Original article

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Effect of percutaneous endoscopic gastrostomy on gastrointestinal motility: evaluation by gastric-emptying scintigraphy

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Purpose **Firstly, to assess the effect of percutaneous endoscopic gastrostomy (PEG) tube placement on gastric emptying, gastrointestinal (GI) tract motility and the rate of gastroesophageal reflux (GER). Secondly, to confirm whether correlations exist between drug absorption behaviour and GI tract motility using the combination method of absorption function analysis with the motility study.**

Methods **Subjects comprised 11 patients with neurological dysphagia. Gastric-emptying scintigraphy was performed both before PEG via nasogastric tube feeding and after PEG placement. After fasting for more than 8 h, each patient was administered 111 MBq of ^{99m}Tc-labelled diethylenetriaminepentaacetic acid (DTPA) with a 100 ml liquid meal via a nutrition tube. Dynamic imaging was performed immediately after administration of a radiolabelled liquid meal for a 1 h period and static imaging was performed after 1, 2, 3 and 6 h. Gastric emptying half-time (T_{50}) was calculated in each patient, and GER ratio and GI transit rate were also evaluated. Simultaneously, we administered 10 mg of famotidine in six of the 11 patients and measured serum concentrations of famotidine at 0, 1, 2, 3 and 6 h. Using the time–concentration curve of famotidine, the maximum concentration of famotidine (C_{max}) and area under the curve of famotidine (AUC_f) were calculated for each patient.**

Results **In seven of 11 patients, T_{50} changed after PEG placement, but not significantly. The GER ratio was significantly decreased and complicated pneumonia improved after PEG placement. GI transit rate for each GI segment was unchanged after PEG placement. Significant linear correlations were identified between T_{50} and both C_{max} and AUC_f.**

Conclusion **Gastric-emptying scintigraphy with ^{99m}Tc-DTPA was effective in the evaluation of GI transit before and after PEG, as well as in assessing GER. Motility and famotidine absorption were maintained after PEG placement. Significant linear correlations were found between T_{50} and both C_{max} and AUC_f. These findings suggest that drug absorption may have some relationship between T_{50}. The result may be more reliable with a larger population.** ***Nucl Med Commun*** **29:562–567 © 2008 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Introduction

Percutaneous endoscopic gastrostomy (PEG) was first described in 1980 by Gauderer *et al.* [1]. This method is minimally invasive, technically simple and inexpensive. PEG has thus been widely accepted to achieve an enteral access route in patients with dysphagia who require chronic nutritional support. Previous reports have discussed the effect of PEG on gastroesophageal reflux (GER) [2–7], and some reports [3,4] have shown negative effects on GER. Few reports, however, have discussed whether changes in whole gastrointestinal (GI) tract motility occur with PEG. Various gastroesophageal motor studies have been reported, including both nuclear studies and non-nuclear studies such as ultrasonography [8] and electrography [9]. However, some limitations in non-nuclear studies are seen when evaluating whole GI tract motility. The present study considered the effects of PEG placement on gastric emptying, rate of GER and

whole GI tract motility by implementing GI tract scintigraphy using ^{99m}Tc-diethylenetriamine pentaacetic acid (DTPA) with a liquid meal. We assessed drug absorption behaviour after famotidine administration in six of 11 cases to confirm whether correlations exist between drug absorption behaviours and GI tract motility.

Methods

Patients

This investigation complied with the tenets of the Declaration of Helsinki promulgated in 1964 and was approved by the Institutional Review Board.

Characteristics of patients are presented in Table 1. We evaluated 11 patients (seven men, four women; mean age, 82.4 ± 10.1 years; range, 67–98 years) who were treated with the PEG procedure. Of these, nine patients displayed sequelae of cerebrovascular disease and two were suffering from spinocerebellar degeneration. Oral ingestion was difficult due to neurological dysphagia and all had received nutritional management by nasogastric tube for several years. None of the patients had a history of previous abdominal surgery. All patients underwent PEG using a pull-type PEG kit (Ponsky 'Pull' PEG Kit; Bard, Georgia, USA). PEG feeding was started after a 48 h observation period. Elental (Ajinomoto, Tokyo, Japan) was used for regular feeds. The volume of feeding was gradually increased, reaching $200\,\mathrm{ml \cdot h^{-1}}$ with a total of 1000 ml, three times per day. Total daily caloric content was 1000–1500 kcal.

