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# Constipation Is More Frequent Than Diarrhea in Patients Fed Exclusively by Enteral Nutrition: Results of an Observational Study

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## Abstract

*Background:* Digestive complications in enteral nutrition (EN) can negatively affect the nutrition clinical outcome of hospitalized patients. Diarrhea and constipation are intestinal motility disorders associated with pharmacotherapy, hydration, nutrition status, and age. The aim of this study was to analyze the frequency of these intestinal motility disorders in patients receiving EN and assess risk factors associated with diarrhea and constipation in hospitalized patients receiving exclusive EN therapy in a general hospital. *Materials and Methods:* The authors performed a sequential and observational study of 110 hospitalized adult patients fed exclusively by EN through a feeding tube. Patients were categorized according to the type of intestinal transit disorder as follows: group D (diarrhea, 3 or more watery evacuations in 24 hours), group C (constipation, less than 1 evacuation during 3 days), and group N (absence of diarrhea or constipation). All prescription drugs were recorded, and patients were analyzed according to the type and amount of medication received. The authors also investigated the presence of fiber in the enteral formula. *Results:* Patients classified in group C represented 70% of the study population; group D comprised 13%, and group N represented 17%. There was an association between group C and orotracheal intubation as the indication for EN ($P < .001$). Enteral formula without fiber was associated with constipation (logistic regression analysis: $P < .001$). *Conclusion:* Constipation is more frequent than diarrhea in patients fed exclusively by EN. Enteral diet with fiber may protect against medication-associated intestinal motility disorders. The addition of prokinetic drugs seems to be useful in preventing constipation. (*Nutr Clin Pract*. XXXX;xx:xx-xx)

## Keywords

enteral nutrition; constipation; diarrhea; dietary fiber

Enteral nutrition therapy (ENT) is indicated for patients unable to be fed orally or unwilling to consume adequate dietary intake orally, due to diseases of the gastrointestinal tract, orotracheal intubation, or neurological disorders with impairment of consciousness.[1,2]

ENT does carry risks. Digestive and metabolic complications can negatively influence patients' clinical outcome.[2] Among the digestive complications of ENT, disorders of intestinal motility are mainly represented by diarrhea[3] and constipation.[2]

Among the several clinical definitions of diarrhea, the most commonly used is the evacuation of 3 or more watery stools in 24 hours. In hospitalized patients receiving enteral nutrition (EN), the frequency of diarrhea is reportedly between 14.7% and 72.0%.[4] A higher frequency of diarrhea is associated with longer hospital stay and increased financial cost to the healthcare provider.[4-8] Diarrhea is associated with advanced age, prescription drugs, certain clinical conditions, length of hospitalization, and the use of EN.[7,9,10]

Constipation is characterized by less than 1 evacuation in a period of 3 days.[9] It has been associated with longer intensive care unit (ICU) hospitalization, feeding intolerance, and difficulty in weaning artificial ventilation.[11] The main causes of constipation among patients receiving EN are specific medications and dehydration.[2,12] Benzodiazepines and opioids are the most common drugs to retard intestinal tract motility.[13,14]

Soluble and insoluble fibers have been recommended to normalize bowel function.[15-17] Soluble fibers inhibit the absorption of glucose, reduce gastric emptying, and decrease the levels of cholesterol and triglycerides.[15-17] Insoluble fibers increase fecal mass, provide stimulus to optimal intestinal functioning, and can prevent intestinal constipation.[15-17] Formulas of EN enriched with fiber are designed to normalize

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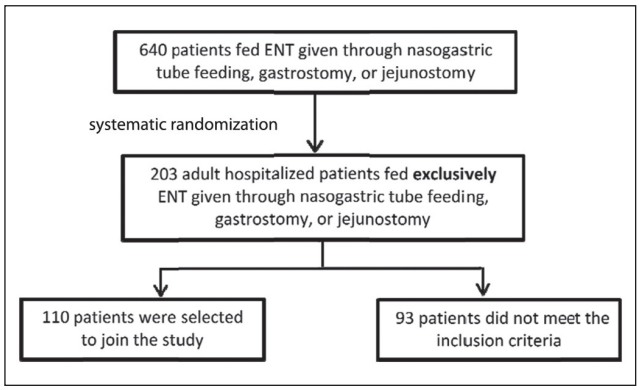


