Tropical Journal of Pharmaceutical Research August 2023; 22 (8): 1699-1704
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
http://dx.doi.org/10.4314/tjpr.v22i8.22

Original Research Article

Use of enteral nutrition and factors influencing feeding intolerance in severely ill patients in the intensive care unit

Fen Tang, Pai Liu, Chunyan Wang*
*Department of Critical Care Medicine, West China Hospital, **West China School of Nursing,** Sichuan University, Chengdu, China*

For correspondence: **Email: 17381988443@163.com; **Tel:** +86-013693443560*

Sent for review: 14 April 2023 *Revised accepted: 26 July 2023*

Abstract

Purpose: *To investigate the use of enteral nutrition (EN) and factors influencing feeding intolerance (FI) in severely ill patients in intensive care unit (ICU).*
Methods: *Retrospective data collection was performed on records of 247 severely ill patients admitted to ICU of the West China Hospital, Chengdu, China between January 2020 and December 2022. Data were divided into two groups: FI group (n = 107) and non-FI group (n = 140). Influencing factors of FI were analyzed by univariate and multivariate analysis, and the use of EN was analyzed.*
Results: *Defined daily doses (DDDs) of enteral nutrition emulsion TPF-T (Ruineng), enteral nutrition suspension (Baipuli) and enteral nutrition emulsion TPF (Ruixian) were most prevalent. The DDDs of enteral nutrition suspension (Nengquanli 1.5) increased, while that of Nengquanli 1.0 decreased. Univariate analysis showed significant differences between FI and non-FI groups in start time of EN, addition of dietary fiber, Acute Physiology and Chronic Health Evaluation (APACHE) II score, use of sedatives, types of antibiotics used, use of vasoactive drugs and oral potassium preparation, mechanical ventilation and hypoalbuminemia ($p < 0.05$). Multivariate analysis showed that addition of dietary fiber, APACHE II score ≥ 20 points, sedatives use, types of antibiotics used ≥ 2, oral potassium preparation and hypoalbuminemia were independent risk factors of FI.*
Conclusion: *Use of EN in ICU is consistent. Factors that influence FI in critically ill patients include dietary fiber, APACHE II score, use of sedatives, use of antibiotics, use oral potassium preparations and hypoalbuminemia. Knowledge of these risk factors and timely measures are of great significance in avoiding FI in ICU.*

Keywords: *ICU, Enteral nutrition, Feeding intolerance, Influencing factors*

Tropical Journal of Pharmaceutical Research is indexed by Science Citation Index (SciSearch), Scopus, Web of Science, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Journal Citation Reports/Science Edition, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts

INTRODUCTION

Due to influence of various factors such as organ dysfunction, mechanical ventilation, medications, etc., severely ill patients in intensive care unit (ICU), who are in critical condition, have poor physical fitness and their body easily falls into a state of negative nitrogen balance, such that they need timely administration of nutritional supplements [1]. However, due to factors such as impaired gastrointestinal function, gastrointestinal complications, sepsis and systemic inflammation, critically ill patients in ICU are prone to malnutrition. According to relevant

research reports, incidence of malnutrition in critically ill patients is high in China, with an incidence of more than 50 % [2].

Enteral nutrition (EN) is a method of providing nutrition through gastrointestinal tract when oral intake is inadequate or not possible. It involves delivering a nutritionally complete liquid formula containing macronutrients (carbohydrates, proteins and fats), micronutrients (vitamins and minerals) and sometimes fiber directly into the stomach or small intestine. EN is administered via various routes including oral, nasogastric, nasoenteric, gastrostomy, or jejunostomy tubes. Based on progress of concept of enteral nutrition, some researchers believe that early EN in ICU critically ill patients can maintain physiological function of gastrointestinal tract, reduce risk of death and shorten recovery process [3].

However, although EN is relatively safe, some patients still experience feeding intolerance (FI) such as diarrhea, abdominal distension and nausea, which not only causes interruption of EN, but may also lead to aggravation of underlying diseases. [4,5]. Feeding intolerance (FI) refers to inability of patient to tolerate (EN) or development of adverse symptoms or complications during administration of EN. It is an important consideration in management of critically ill patients in intensive care unit (ICU). There are few clinical studies on factors influencing development of FI during the course of EN administration in critically ill patients. This signifies a lack of targeted intervention in this regard. Therefore, the aim of this study was to investigate the use of EN and the factors influencing FI.