Scan protocol

We performed gastric-emptying scintigraphy before and 2 weeks after PEG placement. Any medication that had the potential to interfere with gastric motility, such as narcotic analgesics, anticholinergics, antidepressants, calcium channel blockers and H_2 blockers were discontinued for ≥ 24 h before scintigraphy. After fasting for > 8 h, each patient was administered 111 MBq of ^{99m}Tc-DTPA in a total of 100 ml with 300 kcal per 80 g of liquid meal via a nutrition tube. Elental (Ajinomoto, Tokyo, Japan) was used for both test meal and regular feeds. Elental is presented in powdered form and reconstituted using tap water. The content of the Elental is as follows [10]: amino acids, 17.2%; carbohydrates, 79.4%; lipids, 0.7%; and electrolytes, 2%. We administered ^{99m}Tc-diethylenetriaminepentaacetic acid (DTPA) as a radiotracer and used a dual-head gamma camera system (Millennium VG; GE Yokogawa Medical Systems, Tokyo, Japan). First, we administered a ^{99m}Tc-DTPA-labelled liquid meal via a nutrition tube and conducted dynamic scanning for 1 h. We then obtained 10 min static scans of both lungs and the abdomen after 1, 2, 3 and 6 h. Dynamic imaging was performed at a rate of 1 frame per min in a format of 128×128 pixels for 60 min using a low-energy high-resolution collimator. Photopeak settings were 20% at 140 keV for ^{99m}Tc. Static imaging was performed in a format of 1024×1024 pixels using a low-energy high-resolution collimator. All patients were supine during this study. The dual heads of the gamma camera were in the anterior and posterior positions and anterior projection images were obtained.

Image data analysis

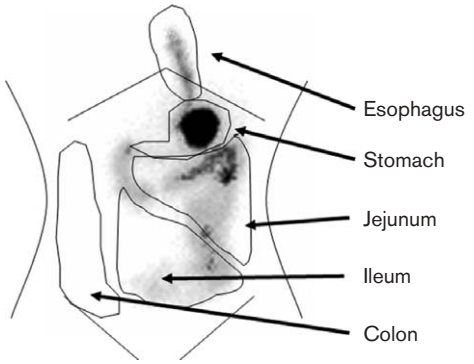
Image data were analysed using a workstation (Genie P & R, version 2.5s; GE Yokogawa Medical Systems). Gastric-emptying half-time (T_{50}) was determined as the time required to reach half the peak gastric counts using continuous imaging data with decay correction. We also evaluated GER ratio and GI transit rate. GER ratio was calculated as the ratio of oesophageal activity to gastric activity using continuous imaging data from start of acquisition to 3 h with decay correction. The maximum value in this time was used as the GER ratio. We considered a GER ratio limit for normal less than 4.0% [3]. GI transit rate was calculated by dividing the GI tract activity into five segments: oesophagus, stomach, jejunum, ileum, and colon (Fig. 1). Regions of interest (ROIs) for the jejunum and ileum were located by drawing a diagonal midline that approximately divided the field of the whole small intestine. Counts for each segment were measured from each ROI and the relative percentage of each ROI compared to the total count of the image (GI transit rate) were calculated and a time–GI transit rate curve was generated for each ROI. The area under the curve of each GI segment (AUC_s, AUC_j, AUC_i

Table 1 Clinical characteristics of the patients

Patient	Age (years)	Sex	Disease	Other diseases	Medication
1	89	M	SCVD	Hypertension	Antihypertensive agent
2	71	M	SCVD	Pneumonia	Antibiotics, anti-thrombotic agents
3*	72	M	SCVD	Hypertension, gastritis	Antihypertensive agent, H_2 blocker
4*	67	M	SCD	Pneumonia, gastritis	Antibiotics, H_2 blocker
5	94	F	SCVD	Pneumonia, oesophagitis	Antibiotics, H_2 blocker
6*	91	M	SCVD	Pneumonia, hypertension	Antibiotics, antihypertensive agent
7*	91	F	SCVD	None	None
8	79	M	SCVD	Pneumonia, hypertension	Antibiotics, antihypertensive agent
9	82	F	SCVD	Hypertension	Antihypertensive agent
10*	82	M	SCD	Pneumonia	Antibiotics
11*	98	F	SCVD	None	None

SCVD, sequela of cerebrovascular disease; SCD, spinocerebellar degeneration.
*Famotodine absorption study was performed.

