

## Review Article

Noushin Mousazadeh (PhD)<sup>1</sup>Hamideh Hakimi (PhD)<sup>2</sup>Hamid Sharif-Nia (PhD)<sup>1,3</sup>Safoura Dorri (PhD)<sup>4\*</sup>

1. Amol Faculty of Nursing and Midwifery, Mazandaran University of Medical Sciences, Sari, Iran

2. Social Determinants of Health Research Center, Faculty of Nursing and Midwifery, Qazvin University of Medical Sciences, Qazvin, Iran

3. Psychosomatic Research Center, Mazandaran University of Medical Sciences, Sari, Iran

4. Nursing and Midwifery Care Research Center, Isfahan University of Medical Sciences, Isfahan

**\* Correspondence:**

Safoura Dorri, Nursing and Midwifery Care Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

**E-mail:** s\_dorri86@yahoo.com**Tel:** 03137927551**Received:** 7 Feb 2024**Revised:** 12 June 2024**Accepted:** 29 June 2024**Published:** ?? 2024

## Disadvantages of various methods of gastrointestinal feeding in patients admitted to the intensive care unit: A systematic review

### Abstract

**Background:** Gastrointestinal tube feeding is one of the most important and beneficial methods of nutrition in patients admitted to the intensive care unit. There is still no consensus on the best nutritional method that will lead to fewer complications. This study aimed to investigate the disadvantages of different methods of tube feeding in patients admitted to the adult intensive care unit.

**Methods:** The present study is a review study conducted in 2022. Articles published in the English language databases including Web of Science, Scopus, Science Direct, and PubMed, between 2000 and 2022 were used.

**Results:** In the initial search phase, 2893 articles were obtained. In the next step, after the review of titles and abstracts, 760 articles remained. Finally, based on inclusion criteria and full text review, 14 related articles were selected. Disadvantages of tube feeding methods were classified into four categories: "respiratory complications", "gastrointestinal complications", "metabolic complications" and "bed occupancy".

**Conclusions:** Based on the results of this study, in terms of complications, intermittent and continuous methods are safer and more preferable than the bolus method. However, low-speed bolus feeding has fewer side effects.

**Keywords:** Intensive care units, Enteral nutrition, Nutritional support, Feeding method, Gastrointestinal tract.

**Citation:**

Mousazadeh N, Hakimi H, Sharif-Nia H, Dorri S. Disadvantages of various methods of gastrointestinal feeding in patients admitted to the intensive care unit: A systematic review. Caspian J Intern Med 2025; 16(1): 28-36.

ICU patients are in a high metabolic state (catabolism) due to their disease and the nature of the ward. Therefore, nutritional support is one of the basics of their care and treatment (1). Previous studies have shown that intestinal feeding is preferable to intravenous feeding. It is the common way of providing nutritional support to patients who are unable to be fed orally (2). Patients in the intensive care units, especially ICUs whose diets change extensively, need to have nutritional support, especially during the first 24 to 48 hours after admission (1). Early initiation of intestinal nutrition allows these patients to benefit from its nutritional and non-nutritional advantages such as maintaining intestinal integrity and improving the function of immune system (3). However, this method has its disadvantages that include inadequate food intake in the acute phase of the disease, gastrointestinal dysfunction, diarrhea, vomiting, nausea, constipation, dumping syndrome, hyperglycemia, hypercapnia, electrolyte disturbances and also the risk of aspiration. These complications can be controlled to some extent by choosing the best feeding method (2, 3). parenteral nutrition (PN) may lead to better nutritional outcome, but the results of meta-analysis showed that it is related with more infectious side effects due to the high sugar content of formulas and the catheters to access the vein (3, 4). Therefore, intestinal nutrition is a more suitable method for critically ill patients who are not able to receive food orally (3). There are several methods of intestinal feeding including continuous, periodic, intermittent, and bolus (5).



Depending on the prescription method, different strategies such as feeding bags, syringes and electronic feeding pumps are used (2). To determine the most appropriate nutritional method, the physician must consider many factors such as the patient's age, conditions, nutritional status and needs, gastrointestinal tract, gastrointestinal tolerance, type of formula and patient mobility. The need for feeding pump and its cost should also be considered (5). Continuous feeding is done using a feeding pump (high-pressure pumps in two types: Positive displacement and Centrifugal feed pumps). The rate for the first 24 hours is 20 to 50 ml per hour. The feeding rate will be increased by 10 to 25 ml every 4 to 24 hours to reach the desired rate (6). While continuous feeding is the preferred method in most ICUs, only a few outdated studies support it (5). Nutritionists, on the other hand, suggest that continuous feeding is not a physiological method compared to intermittent feeding and may have adverse consequences for critically ill patients (2).

