of liver and kidney is normal, they have no serious chronic diseases and sepsis. (3) Immunosuppression enhancer is not used half year before the surgery, there is no history of chemotherapy, radiotherapy, there is also no obvious and important viscera metastasis before the surgery. (4) There are no metabolic abnormalities of congenital amino acid or other metabolic disease and abnormal reactivity disease, of which there are 25 cases of ovarian cancer, 14 cases of endometrial cancer, 21 cases of cerical cancer. In aspects of patients' age, sex, disease, surgery time and way, anesthesia, and intraoperative blood loss and so on in the

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control group and treatment group, there is no statistical significance (P>0.05), which is comparable.

Method of enteral nutrition

When the internal environment is stable after the surgery, control group and treatment group are given postoperative nutritional support for 7 days respectively, with equal nitrogen and equal heat, for nonprotein heat, its 60% is provided by glucose and its 40% is provided by the fat emulsion. The amino acid preparations is 8.5% (Novamin); 25% ~ 35% of nitrogen source in treatment group is provided by force peptide [N (2) - L - alanyl - L - GLUTAMINE], fat emulsion is 20% of the intralipid; patients in the control group and treatment group are given peripherlly inserted centrl ctheter in internal jugular before the trial, 3L nutraceutical in bags is matched and infused through venous duct in internal carotid.

Observation index

Immune indexes

Peripheral venous blood is extracted on the day before the operation and the morning of the first day and ninth day, immune globulin (IgG, IgA, IgM) is detected with image immune turbidity and optical protractor in United States Beckman Corporation through using dividing method with turbidity and light, T-lymphocyte subsets is detected with FCM (flow cytometry) B-DFACSC in BD Asian companies in the United States.

Nutrition indicators

Total protein, albumin, prealbumin is detected through extracting peripheral venous blood on the day before the operation and the morning of the first day and ninth day respectively. DXC800 automatic biochemical analyzer of United States Beckman Corporation is applied for detection.

STATISTICAL ANALYSIS

SPSS13.0 statistical software is applied in analysis. The result is denoted with ± s, compare two groups of count data and test them with x^2, t test or rank sum inspection is applied for comparing two groups of counting data. The data is given ANOVA for repeated measurement. Taking P<0.05 as the difference is significant.

RESULTS

The comparison of immune indexes within two groups of patients

As we can see from table 1, the difference value comparison of humoral immunity and cellular immunity index between EIN group and EN group 1 day before the surgery has no significance (P>0.05). These indicators of the two groups in the first postoperative day have decreased compared with 1 day before operation, the difference has statistical significance (P<0.05); the expression of the IgG, CD4 +, CD4 + / CD8 + between the two groups exist significant difference after 9 days of the surgery, but also the expression of IgG, CD4 +, CD4 +/ CD8 + in EIN Group has significantly rebounded compared with EN group (P<0.05). Compare the difference value between these two groups on postoperative 1 day, preoperative 1 day and postoperative 1 day respectively, there is no statistical significance (P>0.05).

Variance analysis for repeated measurement data of two groups has been performed, it showed that the difference of lgG, CD4 +, CD4 +/ CD8 + between two groups is the result due to the interaction between different nutrition support and time measuring, and both play a very significant role. The change of IgM and IgA, CD8 + is due to the measuring time and other factors, different nutrition support and its change have no significant effect (specific value of P is shown in table 2).

As we can see from table 3, the comparison difference of these nutrition indicators between EIN group and EN group on 1 day before surgery has no significant difference (P>0.05); these indexes of two groups on the first day after surgery has reduced compared with 1 day before surgery, the difference was statistically significant (P<0.05); the PA value between two groups on the ninth day after surgery exists significant difference, and PA value in EIN group has picked up dramatically than it in the EN group (P<0.05). Compare the difference between ALB and TP in two groups on 1 day after surgery and 1 day before surgery, there is no statistical significance (P>0.05). We further perform variance analysis of repeated measurement data for two groups, it shows that the difference between two groups of PA is due to the result of interaction between different nutrition support and measuring time, and both play a very significant role. The change of ALB and TP is due to measuring time and other factors, different nutrition support and its change has no significant effect (specific value of P is shown in table 4).

The results

Integrate above analysis results: Nutrition and immune indexes of two groups on 1 day after surgery has decreased compared with 1 day before surgery, all the indexes have rebounded on the ninth day after surgery. Where prealbumin (PA), immuno globulin (IgG), differentiation antigen 4 (CD4 +), differentiation antigen 4 / differentiation antigens9 (CD4+/ CD8+) in the group of enteral immunonutrition (EIN group) has rebounded significantly when compared with the group of conventional enteral nutrition (P<0.05), and the difference of PA, IgG, CD4+, CD4 +/CD8 + between the two groups is the result which is due to the interaction between different nutrition support and measuring time and both have significant effects (P<0.05).

