Randomised Controlled Trial

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Does enteral nutrition require continuity of management: a randomized controlled study

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Objective: To explore a set of enteral nutrition therapy continuity management programs for intensive care unit patients based on the theoretical study of circadian rhythm mechanism.

Methods: The control group followed routine nursing management. Patients in the experimental group were implemented with an enteral nutrition continuity management program, and their eating behavior was adjusted 3 days before the end of tube feeding. Food intake was intermittent at 2, 3, and 4 h on the first day, the second day, and the third day of intervention, respectively, and all patients stopped eating at night. Abdominal distension assessment, appetite assessment, application of gastric motility drugs, and patient satisfaction were compared between the two groups after tube feeding.

Results: Three days after the end of tube feeding, abdominal distention assessment, bowel sound auscultation, and appetite assessment were statistically different ($P < 0.05$) between the two groups. There were differences in the first day (15 vs. 6, $P < 0.05$), the second day (9 vs. 3, $P < 0.05$), and the cumulative number (17 vs. 7, $P < 0.05$) of gastrointestinal drugs, but no differences in the third day (2 vs. 1, $P > 0.05$). There was a statistical difference in nursing intervention (6.0 vs. 7.0, $P < 0.05$) and psychological nursing (6.0 vs. 7.0, $P < 0.05$), but no statistical difference in health education, medical environment, and nursing attitude ($P > 0.05$).

Conclusion: Enteral nutrition continuity management program has a good preventive effect on the gastrointestinal symptoms of intensive care unit patients after the end of tube feeding.

Keywords: circadian rhythm, continuity of management, enteral nutrition

Introduction

In recent years, the prevention and management of early intolerance symptoms in intensive care unit (ICU) patients with enteral nutrition therapy and the analysis of its influencing factors have attracted the attention of many scholars. However, there are relatively few studies on nursing management strategies after long-term nutrition therapy[1,2]. In normal circumstances, the body has a robust circadian rhythm, which is regulated and influenced by eating behavior. When eating behavior changes, the function of the brain–gut axis is affected, and the robustness of the clock oscillator of the digestive organ is reduced, leading to a series of adverse reactions. Such as the disruption of glucose homeostasis, decreased diversity of gut microbiome, and even sleep disturbances[3–5]. For severe patients with widespread circadian rhythm disorder and altered eating behavior, due to the continuous weakening of the circadian rhythm regulation ability of the body along with the degree of disease, treatment environment, and other factors, the endogenous rhythm regulation ability of the patients is constantly reduced; as a result, the occurrence of abdominal distention, loss of appetite, anorexia, and other events often occur in the stage of tube feeding withdraw stage[6–8]. What's worse, this phenomenon even continues in the daily life for some patients after being discharged from hospital, which seriously affects the quality of their life[9]. However, Matenchuk *et al.*[10] proposed through literature studies that for patients with widespread circadian rhythm disorder, it can effectively promote the smooth regression of circadian rhythm and maintain the normal expression of digestive system function by simulating physiological feeding behavior regulation of the body. At the same time, Zeb *et al.*'s[11] study also suggested that

HIGHLIGHTS

- For critically ill patients, there is a huge discrepancy between diurnal persistent eating behaviors and our physiological ingestive behaviors, and the dietary intervention protocol in this study can effectively promote a smooth transition of eating behaviors in patients.
- The dietary intervention program constructed in this study can effectively reduce the risk of bloating and loss of appetite at the end of tube feeding and reduce the frequency and dosage of gastric stimulant drugs in patients.

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eating signals have a direct regulatory effect on the circadian rhythm of the body and digestive system, and affect the function of the body's digestive system. Therefore, before the end of enteral nutrition therapy for ICU patients, how to take the scientific feeding behavior regulation smooth return to promote the body's physiological eating behaviors has important clinical significance. In attention, study based on the mechanism of circadian rhythm of enteral nutrition continuity management is still relatively rare. Therefore, based on the theoretical mechanism of circadian rhythm, this study aims to explore a set of continuity management programs for enteral nutrition therapy in critically ill patients and to verify the effect of its clinical application.

