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• CLINICAL RESEARCH •

The influence of Enteral Nutrition in postoperative patients with poor liver function

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Abstract

AIM: To investigate the safety, rationality and the practicality of enteral nutritional (EN) support in the postoperative patients with damaged liver function and the protective effect of EN on the gut barrier.

METHODS: 135 patients with liver function of Child B or C grade were randomly allocated to enteral nutrition group (EN, 65 cases), total parenteral nutrition group (TPN, 40 cases) and control group (CON, 30 cases). Nutritional parameters, hepatic and kidney function indexes were measured at the day before operation, 5th and 10th day after the operation respectively. Comparison was made to evaluate the efficacy of different nutritional support. Urinary concentrations of lactulose(L) and mannitol(M) were measured by pulsed electrochemical detection(HPLC-PED) and the L/M ratio calculated to evaluate their effectiveness on protection of gut barrier.

RESULTS: No significant damages in hepatic and kidney function were observed in both EN and TPN groups between pre- and postoperatively. EN group was the earliest one reaching the positive nitrogen balance after operation and with the lowest loss of body weight and there was no change in L/M ratio after the operation (0.026±0.004) at the day 1 before operation, 0.030±0.004 at the day 5 postoperative and 0.027±0.005 at the day 10 postoperative), but the change in TPN group was significant at the day 5 postoperative (0.027±0.003 *vs* 0.038±0.009, $P<0.01$).

CONCLUSION: EN is a rational and effective method in patients with hepatic dysfunction after operation and has significant protection effect on the gut barrier.

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INTRODUCTION

Liver is the central organ for production and utilization of nutrients and plays a key role in metabolism. In chronic liver disease severe protein-calorie malnutrition can seriously damaging the capacity of liver regeneration, however nutritional support can improve the postoperative outcome[1]. Parenteral nutrition (PN) has been used clinically[2], but its limitations of the incomplete nutritional constituent[3], catheter-related or endogenous complication[4], metabolic complications and liver dysfunction restrict its use in hepatic damaged patients[5]. In the mid 1980s, along with the recognition of the relevance of the gut barrier and endogenous infection[6,7], enteral nutrition (EN) has been widely used[8], but how does it effect on poor liver function remaining unclarified.

It is the aim of this study: (1) To investigate the safety, rationality and feasibility in performing EN in postoperative patients with poor liver function. (2) To study the influence of EN on gut barrier.

MATERIALS AND METHODS

Patients and groups

According to the later Enrolled criterion, 135 patients were enrolled and randomly divided into 3 groups: EN (n=65), TPN (n=40) and CON (n=30) (Table 1).

Enrolled criterion is: (1) Hospitalized adult patients from July 1998 to October 2001 with chronic liver damage requiring operative treatment; (2) The hepatic function was graded as Child B or C; (3) A patience of at least 7 days' nutritional support after the operation; (4) Except the primary disease, no other factors affecting the metabolism (5) With the agreement of the patients to join the program.

Table 1 Grouping of patients

	CON (n=30)			TPN(n=40)			EN(n=65)		
	Cases	Grade		Cases	Grade		Cases	Grade	
		B	C		B	C		B	C
PVH	13	10	3	14	8	6	21	10	11
HCC	4	2	2	11	7	4	10	5	5
CLA	1	-	1	3	1	2	8	-	8
ROBD	7	3	4	7	3	4	15	5	10
CLT	3	1	2	3	2	1	10	3	7
Others	2	1	1	2	-	2	1	-	1

PVH: Portal venous hypertension; HCC: hepatocellular carcinomar; CLA: Cholangiocarcinoma; ROBD: Reoperation of bile duct; CLT: cholelithiasis.

Reagents used

(1) 20 % and 30 % Intralipid (Beijing, Fresenius); (2) 8.5 % Novamin (Sino-swed Pharmaceutical Corp. LTD); (3) Nutrison Fibre (Nutrisia); (4) manitol (Sigma); (5) lactulose (Sigma).

Procedures

Deferent Nutrition supports were used: In TPN group, 30 cal· kg^{-1}· d^{-1} energy and 0.16 g· kg^{-1}· d^{-1} nitrogen were given. 1/4-1/3 nonprotein calories were provided by fat and carbohydrate. The ratio of N: nonprotein calorie=1:168. The source of nitrogen was Novamin (8.5 %) and the source of fat was from Intralipid (20 % or 30 %). Essential trace elements and vitamins were given and the solution was given via peripheral infusion from the day 1 after the operation and lasted at least 7 days. In EN group, Nutrison Fibre was given. After 2 days of TPN, EN begun on the day 3 after the operation via the jejunostomy tube placed during the operation. On the first day, 500 ml Nutrison Fibre was given, which was increased progressively each day till 1 500 ml/d while TPN was deceased progressively till totally substituted. This was used given at least for 7 days. The temperature of Nutrison Fibre were kept at 25-30 ℃ and infused in 12-24 h. The rate was adjusted according to the need. In CON group, nutritional support was not performed or performed not regularly.

