Effect of appetite-conditioned reflex stimulation on early enteral nutrition tolerance after surgery

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Abstract

***Objective* : This study aimed to discuss the effects of appetite-conditioned reflex stimulation on the early enteral nutrition (EEN) tolerance, complications, and postoperative hospital stay in patients who underwent surgery.**

***Methods* : Seventy patients who underwent laparoscopic radical resection of colorectal cancer surgery in our hospital between February and December 2017 were randomly divided into a stimulated appetite group (experimental group, including visual stimulation, nasal stimulation, taste stimulation and hearing stimulation) and a control group (n = 35). Both groups received EEN. EEN tolerance, complications, and postoperative hospital stay were then compared between the groups.**

***Results* : Sixty-six patients, including 34 in the experimental group and 32 in the control group, completed the relevant experiment. The experimental group had significantly lower incidence rates of nausea, vomiting, bloating, use of prokinetic drugs, and gastric tube replacement ($P < 0.05$), and shorter tolerable regular eating time (5.0 ± 1.0 d vs 6.4 ± 1.9 d, $P < 0.05$) and postoperative hospital stay (7.0 ± 2.0 d vs 8.0 ± 1.8 d, $P < 0.05$) than the control group. No significant difference in complication rate was detected ($P > 0.05$).**

***Conclusion* : Appetite-conditioned reflex stimulation can improve EEN tolerance, decrease the risk of complications, and shorten ordinary diet recovery time and hospital stay.** (Acta gastroenterol. belg., **2020**, 83, **527-531**).

Key words : early enteral nutrition (EEN), tolerance, colorectal cancer.

Introduction

Patients with colorectal cancer have long operative times, extensive surgery, increased body catabolism, and long postoperative fasting duration. Therefore, postoperative nutritional support is highly important for patients with colorectal cancer. Early enteral nutrition (EEN) after surgery has been widely used in clinical settings as an important measure to promote postoperative rehabilitation according to the concept of rapid rehabilitation surgery (1). EEN via a nasogastric tube is the preferred method for immediate feeding of patients with multiple injuries because it is easy, and therefore, not time consuming to implement (2). EEN can restore or maintain intestinal function and reduce complications (3, 4). EEN includes nutrition and non-nutrition roles, of which the former mainly provides nutrients, but the latter includes roles of protection of the intestinal barrier function, stimulation of gastrointestinal hormones, release of enzymes, immunity, and metabolism. Its non-nutritional roles have increasingly become prominent (5). A previous study reported that approximately 70% of patients with cancer may develop malnutrition, which is more serious in old patients because their compromised physiology, poor responses to stressors, poor nutrient absorption, and insufficient nutrient intake (6, 7).

Studies have shown that EEN can improve patients' nutritional level, reduce complications, and shorten hospital stay (8, 9), but discomfort symptoms (inculding nausea, vomiting and abdominal distension) have been frequently observed in patients who receive EEN. These discomfort symptoms can reduce EEN compliance, which can lead to further decreased compliance (10) and even to discontinuation of the EEN. Therefore, this study aimed to discuss the potential effects of appetite-conditioned reflex stimulation on the EEN tolerance, complications, and postoperative hospital stay of patients who underwent surgery. Our data can be used to survey strategies to increase EEN tolerance.

Materials and methods

Objective

This study was a prospective randomized controlled trial. The inclusion criteria mainly comprised the following : (1) patients diagnosed as having colorectal cancer through preoperative pathological diagnosis ; (2) patients aged 18-80 years ; (3) patients without distant metastasis on imaging examination and suitable for elective laparoscopic surgery ; (4) patients with a preoperative body mass index (BMI) of 17.5-27.5 kg/m^2 and preoperative serum albumin (ALB) level of ≥30 g/L ; (5) patients with an APACHE-II score of ≤20 ; and (6) patients who agreed to enroll and signed

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Submission date : 22/12/2019
Acceptance date : 13/05/2020

the informed consent form. The exclusion criteria were as follows : (1) patient without a history of abdominal surgery ; (2) patients who received chemotherapy and hormone therapy ; (3) pregnant patients ; (4) patients who used gastrointestinal motility drugs 24 hours before surgery ; (5) patients with combined gastroesophageal reflux disease ; and (6) patients with APACHE-II scores of >20. The termination criteria were as follows : (1) tumor distant metastasis and treatment with palliative surgery alone ; (2) intraoperative blood loss of >600 ml or intraoperative blood transfusion ; (3) operation time of >6 h ; and (4) use of the Miles surgical approach. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of the Second Affiliated Hospital of Kunming Medical University. Written informed consent was obtained from all patients.