**Figure 1.** Patient recruitment diagram. ENT, enteral nutrition therapy.

intestinal transit and reduce laxative use.[8] The use of fiber in critically ill and postsurgical patients may reduce diarrhea frequency,[17] and insoluble fibers may reduce constipation in patients on chronic ENT.[17]

However, there is insufficient evidence to support the routine use of fiber in EN formulas for adequate maintenance of intestinal motility.[18] Especially in critically ill patients, a systematic review comparing the effects of EN with and without fiber did not find any difference in terms of intestinal motility.[18] The aim of our study was to determine the frequency of diarrhea and constipation and factors associated with them among hospitalized patients fed exclusively by ENT in a general hospital.

## Patients and Method

We performed a sequential and observational study at São Joaquim Hospital of Beneficência Portuguesa in the city of São Paulo, State of São Paulo, Brazil. The Ethics Committee in Research of São Joaquim Hospital of Beneficência Portuguesa of São Paulo, Brazil, and the Ethics Committee for Analysis of Research Projects of the Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo approved the study.

From July to October 2008, 203 adult hospitalized patients were recruited using a systematic table of randomization among 640 patients fed ENT via tube feeding, gastrostomy, or jejunostomy. Patients were followed by a multidisciplinary team composed of experts in nutrition therapy as described elsewhere.[19]

Inclusion criteria were age older than 18 years, receiving exclusive ENT, and providing informed consent (when the patient was not able, a legal representative provided consent). Exclusion criteria were use of oral or parenteral nutrition (PN) in addition to EN and the presence of colostomy or ileostomy.

For the sequential design of the study, patients were followed daily for 21 consecutive days unless discharge or death.

**Table 1.** Nutrient Composition Formulas

| | Standard Formula | Fiber Formula | Specialized Formula |
|---|---|---|---|
| kcal/mL | 1.2 | 1.2 | 1.0–1.3 |
| Carbohydrate, % | 56 | 56 | 33–73 |
| Protein, % | 14 | 14 | 10–18 |
| Lipid, % | 30 | 30 | 14–49 |
| Fiber, g/mL | 0 | 1.5 | 0 |

All data were collected directly from the patient's records by the study authors on a daily basis.

A total of 110 patients were enrolled; the remaining 93 patients did not meet inclusion criteria. Figure 1 illustrates patient recruitment. Patients were classified into 3 groups according to intestinal transit disorder for analysis: group D (diarrhea—defined as patients passing 3 or more watery stools in 24 hours[4]), group C (constipation—defined as patients with less than 1 evacuation in 3 days[9]), and group N (absence of diarrhea and constipation). All patients were classified according to the occurrence of the first event.

Patients were also categorized according to the presence of fiber in the EN formula as group with fiber (patients who received enteral diet with soluble and insoluble fiber at a dose of 1.5 g/100 mL for at least 5 sequential days) and group without fiber (patients who received enteral diet without fiber for only 2 sequential days). Table 1 shows the nutrient composition of formulas used in the study. Levine feeding tube (CPL Medical's, São Paulo, Brazil) and Dobbhof feeding tube (Tyco Healthcare, Birmingham, UK) were used.

All prescription drugs were recorded and the patients were analyzed according to the type and amount of medication they received from the beginning of the study until the last day of the motility disorder in groups C and D. For group N patients, all drugs were recorded and analyzed until the last day of the study.