The sample preparation including: (1) urine sample: The patient drank the test solution, containing 2 g lactulose, 1 g mannitol in fasted condition or injected on 1 day before operation, 5th and 10th day after the operation respectively. Urine was collected for a total of 6 h and being added 0.1 ml of 10 g/L thimerosal as preservative. The total volume was recorded and 20 ml sample was stored at -20 ℃ until analysis by the HPLC-PED; (2) blood sample: Venous blood samples were achieved during fasting on 1 day before operation, 5th and 10th day after operation respectively for analysis.

Such Monitoring markers were measured: (1) Nutritional status marker: Transferrin (TRF), Prealbumin (PAB), Total protein (TP), Albumin (ALB), the alteration of weight (w) and circumference of upper arm (COUA) postoperatively, and accumulative nitrogen balances in the first 7 days after operation (ANE); (2) Liver and kidney function, electrolytes: Total bilirubin (TB), Direct bilirubin (DB), Albumin (ALB), Total protein (TP), Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Creatinine (Cr), Blood urea nitrogen(BUN), Potassium (k+), Sodium (Na+), Calcium (Ca2+); (3) Gut barrier marker: Urinary ratio of lactulose and Mannitol (L/M)[9,10].

Statistical analysis

The data was expressed as mean ± standard error. Experimental results were analyzed by analysis of variance and *t* tests for multiple comparisons. $P<0.05$ was considered statistically significant.

RESULTS

All 135 patients, except one cirrhotic patient (CON) with portal hypertension died due to MSOF at the 26th day after operation, all completed the treatment and were discharged. In EN group, there were 32 patients complained for abdominal distention and diarrhea but disappeared by adjusting the temperature and infusion rate, given domperidone or antidiarrheal agent.

Nutritional status marker (Table 2)

In all three groups, on the 5th day postoperatively, the level of TRF, TP, and ALB declined significantly ($P<0.05$), but in EN and TPN groups, they recovered on the 10th day. Comparing with TPN, the level of TP in EN group on the 10th day was higher with significant difference ($P<0.05$). In CON group, on the 10th day PO, the level of TRF, PAB, TP and ALB were all significantly lower than these in EN and TPN groups ($P<0.05$). The W and COUA loss in CON group were significantly more than those in EN and TPN groups ($P<0.05$), and in EN group were lower than that in TPN group. Among these, EN group reached positive nitrogen balance the earliest ($P<0.05$).

Table 2 Changes of nutritional status

Parameters	Control(*n*=30)			TPN(*n*=40)			EN(*n*=65)		
	1st BO*	5th PO**	10th PO	1st BO	5th PO	10th PO	1st BO	5th PO	10th PO
TRF(g/L)	1.1±0.6	0.9±0.3	0.8±0.6	1.2±0.4	1.0±0.6	1.2±0.3	1.3±0.6	1.2±0.5	1.2±0.6
PAB(mg/L)	657±232	591±220	595±213	690±214	669±228	667±239	681±228	719±177	690±221
TP(g/L)	63.6±12.9	46.3±9.7	48.1±9.7	66.6±12.2	48.3±10.1	50.4±9.6	70.1±7.9	55.7±7.8	63.5±8.9
ALB(g/L)	30.8±4.9	29.2±5.9	29.1±4.8	31.4±4.9	30.8±7.1	31.8±5.0	36.5±6.1	30.7±4.0	32.9±3.9
ANE		32.4±10.8 $mg\cdot kg^{-1}\cdot 7\ d^{-1}$			105.3±9.4 $mg\cdot kg^{-1}\cdot 7\ d^{-1}$			185.3±8.4 $mg\cdot kg^{-1}\cdot 7\ d^{-1}$	
W(kg)		-3.3±1.7			-2.4±1.1			-2.1±0.9	
COUA	23.5±1.2	-	22.2±1.3	23.6±1.1	-	23.2±1.3	24.4±2.6	-	23.7±2.2

BO: Before operation; PO: After operation;ANE: accumulated nitrogen banlance; W: weight change; COUA: circumference of upper arm.

