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Original Article

Effect of fast-track rehabilitation on liver cirrhosis patients with portal hypertension after surgical therapy

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Abstract: Fast-track (FT) rehabilitation has proved to be successful in enhancing postoperative recovery, shorting hospital stay and reducing postoperative complications. This study aimed to evaluate the efficacy of FT rehabilitation protocol by a prospective study on liver cirrhosis patients with portal hypertension after surgical therapy. Pericardial vascular amputation and splenectomy surgery were performed in accordance with the guidelines of FT rehabilitation protocol or the conventional treatment. Recovery parameters included the post-operative complications, functional recovery of important organs, and post-operative rehabilitation time. A total of 26 patients underwent FT rehabilitation [fast-track surgery (FTS) group], and 20 patients underwent conventional treatment (control group). Compared with control group, FTS group had shorter time of gastrointestinal dysfunction, less blood plasma usage, less nutritional drugs costs ($P < 0.01$), shorter hospital stay ($P=0.039$) and fewer total complications ($P=0.001$). In FTS group, the serum prealbumin and transferrin levels returned to the preoperative level on day 8 after operation, which was significantly shorter than of the control group ($P < 0.05$). In conclusion, FTS rehabilitation could effectively decrease postoperative complications and promote rehabilitation, which is safe, rational and effective on liver cirrhosis patients with portal hypertension.

Keywords: Liver cirrhosis, portal hypertension, fast-track rehabilitation, complication

Introduction

Liver cirrhosis patients with portal hypertension usually present complex clinical and pathophysiological changes in preoperative period, thus leading to high incidence of postoperative complications [1]. The fast-track (FT) rehabilitation is a new concept introduced by Bardram *et al*. in 1995, and has been confirmed by the evidence-based medicine to be an effective approach in reducing the surgical stress, maintaining homeostasis, accelerating the rehabilitation of patients and shortening hospital time [2]. The main protocols of FT rehabilitation include avoidance of preoperative fasting, avoidance of preoperative bowel cleansing, optimizing perioperative and postoperative analgesia, early oral feeding and ambulation, and maintaining fluid balance [3]. Currently FT rehabilitation has been widely investigated and applied in the surgical treatment of gastrointestinal tumors [4], but there are few reports on the application for liver cirrhosis patients with portal hypertension. This study aimed to test whether FT rehabilitation could promote surgery recovery and decrease postoperative complications in liver cirrhosis patients with portal hypertension.

Subjects and methods

Patients

A total of 46 patients with liver cirrhosis and portal hypertension were included in this study, and all the patients underwent pericardial vascular amputation and splenectomy surgery. Then they were randomly divided into the fast-track surgery group (FTS group) and the conventional treatment group (control group).

Inclusion criteria were as follows: patients were aged between 18 and 75 years old, and liver cirrhosis with portal hypertension and hypersplenism were confirmed by imaging diagnosis. The liver function was A or B levels. All patients

have normal gastrointestinal function and surgical indications. Exclusion criteria: patients complicated with serious heart disease, endocrine or metabolic disease (such as, diabetes, hyperthyroidism, pancreatitis, etc) or Child C level of liver function. For all patients, preoperative ascites should be eliminated and liver function be improved to Child A level.

Conventional treatment procedures

Perioperative conventional treatment mainly includes the following procedures: (1) The blood hemogram, liver function and blood coagulation were tested and the hypersplenism degree was evaluated. Then for the patients with abnormal hemogram, bone marrow examination was made to ensure good bone marrow hematopoietic function; (2) Propranolol and somatostatin were used to decrease portal vein pressure and prevent upper gastrointestinal bleeding; (3) Liver function and nutrition risk were estimated, branched-chain amino acids were given to patients with liver function of Child B, and plasma or albumin was administrated to patients whose albumin were less than 28 g/L, and spironolactone and dihydrochlorothiazede were applied to patients with ascites; (4) The patients with abnormal blood coagulation received vitamin K infusion to reduce intraoperative hemorrhage; (5) All patients were given third-generation cephalosporins antibiotics from preoperative 1 h to postoperative 1 week; (6) The daily fluid intake should be limited in about 2500 mL to avoid liquid overload; (7) Parenteral nutrition with PN formulation was used if patients' intestinal function could not be restored; (8) Anticoagulant was given to patients whose platelet number was higher than 300×10^9/L to avoid acute portal vein thrombosis.