For statistical analysis purposes, we excluded patients with diarrhea or constipation on the first day of the study when they had these intestinal motility disorders prior to receiving EN. We considered all therapeutic drug classes that could influence intestinal transit regardless of administration method (via feeding tube, orally, or intravenously) (Table 2). We studied demographic variables (age and gender), ENT variables (indication, type, and feeding tube location), hospitalization (ward or ICU), and clinical outcome (Table 3). Serum albumin level (g/dL) was measured on days 1, 10, and 21 in patients who remained in the study. Study data were stored in an electronic database, in spreadsheet format, using Microsoft Office Excel 2007 software (Microsoft Corp, Redmond, WA), through a process of double entry to minimize the risk of error. The patients were statistically analyzed according to the categorizations as follows: intestinal transit (groups C, D, or N), presence of fiber in EN (group with or without fiber), and the amount of prescribed drugs that could influence intestinal motility.

**Table 2.** Association Between Intestinal Disorders and Drugs Influencing Intestinal Transit[1,2,5,9,12]

| | Group C: Constipation (n = 8, 20%)[a] | Group D: Diarrhea (n = 13, 32.5%)[b] | Group N: Absence of Diarrhea and Constipation (n = 19, 47.5%) | *P* Value |
|---|---|---|---|---|
| Analgesic | 21.05 | 20.00 | 20.00 | .575 |
| Antibiotic | 14.69 | 24.77 | 20.03 | .153 |
| Anticholinergic | 19.00 | 19.00 | 22.16 | .175 |
| Anticonvulsant | 17.50 | 20.42 | 21.82 | .369 |
| Antidiabetic | 20.00 | 20.00 | 21.05 | .575 |
| Antidiarrheal | 16.25 | 23.88 | 19.97 | .206 |
| Antidopaminergic | 9.94 | 18.42 | 26.37 | .002 |
| Antiemetic | 19.38 | 20.65 | 20.87 | .934 |
| Antihistamine | 19.50 | 19.50 | 21.61 | .322 |
| Antiparkinsonian | 19.00 | 22.00 | 20.11 | .415 |
| Antipsychotic | 17.00 | 20.35 | 22.08 | .297 |
| Benzodiazepines | 26.31 | 16.08 | 21.08 | .091 |
| Calcium channel blocker | 19.00 | 19.23 | 22.00 | .572 |
| Diuretic | 24.88 | 16.12 | 21.66 | .183 |
| $H_2$ antagonist | 25.38 | 19.69 | 19.00 | .069 |
| Laxative | 19.50 | 22.58 | 19.50 | .119 |
| Nonsteroidal anti-inflammatory | 16.63 | 26.35 | 18.13 | .078 |
| Opioid | 18.69 | 21.19 | 20.79 | .842 |
| Trace elements | 19.50 | 19.50 | 21.61 | .322 |
| Tricyclic antidepressant | 22.50 | 20.00 | 20.00 | .135 |
| Vasodilator | 17.63 | 19.00 | 22.74 | .411 |

[a]Defined as patients with less than 1 evacuation in 3 days.[9]
[b]Defined as patients passing 3 or more watery stools in 24 hours.[4]

### *Statistical Analysis*

For qualitative variables, we used $\chi^2$ or Fisher's exact test to verify association between variables and groups. Logistic regression was performed with the variables age, sex, hospitalization place, diagnosis, fiber, and treatment with norepinephrine, with dependant variables being groups D and C to determine their risk relative to group N. Wilcoxon *W* test was performed to compare the amount of drug among groups C and D as compared with group N, with groups with and without fiber classified in this analysis. A significance level of 5% was used. Analyses were performed using the statistical program PASW 18 for Windows (SPSS, Inc, an IBM Company, Chicago, IL).

## Results

Group C represented 70% of the study population (n = 77), whereas groups D and N represented 13% (n = 14) and 17% (n = 19), respectively.

In group D, 42.8% of patients had only 1 episode of diarrhea, 42.8% had 2 or 3 episodes, and 14.3% had 7–10 episodes. Diarrhea occurred more than 2 consecutive days in 30% of patients in group D. In group C, 75% of patients had a single episode of constipation, with an average duration of 5.7 days.

