Risk Factors for Gastrointestinal Symptoms post Enteral Nutrition Initiation via a Gastrostomy Tube

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ABSTRACT

Background: *Percutaneous endoscopic gastrostomy (PEG) facilitates long-term enteral nutrition. However, parenteral nutrition prior to PEG tube placement can cause impaired gastrointestinal function. Additionally, upon initiation of enteral feeding via a PEG tube, some patients suffer from gastrointestinal symptoms (e.g., vomiting, diarrhea), which reduce their quality of life and increase the nursing workload.*

Method: *This retrospective study included 155 patients upon whom the author performed PEG as the attending physician. Enteral nutrition was started through the PEG tube on the third day after its placement. The following characteristics were analyzed: age, gender, indications for PEG, preoperative enteral nutrition, administered liquid nutrients, daily dosage of nutrients, serum albumin levels, serum alanine aminotransferase levels, serum creatinine levels, serum hemoglobin levels, and vomiting or diarrhea within seven days after the initiation of PEG feeding. A logistic regression model was used to identify the risk factors contributing to gastrointestinal symptoms, and three variables were sequentially introduced into the model—preoperative non-enteral nutrition, hypoalbuminemia, and administration of non-elemental diets.*

Results: *Vomiting and diarrhea occurred in 10 and 15 patients, respectively. There were significant differences in administered nutrients and serum albumin levels between patients with and without gastrointestinal symptoms. Multivariate analysis revealed that the adjusted odds ratios for administration of non-elemental diets and serum albumin level ≤ 3.2 g/dL were 8.05 (95% confidence interval (CI): 2.66–24.4; $p < 0.001$) and 3.81 (95% CI: 1.33–10.9; $p < 0.05$), respectively.*

Conclusion: *The administration of non-elemental diets and a serum albumin level ≤3.2 g/dL were significant risk factors.*

Keywords: *albumin, diarrhea, elemental diet, percutaneous endoscopic gastrostomy, vomiting*

ABSTRAK

Latar belakang: *Gastrostomi endoskopik perkutan (GEP) membantu pemberian nutrisi enteral jangka panjang. Walaupun demikian, pemberian nutrisi parenteral sebelum penggantian pipa GEP dapat menyebabkan gangguan fungsi gastrointestinal. Selain itu, setelah inisiasi pemberian makanan enteral melalui selang GEP, beberapa pasien dapat mengalami gejala-gejala gastrointestinal (misalnya, muntah, diare), yang dapat menurunkan kualitas hidup mereka dan meningkatkan beban perawatan.*

Metode: *Studi retrospektif ini mengikutsertakan 155 pasien yang menjalani prosedur GEP di bawah pengawasan penulis sebagai dokter yang merawat. Nutrisi enteral mulai diberikan melalui pipa GEP pada hari ketiga setelah pipa diganti. Beberapa karakteristik yang dianalisis dalam studi ini adalah sebagai berikut: usia, jenis kelamin, indikasi GEP, nutrisi enteral pre-operatif, nutrisi cair yang diberikan, dosis nutrisi harian, kadar albumin serum, kadar alanine aminotransferase serum, kadar kreatinin serum, kadar hemoglobin serum, dan muntah atau diare dalam 7 hari setelah pemberian makan melalui GEP. Model regresi logistik digunakan*

untuk mengidentifikasi faktor risiko yang berkontribusi terhadap gejala-gejala gastrointestinal, dan tiga variabel secara berurutan dimasukkan ke dalam model – nutrisi non-enteral pre-operasi, hipoalbuminemia, dan pemberian diet non-elemental.