In periodic method, feeding was done via a feeding pump in less than twenty four hours and usually between eight to twenty four hours. The speed and amount of feeding can be changed based on patient's tolerance (5). This method can be used when there is a feeding tube in the stomach or intestines. Also, this method allows the patient to be more mobile due to the fact that the patient is not dependent on the feeding pump. In terms of mortality, there was no significant difference between periodic and continuous tube feeding (6). Only one study showed that patients who received periodic tube feeding had a shorter hospital stay (7). In the intermittent feeding method, feeding was done for twenty to sixty minutes via a pump or feeding bag by the help of gravity (feeding with gravity is better tolerated). In this method, two hundred and forty to seven hundred and twenty cc of food are given to the patient over 20-60 minutes, 4 to 6 times a day.

This method is more physiologic than the continuous and cyclic method and it provides more mobility for the patient. The study of Ichimaru revealed that there is no difference between the two methods of continuous and intermittent feeding in terms of complications (5). In the bolus method, food enters the gastrointestinal tract using a syringe and under the force of gravity. It is done for 4 to 10 minutes and 3 to 6 times a day with a volume of 240 cc. Due to the speed of feeding in this method, diarrhea and aspiration are common. The results of a study showed that bolus feeding has a better nitrogen balance compared to continuous feeding. Continuous drip feeding, can lead to the loss of fat and protein along with the separation of a fat layer within the bag (8).

Despite the benefits of intestinal nutrition in critically ill patients, results of studies show that nutritional support is still not optimal in intensive care units (1). The results of a study showed that patients in an intensive care unit received only 49.1% of their nutritional needs (9). The study of Lee and Kang showed that patients received only 51% of the ordered food volume of food (10). Based on the above mentioned findings, health care providers and researchers tried to determine what factors obstruct proper gastrointestinal nutrition in critically ill patients. Gastrointestinal nutrition was often inadequate or eliminated, or in some cases other therapeutic interventions were preferred (1).

Considering the diversity of results reported in the studies, the answer to the question "Which gastrointestinal feeding method is more suitable for ICU patients?" is still unanswered. Gastrointestinal nutrition has been used in patients in ICU for many years. The policies related to these procedures are periodically changed and updated. There is also a growing body of evidence. But there is controversy and uncertainty about choosing preferred method (5). Despite the widespread use of intermittent and continuous tube feeding methods, it is still not clear why these methods are more useful (11).

However, too little information is available to recommend a particular method of gastrointestinal nutrition. Based on the research team experience, intermittent bolus method using a syringe is the dominant method of supportive nutrition. Unfortunately, in many cases, this method of feeding is done with improper speed and pressure, which can lead to other complications. Due to the importance of nutrition and the selection of the best method of gastrointestinal nutrition in ICU, the present review was performed to investigate the disadvantages of different types of gastrointestinal nutrition.

## Methods

This review study was conducted in 2022. The research was approved by the Vice Chancellery for Research of Mazandaran University of Medical Sciences (Research Ethics Committee of Mazandaran University of Medical Sciences with approval ID: IR.MAZUMS.REC.1400.11556). English language databases including Web of Science, Scopus, Science Direct, and PubMed were searched. Search was conducted using enteral feeding, enteral nutrition, intensive care unit, cyclic method, continuous method, bolus method, intermittent method, nutritional support, tube feeding as keywords.

First, the titles of the articles were checked with the objectives of the study. Then the abstracts of remained articles were read and examined. Finally, the full text of the articles were assessed and their relationship with the objectives of the study were reviewed. Articles were searched by two researchers independently and all articles were evaluated by them. The inclusion criteria were: experimental and quasi-experimental studies, the relevancy and having the characteristics of a scientific paper based on the Critical Appraisal Skills Program (CASP). The exclusion criteria were: inadequate information in the

articles and the unavailability of the full text (such as studies presented in congresses).