General data

Seventy patients treated in the Department of Gastrointestinal Surgery, Second Affiliated Hospital of Kunming Medical University, who underwent colorectal cancer radical surgery were randomly divided into experimental and control groups (n = 35 in each group). Sixty-six patients completed the study, including 34 in the experimental group and 32 in the control group. No significant differences in general data were detected between the two groups ($P > 0.05$, Table 1).

Table 1. **— General data in the two groups**

Index	Experimental group (n=34)	Control group (n=32)	P value
Gender (male/female)	24/10	21/11	0.665
Age ($\bar{\chi} \pm s$ years old)	59.6±11.3	6χ0.7±11.8	0.701
BMI ($\bar{\chi} \pm s$ kg/m^2)	21.2±2.1	21.4±1.8	0.494
Albumin ($\bar{\chi} \pm s$ g/L)	37.8±3.9	38.5±4.2	0.512
Hemoglobin ($\bar{\chi} \pm s$ g/L)	118.4±15.2	121.5±14.9	0.407
TNM stage (I~II/III)	25/9	24/8	0.891
Operation time ($\bar{\chi} \pm s$ h)	3.31±0.64	3.48±0.77	0.315
Intraoperative blood loss ($\bar{\chi} \pm s$ ml)	180±160[a]	160±100[a]	0.458
APACHE-II score	7.0±4.3[a]	7.3±2.4	0.871

Note : [a] indicates that data are not normally distributed, and they are described as median ± interquartile range, and statistical analysis is performed using Wilcoxon rank sum test.

Intervening measures

In the experimental group, the appetite-conditioned reflex stimulation in the patients included the following : (1) visual stimulation : a video showing a patient about 30 min who loves to eat was played for the patients to watch with their families and the hospital staff (30min before meal, 30min/ time, 3 times/day) ; (2) nasal stimulation : fragrant fruit or food were placed beside the patient's bed ; (3) taste stimulation : vitamin C pill in mouth (100 mg/time, 3 times/day) ; (4) hearing stimulation : patients listened to food-related media on headphones (30min/ time, 3 times/day).

The patients in the two groups received an enteral nutritional suspension (NUTRICIA, Wuxi, China) at 6 h after surgery, and the dose was 50 ml/time and 3 h/time. The specific ingredients include water, maltodextrin, whey protein hydrolysate, vegetable oil, vitamins, minerals and trace elements and other essential nutrients. From the second day, the dose was adjusted to 200 ml/ time and 3-4 h/time. If the first artificial feeding of 300ml nutrient solution was well tolerated and the patients were willing to take it orally, the nasal feeding tubes were removed and changed to oral administration. In accordance with the patient's tolerance, liquid diet was transited to regular diet, and the intravenous fluid volume was simultaneously adjusted. Stomach tubes were removed at 12 h after surgery and replaced if intestinal obstruction was detected in the patient. Blood K and ALB levels were measured, and K and ALB were infused if necessary. Blood glucose level was controlled at <10 mmol/L after surgery, and insulin therapy was performed if necessary. Restrictive rehydration was used after surgery, at a dose of ≤2000 ml/d (11). Postoperative out-of-bed activities were voluntarily performed by the patients.

Monitoring indicators

Observation and monitoring indicators mainly included the following : (1) general data : sex, age, BMI, and hematological specimen test ; (2) intraoperative conditions : operation time, intraoperative blood loss, and APACHE-II score after surgery ; (3) EEN tolerance : nausea, vomiting, bloating, diarrhea (>5 times/d), reposition of gastric tube, postoperative tolerance of common dietary time, and postoperative use of gastrointestinal motility medication ; and (4) Nausea, vomiting, bloating, diarrhea and postoperative hospital stay.

The discharge standards were as follows : (1) tolerance of oral diet without peripheral rehydration ; (2) intestinal function recovery ; (3) good pain control ; (4) recovery of ambulation ; and (5) normal body temperature.