Table 1: The comparison of immune indexes within two groups of patients

Grouping	Test index	Preoperative 1d	Postoperative 1d	Postoperative 9d	Difference value between 1d of pre-operation and post-operation	Difference value between postoperative 9d and 1d
EIN Group	CD4+(%)	36.66±3.60	29.93±3.12*	40.95±3.55#	6.72±1.05	11.02±2.03*
	CD8+(%)	21.44±3.35	18.84±3.15*	20.57±3.16	2.60±0.39	1.73±0.41
	CD4+/CD8+	1.71±0.26	1.62±0.24*	2.03±0.27#	0.12±0.06	0.41±0.12*
	IgG (g/L)	9.29±1.10	8.29±1.04*	11.29±1.13#	1.00±0.29	3.00±0.44*
	IgM (g/L)	1.50±0.38	1.17±0.38*	1.66±0.34	0.29±0.10	0.45±0.12
	IgA (g/L)	2.05±0.49	1.72±0.47*	2.10±0.48	0.33±0.08	0.38±0.15
EN Group	CD4+(%)	35.84±2.94	28.92±2.40*	33.83±3.25#	6.91±0.90	4.90±1.52*
	CD8+(%)	22.81±4.74	20.10±4.83*	21.89±4.85	2.71±0.42	1.79±0.45
	CD4+/CD8+	1.63±0.32	1.51±0.34*	1.60±0.31#	0.12±0.05	0.09±0.08*
	IgG(g/L)	9.56±1.52	8.47±1.53*	9.74±1.52#	1.09±0.33	1.27±0.38*
	IgM(g/L)	1.45±0.27	1.13±0.26*	1.57±0.26	0.32±0.08	0.44±0.61
	IgA(g/L)	2.12±0.42	2.12±0.42*	2.12±0.42	0.35±0.06	0.44±0.10

Note: "*" denotes the comparison between 1 day before and after surgery within group has statistical significance, P<0.05; "#" denotes the comparison between EIN group and EN group of 9 days after surgery is statistically significant, P<0.05; * denotes difference value comparison of 9 days after surgery and 1 day after surgery between two groups is statistically significant, P<0.05.

Table 2: The results of ANOVA for repeated measurement between immune index of patients in two groups

	C		Time		Cx Time	
	F	P	F	P	F	P
IgG	1.197	0.278	901.130	0.000*	209.051	0.000*
IgM	0.769	0.384	846.107	0.000*	2.371	0.104
IgA	0.452	0.504	566.861	0.000*	2.734	0.087
CD4+	14.422	0.000*	945.463	0.000*	164.168	0.000*
CD8+	1.559	0.217	955.280	0.000*	0.420	0.615
CD4+/CD8+	8.257	0.006*	254.611	0.000*	132.704	0.000*

Table 3: The changes of nutrition indicators in both groups

Grouping	Test index	Preoperative 1d	Postoperative 1d	Postoperative 9d	The difference value between preoperative and postoperative 1d	The difference value between postoperative 9d and1d
EIN Group	ALB (g/L)	36.4±3.1	31.2±2.5*	34.9±2.9	5.2±1.5	3.7±1.2
	PA (mg/L)	233±28	190±27*	203±25#	43±8	12±6*
	TP (g/L)	65.7±3.9	60.1±3.3	61.7±3.4	5.6±1.4	1.6±0.6
EN Group	ALB (g/L)	36±2.6	31.2±2.0*	34.6±2.5	4.8±1.2	3.4±1.2
	PA (mg/L)	233±28	185±28*	215±29#	40±10	30±9*
	TP (g/L)	65.5±3.9	60.1±2.8*	61.6±3.1	5.4±1.8	1.6±0.7

Note: "*" denotes the comparison between 1 day before and after surgery within group has statistical significance, P<0.05; "#" denotes the comparison between EIN group and EN group of 9 days after surgery is statistically significant, P<0.05; * denotes difference value comparison of 9 days after surgery and 1 day after surgery between two groups is statistically significant, P<0.05.

Table 4: The analysis result of repeated measurement variance for the nutritive index of patients in two groups

	C		Time		C × Time	
	F	P	F	P	F	P
ALB	0.073	0.789	559.018	0.000*	0.697	0.477
PA	0.002	0.963	893.715	0.000*	57.325	0.000*
TP	0.012	0.914	530.985	0.000*	0.150	0.756

Note: C is treatment factor and Time is measuring Time, C × Time is the synergistic effect between measuring time and treatment factor, "*" denotes P<0.05, which has significant differences.