## Results

In the initial search phase, 2893 articles were obtained. In the next step, after the review of titles and abstracts, 760 articles remained. Finally, based on the inclusion criteria and full text review, 14 related and valid articles were selected using CASP check list. The articles included in the research are presented in table 1.

**Table1: characteristics of the articles**

Authors and year	Sample Size	Patient's characteristics	Feeding Method			Follow up	Results
			Bolus feeding	Intermittent feeding	Continuous feeding		
Rhoney et al, 2002 (12)	152	Patients with Acute Brain Injury (GCS 7) Age: 16-93	86	-	66	Stomach dilation, Reduced bowel sounds, Aspiration, Stomach residue > seventy five ml for four consecutive hours, Diarrhea, Haematemesis, Melena, VAP	The amount of calories and average protein intake in bolus feeding was higher than continuous feeding and statistically significant difference. -achieving nutritional goal is longer in bolus Vs. continuous. Feeding intolerance was more in bolus feedings (P=0.009). The duration of hospitalization and mortality were the same in both groups. Aspiration pneumonia was occurred more often in bolus feeding than in continuous feeding, but it was not statistically significant.
Steevens et al, 2002 (13)	18	Patients with Brain Injury Age: 18-70	-	5 Males and 4 females Start Volum feeding: 125 mL by gravity (Q 4h). Increased Q12 h until the target volume.	7 males and 2 females continuous feeding. Started with 25 mL/h. increased Q12h until the target volume.	The tolerance of the gastrointestinal tract, pulmonary aspiration and nutritional indicators	The continuous method had less gastrointestinal complications (diarrhea) than the bolus method. One case of aspiration was seen in intermittent feeding. Both groups reached the target volume within 7 days.
Serpa et al, 2003 (14)	28	Hospitalized 18-80 years ICU	-	Feeding 24 hours every 3 hours and feeding at the rate of one hour	Feeding 24 hours a day	Nausea, vomiting, abdominal distension, residual volume, aspiration	No significant difference regarding nausea and vomiting, aspiration, abdominal distension, residual volume and tube obstruction.

Authors and year	Sample Size	Patient's characteristics	Feeding Method			Follow up	Results
			Bolus feeding	Intermittent feeding	Continuous feeding		
MacLeod et al, 2007 (15)	168	Over 18 years Under the ventilator	-	feed pump Duration 30 to 60 minutes every 4 hours	Feeding pump 24 hours	Reach the target volume and calories 200 cc, 1.0 cal/mL Diarrhea and vomiting and aspiration pneumonia	Difference in diarrhea, vomiting, and pneumonia were not statistically significant in the two groups (p > 0.45). Both groups reached the target volume within 7 days (p > 0.05). The intermittent group reached the target volume sooner than the continuous group.
Maurya et al, 2011 (16)	40	Male patients with head injury connected to a ventilator	Blues every three hours for 18 hours and 6 hours of night rest	-	18 hours continuous and 6 hours of night rest	Respiratory rate and energy consumption at rest REE every 30 minutes for 24 hours. Blood sugar measurement every 4 hours Control of feeding intolerance, aspiration, diarrhea	RQ and REE, blood sugar, diarrhea in two groups had no significant statistical difference. Aspiration in continuous group was lower than bolus P=0.002
Abdelsalam et al, 2012 (17)	40	Age 20 to 80 years	Feeding for one hour every three hours	-	Feeding with a 24-hour pump	Aspiration and reaching the target volume within 72 hours	On the first day, food intake was higher in the continuous feeding than in the blues, but there was no difference in the following days, which was not statistically significant. Aspiration did not occur in both groups.
Kadamani et al, 2014 (18)	30	Age 20 to 80 years under ventilator	Every 4 to 6 hours feeding for 10 to 15 minutes	-	Continuous feeding 24 hours a day	Aspiration and nausea vomiting diarrhea constipation residual volume within seventy two hours	The difference in the incidence of aspiration, nausea, vomiting and diarrhea in two groups was not statistically significant. In terms of constipation, there was a significant difference and more occurred in the continuous group.
Shahriari et al, 2015 (19)	50	18-65 years old, Hospitalized in ICU	10-20 minutes 6 times in 24 hours by syringe	-	Feeding pump within 24 hours	Measuring the residual volume of the stomach every 4 hours with a syringe Measuring blood sugar every 4 hours with a glucometer Measurement of proalbumin at the beginning and four days later	In the continuous feeding group, blood sugar (BS) levels decreased on the 4th day compared to the first day, and in the bolus feeding group, blood sugar increased on the second day. Prealbumin level increased in the continuous group.