METHODS

Patients

Two hundred and forty-seven (247) critically ill patients, who were hospitalized in the ICU of West China Hospital, Chengdu, China from January 2020 to December 2022, were retrospectively selected and randomly divided into FI group and non-FI group. Among them, there were 152 male patients and 95 female patients with age range of 21 to 79 years, and an average of 58.49 ± 9.14 years. Disease types: 161 patients after surgery for lung diseases, 47 patients with lung infection and 39 patients with stroke. This study complied with the requirements of the Declaration of Helsinki [6] and received ethical approval from West China Hospital. China (approval no. 20-WCH-031).

Inclusion criteria

Patients whose records met the following criteria were included: Consent to use of EN, aged over 18 years, no malnutrition before entering the ICU, acute physiology and chronic health status scoring system II [7] (acute physiology and chronic health evaluation II, APACHE II) ≥ 10 points and Length of stay in ICU exceeding 7 days.

Exclusion criteria

Patients whose records met the following criteria were excluded from the study: Presence of digestive tract disease, EN contraindication, organ dysfunction, consciousness, cognitive dysfunction, severe ischemic encephalopathy or craniocerebral disease, those with incomplete clinical data, a history of bowel surgery, end-stage chronic diseases and use of immunosuppressants one month before hospitalization.

Data collection

Statistics on the frequency of EN preparations (defined daily doses, DDDs) and general information of patients including gender, age and type of disease were collected. Relevant literature was consulted and combined with previous data from the hospital to identify factors that may cause FI. Patient data such as EN start time, dietary fiber addition, catheterization method, APACHE II score, application of sedatives, application of antibiotics, application of vasoactive drugs, oral potassium preparations, mechanical ventilation and hypoalbuminemia were also collected.

FI Judgment Criteria [8] was used from the beginning of EN administration to assess FI situation for 7 days. Occurrence of any of the following situations suggests FI:

Diarrhea

Three or more defecations per day with defecation volume of greater than 200 g per day, accompanied by changes in stool properties such as loose stools, abdominal distension with 2 intra-abdominal pressure measurements greater than 12 mmHg, gastric residual overdose with gastric content greater than 200 mL/6 h.

Constipation

No bowel movement for greater than or equal to 3 days, weakened or the absence of bowel

sounds, vomiting or regurgitation and gastrointestinal bleeding.

Data analysis

SPSS 20.0 statistical software was used for the analysis of data. Measurement data were expressed as mean ± standard deviation (SD) while count data were expressed as rate (%) and tested by χ^2-univariate and multivariate. Logistic regression was used to analyze the influencing factors of FI. $P < 0.05$ indicates statistically significant differences.

RESULTS

EN usage in ICU

Enteral nutrition emulsion TPF-T (Rueneng), enteral nutrition suspension sp (Baipuli) and enteral nutrition emulsion TPF (Ruixian) DDDs were ranked among the top three. Enteral nutrition suspension (Enteral Nutrition 1.5) DDDs showed an increasing trend, while DDDs of enteral nutrition suspension (Energy 1.0) showed a decreasing trend (Table 1).

Univariate analysis affecting FI in critically ill patients

According to results of FI, patients were divided into FI group (n =107) and non-FI group (n =140) and there was no significant difference between the two groups in terms of gender, age and catheterization method ($p > 0.05$). There were however, statistically significant differences in EN start time, dietary fiber addition, APACHE II score, use of sedatives, antibiotics used, use of vasoactive drugs, oral potassium preparations use, mechanical ventilation, and hypoalbuminemia (Table 2, $p < 0.05$).

Multi-factor analysis influencing FI

Occurrence of FI in critically ill patients was used as the dependent variable, while EN start time, dietary fiber addition, APACHE II score, application of sedatives, types of antibiotics, application of vasoactive drugs, use of oral potassium preparations, mechanical ventilation and hypoalbuminemia were used as dependent variables. Independent variables were included in Logistic regression analysis. The results showed that no dietary fiber was added, APACHE II score ≥ 20 points, sedatives use, antibiotics ≥ 2 types, oral potassium preparations use and hypoalbuminemia were independent risks affecting FI in ICU critically ill patients ($p < 0.05$). (Table 3 and Table 4).

DISCUSSION

In recent years, nutritional support has been applied in comprehensive treatment of patients in modern medicine and it plays an important role. For critically ill patients in ICU, EN is first choice [9].