Table 3 Changes of liver and kidney function, electrolytes

Parameters	Control(*n*=20)			TPN(*n*=26)			EN(*n*=30)		
	1st BO	5th PO	10th PO	1st BO	5th PO	10th PO	1st BO	5th PO	10th PO
TB (μmol/L)*	92.3±37.8	71.7±34.5	41.8±35.8	86.3±46.8	68.7±33.8	45.7±33.2	119.8±73.0	96.3±54.4	64.3±47.3
DB(μmol/L)*	53.3±28.6	39.2±23.3	16.5±11.7	50.4±33.7	38.4±22.6	17.7±12.3	60.8±50.2	42.8±32.7	31.9±29.2
TP(g/L)*	63.6±12.9	46.3±9.7	48.1±9.7	66.6±12.2	48.3±10.1	50.4±9.6	70.1±7.9	55.7±7.8	63.5±8.9
ALB(g/L)	30.8±4.9	29.2±5.9	29.1±4.8	31.4±4.9	30.8±7.1	31.8±5.0	36.5±6.1	30.7±4.0	32.9±3.9
AST(U/L)#	71.7±28.9	91.3±33.5	78.7±28.1	73.4±30.6	89.9±35.7	67.7±39.1	94.8±47.8	104.4±80.7	69.6±23.8
ALT(U/L)#	54.7±31.1	101.4±44.9	85.3±33.7	58.7±32.3	99.3±56.2	78.7±35.5	109.1±82.7	148.4±180	67.1±50.1
Cr(μmol/L)	72.9±28.8	82.1±23.3	69.5±37.9	73.9±35.3	80.1±22.9	67.5±33.7	77.4±16.5	80.6±24.7	77.1±19.6
BUN(mmol/L)	6.9±3.3	8.4±3.5	5.9±3.4	7.1±4.1	8.2±3.7	5.6±3.2	5.5±1.8	6.9±4.9	6.0±3.2
K(mmol/L)	3.9±0.5	5.3±1.1	3.8±0.7	3.8±0.6	4.4±0.9	4.3±1.1	4.1±0.5	4.3±0.8	4.4±0.2
Na(mmol/L)	136.5±14.7	139.3±18.3	145.8±15.4	132.7±15.9	140.3±13.7	138.8±7.3	138.3±7.1	135.3±5.7	137.0±7.4
Ca(mmol/L)	2.35±0.39	1.99±0.18	2.17±0.31	2.32±0.43	2.67±0.27	2.27±0.34	2.21±0.22	2.07±0.14	2.24±0.17

*among all 3 groups, between day 1 preopratively and day 10 postoperatively, $P<0.01$; # at day 10 postoperatively, the levels were lower in EN and TPN group than in CON group, $P<0.05$.

Liver and kidney function, electrolytes (Table 3)

After operation, the levels of TB, DB declined significantly in all three groups ($P<0.01$). Same increase could be found in patients with hepatic lobectomy, radical operation of Cholangiocarcinoma, severe portal hypertension and emergency operation, but with no statistical significance. On the 10th PO, the levels of AST and ALT were lower in EN and TPN group than those in CON group ($P<0.05$), but no difference was seen between EN and TPN group. The levels of Cr and BUN increased in EN and TPN group on the 5th day, but recovered on the 10th day. No electrolyte imbalance occurred in EN and TPN group.

Gut barrier marker (Table 4)

In EN group, the L/M ratio did not chang after operation. In TPN and CON groups, they increased on the 5th day ($P<0.01$) and declined at 10th day. In both TPN and CON groups, the difference of L/M ratio between preoperation and postoperation was significant.

Table 4 Changes of L / M ratio

	1st BO	5th PO	10th PO
CON(*n*=30)	0.028±0.004	0.037±0.017	0.031±0.010
TPN(*n*=40)	0.027±0.003	0.038±0.009	0.030±0.006
EN(*n*=65)	0.026±0.004	0.030±0.004	0.027±0.005

DISCUSSION

Present status of clinical nutritional support in patients with poor hepatic function

The liver plays a central role in nutritional homeostasis and any liver disease can lead to abnormal nutrient metabolism with the subsequent malnutrition. Severe protein-calorie malnutrition in patients with advanced liver disease can seriously undermine the capacity for liver regeneration and functional restoration. Appropriate nutritional support is helpful to these patients.