Table 3 reports patient characteristics by group. Group C had more patients hospitalized in the ICU compared with groups D and N ($P = .0297$), but logistic regression did not identify a relationship between the variable hospitalization site and the presence of constipation ($P = .171$).

There was an association between group C and orotracheal intubation as the indication for EN ($P < .001$). Patients were followed for 21 days or left the study (reasons for dropout described in Table 3). Resumption of oral intake was significantly higher in group N (31.6%). Group C had a higher mortality compared with other groups (23.4%; $P = .0367$) (Table 3).

To evaluate severity of illness, we considered the use of norepinephrine as a predictor of critical risk. In the logistic regression, norepinephrine use was not significant when compared with some variants (gender, age, hospitalization, fiber). Norepinephrine use was not significantly different between the diarrhea and constipation groups ($P > .05$). Serum albumin levels were not useful in predicting the frequency of diarrhea on any study day, regardless of any cutoff level used ($P > .05$).

All patients were initially given EN without fiber. The fiber group, on average, began using formula with fiber 8 days after

**Table 3.** General Characteristics of 110 Patients Fed Exclusively Enteral Nutrition

| | | Group C: Constipation (n = 77, 70%)[a] | Group D: Diarrhea (n = 14, 13%)[b] | Group N: Absence of Diarrhea and Constipation (n = 19, 17%) | *P* Value |
|---|---|---|---|---|---|
| Age (>65 y) | | 58 (75.0) | 10 (71.4) | 15 (78.9) | .8857 |
| Female gender | | 40 (52.0) | 9 (64.3) | 12 (63.2) | .5746 |
| Hospitalization (ICU) | | 64 (83.0) | 9 (64.3) | 11 (57.9) | .0297 |
| EN indication | Dysphagia | 11 (14.3) | 5 (35.7) | 7 (36.8) | <.0001 |
| | Acute respiratory failure | 1 (1.3) | 0 | 1 (5.3) | |
| | Orotracheal intubation | 52 (67.5) | 4 (28.5) | 5 (26.3) | |
| | Neurologic | 3 (3.9) | 3 (21.4) | 1 (5.3) | |
| | Impaired consciousness | 9 (11.7) | 2 (14.3) | 7 (26.4) | |
| | Tracheostomy | 1 (1.3) | 0 | 0 | |
| Feeding tube | Gastrostomy | 1 (1.3) | 1 (7.1) | 2 (10.5) | .1523 |
| | Nasogastric | 66 (85.3) | 10 (71.4) | 15 (78.9) | |
| | Postpyloric | 10 (13.0) | 3 (21.4) | 2 (10.5) | |
| Outcome | Completed the study (21 days) | 40 (51.9) | 9 (64.3) | 10 (52.6) | .0367 |
| | Nutrition therapy discharge | 1 (1.3) | 0 | 0 | |
| | Hospital discharge | 2 (2.6) | 2 (14.3) | 2 (10.5) | |
| | Parenteral nutrition | 0 | 1 (7.1) | 0 | |
| | Oral nutrition | 16 (20.8) | 2 (14.3) | 6 (31.6) | |
| | Death (before 21 days) | 18 (23.4) | 0 | 1 (5.3) | |

Values presented as No. (%). EN, enteral nutrition; ICU, intensive care unit.
[a]Defined as patients with less than 1 evacuation in 3 days.[9]
[b]Defined as patients passing 3 or more watery stools in 24 hours.[4]

EN initiation. Only 2 patients changed from EN with fiber to EN without fiber after a period of 5 and 8 days, respectively. The average amount of fiber received in the fiber group was 20.6 g/d.

There was a significant association between constipation and the group without fiber. Constipation corresponded to 75.7% of the group without fiber and represented only 13.1% of the group with fiber ($P < .001$). Logistic regression indicated that EN without fiber may increase the risk of constipation up to 7 times ($P = .014$).