Table 1: Use of EN in ICU Department from January 2020 to December 2022

Name	2020		2021		2022	
	DDDs	Sorted	DDDs	Sorted	DDDs	Sorted
Enteral Nutrition Powder TP (Ansul)	104	5	125	4	119	5
Enteral Nutrition Suspension sp (Baiprel)	184	2	196	2	204	2
Short Peptide Enteral Nutrition Powder (Baipusu)	51	8	46	10	27	10
Enteral Nutritional Suspension (Energy 1.5)	16	11	54	8	131	4
Enteral nutrition suspension (energy 1.0)	120	4	113	5	32	9
Enteral Nutrition Emulsion TPF-D (Raydai)	71	6	60	7	66	7
Enteral Nutrition Emulsion TPF-HE (Ruigao)	22	10	24	11	21	11
Enteral Nutrition Emulsion TPF-T (Rueneng)	215	1	234	1	229	1
Enteral Nutrition Emulsion TP (Ruisu)	37	9	48	9	43	8
Enteral Nutrition Powder AA (Vivo)	68	7	78	6	81	6
Enteral Nutrition Emulsion TPF (Ruixian)	153	3	162	3	157	3

DDDs = defined daily doses

Table 2: Univariate analysis of factors influencing FI in critically ill patients

Relevant factor	FI group (n=107)	Non-FI group (n=140)	x^2	*P*-value
Gender			0.693	0.405
Male	69 (45.39)	83 (54.61)		
Female	38 (40.00)	57 (60.00)		
Age			4.824	0.028
<60 years	32 (34.41)	61 (65.59)		
≥60 years	75 (48.70)	79 (51.30)		
EN start time (day)			45.26	<0.001
<2 days	52 (29.71)	123 (70.29)		
≥2 days	55 (76.39)	17 (23.61)		
Added dietary fiber			44.45	<0.001
Yes	34 (24.64)	104 (75.36)		
No	73 (66.97)	36 (33.03)		
Intubation method			2.796	0.094
Oral	11 (30.56)	25 (69.44)		
Nasal feeding tube	96 (45.50)	115 (54.50)		
APACHE II score (points)			15.28	<0.001
<20	42 (31.82)	90 (68.18)		
≥20	65 (56.52)	50 (43.48)		
Apply sedatives			7.684	0.006
Yes	48 (55.17)	39 (44.83)		
No	59 (36.88)	101 (63.13)		
Types of antibiotics used (species)			34.73	<0.001
<2	20 (20.41)	78 (79.59)		
≥2	87 (58.39)	62 (41.61)		
Use of vasoactive drugs			9	0.003
Yes	28 (63.64)	16 (36.36)		
No	79 (38.92)	124 (61.08)		
Oral potassium preparations			40.8	<0.001
Yes	71 (66.36)	36 (33.64)		
No	36 (25.71)	104 (74.29)		
Mechanical ventilation			21.61	<0.001
Yes	79 (56.03)	62 (43.97)		
No	28 (26.42)	78 (73.58)		
Hypoalbuminemia			33.28	<0.001
Yes	74 (62.18)	45 (37.82)		
No	33 (25.78)	95 (74.22)		

Table 3: Description of independent and dependent variables assignment

Variable	Code	Assignment
EN start time	X1	1= ≥2 days; 0=<2 days
Added dietary fiber	X2	1=no; 0=yes
APACHE II score	X3	1=≥ 20; 0=<2
Apply sedatives	X4	1=yes; 0=no
Types of antibiotics used	X5	1= ≥2 species; 0=<2 species
Use of vasoactive drugs	X6	1=yes; 0=no
Oral potassium preparations	X7	1=yes; 0=no
Mechanical Ventilation	X8	1=yes; 0=no
Hypoalbuminemia	X9	1=yes; 0=no
FI	Y1	1=yes; 0=no

Note: When Y1 is coded as 1, it indicates that the patient experienced feeding intolerance, while a code of 0 signifies the absence of feeding intolerance

Amongst EN preparations used in ICU Department of the hospital from January 2020 to December 2022, enteral nutrition emulsion TPF-T (Rueneng) DDDs ranked first, because omega-3 fatty acids contained in it have various physiological functions, such as regulation of blood lipids, participation in metabolic breakdown of arachidonic acid, dilation of blood vessels and inhibition of inflammation. Therefore, it has relatively good effects on sepsis, cardiovascular disease, hyperlipoproteinemia, and stroke. In addition, carbohydrates are inevitably added to EN, which generates carbon dioxide and increases respiratory burden of patients.