Fig. 1



Gastrointestinal tract activity was divided into five segments: oesophagus, stomach, jejunum, ileum, and cecum/colon. ROIs for the jejunum and ileum were located by drawing a diagonal midline that approximately divided the field of the whole small intestine.

and AUC_c) was calculated in each patient using the trapezoid formula and compared between before and after PEG.

Famotidine absorption study

Simultaneous administration of famotidine was performed in conjunction with a scintigraphic study for six of the 11 subjects. This study was performed both pre-PEG and post-PEG using exactly the same technique. All six patients were free from famotidine medication at least 3 days before this study. We administered 10 mg of famotidine via a nutrition tube. Blood samples were obtained through a forearm venous catheter for multiple blood samplings and placed in heparinized vials. Samples were extracted just before and at 1, 2, 3 and 6 h after administration of famotidine. Blood samples were centrifuged and the plasma immediately stored at $-20^{\circ}C$ until assay. Blood samples were delivered to Okayama University for analysis. Concentrations of famotidine in plasma were determined using high-performance liquid chromatography (HPLC). The maximum concentration of famotidine (C_{max}) and the area under the curve of famotidine (AUC_f) were calculated using the trapezoid formula and the results compared with T_{50}.

Statistical analysis

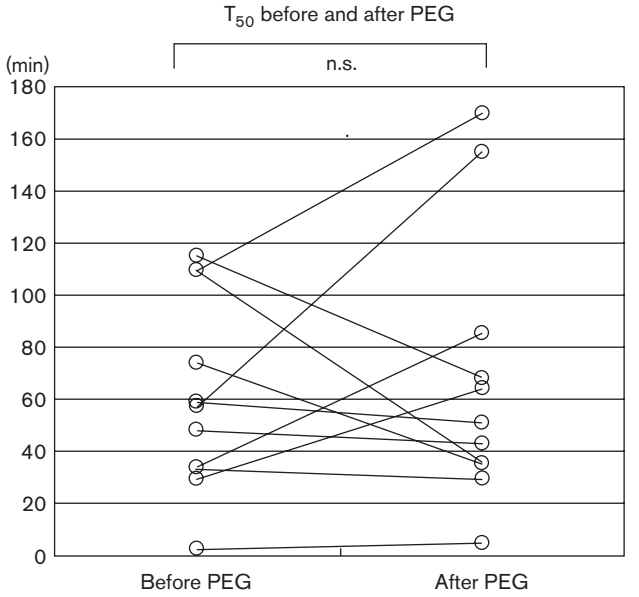
A non-parametric Wilcoxon signed-ranks test was used for statistical comparisons between the two evaluations of scintigraphic T_{50} and GER ratio. Pearson's regression analysis was used to evaluate correlations between T_{50} and both C_{max} and AUC_f. Values of $P < 0.05$ were considered significant.

Results

Gastric-emptying half-time (T_{50})

Changes in T_{50} between pre-PEG and post-PEG placement are shown in Fig. 2. The T_{50} of pre-PEG and post-

Fig. 2



Changes in T_{50} before and after PEG. T_{50} was decreased in three of 11 patients, and increased in four patients. However, no significant changes in T_{50} were identified after PEG placement.

PEG placement (mean ± SD) was 60.9 ± 37.3 and 67.3 ± 51.8, respectively. T_{50} shortened in three patients and increased in four patients after PEG placement, but no significant changes were identified in any patients.