Authors and year	Sample Size	Patient's characteristics	Feeding Method			Follow up	Results
			Bolus feeding	Intermittent feeding	Continuous feeding		
Chowdhury et al, 2016 (20)	360	Over 18 years old under ventilator	Feeding pump blues		Continuous feeding pump	Vomiting, diarrhea, constipation, regurgitation and aspiration and pneumonia caused by aspiration	Bolus feeding resulted in a significant increase in gastric volume, superior mesenteric artery blood flow compared to continuous feeding, and the rate of return to fasting volume was faster in bolus feeding than continuous (P < 0.0011). Both types of feeding decrease the amount of water in the small intestine. Both feeding resulted in a decrease in plasma ghrelin concentration, although this was greater in bolus type. The type of bolus also leads to an increase in concentration of insulin and peptide YY Which was not observed with continuous feeding.
Evans et al, 2016 (21)	50	Patients 18-89 years old Hospitalized in ICU	26	-	24	Blood glucose, insulin use, feeding volume and prescribed calories	No statistical difference was observed between blood sugar level, insulin use, gavajo volume, caloric intake between the two groups.
Anandika et al, 2019 (22)	21	Age 18 to 75 years	The food was drawn with a 5 cc syringe within 5 to 10 minutes	-	-	Diarrhea, aspiration, pneumonia, nausea and flatulence within 7 days	%۶۷ diarrhea %۵۲ aspiration of stomach contents %۳۳ of aspiration pneumonia %۲۵ nausea %۵ flatulence
Mahran et al, 2019 (23)	50	18 years and older who were connected to a ventilator for more than 48 hours.	-	group1 (Intervention): intermittent feeding for 5 minutes every 4 hours group2 (Control): intermittent feeding for 10 minutes every 2 hours groups fasted for eight hours.	-	Intervention for three days Measurement of intra-abdominal pressure, examination of gastrointestinal complications	Intra-abdominal pressure in group 2 was higher before the first feeding (P = 0.03), but in the group1 it was higher after the second and third feeding (P = 0.02) Vomiting and diarrhea were not significantly different but Constipation and abdominal distension were more in group1.
Seyyedi et al, 2020 (24)	34	Under the ventilator. Age 18 to 85 without gastrointestinal problems. Review within a week	Feeding at a rate of 75 cc every three hours		Feeding at a rate of 25 cc per hour	Phosphorus level measurement blood sugar	Phosphorus level was increased in two groups, which difference was not significant. There was no difference in BS but the glucose level in the continuous was lower than blous.

Authors and year	Sample Size	Patient's characteristics	Feeding Method			Follow up	Results
			Bolus feeding	Intermittent feeding	Continuous feeding		
Dong et al, 2021 (25)	59	Patients over 18 years old connected to a ventilator		32 people intermittent feeding, 200-250 ml of food solution by pump 4-5 times a day.	27 people fed continuously and uniformly with a pump	Rectus femoris thickness and cross-sectional area, indicators related to nutritional status [hemoglobin, albumin, perialbumin and BS] were recorded. Incidence of: diarrhea, length of stay in ICU, vomiting, constipation, gastric residual volume and aspiration, within seven days	In both groups atrophy of Rectus femoris muscle occurred ( $P > 0.05$ ). There was no statistical difference in the amount of hemoglobin and blood sugar, diarrhea, vomiting, constipation, aspiration, length of stay in the two groups. In intermittent feeding group abnormal gastric residual volume was significantly lower than the continuous.

## Discussion

In this section, the findings of the study are presented based on respiratory, gastrointestinal, metabolic complications and bed occupancy.