Methods

Study design

This is a two-arm parallel-group randomized controlled trial designed to improve gastrointestinal symptoms during the withdrawal phase of enteral nutrition therapy in critically ill patients, so we used a nonequivalent control group and a pretest/posttest design. The work has been reported in line with the CONSORT criteria, Supplemental Digital Content 1, http://links.lww.com/MS9/A487. The study consists of two parts, namely, the formulation of the dietary management plan and clinical application practice. Patients in both groups followed the routine diagnosis and treatment procedures of enteral nutrition. Enteral nutrition therapy could not be terminated in all patients at the same time due to the differences in patients' conditions, so a nonconcurrent randomized controlled trial was used to carry out the clinical study. According to the doctor's treatment plan, we selected patients who met the inclusion and exclusion criteria in 3 days and randomly divided them into the control group and the experimental group in a ratio of 1:1 by using the random number arrangement method. The control group did not perform any intervention measures during the tube feeding withdrawal stage, and the experimental group received dietary plan management during the tube feeding withdrawal stage. All data surveys were cross-collected by ICU and EICU staff, and if the patients were transferred out of the ICU, the data was conducted by nursing staff in clinical departments. None of the investigators knew the grouping of patients. Ethical approval was obtained from our hospital (2022-028).

Participants and selection procedure

Sixteen patients in our hospital who met the inclusion and exclusion criteria were selected for the clinical pretrial from July 20 to 26, 2023. The incidence of abdominal distension events during the tube feeding withdrawal stage was taken as the main outcome index. The results showed that the incidence was 75% in the control group and 40% in the experimental group, and the test standard value was 0.05 and β value was 0.02. The statistical software PASS 11.0 was used to calculate the total sample size for this study of 60 cases. Considering the instability of the disease for ICU patients, the rate of loss to follow-up was increased by 10%, and the final sample size was 66 cases. Inclusion criteria: patients were 18 years or older, with self-consciousness in the withdrawal stage of tube feeding, feeding times were 7 days or more, no immunosuppressants were used, patients and their families are willing to cooperate with this study. Exclusion criteria : gastrointestinal symptoms have been present during enteral nutrition therapy or auxiliary means such as drugs are used to maintain enteral nutrition therapy, severe electrolyte disorder exists; its diagnostic criteria refer to the study reported by Wang *et al.*[12], severe liver disease, hyperthyroidism, and diabetes mellitus. Criteria for shedding: the patient was transferred to another hospital after enteral nutrition treatment. Figure 1 illustrates the study design flowchart and process stages. Verbal or written informed consent was required from both the patients and their families.

Study procedure

Our research team was established before the study and consisted of three chief physicians and two head nurses from the ICU, one archiater in gastroenterology, and two master nurses in the field of critical care nursing have their research focus centered on enteral nutrition therapy for critically ill patients. Both of them have currently obtained qualifications as certified nutritional therapists. They mainly constructed the diet management plan preliminarily and invited relevant experts for letter consultation. The study was conducted from August 1 to October 15, 2023. Between the two groups in this study, only the feeding management before the end of enteral nutrition therapy was different, and other nursing measures were consistent. Patients in both groups received routine nursing care according to nutritional treatment guidelines[13], including raising the head of a bed 30°–45° during enteral nutrition support. The residual stomach was monitored every 4 h. During the intervention, the medical staff strictly implemented the hand hygiene system. The discontinuation time of enteral nutrition therapy prescription for patients in the two groups was determined by three ICU archiaters according to the joint assessment of patients' conditions. Follow-up investigations and interventions were conducted based on the diagnosis and treatment opinions of the current department when patients were transferred to the general ward during the intervention period.