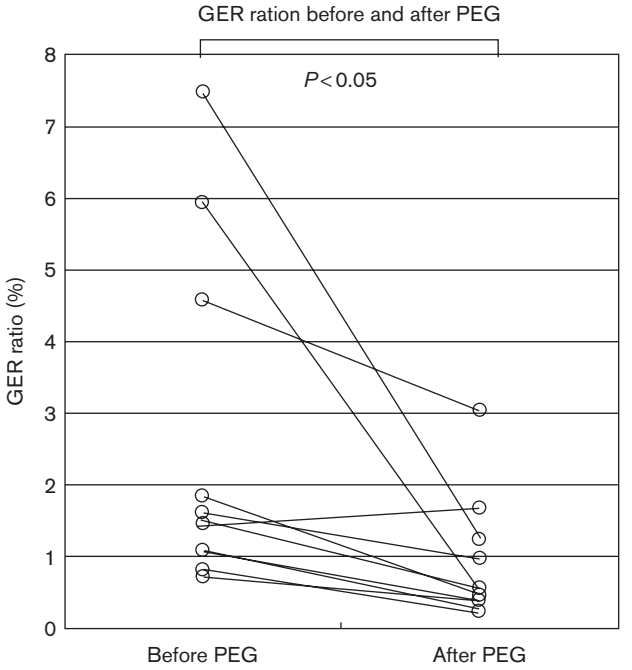
Gastroesophageal reflux ratio

Changes in GER ratio before and after PEG placement are shown in Fig. 3. GER ratio of pre-PEG and post-PEG placement (mean ± SD) was 2.53 ± 2.33 and 0.88 ± 0.85, respectively. GER ratio decreased significantly after PEG placement. Six of the 11 patients suffered from aspiration pneumonia before PEG placement, five of the six patients improved after the PEG placement. Among those five patients, three patients were scintigraphically positive for GER before PEG, all of these three patients showed as decreased GER ratio within normal limit after PEG placement. A representative case is presented in Fig. 4. In association with this finding, aspiration pneumonia improved in all five patients. However, one patient who displayed continued GER after PEG placement did not recover from aspiration pneumonia.

Gastrointestinal transit rate

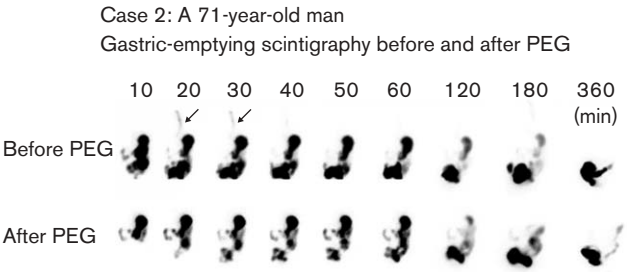
GI transit rate was calculated in each segment. Time–GI transit rate curves of each GI segment before and after PEG placement are presented in Fig. 5. In pre-PEG placement, area under the curve of each GI segment (AUC_s, AUC_j, AUC_i and AUC_c) (mean ± SD) were 120.77 ± 54.09, 100.27 ± 50.76, 171.35 ± 63.64 and 130.66 ± 51.20, respectively, while in post-PEG placement, those were 93.51 ± 24.48, 126.87 ± 64.23,

Fig. 3



Changes in GER ratio. GER ratio was significantly decreased after PEG placement.

Fig. 4



	GER ratio (%)
Before PEG	5.93
After PEG	0.56

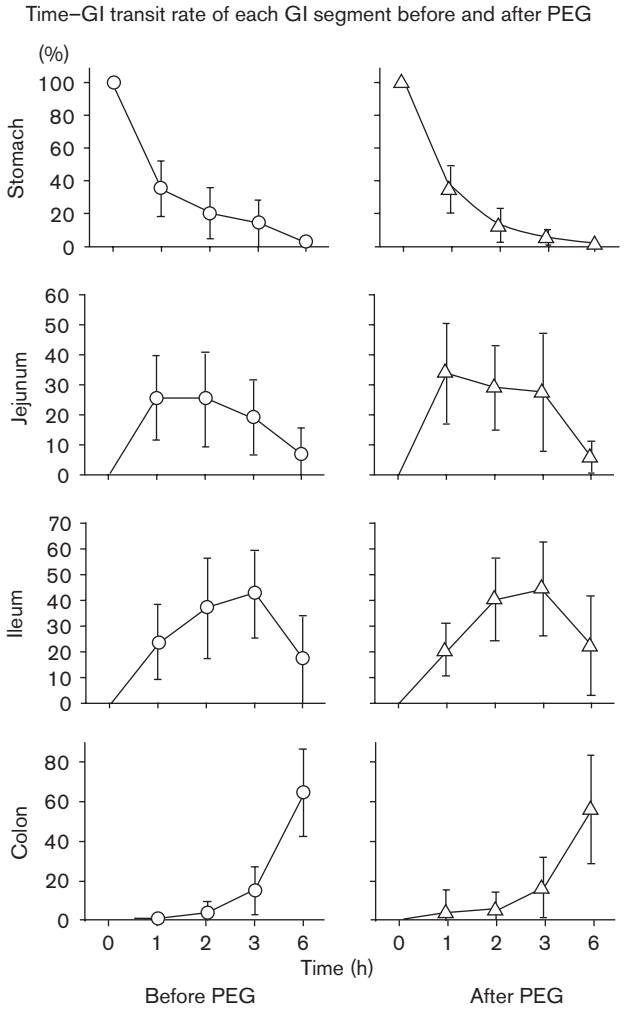
The case is a 71-year-old man. This patient suffered from GER (arrows) and aspiration pneumonia before PEG placement. After PEG placement, GER reflux disappeared and GER ratio decreased.