**Respiratory complications:** Aspiration followed by pneumonia is among the findings mentioned in the articles included in the study. According to the studies, the most common complication of tube feeding is aspiration. The results of studies in this field are different and each study had its own conclusion. Several studies have shown that the rate of aspiration was similar in continuous, bolus and intermittent feeding and there was no difference between these methods (18, 25). According to these studies, there were no statistically differences between the continuous and bolus feeding on the rate of aspiration or diarrhea ( $P > 0.05$ ). Some studies have reported different results. For example, the results of the Maurya study in 2011 showed that the rate of aspiration in continuous feeding is lower than that of bolus (16). Also, Rhoney et al. 2002 in their study found that the incidence of aspiration in bolus method was more than continuous (12). Maurya and Rhoney's studies were both performed on patients with head and brain injury. Their sample size was 40 and included 152 patients, respectively. However, these studies have suggested that continuous bolus feeding is preferable in terms of aspiration, based on the results of other studies that have shown no significant difference, such a claim cannot be made with certainty and further research and evidence is still needed.

Comparison of continuous versus intermittent feeding showed that in most studies, there was no statistically significant difference between the methods in terms of aspiration. Only the results of the study by Juan et al. 2020

indicate that in the continuous feeding method, aspiration pneumonia was more than the intermittent method (26). We did not find a study that compared all three methods. Therefore, conclusions are difficult and further experimental studies with three groups are still needed. However, in terms of aspiration, it may be hypothesized that intermittent and continuous feeding is preferable to bolus method. This hypothesis is supported by the fact that bolus feeding rapidly affects the lower esophageal sphincter (LES) pressure and may increase the likelihood of aspiration. Coben et al. measured the effect of both continuous and continuous bolus methods on the pressure of LES. The results showed that bolus feeding reduced the pressure of the LES (27) and was associated with an increased risk of aspiration.

Another point to consider is that in all the mentioned studies, the duration of feeding was more than 10 minutes in all methods. Only in the study by Anandika (2019) where feeding time was less than 10 minutes (5 to 10 minutes), the incidence of aspiration of gastric contents was reported to be 52% (22). It seems that in all feeding methods, if the feeding speed is reduced, the risk of aspiration will also be reduced. Respiration has only been studied in the study of Maurya et al., and they found no differences between all methods (16).

**Gastrointestinal side effects:** Gastrointestinal side effects reported in the articles were: nausea and vomiting, stomach volume, tube obstruction, bloating, intolerance to nutrition and impaired food absorption. Rhoney et al. (2002) reported that the rate of feeding intolerance was higher in the bolus method than in the continuous method. The stomach volume increase in the bolus method was more than the



continuous method (12). Anandika et al. (2019) found that 67% ICU patients suffered from diarrhea and 25% of them developed nausea after bolus method (22). This result is while the findings of many studies showed that the amount of remaining stomach volume and the incidence of diarrhea and vomiting, constipation and bloating are the same in both bolus and continuous feeding methods (14, 18). Comparison of two intermittent and continuous methods in terms of diarrhea and vomiting, both methods have been reported to be the same (15, 17).

Comparison of two intermittent and continuous methods in terms of diarrhea and vomiting showed same rate in both (15, 25). While the results of a study by Hiebert showed that the number of defecation in continuous feeding was less than intermittent (28). The results of some studies indicate that continuous and intermittent feeding reduce vomiting, diarrhea and constipation compared to bolus feeding (13, 21, 29). The results of a study that examined the effect of feeding speed on intra-abdominal pressure showed that feeding speed is an effective factor in increasing intra-abdominal pressure (23). The summary of the included articles shows that the high feeding speed is related to more gastrointestinal complications. Therefore, intermittent and continuous feeding, if performed at low speed, are preferable to rapid bolus feeding. Considering the different results in gastrointestinal complications, if a study is done with all the feeding methods, it is possible to find valid results.

**Metabolic effects:** The level of insulin and blood sugar, protein and calorie intake were assessed in the articles. Acute changes in blood sugar can increase the permeability of endothelial cells membrane and worsen the patient's clinical condition (30). A 2016 study by Chowdhury et al. showed that bolus feeding resulted in an increase in insulin concentration compared to fasting, whereas in continuous feeding, there was a slight increase in insulin concentration ( $P = 0.0024$ ). They also showed that bolus feeding increased insulin and YY peptide concentrations compared to continuous feeding (20). Shahriari et al. 2015 reported that the amount of blood sugar in continuous feeding on the fourth day decreased compared to the first day and in the bolus method blood sugar increased significantly on the second day (19). Other studies did not report a statistically significant difference in blood sugar levels between bolus and continuous and intermittent feeding methods (16, 21, 24, 25). Comparing continuous and bolus nutrition showed that continuous nutrition is more effective than the bolus method in controlling blood sugar and preventing fluctuations in blood sugar levels. Continuous feeding can

also provide better nutritional status by increasing pre-albumin levels (19).