The group without fiber corresponded to 71.43% of the diarrhea group, but this association was not significant ($P > .05$).

Therapeutic drug classes were used with similar frequency among the 3 groups ($P > .05$) with the exception of the antidopaminergic domperidone, a prokinetic that was used less frequently in group C ($P < .05$) (Table 2). The use of antidopaminergic agents decreased the constipation risk factor by 17% and the diarrhea risk factor by 15% on logistic regression when comparing the constipation and diarrhea groups with group N (fiber and use of antidopaminergic agent) ($P = .02$). In the group without fiber, the use of $H_2$ antagonist drugs was associated with constipation ($P = .013$), but in the group with fiber, there was no such association ($P = .83$). In the group without fiber, treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) was associated with a higher frequency of diarrhea ($P = .021$); this association was not found in the group with fiber ($P = 1.0$).

## Discussion

The reported frequency of diarrhea in patients on ENT varies from 14.7% to 72%.[4,6,7,9,13] This is probably related to the variety of definitions of diarrhea in the literature (from 1–5 bowel movements per day and consideration of stool consistency) and the patient population studied. In the present study, we defined diarrhea as 3 or more liquid stools in 24 hours. We found a diarrhea frequency of 13%, similar to the study that used the same definition and studied a similar patient group.[4]

Recently, the Clinical Nutrition Task Force of the International Life Sciences Institute Brazil published 2 books describing indicators for the evaluation of ENT and PN therapy quality. "Frequency of diarrhea in ENT" was chosen by a multidisciplinary team of specialists in PN and EN as the second best quality indicator listed in these publications. This indicator is applicable and simple to use and was considered very important. In our study, the observed frequency of diarrhea (13%) was close to the suggested target of less than 10% in patients receiving ENT.[20]

Some studies relate hypoalbuminemia to higher frequencies of diarrhea due to decreased intestinal absorption of nutrients.[5-8] However, in our study, we found no significant association between hypoalbuminemia and diarrhea. In addition, we did not observe a statistically significant association when using different serum albumin level cutoff points. This could be explained by the frequency of hypoalbuminemia in our population, with an average blood albumin level of 2.95 ± 1.25 g/dL.

According to our study, constipation was the most common intestinal motility disorder in ENT patients. Constipation seems to be discussed less frequently than diarrhea, perhaps because it requires less attention of the multidisciplinary team involved in the patients' management.

Constipation as well as its implications seems to obtain very little attention, but this disorder could be often concomitantly present with gastroparesis, ileoparesis, and consequently a delay of nutrition support. Inadequate nutrient intake could interfere in the prognosis.[21]

Evaluation of the frequency of constipation is also described as a quality indicator, with a target of less than 20%.[20] In the literature, this frequency ranges from 15.7%–29.7% according to the different definitions for constipation.

Another observational study, also conducted in Brazil, focused on constipation in the ICU at a school hospital. The authors found a frequency of 69.9% of constipation in critically ill patients.[22] Constipation definition was the same as that used in our study, and the frequency was very similar to the one that we found. An important conclusion of this study was that early EN (<24 hours) was associated with less constipation.[22] Our study was not designed to analyze this.

The study by Mostafa et al[14] shows that constipated patients failed to wean from mechanical ventilation due to impaired function of respiratory muscles, caused by distension and restlessness. This could explain the relationship we found between orotracheal intubation and constipation frequency. Another study that confirmed this relationship showed an increase in the duration of mechanical ventilation among patients who remained constipated for more than 6 days in the ICU.[21] This could be related to the effects of intra-abdominal pressure increase, which can reduce lung compliance, increase pleural and intrathoracic pressure, and also cause respiratory problems.[21]

Mortality was associated with constipation; this finding, although interesting, must be interpreted with caution because our study was not designed to analyze this, and the logistic regression did not confirm this relationship.