183.08 ± 52.36 and 126.63 ± 51.08, respectively. The AUC of each GI segment did not change significantly between before and after PEG placement and GI transit rate for each GI segment remained stable after PEG placement.

Famotidine absorption study

The time–concentration curve of famotidine for the six patients is presented in Fig. 6. This study was performed

Fig. 5



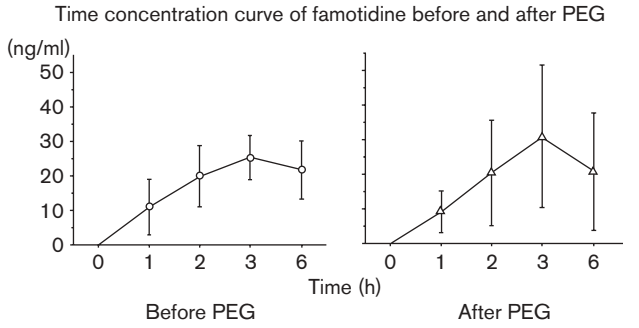
This shows dynamic percentage curves for each GI segment before and after PEG placement. Each point shows mean ± SD. The percentage of each GI segment did not change significantly between before and after PEG placement.

both pre-PEG and post-PEG using exactly the same technique. The AUC_f of pre-PEG and post-PEG placement (mean ± SD) was 108.48 ± 37.69 and 115.14 ± 68.48, respectively. AUC_f did not change significantly between before and after PEG placement. Significant linear correlations were seen between T_{50} and both C_{max} (Fig. 7) and AUC_f (Fig. 8)

Discussion

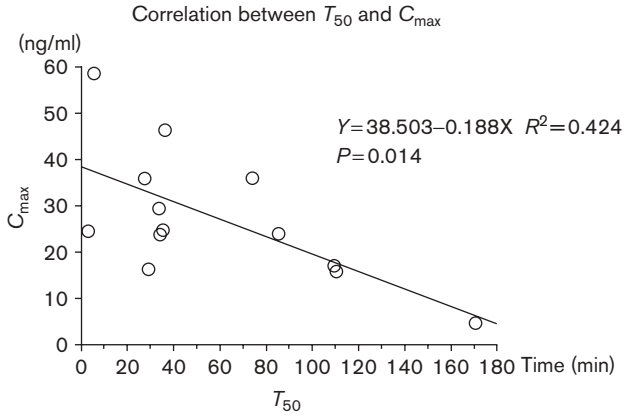
We evaluated changes in T_{50}, GER ratio and GI transit rate by dynamic gastrointestinal scintigraphy using a ^{99m}Tc-DTPA-labelled liquid meal. T_{50} decreased in three patients and increased in four patients, but was not significantly changed after PEG placement. In five of the six patients in which aspiration pneumonia was discovered during NGT nutrition, pneumonia improved after PEG placement. In association with this finding, among

Fig. 6



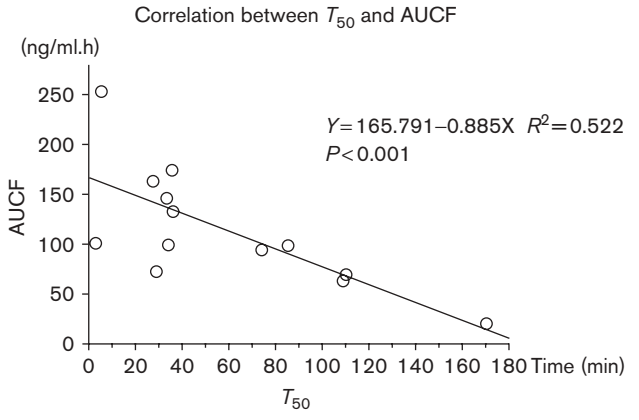
This shows the time–concentration curve of famotidine in six patients before and after PEG placement. Each point shows mean ± SD. The time–concentration curve profile did not change significantly after PEG placement.