***Hasil:** Muntah dan diare masing-masing terjadi pada 10 dan 15 pasien. Terdapat perbedaan yang bermakna antara nutrisi yang diberikan dan kadar albumin serum pada pasien yang mengalami dan tidak mengalami gejala-gejala gastrointestinal. Analisis multivariat menunjukkan bahwa odds ratio yang disesuaikan untuk pemberian diet non-elemental dan kadar albumin serum ≤ 3.2 g/dL adalah 8.05 (Interval Kepercayaan (IK) 95%: 2.66–24.4; p < 0.001) dan 3.81 (95% CI: 1.33–10.9; p < 0.05), secara berturut-turut.*

***Simpulan:** Pemberian diet non-elemental dan kadar albumin serum ≤3.2 g/dL merupakan faktor risiko yang bermakna.*

***Kata kunci:** albumin, diare, diet elemental, gastrostomi endoskopik perkutan, muntah*

INTRODUCTION

"If the gut works, use it." The key to achieving successful nutrition is gastrointestinal tract feeding access. The purpose of enteral nutrition is to sustain mucosal barrier function, along with intestinal immune response and normal flora, by maintaining gastrointestinal mucosal integrity.[1] Percutaneous endoscopic gastrostomy (PEG) facilitates long-term enteral nutrition.[2]

The American Society for Parenteral and Enteral Nutrition and the Japanese Society for Parenteral and Enteral Nutrition have recommended the use of gastrostomy tubes for patients whose nutritional intake is likely to be qualitatively or quantitatively inadequate for a period exceeding four weeks.[3] However, parenteral nutrition prior to PEG tube placement can cause impaired gastrointestinal function.[4] Additionally, upon initiation of enteral feeding via a PEG tube, some patients suffer from gastrointestinal symptoms (e.g., vomiting, diarrhea), which reduce their quality of life and increase the nursing workload. Furthermore, aspiration pneumonia and dehydration due to diarrhea are life-threatening complications of enteral nutrition.

The aim of this study was to identify the risk factors contributing to gastrointestinal symptoms when liquid nutrients, which are frequently used in clinical practice, were administered after PEG tube placement.

METHOD

This retrospective study included 185 patients upon whom the author performed PEG as the attending physician from August 1, 2011 to March 31, 2020. Excluded from the study were: 24 patients receiving enteral nutrition with semi-solid medical foods; five patients having a previous history of pylorus-preserving gastrectomy or esophagectomy with gastric tube reconstruction; and one patient with no enteral feeding after PEG tube placement. One hundred fifty-five patients were investigated.

Before PEG tube insertion, there were no instances of fever, hypoxemia, vomiting, or diarrhea among the patients. All patients received 1 g ceftazidime intravenously twice daily for three days as antibiotic prophylaxis, and a 24-Fr PEG tube was placed using the modified introducer technique without complications. Enteral nutrition through the PEG tube was started on the third day after its placement. A gravity-controlled method was used to administer liquid nutrients (600–1,200 kcal/day) at a speed of 250–400 mL/h.

Patient data extracted from medical records included the following: age, gender, indications for PEG, preoperative enteral nutrition, administered liquid nutrients, daily dosage of nutrients, serum albumin levels, serum alanine aminotransferase levels, serum creatinine levels, serum hemoglobin levels, and gastrointestinal symptoms (vomiting or diarrhea) within seven days after the initiation of enteral feeding via a PEG tube. Diarrhea was defined as liquid or loose stool at least three times a day, and stool sample-based tests confirmed non-infectious causes. A logistic regression model was used for identifying the risk factors that contributed to gastrointestinal symptoms, and three variables were sequentially introduced into the model—preoperative non-enteral nutrition, serum albumin level ≤ 3.2 g/dL, and administration of non-elemental diets. Youden index (sensitivity = 59.2%; specificity = 72.0%) was used to obtain the abovementioned cut-off value for serum albumin level upon the onset of gastrointestinal symptoms in the receiver operating characteristic curve analysis (area under the curve = 0.666; 95% confidence interval (CI): 0.557–0.775).

The present study was approved by the institutional ethics committee. Informed consent was obtained from

the patients or their families. Statistical analysis was performed with EZR (Easy R, Version 1.37, Saitama, Japan), and *p* values of less than 0.05 were considered to be statistically significant.[5] The author used the two-sided Mann–Whitney U test or the Fisher's exact test for the differences between the two groups.