However, enteral nutrition emulsion TPF-T (Rueneng) has a high-fat and low-sugar content with less carbohydrate, hence it helps patients maintain normal respiratory function, especially in patients with lung function damage. Enteral nutrition suspension sp (Baiprex) DDDs ranked second because it is easily absorbed, have less fecal residue, and quickly supplement nutrients needed by patients. Enteral nutrition emulsion

Table 4: Logistic multiple regression analysis affecting FI in ICU critically ill patients

Factor	Beta	SE	Wald X^2	OR value	95% CI	*P*-value
Added dietary fiber	-1.673	0.679	5.138	3.256	0.068~0.591	0.004
APACHE II score	1.570	0.172	8.519	2.706	1.348~7.151	0.008
Apply sedatives	1.914	0.730	4.651	1.024	1.472~9.113	0.037
Types of antibiotics Used	1.844	0.613	3.148	2.483	1.518~8.742	0.011
Oral potassium Preparations	1.490	0.548	6.857	1.267	1.581~10.164	0.032
Hypoalbuminemia	2.158	0.491	4.482	1.526	1.858~5.541	0.028

Note: *Beta (β): Beta represents regression coefficient or estimated effect size of a predictor variable in logistic regression model: SE (Standard Error): SE is the standard deviation of sampling distribution of beta coefficient: Wald X^2 (Wald Chi-square): Wald Chi-square statistic is a measure of overall significance of predictor variable in logistic regression model; OR value (Odds Ratio): Odds ratio represents ratio of the odds of an event occurring in one group (e.g. patients with certain characteristics) to the odds of the event occurring in another group (e.g. patients without those characteristics); 95 % CI (Confidence Interval):*

TPF (Ruixian) DDDs have always been ranked third [4]. It provides high energy, supplements all nutrients needed by patients and is added with dietary fiber to protect the physiological functions of gastrointestinal tract. Enteral nutrition suspension (capacity 1.5) gradually replaced enteral nutrition suspension (capacity 1.0) and its DDDs increased as seen from results in this study. This increase is because enteral nutrition suspension (capacity 1.5) has higher energy density and is thus ideal for diabetics, those with constipation and patients who do not want to eat.

During the use of EN, some critically ill patients in ICU will experience FI, which may affect function of EN and this could be detrimental to recovery of patients [3,10]. Among the 247 ICU critically ill patients in this study, 107 patients (43.32 %) had FI, indicating that the FI situation in ICU critically ill patients is relatively serious. The results of multivariate analysis showed that no added dietary fiber, APACHE II score ≥ 20 points, use of sedatives, application of ≥ 2 types of antibiotics, oral potassium preparations use and hypoalbuminemia were independent risk factors for FI in ICU critically ill patients. This could allude to the fact that dietary fiber can generate fermented substances, maintain stability of intestinal flora, protect the intestinal biological barrier and reduce occurrence of FI [11]. Hence, for patients with high risk of FI, one could choose to add dietary fiber nutritional preparations such as enteral nutrition emulsion TPF (Rui Xian). Patients with APACHE II score ≥ 20 points are more seriously ill, have weaker gastrointestinal function, slow gastrointestinal motility and emptying and have a higher risk of FI [4]. Therefore, patients with APACHE II score ≥ 20 points need to be alert to the risk of FI. Sedatives are among commonly used drugs for critically ill patients in ICU. They can relieve pain, but they also relax the lower esophageal sphincter, which may lead to fluid reflux [5]. When using sedatives, risk of FI in patients needs to be considered. Excessive use of antibiotics destroys the stability of intestinal flora, increase drug resistance of harmful bacteria, lead to decreased intestinal function and makes patient prone to diarrhea [8]. Therefore, rational use of antibiotics is important in avoiding FI phenomenon. Potassium preparations taken orally are more irritating to gastrointestinal tract and may easily cause retention of intestinal content [12,13]. Therefore, oral administration of potassium preparations on empty stomach should be avoided. Level of albumin in patients with hypoalbuminemia is low and albumin is an important nutrient that can inhibit inflammatory response and protect function of gastrointestinal tract. When albumin level is less than 35 g/L, it indicates that nutritional status of the body is poor with a high risk of FI [2], thus monitoring albumin index is necessary and supplementing albumin can improve nutritional status.