Fig. 7



Comparison of T_{50} and C_{max}. A significant linear correlation was identified.

Fig. 8



Comparison of T_{50} and AUC_f. A significant linear correlation was identified.

those five patients, three were scintigraphically positive for GER before PEG, all of the three patients showed a decreased GER ratio within normal limit and pneumonia improved after PEG placement. Cole *et al.* [3] found that the GER ratio is normally 4.0%. All patients after PEG placement showed a low GER ratio within this limit. Our findings suggest that PEG placement, and to be free from NGT nutrition, does not worsen GER or aspiration pneumonia. These findings are consistent with previous reports that have mentioned that PEG placement does not worsen GER [2,5–7]. None of the previous reports have shown changes in T_{50} or GI transit rate between before and after PEG. In our study, T_{50} did not significantly change after PEG placement. AUC of each GI segment did not significantly change after PEG placement and GI transit rate remained stable after PEG placement. We have deleted 'gastrointestinal motility' and corrected as follows.

These findings suggest that fixation of the stomach using PEG procedures is not always detrimental to gastric emptying. We consider that most PEG procedure fixes anterior, middle portion of the stomach, therefore this procedure might not affect both of the gastric fundic lag phase and gastric antral motility. Both of lag phase and gastric antral motility are important in considering gastric emptying motility.

We evaluated famotidine absorption simultaneously in six of the 11 patients. AUC_f did not change significantly between before and after PEG placement, suggesting that PEG procedures are also not always detrimental to drug absorption. Analyses also identified significant linear correlations between T_{50} and both C_{max} and AUC_f. Haruta *et al.* [11] found that the plasma concentration–time profile was able to be predicted using individual gastrointestinal scintigraphic data and a GI-transit–absorption model. This finding suggests that drug absorption may have some relationship with T_{50}. Some reports have noted that motility of the stomach changes when H_2 receptor blockers or proton pump inhibitors such as famotidine are administered [12,13]. In addition, H_2 receptor blockers are suggested to provide cholinergic properties that influence GI motility [14,15]. We evaluated influences on the stomach of not only PEG, but also famotidine, as we administered ^{99m}Tc-DTPA and famotidine at the same time. A famotidine plasma concentration of $13\,ng \cdot ml^{-1}$ reportedly inhibits gastric-acid secretion by 50% [16]. In this study, because famotidine dosage was low, gastric emptying was completed in most patients before reaching $13\,ng \cdot ml^{-1}$. In addition, a time lag is thought to exist between pH increases and motility change. In fact, one report has mentioned that gastric pH begins to rise with administration of 20 mg of oral famotidine after 2 h [17]. In addition, another report describes comparatively minor cholinergic properties for

famotidine among H_2 receptor blockers [15]. Given that only 10 mg of famotidine was used in this study, the influence of any pH change on gastric motility is low.

Limitations

First, the subject population especially drug absorption in this study was small and findings may differ in another study. Second, ROIs for the stomach and colon were easily identified because of the characteristic anatomy, but ROIs for the jejunum and ileum were located by drawing a diagonal midline that approximately divided the field of the whole small intestine, meaning that reproducibility may be low and interobserver and intraobserver variations may be large. Finally, this study was conducted under fasted conditions, which may offer differing results to fed conditions. Further studies are required to clarify these issues.

Conclusion

Gastric-emptying scintigraphy with ^{99m}Tc-DTPA was effective in the evaluation of GI transit before and after PEG, as well as for assessing GER. GER significantly decreased after PEG placement and complications of GER and aspiration pneumonia typically disappeared after PEG placement. Motility and famotidine absorption were maintained after PEG placement. Significant linear correlations were identified between T_{50} and both C_{max} and AUC_f. These findings suggest that drug absorption may have some relationship between T_{50}. The result may be more reliable with a larger population.

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