Control group

The control group received routine nursing intervention according to the guidelines[13] recommended before the end of enteral nutrition therapy, including raising the head of a bed and monitoring stomach residues every 4 h. After enteral nutrition treatment, the patient was instructed to eat orally in the semi-decubitus or semi-sitting position in the early stage. In the process of eating, the head is tilted forward 45° to expand the throat channel, and the amount of single mouth intake gradually increases to the normal amount according to the patient's tolerance. As for the food traits, the gradual transformation process from liquid to semi-liquid and solid food was followed.

Experimental group

After careful discussion, the research team concluded that day–night eating behavior would lead to the disorder of ghrelin secretion, long-term continuous nutrition pumping would increase the risk of tube feeding dependence, and intermittent eating could promote the recovery of brain–gut axis nerve reflex mechanism. Based on these observations, we developed a dietary management plan for the experimental group. The management mainly reflected in the patient from day and night continuous

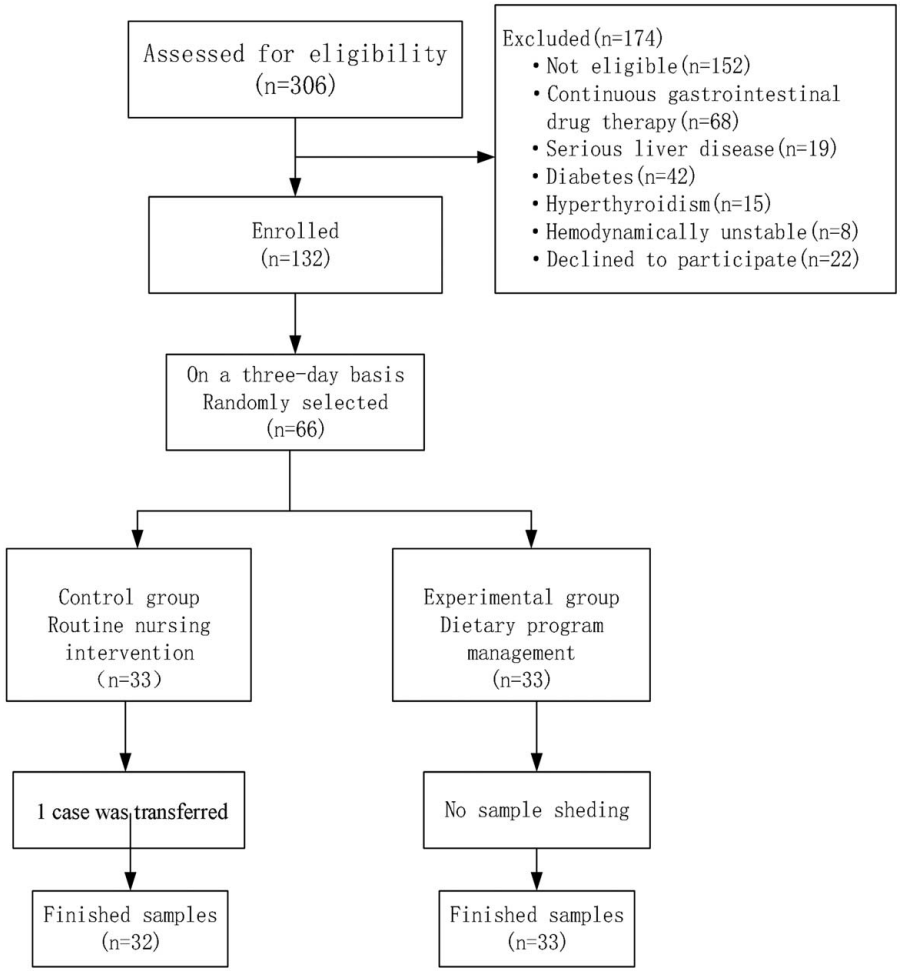

Figure 1. Study consort diagram.