Fast-track rehabilitation procedures

Based on conventional treatment, FTS group patients received fast-track rehabilitation procedures as follows: (1) Enteral nutrition (the Huarui Pharmaceutical Company) was given through the preset nasojejunal feeding tube gradually from postoperative 24 h. We encouraged patients to ambulate early on postoperative 2nd day, in order to facilitate early recovery of intestinal function. The three-cavity feeding tube was pulled out after postoperative anal exhaust, and then semi-liquid diet was gradually transited to solid food. The blood plasma was administered appropriately to maintain serum albumin concentration more than 30 g/L according to the postoperative liver function and serum albumin level. (2) Low-dose diuretics infusion was used in order to prevent the occurrence of ascites, and gradually changed to oral diuretics until intestinal function recovery. (3) Less or none salt-containing liquid was given on postoperative 2 d, and postoperative daily potassium supplying was kept at 5-6 g to maintain serum potassium higher than 4 mmol/L. (4) The drainage fluid color was observed every day, and once mass ascites appeared, we clipped or pulled out the drainage tube and applied plasma or artificial colloids to increase colloid osmotic pressure. (5) We applied proton pump inhibitor to prevent the occurrence of portal hypertensive gastropathy after operation. After patients' oral feeding, we encouraged patients to eat more digestible foods following "low-salt, low-fat, high-quality proteins" principles. (6) With the co-operation of nursing staff, we paid attention to improve psychological guidance and enhance the patients' confidence to overcome diseases.

Obversation indexs

In the study, our clinical indexes were included as follows: (1) General conditions: weight, temperature, pulse, respiration, abdominal distension, postoperative exhaust time, hospital stay, and plasma dosage. (2) Clinical complications: surgical complications, ascites, blood loss, hypoproteinemia. (3) Laboratory test indicators: nutritional and metabolic indexes (prealbumin, transferrin). Discharge criteria included stopping the infusion, normal diet, normal temperature, no ascites, and good ambulation.

Statistical analysis

Data were analysed using SPSS16.0 software for windows, and the chi-square test was used for categorical data and the t-test for continuous data. P values < 0.05 were considered statistically significant.

Results

Forty-six patients were recruited in our study. There were 26 cases in FTS group with the average age of 47.85±8.44 years old, and the fast-track surgery was applied during entire

Table 1. Patient preoperative characteristics

Characteristics	FTS group (n=26)	Control group (n=20)	*P* value
Sex (Male/Female)	16/10	14/6	0.55
Age ($\bar{x}$±s yr)	47.85±8.44	45.25±10.63	0.361
Weight ($\bar{x}$±s kg)	65.23±7.41	67.35±7.66	0.348
Cardiovascular disease (Yes/No)	4/22	2/18	0.924
Child grading A/B	9/17	9/11	0.474
Anemia degree (Mild/Moderate/Severe)	2/14/10	2/11/7	0.947
Varicose veins degree (Mild/Moderate/Severe)	3/17/6	2/10/8	0.463

Table 2. The comparison of postoperative characteristics and complications between two groups

Postoperative indexes	FTS group (n=26)	Control group (n=20)	*P* value
First-exhaust time (h)	52.65±6.80	71.1±10.35	0.000
Solid-food tolerance time (d)	5.73±2.66	7.65±3.33	0.035
Plasma dosage (g)	30.15±5.87	36.05±7.22	0.004
Hospital stay time (d)	20.77±8.94	27.1±11.23	0.039
Average nutrition fee (¥/d)	241.58±33.21	349.5±47.04	0.000
Complications	3	11	0.001
Hydrothorax	1	3	
Left subphrenic dropsy	1		
Incision infection	1	1	
Ascites	0	5	
Hyponatremia	0	1	
Hepatorenal syndrome	0	1	

Table 3. The comparison between preoperative and postoperative pre-albumin (mg/L)

	FTS group	Control group	t value	*P* value
Preoperative	198.46±54.93	195.75±62.37	0.156	0.876
Postoperative 8th day	174.81±50.19	133.05±46.99	2.875	0.006*
t value	1.485	3.670		
P value	0.150	0.002		

perioperative period. There were 20 cases in control group with the average age of 45.25± 10.63 years old, and the conventional treatment was applied during entire perioperative period. There were not significant differences in gender, age, weight, admission liver function of Child grading, preoperative cardiovascular disease, preoperative anemia degree, and preoperative varicose veins degree between two groups (P > 0.05) (**Table 1**). There were significant differences in first-exhaust time, solid-food tolerance time, plasma dosage, average nutrition fee, hospital stay time, and postoperative complications between two groups (P < 0.05) (**Table 2**).

There was no significant difference on preoperative pre-albumin between two groups (P > 0.05), while pre-albumin was significantly higher in FTS group than in control group on postoperative 8th day (P=0.006). For FTS group, there was no significant difference in pre-albumin between preoperative and postoperative values (P=0.150). For control group, the postoperative pre-albumin level was significant lower than that in preoperative value (P=0.002) (**Table 3**).