**Bed occupancy:** The death rate and the length of stay were two indicators that existed in the articles, but these indicators were investigated in only two studies. In Rhoney et al.'s research, the mortality rate was the same in both bolus and continuous feeding groups (20). Dong et al.'s found in their research that the length of hospitalization did not differ in the groups (25). Therefore, although there is a lack of evidence, it is not possible to make a definite conclusion, but it seems that there is no difference in this respect between tube feeding methods.

In general, the results of various studies show that continuous and intermittent feeding is preferable to the bolus method. Although, if the bolus feeding is done less quickly, many of the mentioned complications can be prevented. Therefore, it seems that the speed of feeding is an important factor in preventing complications, so, the lower the speed of feeding, the less likely complications will occur. The results of the investigations showed the preference of enteral nutrition. By considering the disadvantages of each tube feeding method and according to the facilities and human resources in each medical center, one of the nutritional support methods can be chosen. Although choosing one method for all patients cannot be a correct approach.

## Acknowledgments

The research team would like to thank the Research Vice-Chancellery of Mazandaran University of Medical Sciences.

**Funding:** Mazandaran University of Medical Sciences (grant number: 11556).

**Ethics approval:** IR.MAZUMS.REC.1400.11556.

**Conflict of interests:** There is no conflict of interest.

**Authors' contribution:** NM contributed in the conception of the work, conducting the study, revising the draft, approval of the final version of the manuscript, and agreed to all aspects of the work. HH contributed in the conception of the work, drafting and revising the draft, approval of the final version of the manuscript, and agreed to all aspects of the work. HS-N contributed in the conception of the work, conducting the study, revising the work. SD contributed in the conception of the work, drafting and revising the draft, approval of the final version of the manuscript, and agreed to all aspects of the work.