eating to intermittent eating during the day and no eating at night. According to the recommendation of "ESPEN guideline on hospital"[14], the energy intake requirement of severe patients during disease recovery is 30–35 kcal/kg/d, and the total daily energy requirement of each patient is roughly calculated. Based on the research basis of Menculini *et al.*[15], Kaczmarek *et al.*[16], and the expert letter consultation. Our research team carried out a full discussion and then proposed that the patients should be managed with a dietary plan 3 days before the end of enteral nutrition therapy. The plan contents were as follows: intermittent food intake was carried out at intervals of 2, 3, and 4 h on day 1, day 2, and day 3, respectively, and each intake was calculated by dividing the total amount of patients' needs by the number of feeding times per day. All patients stopped eating at night. In terms of diurnal eating behavior, for example, for a patient of 50 kg, the recommended energy intake is about 1500–1750 kcal, and ~1500 ml enteral nutritional emulsion is required. The feeding time and feeding amount are shown in Table 1.

Outcome measures

Based on the clinical investigation results of digestive tract symptoms in patients at the early stage of oral feeding (within 3 days) and the status quo of domestic and foreign reports, the research team discussed and formulated the following observation indicators: abdominal distention assessment: abdominal distention was assessed by the numerical rating scale in conjunction with bowel sound auscultation. The numerical rating scale was formulated, in which 0 points represented no abdominal distension, one to three points mild abdominal distension, four to six points moderate abdominal distension, and seven to 10 points severe abdominal distension[17]. The assessment criteria of bowel sound was implemented and judged according to the guidelines of "digestive system diseases"[18]. The scales and the assessment time of bowel sound were all before the patient took

Table 1

Eating management plan.

Time food intake	8:00	10:00	11:00	12:00	14:00	16:00	17:00	18:00
Intervention day 1 (eat about 250 ml[a])	√	√		√	√	√		√
Intervention day 2 (eat about 370 ml[a])	√		√		√		√	
Intervention day 3 (eat about 500 ml[a])	√			√		√		

[a]Take a weight of 50 kg as an example.

the medicine every morning. Appetite assessment: visual analog scale was used to assess the appetite of patients on the first day after the nutritional treatment. The patients selected appropriate values according to their conditions to indicate their appetite, where 0 points mean no appetite at all and 10 points mean very good appetite[19]. Application of gastric motility drugs: based on the diagnosis and treatment opinions of the patients in the current department, the application of domperidone and mosapride drugs promoting gastrointestinal motility in the two groups was collected and recorded, and the application conditions of drugs were implemented by relevant doctors according to clinical diagnosis and treatment standards. Patient satisfaction: a self-made satisfaction rating scale was used to investigate and record the medical environment, health education, nursing intervention, nursing attitude, and psychological nursing of patients before the end of enteral nutrition treatment. At the same time, to reduce the risk of human bias, an allocation plan concealment was implemented during the collection of all outcome indicators of patients. That is, participants in the ICU and EICU treatment unit conducted cross-evaluation on the transferred patients.

Data analysis

SPSS 24.0, software was used for data analysis. The quantitative data were tested for normality. Normally distributed data were statistically described by means and SDs. Nonnormally distributed data were statistically described by quartile. Frequencies and percentages were statistically described. The t test, Mann–Whitney U test, or χ^2 test was used to determine the homogeneity of the two groups. Repeated measurement data were analyzed by generalized linear mixed models. The rank sum test was used to compare between grade data groups. Test level $\alpha = 0.05$, when P value < 0.05 means the difference was statistically significant.

Results

Participant

During the intervention period, 306 patients were recruited (136 patients did not meet the inclusion criteria, 38 patients or their families refused to participate in the study). Sixty-six patients were randomly selected from 130 patients and divided into a control group and an experimental group in a 1:1 ratio. One case in the control group was transferred to another hospital. Finally, a total of 65 cases were completed (Fig. 1). Prior to the intervention, there was no statistical significance in age (57.96 ± 15.23 vs. 60.34 ± 10.24), BMI (21.76 ± 2.47 vs. 22.44 ± 1.95), and other general data of enteral nutrition treatment patients between the two groups (Table 2).