CONCLUSION

Use of EN in critically ill patients is relatively consistent throughout the study period. Some factors that influence FI include no added dietary fiber, APACHE II score, application of sedatives, application of antibiotics, use of oral potassium preparations and hypoalbuminemia. Knowledge of these risk factors and timely measures are of great significance in avoiding FI in critically ill patients.

DECLARATIONS

Acknowledgements

None provided.

Funding

None provided.

Ethical approval

This study received ethical approval from West China Hospital. China (approval no. 20-WCH-031).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

Open Access

REFERENCES

1. *Hartwell JL, Cotton A, Wenos CD, Timsina L, Zarzaur BL, Rozycki G. Early Achievement of enteral nutrition protein goals by intensive care unit day 4 is associated with fewer complications in critically injured adults. Ann Surg 2021; 274(6): e988-e994.*
2. *Secombe P, Harley S, Chapman M, Aromataris E. Feeding the critically ill obese patient: a systematic review protocol. JBI Database System Rev Implement Rep 2015; 13(10): 95-109.*
3. *Mehta NM, Bechard LJ, Cahill N, Wang M, Day A, Duggan CP, Heyland DK. Nutritional practices and their relationship to clinical outcomes in critically ill children – an international multicenter cohort study. Crit Care Med 2012; 40(7): 2204-2211.*
4. *Nkwocha CC, Ekeanyanwu RC, Okagu IU. Nutritional and antinutritional composition of Synsepalum dulcificum seeds. Trop J Pharm Res 2022; 21(4):779-785 doi: 10.4314/tjpr.v21i4.14*
5. *Tuncay P, Arpaci F, Doganay M, Erdem D, Sahna A, Ergun H, Atabey D. Use of standard enteral formula versus enteric formula with prebiotic content in nutrition therapy: A randomized controlled study among neuro-critical care patients. Clin Nutr Espen 2018; 25: 26-36.*
6. *World Medical Association. World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects. JAMA 2013; 310(20): 2191-2194.*
7. *Finlay S, Asderakis A, Ilham A, Elker D, Chapman D, Ablorsu E. The role of nutritional assessment and early enteral nutrition for combined pancreas and kidney transplant candidates. Clin Nutr Espen 2017; 17: 22-27.*
8. *Gao H, Yao J, Lu L, Dou L, Chang W. Clinical study of acute gastrointestinal injury classification in early enteral nutrition in patients under intensive care. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue 2014; 26(4): 214-218.*
9. *Chlebowski RT, Beall G, Grosvenor M, Lillington L, Weintraub N, Ambler C, Richards EW, Abbruzzese BC, McCamish MA, Cope FO. Long-term effects of early nutritional support with new enterotropic peptide-based formula vs. standard enteral formula in HIV-infected patients: randomized prospective trial. Nutrition 1993; 9(6): 507-512.*
10. *Arunachala MT, Chapple LS, Lange K, Marathe CS, Horowitz M, Peake SL, Chapman MJ. Gastrointestinal dysfunction during enteral nutrition delivery in intensive care unit (ICU) patients: Risk factors, natural history, and clinical implications. A post-hoc analysis of The Augmented versus Routine approach to Giving Energy Trial (TARGET). Am J Clin Nutr 2022; 116(2): 589-598.*
11. *Joffe A, Anton N, Lequier L, Vandermeer B, Tjosvold L, Larsen B, Hartling L. Nutritional support for critically ill children. Cochrane Db Syst Rev 2016; 2016(5): D5144.*
12. *Lou JQ, Li Q, Cui QW, Zhang P, Sun H, Tang H, Zhuang MM, Sun Y. A prospective randomized controlled study on the curative effects of enteral immunonutrition support therapy in adult burn patients at nutritional risk. Chin J Burns 2022; 38(8): 722-734.*
13. *Lydia DE, Mohandas A, Priya S, Monica SJ, Gajdacs M, Khusro A, Alghamdi S, Almehmadi M, Kahrizi D, Sahibzada MUK. Physicochemical properties, nutrient profile, microbial stability, and sensory evaluation of cupcakes enriched with pomegranate seed oil. Cell Mol Biol 2021; 67(4): 33-41.*