PN and EN are two major nutritional supports clinically. What has been proved is that long-term TPN may aggravate the liver damage[11]. In recent years, there have been some advance in studies on various formulas including the branched chain amino acid (BCAA)[13] and MCT/LCT[14] in patients with poor hepatic function[12], but there are still some problems: (1) How does lipid affect the nutrient metabolism; (2) What is the rational and safe dose and the suitable percentage of lipid supplied as the energy source[15,16]; (3) The expensive cost. These problems impede the extensive use of PN which on long-term use may cause atrophy of intestinal mucosa and lead to the gut barrier dysfunction[17]. The consequent enteric bacterial translocation would also cause endogenous infection even multiple organ failure (MOF) and death. EN is a more physiological, cheaper and has protection function on gut barrier. But when using EN[18,19], the later three facts are inevitable: (1)The gastrointestinal tract should be intact; (2) Patient should be able to tolerate the indwelling nasogastric tube;(3) In case of hypertonic, patient may have abdominal distention, diarrhea, and sometimes nausea and vomiting and enhancement of the liver burden. There had been reported on using EN in patients with alcoholic cirrhosis and obstructive jaundice[20,21], but in patients with worse liver function or sustain the hepatic lobectomy, radical operation of cholangiocarcinoma, severe portal hypertension with upper gastrointestinal hemorrhage, the selection of nutritional support is troublesome.

Evaluation of EN and its influence on liver function

En has been proven to be an efficient nutritional support[22,23], which is prefer to TPN. In this study, in both EN and PN groups, the patients' nutritional status was much better than CON group. Compare with PN groups, in weight loss and circumference of upper arm, EN group were much less and the positive nitrogen balance was reached much earlier.

Liver is the key organ in maintaining the carbohydrate, lipid and protein metabolism and the stabilization of internal environment. Also it is the site of biochemical pathways responsible for production and utilization of nutrients and other chemicals. It plays a central role in carbohydrate, lipid and nitrogen metabolism. Therefore it is not surprising that chronic liver disease has great metabolic impact. On the base of this, the impact and irritated responsiveness of the operation may aggravate the burden of liver and ultimately affect the outcome of the patients[24-26]. On the other hand, we can suspect that if the nutrients were absorbed via liver, the liver could utilize the nutriment as the substrate to repair and rebuilt hepatic cell so as to promote its recover[27]. Whether it is beneficial or harmful, our study have performed some useful study in finding this method for support sufficient nutriment at the same time to avoid further liver damage in such patients.

In 42/65 patients of Child C grade EN group, after EN, had their levels of ALT, AST, TB and DB declined, and their Cr and BUN did not increased. There were no signs of aggravating damage of liver and kidney. The successful use of Nutrison Fibre indicates that whether the BCAA is absolutely necessary in EN needs further study.

EN can protect the gut barrier

In patients with poor liver function, infection is a familiar complication and threat[28]. Except for the depression of cellular immunity[29], the bacteria translocation is the most probable reason of infection after the operation[30]. Because of the translocation of the germ and endotoxin, the consequent systemic inflammatory reaction and sepsis and the dysfunction of renal, lung and cardiac system would even threaten the patient' s life. The gut barrier plays a the major role in preventing bacteria translocation and block the subsequent malign reaction, which is the "trigger" of MSOF[31,32]. Keeping the integrity of gut barrier is important to decrease the morbidity and mortality after operation.

In our study, the L/M probe was selected to monitor the status of gut barrier. The result showed: the L/M ratio of EN group was 0.026±0.004 in day 1 before the operation, 0.030±0.004 in day 5 postoperatively and 0.027±0.005 in day 10 postoperatively, the change was not significant, but it was markedly elevated in TPN and CON group after operation as follow. It indicated: EN could protect the gut barrier remarkably, the rational mechanisms were (1) The stimulation on the bowl wall may increase the blood perfusion[33,34]; (2) The stimulation on the bowl wall may accelerate the secretion of pancreas and biliary duct to prevent shrinking of gut mucosa; (3) EN supplies the substrate of intestinal mucosal cell metabolism directly; (4) The fiber[35-38] ingredient of Nutrison may also protect the gut barrier.

Clinical observation

In our study, we found through the upper jejunostomy tube placed during the operation, good nutrition support and good tolerance and good controllability are approached. The tube can be hold for at least 4 weeks. With good nursery, it can be kept fairly long, the longest one in our study is 94 days and no complications occurred.

In our study, the rate of ascites was 83.6 %, 93.3 % and 90.0 % in EN group, PN group and CON group, respectively, till discharge, the subsidence of them were 86.6 %, 61.3 % and 75 %. In EN group the ascites subsided earliest and liver function recovered faster.

The lowest rate of fever and the shortest fever time indicated that the risk of infection is low in EN. It is owed to the protection of the gut barrier.

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