Table 2

Patient characteristics at baseline.

Variables	Routine nursing intervention ($n = 32$)	Dietary program management ($n = 33$)	$t/\chi^2/z$	P
Gender, n (%)			0.423	0.515
Male	20 (62)	18 (56)		
Female	12 (38)	15 (44)		
Age, mean (SD)	57.68 ± 15.39	60.54 ± 10.15	0.886	0.379
APACHE II score, mean (SD)	11.88 ± 2.31	11.03 ± 2.64	1.376	0.174
Body mass index, M (Q_{25}, Q_{75})	22.4 (19.8, 23.7)	22.6 (20.8, 24.0)	1.011	0.312
Tube feeding day, M (Q_{25}, Q_{75})	8.5 (8.0, 10.0)	8.0 (7.0, 9.0)	1.417	0.156
ICU length of stay, M (Q_{25}, Q_{75})	9.0 (8.0,11.0)	9.0 (7.0,11.0)	1.197	0.231
Primary disease, n (%)			2.787	0.594
Respiratory failure	6 (18)	9 (28)		
COPD	9 (28)	6 (18)		
Cerebral trauma	4 (12)	7 (21)		
Cerebral infarction	8 (25)	5 (15)		
Other	5 (17)	6 (18)		

APACHE II, Acute Physiology and Chronic Health Evaluation II; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit.
Proportions were compared using χ^2 test.
Normal distribution data were compared using analysis of t test.
The abnormal distribution data were tested by a nonparametric test.

Effect of dietary program management

Through dietary plan management for patients in the experimental group, the experimental results are as follows (Table 3).

Abdominal distention assessment

The results of repeated measurement analysis of variance for abdominal distension score showed that there were significant differences in abdominal distension score of patients at different time points ($F_{time} = 70.753$, $P < 0.001$), and there was no statistical difference in the interaction effect ($F_{intervention \times time} = 0.060$, $P = 0.807$), but there were statistical differences between intervention ($F_{\text{intervention}} = 70.753$, $P < 0.001$). Results showed that abdominal distention scores did not change over study time in both groups (Table 4, Fig. 2). At the same time, there were statistical differences in bowel sound auscultation evaluation within 3 days between the two patients ($P < 0.05$), and the intestinal peristalsis in the experimental group was significantly better than that the control group.

Appetite assessment

The appetite assessment results of patients in the two groups on the first day after the end of tube feeding showed that the appetite assessment of patients in the experimental group was better than the control group (4.5 vs. 6), and the difference was statistically significant ($z = 2.677$, $P = 0.007$).

Application of gastric motility drugs

There was a statistical difference in the drug application of the digestive tract on the first day ($\chi^2 = 5.366$, $P = 0.021$) and the second day ($\chi^2 = 3.910$, $P = 0.048$) of drug use in the two groups after enteral nutrition treatment, but there was no statistical difference in the number of drug use on the third day ($\chi^2 = 0.001$, $P = 0.978$). Overall, the number of patients in the experimental group was significantly less than that in the control group ($\chi^2 = 7.104$, $P = 0.008$).

Patient satisfaction

Patient satisfaction is a subjective index to evaluate the quality of medical care. Good satisfaction can not only effectively improve the enthusiasm for medical care but also promote the rehabilitation of patients to some extent. At the end of the study, an analysis of the patient satisfaction survey found statistically

Table 3

Abdominal distension score, bowel sounds, appetite assessment, application of gastric motility drugs, and patients satisfaction by randomized groups.