Another important potential etiology of constipation is hydration status.[2,12] Typically, patients in our study received 100 mL of water 6 times per day via the feeding tube, as per protocol. However, we did not strictly monitor fluid supply via tube feeding and intravenously, which would include saline hydration and water for medication. This is a limitation of our study.

The use of prokinetic drugs in conjunction with ENT has been proposed to reduce gastric stasis.[23] The medications most commonly used for this purpose are metoclopramide and domperidone. Metoclopramide is rarely used in clinical practice because it interacts with other drugs and can cause extrapyramidal reactions or, when associated with anticholinergic drugs, has reduced effects on gastrointestinal motility.[24]

Domperidone works as a peripheral dopamine blocker, antiemetic, and modifier of gastrointestinal functions.[24] In our study, we found that domperidone was beneficial for the prevention of intestinal motility disorders.

In the group without fiber, $H_2$ antagonist treatment was associated with a higher frequency of constipation, but this association disappeared when patients received fiber-enriched EN formulas. The $H_2$ antagonists are frequently prescribed in the ICU for prophylaxis of gastrointestinal disorders associated with stress.[25] However, the reduction of stomach acid due to the effect of $H_2$ antagonists could alter the microbiota of the gastrointestinal tract, thus increasing or decreasing intestinal motility.[26]

In the group without fiber, NSAID treatment was associated with diarrhea frequency, but this association was not significant among patients receiving fiber-enriched EN formulas. NSAIDs may modify the intestinal microbiota by inhibiting cyclooxygenase-1 (COX-1); as a side effect, there is a reduction of stomach acid associated with gastrointestinal disturbances such as diarrhea and constipation.[24]

We observed that the EN with fiber may be useful against adverse effects of medication associated with intestinal motility disorders.

The addition of fiber to EN formulas and hydration protocols have been suggested for the prevention of intestinal motility disorders,[8,9,12,27,28] but there is a lack of strong evidence to support the systematic use of fiber for constipation prevention.[15-18,29-31] A review found significant benefits only in surgical and critically ill patients.[17]

In a prospective, randomized, controlled study in elderly patients divided into groups with standard EN vs fiber-enriched EN, improvement of stool frequency and consistency was seen in the group receiving EN with fiber.[16] A meta-analysis of 7 randomized controlled trials compared EN formulas with and without fiber and found no significant

effect on diarrhea prevention. Another meta-analysis of 51 studies (43 randomized controlled trials) found that supplementation of EN with fiber can reduce the frequency of diarrhea.[28]

In 2009, an analysis of 6 studies in critically ill patients on mechanical ventilation (5 with soluble fiber and 1 with insoluble fiber [soy polysaccharide]) showed no significant difference between the groups with a standard diet vs a fiber-enriched diet concerning intestinal motility disease, mortality, infection, and days of artificial ventilation.[30]

The Canadian guideline supports the lack of concrete evidence for routine recommendation of fiber-enriched EN.[18] In 2010, Chittawatanarat et al[32] evaluated 2 groups of surgical ICU patients with sepsis on ENT (standard vs fiber-enriched EN formulas) and found no significant difference in the frequency of diarrhea between groups. In our study, the presence of fiber in EN seemed to be important in constipation prevention but had no effect on diarrhea frequency.

The logistic model of statistical analysis allows the comparison of multiple factors and eliminates the confounding between variables. Because of the observational design of our study, no finding here can be interpreted as a causal relationship.

An important limiting factor of our study was the retrospective classification of patients into categories according to intestinal motility and enteral feeding. In this sense, prospective, randomized, double-blind protocols for ENT are necessary to clarify the influence of drug therapy and EN with fiber on intestinal motility disorders.

## Conclusion

Constipation was more frequent than diarrhea in patients receiving exclusively ENT, mainly in patients receiving EN formula without fiber. Constipation was associated with artificial ventilation. The addition of prokinetic drugs was associated with constipation prevention. Enteral diet with fiber might protect against medication-associated intestinal motility disorders and was associated with constipation prevention in enterally fed patients.

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