RESULTS

Patients' backgrounds are summarized in Table 1, and administered liquid nutrients are shown in Table 2. The median age of patients was 81 years, and 54.2% of patients (84/155) were females. Approximately three-fourths of indications for PEG were dementia (40.0%, 62/155) and cerebrovascular disease (36.8%, 57/155). Gastrointestinal symptoms occurred in 25 (16.1%) patients; vomiting and diarrhea occurred in 10 (6.5%) and 15 (9.7%) patients, respectively. The differences were significant in administered nutrients and serum albumin levels between patients with and without gastrointestinal symptoms. Multivariate analysis revealed that the adjusted odds ratios for administration of non-elemental diets and serum albumin level ≤3.2 g/dL were 8.05 (95% CI: 2.66–24.4; $p < 0.001$) and 3.81 (95% CI: 1.33–10.9; $p < 0.05$), respectively (Table 3).

Table 1 Patients' backgrounds (n = 155)

	Overall	Gastrointestinal symptoms*		p
		Positive (n = 25)	Negative (n = 130)	
Age (y) , median	81	81	81	0.554
Female, n (%)	84 (54.2)	14 (56.0)	70 (53.8)	1
Indications for PEG, n (%)				0.0851
Dementia	62 (40.0)	10 (40.0)	52 (40.0)	
CVD	57 (36.8)	6 (24.0)	51 (39.2)	
Sarcopenia	24 (15.5)	6 (24.0)	18 (13.8)	
Malignancy	5 (3.2)	3 (12.0)	2 (1.5)	
Parkinson's disease	4 (2.6)	0	4 (3.1)	
Schizophrenia	3 (1.9)	0	3 (2.3)	
Preoperative enteral nutrition, n (%)	101 (65.2)	12 (48.0)	89 (68.5)	0.0662
Administered liquid nutrients, n (%)				0.00253
Elemental diets	84 (54.2)	6 (24.0)	78 (60.0)	
Polymeric formulae	57 (36.8)	15 (60.0)	42 (32.3)	
Oligomeric formulae	14 (9.0)	4 (16.0)	10 (7.7)	
Daily dosage of nutrients (mL), median	900	900	900	0.580
Serum albumin level (g/dL), median	3.3	3.0	3.3	0.00855
Serum alanine aminotransferase level (IU/L), median	18	16	18	0.969
Serum creatinine level (mg/dL), median	0.56	0.57	0.56	0.461
Serum hemoglobin level (g/dL), median	11.8	11.1	11.9	0.160

*: vomiting or diarrhea within seven days after the initiation of enteral feeding via a gastrostomy tube, CVD: cerebrovascular diseases (cerebral infarction, cerebral hemorrhage, subarachnoidal hemorrhage, or subdural hemorrhage), PEG: percutaneous endoscopic gastrostomy.

Table 2. Administered liquid nutrients after PEG tube placement

	kcal/mL	n
Elemental diets (n = 84)		
ELENTAL®; EA Pharma, Tokyo, Japan	1.0	84
Oligomeric formulae (n = 14)		
Twinline-NF Liquid for Enteral Use®; Otsuka Pharmaceutical, Tokyo, Japan	1.0	14
Polymeric formulae (n = 57)		
L-8®; Asahi Kasei Pharma, Tokyo, Japan	1.0	18
ENSURE H®; Abbott Japan, Tokyo, Japan	1.5	13
RACOL-NF Liquid for Enteral Use®; Otsuka Pharmaceutical, Tokyo, Japan	1.0	11
E-7®; Clinico, Tokyo, Japan	1.0	8
Renalen LP®; Meiji, Tokyo, Japan	1.6	2
DIMVest®; Ajinomoto Pharmaceutical, Tokyo, Japan	1.0	2
Medief®; Nestle, Tokyo, Japan	1.0	1
Glucerna®; Abbott Japan, Tokyo, Japan	1.0	1
ISOCAL 2K Neo®; Nestle, Tokyo, Japan	2.0	1

PEG: percutaneous endoscopic gastrostomy.