DISCUSSION

In this study, we found that, in terms of protein synthesis in postoperative body, two groups of serum albumin (ALB), prealbumin (PA) and total protein (TP) on the day after surgery were significantly lower than preoperative 1 day, and after nutritional support treatment, all indicators significantly rosed again 9 days after surgery. Among them, the amount and added amount of serum TP, ALB after surgery in-group of intestinal immune had no obvious difference with that in-group of conventional enteral nutrition, while serum PA recovered significantly both in quantity and postoperative increased amount ($P<0.05$). For its reason, it may be associated with the half-life period of ALB and PA. The half-life period of ALB and PA are 20 days and 2 days respectively, the albumin synthesis of liver has great potential and the body has offered a lot of compensatory to its synthesis, it generally drops after malnutrition's occurring for a few months, and the level of prealbumin in the blood is low, its level drops rapidly, under the condition of lacking protein energy, when the energy of protein intake increase, it can be obviously improved in three days, which can sensitively reflect the level of protein synthesis in body (Peranzoni *et al.,* 2011). But the composition of TP is complicated, therefore, PA can better reflect the metabolism condition of protein synthesis in body (Wisehmeyer and Glutamine, 2012). On the first day after surgery, serum ALB, TP, PA were significantly lower than it before surgery, on the one hand, it is related with preoperative malnutrition and hypoalbuminemia and postoperative traumatic stress reaction. For the postoperative body under the stress state, patients' energy consumption increase, a large number of proteins are broken down for energy supply, resulting into further decline of serum ALB, TP, PA, thus aggravate malnutrition. On the other hand, under the state of anesthesia and surgical stress, the permeability of blood capillary in the whole body increase, a large number of ALB permeate outside of blood vessel. But PA is a negative acute phase protein, it can eliminate toxic metabolic substances in the blood circulation, and it will be consumed gradually. This can also lead to the decline of postoperative ALB and PA (Chen *et al.,* 2010). After1week of nutritional support treatment, serum ALB, TP, PA significantly increased. Although the amount and added amount of serum ALB, TP has no obvious difference between two groups, but it can still be found that the recovery trend of serum ALB and TP in EIN group is faster than EN group. The quantity and added amount of serum PA after surgery rose again significantly ($P<0.05$) and such change is the result of the interaction between two different kinds of enteral nutrition and measuring time. Above changes indicate that glutamine's enforcing role in enteral nutrition can better improve nutritional status in patients with gynecological tumor, and the effect is faster than conventional enteral nutrition. Tumor cells gradually increase the uptake and use of Gln, and it can lead to concentration drop of Gln in blood, and the low level of Gln in blood would cause all the function relying on Gln oxidation and the cells' function of providing nitrogen and carbon precursor (such as intestinal epithelial cell, vascular endothelial cell, T lymphocytes, monocytes, macrophages, etc.) decline and even fail, therefore, replenishing exogenous Gln plays an important role in maintaining the body's metabolism, structure and function of each organ. The body's anti-tumor immunity includes cellular immunity and humoral immunity, etc., the imbalance of body's immune function will make cancer cells evade the monitoring of immune cells for escaping, eventually leading to tumorigenesis (Guohao, 2009) or postoperative recurrence. The ratio CD4 +/CD8 + between the cells of CD4 + and CD8 + can be used as the important indicators of measuring immunosuppression degree of patients after surgery (Cheung *et al.,* 2010). A study shows glutamine is the best material that T lymphocyte replication and function depends on (Peng *et al.,* 2011). This study confirms that this research results shows that the immune indexes of the patients in two groups have declined after surgical trauma, through enteral nutrition support, the expression of IgG, CD4+, CD4+/CD8+ in EIN group on the ninth days after surgery has obviously improved than that in EN group, and such changes are the results of interaction between two different kinds of enteral nutrition and measuring time. Results indicate that compared with conventional enteral nutrition, strengthening the glutamine enteral nutrition can better improve immunosuppression status in patients with gynecological tumors and glutamine may strengthen this effect, the study results are consistent with literature report (Tsering *et al.,* 2012).

Therefore, maintaining its plasma concentration through supplementing exogenous glutamine is conducive to regulate the body's immune function (Coeffier and Dechelotte, 2009). It has positive significance to the postoperative recovery of patients. This also points out the direction and basis for drug research and development of tumor patients in postoperative nutritional health recovery.

CONCLUSION

We could derive the conclusion that: Strengthening the enteral nutrition with glutamine could be more effectively improve the nutritional status of patients with gynecology malignant tumor after operation than conventional enteral nutrition, thus promotes the recovering of patients' immunologic function. But there still exists some deficiencies in this research: this research only expounds the results of the experiment, but does not proposes substantive method of solving problems, which must make this research lack some earning value.

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