Variables	Routine nursing intervention ($n=32$)	Dietary program management ($n=33$)	$t/\chi^2/z$	P
Abdominal distension score, M (Q_{25}, Q_{75})				
The first day	6.0 (4.0, 7.0)	3.0 (2.0, 3.7)	4.737	<0.001
The second day	4.0 (3.5, 5.0)	2.0 (1.0, 2.0)	4.793	<0.001
The third day	4.0 (3.0, 5.0)	1.0 (1.0, 2.0)	5.014	<0.001
Bowel sounds on day 1, *n* (%)			2.634	0.008
Disappearance	12 (37)	6 (18)		
Attenuation	19 (60)	18 (54)		
Normal	1 (3)	9 (28)		
Hyperactivity	0 (0)	0 (0)		
Bowel sounds on day 2, *n* (%)			2.845	0.004
Disappearance	9 (28)	3 (10)		
Attenuation	18 (56)	15 (45)		
Normal	5 (16)	15 (45)		
Hyperactivity	0 (0)	0 (0)		
Bowel sounds on day 3, *n* (%)			3.865	<0.001
Disappearance	4 (12)	1 (3)		
Attenuation	21 (67)	9 (27)		
Normal	7 (21)	21 (64)		
Hyperactivity	0 (0)	2 (6)		
Appetite ratings, M (Q_{25}, Q_{75})	6 (4.0, 8.0)	4.5 (3.0, 5.7)	2.677	0.007
Gastric motility drug use, *n* (%)				
The first day	15 (46)	6 (18)	5.366	0.021
The second day	9 (28)	3 (9)	3.910	0.048
The third day	2 (6)	1 (3)	0.001	0.978
Total users	17 (53)	7 (21)	7.104	0.008
Patient satisfaction, M (Q_{25}, Q_{75})				
Satisfaction with the medical environment	8.0 (6.0, 8.0)	7.0 (6.0, 8.0)	0.921	0.357
Satisfaction of health education	7.0 (6.0, 8.0)	7.0 (6.2, 8.0)	0.617	0.573
Satisfaction of psychological nursing	6.0 (6.0, 7.0)	7.0 (6.0, 8.0)	2.196	0.028
Satisfaction of nursing intervention	6.0 (5.0, 6.5)	7.0 (6.0, 7.7)	3.281	0.001
Satisfaction of nursing attitude	7.0 (6.0, 8.0)	7.0 (6.0, 8.0)	0.695	0.487

Normal distribution data were compared using analysis of *t* test.
The abnormal distribution data were tested by a nonparametric test.
The rank sum test was used for grade data.
Proportions were compared using the χ^2 test or the Fisher exact test.

Table 4

Abdominal distention score results of generalized linear mixed models.

Variables	F	P
Intervention	45.728	<0.001
Time	70.045	<0.001
Intervention × time	1.678	0.190

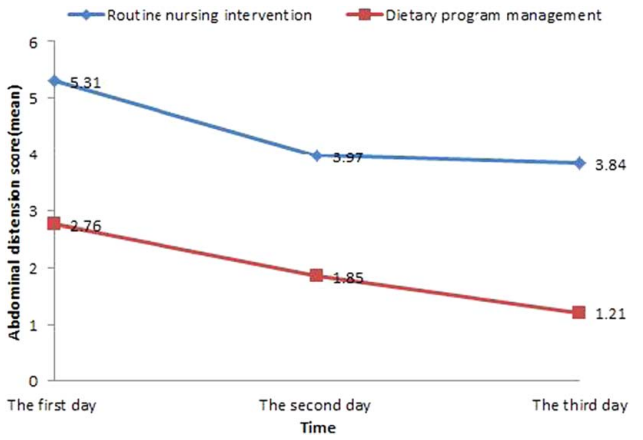

Figure 2. Changes in abdominal distension score.

significant differences between the two groups in terms of nursing intervention evaluation ($z=3.281$, $P=0.001$) and psychological nursing evaluation ($z=2.196$, $P=0.028$). However, there were no statistically significant differences in the aspects of the medical environment ($z=0.921$, $P=0.357$), health education ($z=0.617$, $P=0.573$), and nursing attitude ($z=0.695$, $P=0.487$).