Table 3. Results of the multivariate analysis for identifying the risk factors contributing to gastrointestinal symptoms when liquid nutrients were administered after PEG tube placement

Variables	Crude OR (95% CI)	p	Adjusted OR (95% CI)	p
Preoperative non-enteral nutrition	2.35 (0.988–5.60)	0.0533	2.79 (0.973–7.98)	0.0563
Serum albumin level ≤3.2 g/dL	3.74 (1.46–9.57)	0.00602	3.81 (1.33–10.9)	0.0125
Administration of non-elemental diets	4.75 (1.78–12.7)	0.00188	8.05 (2.66–24.4)	0.000228

CI: confidence interval, OR: odds ratio, PEG: percutaneous endoscopic gastrostomy.

Table 4. Patients with gastrointestinal symptoms leading to death (n = 7)

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Administered nutrients	ED	ED	ED	OF	OF	PF	PF
Age (y)	90	79	75	80	95	69	83
Gender	Female	Male	Female	Female	Female	Male	Female
Indications for PEG	Sarcopenia	Dementia	Sarcopenia	CVD	CVD	Dementia	Dementia
Serum albumin level (g/dL)	2.7	3.0	3.1	3.5	3.0	2.6	2.7
Preoperative enteral nutrition	No	No	Yes	No	No	No	Yes
Gastrointestinal symptoms	Diarrhea	Vomiting	Vomiting	Vomiting	Vomiting	Vomiting	Diarrhea
Causes of death	Heart failure	Pneumonia	Pneumonia	Paralytic ileus	Pneumonia	Pneumonia	Renal failure

CVD: cerebrovascular diseases, ED: elemental diet, OF: oligomeric formula, PEG: percutaneous endoscopic gastrostomy, PF: polymeric formula

DISCUSSION

Elemental diets consist of essential amino acids, glucose, trace elements, and vitamins. Depending on the amino acid composition, elemental diets are easily absorbed and highly digestible. In fact, Horiuchi *et al*. reported that elemental diets were less likely to induce diarrhea than standard liquid diets in bedridden, gastrostomy-fed patients.[6] Additionally, their study revealed that elemental diets were related to more rapid gastric emptying and fewer episodes of aspiration than standard liquid diets, most likely due to their low amounts of lipids.[6] Therefore, the utility of elemental diets is deemed reasonable.

Diarrhea occurs more commonly in tube-fed patients with hypoalbuminemia.[7] Patients with hypoalbuminemia caused by chronic malnutrition experience diarrhea more often than those with acute malnutrition.[8] Hypoalbuminemia is associated with gut edema and impaired nutrient absorption.[9] Early and aggressive nutritional support is needed to prevent hypoalbuminemia whose presence preoperatively may reflect potential malabsorption.

Preoperative enteral nutrition is suggested for maintaining gastrointestinal function; contrary to expectations, preoperative non-enteral nutrition was not a significant risk factor for gastrointestinal symptoms in the present study. Postoperative non-enteral nutrition for only three days may have caused impaired gastrointestinal function. Even when preoperative enteral nutrition has not been performed, patients with a serum albumin level >3.2 g/dL should undergo PEG tube placement and receive postoperative enteral feeding with elemental diets.

In this study, it should be noted that seven patients died from vomiting or diarrhea, and the rate of gastrointestinal symptoms leading to death was 28.0% (7/25) (Table 4). Aspiration pneumonia (57.1%, 4/7) was the most common cause of death. Pump-assisted enteral nutrition or post-pyloric feeding can reduce the risk of aspiration pneumonia.[10,11] However, these methods require pumps and are more difficult to manage than gravity-controlled enteral nutrition.[6] In addition, post-pyloric tubes easily become obstructed and displaced.[6] Semi-solid medical foods may reduce the risk of aspiration pneumonia in gastrostomy-fed patients.[12,13] My department will be conducting further investigation involving more patients receiving semi-solid medical foods.

This study had several limitations. First, patients' gastrointestinal motility may have influenced cases of vomiting or diarrhea. Second, the study design was single-center and retrospective. A multicenter, randomized study is necessary for the reduction of selection bias.

CONCLUSION

The administration of non-elemental diets and a serum albumin level ≤ 3.2 g/dL were significant risk factors for gastrointestinal symptoms when liquid nutrients were administered after PEG tube placement.

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