The general objective data were collected by the members of the research group according to the medical record information for the patients when they were discharged. The patient's progress of oral nutrient solution, independent feeding and subjective indicators of tolerance were recorded by the escort at any time, and the members of the research group collected them every day. The intervention measures were uniformly implemented 8 days after the operation, and the tolerance of nutrient solution and subjective and objective indexes of self-feeding were recorded on the 8th day after the operation.

Statistical analysis

Measurement data with normal distribution were described as mean ± standard deviation and estimated using a *t* test. Data that were not normally distributed were

Table 2. — **EEN tolerance in the two groups**

Index	Experimental group (n=34)	Control group (n=32)	Statistics	P value
Nausea (%)	10(29.4)	19(59.4)	X^2=6.008	0.014
Vomiting (%)	2(5.9)	9(28.1)	X^2=5.872	0.015
Bloating (%)	6(17.6)	14(43.8)	X^2=5.318	0.021
Diarrhea (%)	3(9.7)	8(25)	X^2=3.106	0.078
Usage of gastrointestinal motility drugs (%)	1(3.0)	7(21.9)	-	0.025#
Stomach tube reset (%)	0	5(15.6)	-	0.023#
Toleration regular eating time ($\bar{\chi}$ ± s) d	(5.0±1.0)[a]	(6.4±1.9)	Z=-3.430	0.001

Note : [a] indicates that data are not normally distributed, and they are described as median ± interquartile range, and statistical analysis is performed using Wilcoxon rank sum test. #indicates Fisher exact test.

Table 3. — **Complication and postoperative hospital stay in the two groups**

Index	Experimental group (n=34)	Control group (n=32)	Statistics	P value
Lung infection (%)	0	2(6.3)	-	0.231#
Anastomotic leakage (%)	0	1(3.1)	-	0.485#
SIRS (%)	2(5.9)	0	-	0.493#
Postoperative hospital stay ($\bar{\chi}$ ± s) d	7.0±2.0[a]	8.0±1.8	Z=-2.438	0.015

Note : [a] indicates that data are not normally distributed, and they are described as median ± interquartile range, and statistical analysis is performed using Wilcoxon rank sum test. # indicates Fisher exact test.

described as median ± interquartile range and estimated using the Wilcoxon rank sum test. Counting data were estimated using the c^2 test or Fisher probability method, and a P value of <0.05 was considered a statistically significant difference.

Results

EEN tolerance

The patients in the stimulated appetite group showed significant differences in the incidence rates of nausea (29.4%), vomiting (5.9%), bloating (17.6%), use of gastrointestinal prokinetic drugs (3.0%), replacement of gastric tubes (none), in tolerable regular eating time (5.0 ± 1.0) from those in the control group ($P < 0.05$). However, there were no significant difference in the incidence of diarrhea was detected ($P > 0.05$, Table 2). Five patients in the control group had >500 ml of postoperative drainage volume per day, which was >1000 ml in twice of the patients. The minimum drain time exceeded 2 days.

Comparison of complications and postoperative hospital stay

In the postoperative course, no significant differences in symptoms, including lung infection, anastomotic leakage, and SIRS were detected between the two groups ($P > 0.05$), but the hospital stay duration in the experimental group was shorter than that in the control group ($P < 0.05$, Table 3).

Discussion

In patients with colorectal cancer, owing to abnormal body and tumor metabolisms, intake of nutrients cannot meet the nutritional needs of the body, often resulting in preoperative malnutrition. During anesthesia and surgery, the body is subjected to stress, with high catabolism and negative nitrogen balance, which aggravate postoperative malnutrition. Poor nutrition can lead to a decrease in the of intestinal cells, and the decline in cell proliferation and protein synthesis within the thinned mucosal lining of the lumen lead to mucosal atrophy. As a result, enzyme activity decreased the bowel mucosal healing and intestinal bacterial translocation, which easily occur in patients with postoperative infectious complications, concomitant intestinal mucosa secretion decline, loss of mucus adhesion barrier, and impaired immune function. Furthermore, intestinal mucosal sur-gical trauma can also lead to impaired immune function and reduce the patient's postoperative tolerance to chemotherapy, radiotherapy, etc. The idea of nutritional support in the early postoperative period for patients with nutritional risk due to colorectal cancer has received increasing attention.