Discussion

For critically ill patients, the system of enteral nutrition therapy generally consists of three stages[20]. The first phase is mainly the prevention and treatment of tube feeding intolerance incidents, the second phase is mainly the maintenance of tube feeding, and the last stage is the withdrawal of tube feeding, that is patient from tube feeding to oral feeding stage. At present, there are relatively many reports on the first and second stages of patient feeding, while there are few studies on the withdrawal stage of patient feeding.

For ICU patients, continuous day and night nutrition pumping can increase the body's tolerance to treatment, but at the same time, it also directly leads to the secretion cycle disorder of bile acid, insulin, ghrelin, and other digestive hormones[21,22], resulting in patients with varying degrees of digestive system symptoms during the withdrawal stage of tube feeding. In addition, the continuous pumping of nutrients in the course of enteral nutrition therapy will keep the satiety center of the body in an excited state, resulting in different degrees of anorexia, poor appetite, and other symptoms in the withdrawal stage of tube feeding[23].

In this study, the dietary management plan was formulated mainly based on the nutritional management status of ICU patients. Intermittent energy intake feeding mode was implemented before the end of tube feeding based on the average daily energy demand of patients. It can not only effectively reduce the gastrointestinal metabolic load of patients but also promote gastrointestinal peristalsis to a certain extent. This is done to relieve the early abdominal distension of patients through oral feeding, increase the appetite of patients, and then reduce the application of gastric motility drugs. At the same time, based on the theoretical mechanism that eating signals stimulate the peripheral biological clock to promote the normal expression of the

circadian rhythm of the stomach, liver, and other effectors[24]. This study gradually extended the patients' eating interval, regulated their eating behavior day and night, and changed the single feeding amount so as to promote the recovery of the brain–gut axis reflex mechanism of the patients. To achieve the purpose of reducing the occurrence of early digestive tract events through oral feeding patients and then improve the patient's treatment satisfaction, promote the disease recovery of patients.

Conclusions

Enteral nutrition therapy is one of the common treatment measures for ICU patients. At present, many scholars pay more attention to the prevention and management of intolerance events in patients at the early stage of nutrition therapy, but studies after enteral nutritional treatment are relatively rare. As we all know, continuous day and night food intake is very different from the physiological feeding behavior of our body. Meanwhile, continuous day and night eating behavior can also disrupt the secretion cycle of various hormones in our body, especially in the digestive system. Therefore, for these patients, it is of great significance to explore how to promote the smooth transition of their eating behavior after long-term enteral nutrition therapy. In this study, dietary plans were formulated and applied mainly based on the theoretical study of the circadian rhythm mechanism, and it was found that dietary plans could significantly reduce the risk of abdominal distension, loss of appetite, and application of gastric motility drugs in ICU patients after the end of tube feeding, which has good clinical practice significance for patients' disease prognosis.

Limitation

This research was only carried out on patients who met the inclusion and exclusion criteria in our hospital, and the general applicability of the study plan needs to be further verified by expanding the sample and expanding the region.

Ethical approval

Ethics Committee of the Fourth People's Hospital of Zigong (Approval No. 2022-028).

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

J.D.: carried out the paper writing and research design. C.N.: carried out expert correspondence and quality control. Y.L.: carried out the clinical investigation and statistical analysis. X.W.: carried out the clinical investigation and data analysis.

conflicts of interest disclosure

There are no conflicts of interest.

Research registration unique identifying number (UIN)

Trial registration number: ChiCTR2200059279.

Guarantor

Jinlei Du.

Data availability statement

All data has been uploaded as an attachment.

Provenance and peer review

None.

Supporting information

S1 Dataset. The dataset from which the results of the study were produced (SAV). Please refer to the supplementary material in the text, Supplemental Digital Content 2, http://links.lww.com/MS9/A488.

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