## References

1. Chang SJ, Kim H. Barriers to enteral feeding of critically ill adults in Korea. *Asia Pac J Clin Nutr* 2019; 28: 238-45.
2. Patel JJ, Rosenthal MD, Heyland DK. Intermittent versus continuous feeding in critically ill adults. *Curr Opin Clin Nutr Metab Care* 2018; 21: 116-20.
3. Elke G, van Zanten AR, Lemieux M, et al. Enteral versus parenteral nutrition in critically ill patients: an updated systematic review and meta-analysis of randomized controlled trials. *Critical Care* 2016; 20: 1-14.
4. Peter JV, Moran JL, Phillips-Hughes J. A metaanalysis of treatment outcomes of early enteral versus early parenteral nutrition in hospitalized patients. *Crit Care Med* 2005; 33: 213-20.
5. Ichimaru S. Methods of enteral nutrition administration in critically ill patients: continuous, cyclic, intermittent, and bolus feeding. *Nutr Clin Pract* 2018; 33: 790-5.
6. Brantley S, Mills M. Overview of enteral nutrition. The ASPEN adult nutrition support core Curriculum 2012: 196; 170-84.
7. Lázaro J, Guallar A, Gracia P, Caverni A, Albero R. Continuous enteral nutrition versus single bolus: effects on urine C peptide and nitrogen balance. *Med Clin (Barc)* 2005; 124: 613-5. [in Spanish]
8. Bankhead R, Boullata J, Brantley S, et al. ASPEN enteral nutrition practice recommendations. *JPEN J Parenter Enteral Nutr* 2009; 33: 122-67.
9. Lee M, Kang J. Nutritional support, gastric residual volume and nutritional status during enteral nutrition in intensive care unit patients. *Korean J Adult Nurs* 2014; 26: 621-9. [in Korean]
10. Patel JJ, Hurt RT, McClave SA, Martindale RG. Critical care nutrition: where's the evidence? *Crit Care Clin* 2017; 33: 397-412.
11. Elliott D, Aitken L, Chaboyer W, Marshall A. ACCCN's critical care nursing. 2nd ed. Elsevier Australia 2011; pp: xx-xx. (please add page number)
12. Rhoney DH, Parker D, Formea CM, Yap C, Coplin WM. Tolerability of bolus versus continuous gastric feeding in brain-injured patients. *Neurol Res* 2002; 24: 613-20.
13. Steevens EC, Lipscomb A, Poole GV, Sacks GS. Comparison of continuous vs intermittent nasogastric enteral feeding in trauma patients: perceptions and practice. *Nutr Clin Pract* 2002; 17: 118-22.
14. Serpa LF, Kimura M, Faintuch J, Ceconello I. Effects of continuous versus bolus infusion of enteral nutrition in critical patients. *Rev Hosp Clin Fac Med Sao Paulo* 2003; 58: 9-14.
15. MacLeod JB, Lefton J, Houghton D, et al. Prospective randomized control trial of intermittent versus continuous gastric feeds for critically ill trauma patients. *J Trauma Acute Care Surg* 2007; 63: 57-61.
16. Maurya I, Pawar M, Garg R, Kaur M, Sood R. Comparison of respiratory quotient and resting energy expenditure in two regimens of enteral feeding - continuous vs. intermittent in head-injured critically ill patients. *Saudi J Anaesth* 2011; 5: 195-201.
17. Abdelsalam Y. Continuous versus bolus infusion of enteral nutrition in intensive care unit. *AAMJ* 2012; 10: 154-68.
18. Kadamani I, Itani M, Zahran E, Taha N. Incidence of aspiration and gastrointestinal complications in critically ill patients using continuous versus bolus infusion of enteral nutrition: a pseudo-randomised controlled trial. *Aust Crit Care* 2014; 27: 188-93.
19. Shahriari M, Rezaei E, Bakht LA, Abbasi S. Comparison of the effects of enteral feeding through the bolus and continuous methods on blood sugar and prealbumin levels in ICU inpatients. *J Educ Health Promot* 2015; 4: 95.
20. Chowdhury AH, Murray K, Hoad CL, et al. Effects of bolus and continuous nasogastric feeding on gastric emptying, small bowel water content, superior mesenteric artery blood flow, and plasma hormone concentrations in healthy adults: a randomized crossover study. *Ann Surg* 2016; 263: 450-7.
21. Evans DC, Forbes R, Jones C, et al. Continuous versus bolus tube feeds: Does the modality affect glycemic variability, tube feeding volume, caloric intake, or insulin utilization? *Int J Crit Illn Inj Sci* 2016; 6: 9-15.
22. Anandika DM, Yaddanapudi N. Intolerance among patients on bolus method of intermittent enteral feeding admitted in ICU in a tertiary care hospital. *Nurs Midwifery Res* 2019; 15: 102-7.
23. Mahran G, Mahgoup A, Kamel EZ, Ahmad MM. Effect of 2 enteral feeding schedules on intra-abdominal pressure in patients receiving mechanical ventilation: A randomized controlled trial. *Crit Care Nurse* 2019; 39: 29-35.
24. Seyyedi J, Rooddehghan Z, Mohammadi M, Haghani S. Comparison of the effect of enteral feeding through the bolus and continuous methods on serum phosphorus and glucose levels in patients with mechanical ventilation: A randomized clinical trial. *J Nutr Metab* 2020; 2020: 6428418.



25. Dong J, Liu R, Li L, Yao L. Effects of intermittent feeding and continuous feeding on muscle atrophy and nutritional status in critically ill patients. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue* 2021; 33: 844-8. [in Chinese]
26. Juan W, Zhen H, Yan-Ying F, et al. A comparative study of two tube feeding methods in patients with dysphagia after stroke: a randomized controlled trial. *J Stroke Cerebrovasc Dis* 2020; 29: 104602.
27. Coben RM, Weintraub A, DiMarino AJ Jr, Cohen S. Gastroesophageal reflux during gastrostomy feeding. *Gastroenterology* 1994; 106: 13-8.
28. Hiebert JM, Brown A, Anderson RG, et al. Comparison of continuous vs intermittent tube feedings in adult burn patients. *JPEN J Parenter Enteral Nutr* 1981; 5: 73-5.
29. Wanden-Berghe C, Patino-Alonso MC, Galindo-Villardón P, Sanz-Valero J. Complications associated with enteral nutrition: CAFANE study. *Nutrients* 2019; 11: 2041.
30. Hempel A, Maasch C, Heintze U, et al. High glucose concentrations increase endothelial cell permeability via activation of protein kinase C $\alpha$ . *Circ Res* 1997; 81: 363-71.