After surgical treatment, appetite and diet are known to decline during recovery, which leads to malnutrition. Nutritional status can take up to a year to recover after an operation (12). Long-term parenteral nutrition can lead to iatrogenic intestinal hunger syndrome. Dietary restriction can damage the intestinal mucosal barrier, and long-term parenteral nutrition can lead to intestinal atrophy. If the intestinal barrier is impaired, intestinal bacteria translocation can occur. This translocation predisposes patients to enterogenic infection, a major cause of multiple-organ failure in critically ill patients (6). Owing to the lack of food in the digestive tract, gallbladder contraction, such as gut hormone secretion, is reduced ; thus, biliary sludge and stone easily form in the gallbladder. In addition, hepatic steatosis due to glucose overload and liver function damage occur.

Enteral nutrition has been the first choice in clinical nutrition support. Early postoperative enteral nutri-

tion can promote recovery from peristalsis, and even a small amount of diet, lower than the calorie requirement, is beneficial. This may be because EEN has a local nutritional effect, can stimulate the growth of epithelial cells in the intestinal mucosa, and promotes the secretion of gastrointestinal hormones and the recovery of gastrointestinal function. In addition, the gastric tube can also be removed early to avoid lung infection. The current study indicates that EEN should be the first choice of nutritional support if the intestinal function after colon cancer surgery permits. EEN can provide nourishment and play an important role in intestinal mucosal structure and function integrity, and reduce bacterial and endotoxin translocations (13). EEN can accelerate postoperative immune function and recovery of bowel function in patients with colorectal cancer (14), and improve nutritional function. EEN in critically ill patients can reduce organ failure, infectious complications, and mortality, thereby reducing postoperative hospital stay and reducing hospitalization costs (15). A more important finding is that owing to the lower price of enteral nutrition, it is more suitable for human physiological needs and easily promoted by healthcare workers. According to the guidelines of the European Society of Parenteral and Enteral Nutrition and the American Society of Parenteral and Enteral Nutrition, perioperative nutritional support should be considered in patients with cancer. Furthermore, for patients with severe malnourishment, they recommend performing surgery after administering preoperative nutritional support for >7 days (16, 17). It is important to note that some patients receiving EEN may experience complications such as nausea, vomiting, and aspiration-which can result in lung infection (18) ; of course, these complications lead to reduced compliance (10, 19) and even discontinuation of EEN.

EEN tolerance is related to not only the type, dose, and concentration of enteral nutrition but also the feeding technology used by medical staff. Currently, EEN tolerance is mainly improved by improving gastrointestinal motility via medication as well as use of abdominal massage and Chinese medicine, but some measures may aggravate patient discomfort or cause related adverse reactions, and the efficacy of some measures has not been validated (20).

This study aimed to stimulate eating desire by using 4 appetite-conditioned reflex stimuli, including viewing, smelling, tasting, and hearing. These stimuli are meant to reduce the nausea, vomiting, and diarrhea caused by EEN, as well as decrease use of motility drugs, decrease the number of stomach tub e changes, and shorten the tolerable normal eating time and postoperative hospital stay. The potential mechanisms may be as follows : (1) Vision, smell, taste, and hearing can stimulate peripheral appetite signals that can stimulate the hypothalamus via neurotransmitters, neural pathways, and related hormones. Then, the hypothalamus distributes appetite signals after integrating the appetite regulation network and generates appetite regulatory factors such as orexin and neuropeptide Y, thereby stimulating appetite and enhancing feeding behavior. (2) Vision, smell, taste, and hearing can stimulate cerebral and nerves that induce swallowing. Swallowing reflex causes a vagal anti-inflammatory pathway, which can help acetylcholine with α-7 nicotinic receptors of inflammatory cells to reduce the release of inflammatory mediators, improve postoperative palsy, and stimulate the release of gastrointestinal hormones and food digestion and absorption (21). (3) Vision, smell, taste, and hearing can conduct detailed signals (e.g., smell and color) and abstract signals (e.g., language and character), and then cause conditioned digestive fluid secretion, and help digestion and absorption of food. Moreover, we found no significant difference in the incidence of complications between the two groups ($P > 0.05$), indicating that interventions do not increase the risk of postoperative adverse events.

Taken together, for patients with colon malignancy who receive EEN treatment, stimulus of vision, smell, taste, and hearing can improve EEN tolerance, reduce the risk of enteral nutrition-related complications, and shorten hospital stay, which may be a simple, easy, and safe intervention.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgements

This study was supported by the Foundation of Research Center for Surgical Clinical Nutrition in Yun-Nan Province. We used the funding to collect the data and revise the manuscript.

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