There was no significant difference in preoperative transferrin level between two groups (P > 0.05), while there was significant difference in transferrin level on postoperative 8th day (P=0.009). Compared with preoperative transferrin level, postoperative transferrin level was significantly decreased in control group (P=0.000) but remained unchanged in FTS group (P=0.298) (**Table 4**).

Discussion

Surgery and anesthesia often aggravate the liver function of cirrhosis patients with portal hypertension, and lead to more severe postoperative complications [5], with postoperative complications rate of about 21.8% [6]. In our study, the postoperative complications rate of control group was 17.26%, which was decreased significantly in FTS group (P < 0.01) after

Table 4. The comparison between preoperative and postoperative transferrin (g/L)

	FTS group	Control group	t value	*P* value
Preoperative	2.05±0.35	2.12±0.43	-0.595	0.555
Postoperative 8th day	1.94±0.42	1.62±0.37	2.747	0.009*
t value	1.062	9.026		
P value	0.298	0.000*		

the optimized perioperative management. The hospital stay time was shortened in FTS group compared with control group. In both groups, the level of albumin, pre-albumin and transferrin were all decreased significantly after operation, following with hypoproteinemia. In the postoperative 8 d, the pre-albumin and transferrin values could be restored to closely the preoperative level in FTS group, while the two indicators were lower than those of preoperative levels in control group. It indicated that the optimized nutritional support therapy of FTS group was better than control group on liver protein levels.

Early enteral nutrition demonstrates a variety of advantages in liver cirrhosis patients with portal hypertension [7-10]: (1) Surgery generally causes gastrointestinal congestion and hemodynamic changes that could lead to intestinal hypoperfusion and mucosal damage. Early enteral nutrition can protect the intestinal mucosa, and reduce the entrance of bacteria and endotoxin to liver by intestinal tract, thus reducing liver burden. (2) Parenteral nutrition provides nutrients, especially fatty substances directly to systemic circulation, thus aggravating the burden of the damaged liver with reduced albumin synthesis. However, enteral nutrition can provide nutrients to liver from the portal vein system which meet the physiological needs, and it is beneficial to liver metabolism. In this study, control group received parenteral nutrition and illustrated this point that the significantly decreased postoperative prealbumin and transferrin compared with FTS group that received enteral nutrition. The main purposes of early enteral nutrition for FTS group were to strengthen postoperative gastrointestinal peristalsis and immune function, and accelerate recovery of gastrointestinal function. In our study, the first flatus and tolerance of solid foods of FTS group were significantly earlier than that of control group ($P < 0.05$).

Ascites is one of the major complications of liver cirrhosis with portal hypertension and could influence its prognosis [11]. The patients with preoperative ascites and obvious liver dysfunction were vulnerable to ascites again after operation [12]. In our study, postoperative ascites incidence rate was 25%. Ascites could influence the patients' postoperative recovery, and the prominent manifestations include hypovolemia, reduction of organs' perfusion, loss of serum albumin, decrease of hepatic and renal functions, and hepatorenal syndrome. Mass ascites and severe electrolyte disorder could induce peritoneal interventricular syndrome, abdominal distension and gastrointestinal dysfunction, thus leading to consequent intestinal failure and bacterial translocation [13]. During clinical practice, we found that the development of postoperative complications was often triggered by one initiating factor, such as ascites. Therefore, more attention should be paid to the postoperative ascites and deal with it in time to avoid the prolongation of patients' rehabilitation process. In our study, we took prophylactic diuretic measures for FTS group in the second day after operation, and limited sodium infusion. As a result, the incidence rate of ascites patients was significantly lower in FTS group compared with control group ($P < 0.05$).

Postoperative electrolytes (Na^{2+}, k^{+}) should be monitored and finely controlled due to diuretic treatments [14]. We found that patients who do not be given sodium in the short time after operation (about postoperative two days inside) did not appear hyponatremia but were prone to hypokalemia, which might be caused by postoperative usage of diuretics and special pathophysiologic characteristic (such as the decline of aldosterone inactivated ability). Once hypokalemia appeared, patients were vulnerable to the hepatic encephalopathy and enteroplegia [15]. In our study, the postoperative serum potassium of patients was higher than 4 mmol/L, which can maintain its homeostasis.

In summary, the FTS rehabilitation protocol is a safe, rational multi-disciplinary collaborative process [16, 17] and could effectively decrease post-operative complications and promote post-operative rehabilitation in liver cirrhosis patients with portal hypertension. We should pay more attention to the prophylactic mea-

sures of complications, early usage of enteral nutrition and therapy to ascites promptly so as to accelerate the patients' rehabilitation.

Disclosure of conflict of interest

None.

Authors' contribution

Xia Zhang analyzed the data and wrote the manuscript; Jing Zhang colleccted patients' information; Jun Li and Gang Cui performed all the experiments and collected all the data; Gang Li designed the study and revised the manuscript.

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