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Gastric acidity and duodenogastric reflux during nasojejunal tube feeding in mechanically ventilated patients

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Abstract *Objective*: In order to prevent gastric microbial overgrowth, which may complicate nasogastric feeding, administration of nutrients more distally into the gut has been advocated in intensive care patients, as it offers the advantage of keeping the stomach empty and acid. In this study, we assessed the impact of jejunal feeding upon gastric pH in a group of mechanically ventilated, critically ill patients, with special focus on duodenogastric reflux as a possible cause of gastric alkalinization during jejunal nutrition.
Design: Prospective experimental study.
Setting: Multidisciplinary intensive care unit of a university hospital.
Patients and methods: Gastric pH was recorded by continuous pHmetry over a 4-h period of fasting followed by a 4-h period of nasojejunal feeding at 100 kcal/h in 21 mechanically ventilated, critically ill patients. To determine the contribution of duodenogastric reflux to modifications of gastric acidity, the diet was traced with [^{111}In] DTPA (pentetic acid) in 11 of these 21 patients; gastric contents were aspirated every 30 min, then analysed for measurement of radioactivity, glucose, and bile acid concentration.
Measurements and results: Median intragastric pH increased slightly from 1.59 (1.20–2.73; interquartile range) (fasting) to 2.33 (1.65–4.64) (feeding) ($p = 0.013$), and the length of time that the pH was 4 or above increased from 1 (0–24) to 9 (0–142) min ($p = 0.026$). The variability of pH values and the number of acute alkalinization episodes did not change between the two phases. In 10 of 11 patients in which the diet was labeled with [^{111}In] DTPA, reflux was documented at a given time of the feeding period. Bile acid concentrations in the stomach increased from 392 (61–1076) (fasting) to 1446 (320–2770) μmol/l (feeding) ($p = 0.010$) and mean glucose concentration increased from 59 (28–95) to 164 (104–449) mg/dl ($p = 0.006$).
Conclusion: Duodenogastric reflux is common in mechanically ventilated critically ill patients with nasojejunal feeding tubes. It occurs both during fasting and during nasojejunal feeding. During nasojejunal feeding, moderate alkalinization of the gastric contents occurs as a result of bile and nutrient reflux.

Key words Critically ill · Enteral feeding · Gut dysfunction

Introduction

In the critically ill patient, the importance of providing nutrients by the enteral route has been emphasized; enteral nutrition promotes intestinal perfusion [1], protects the gut mucosa, and may reduce the risk of bacterial translocation [2, 3]. Because gastric emptying is often inadequate in these patients [4, 5], feeding into the small bowel may be preferred over gastric feeding, so that many critical care physicians are now recommending feeding these patients via a nasojejunal tube [6–8]. Indeed, compared to nasogastric feeding, nasojejunal feeding may theoretically prevent stagnation of nutrients in the stomach, thereby avoiding the risk of aspiration [7, 9]. It may also increase the quantity of calories delivered into the gut [10, 11] and prevent microbial colonization of the stomach (a possible cause of retrograde pneumonia) by preserving gastric acid.

In contrast with the increasing interest in nasojejunal tube feeding in intensive care units, very few studies have validated these theoretical advantages in critically ill patients. Particularly, little is known about the possibility of bile and/or nutrient reflux from the duodenum to the stomach during nasojejunal feeding.

In the present study we analyzed the modifications of gastric acidity before and during nasojejunal tube feeding in mechanically ventilated, critically ill patients, with special focus on duodenogastric reflux as a possible cause of gastric alkalinization during jejunal nutrition.

Materials and methods

Patients

During a 6-month period (October 1995 to March 1996), the adult patients admitted to our intensive care unit who were receiving prolonged mechanical ventilation and requiring artificial nutrition were eligible for the study. We excluded patients in whom enteral nutrition was considered to be contraindicated due to recent abdominal surgery, postoperative ileus or uncontrolled hypotension, as well as patients in whom treatment with gastric antisecretory agents (H_2 antagonists, H + K + ATPase inhibitors) could not be interrupted due to active upper gastrointestinal tract erosions, a history of peptic ulcer disease, or chronic treatment with anti-inflammatory drugs. The patients were not selected on the basis of the volume or pH of their gastric aspirates before the investigation.

The day before the study, treatment with the medications known to interfere with gastric secretory function was interrupted and stress ulcer prophylaxis was achieved by intragastric sucralfate, 10 mg three times daily, a medication that does not interfere with gastric acid secretion [12]. All medications were unchanged throughout the study.

The patients were fitted with a double-lumen nasogastrojejunal feeding tube (Dobbhof, Sherwood Medical, Bondoufle, France). The tube was inserted under fluoroscopic guidance at the bedside according to the following procedure: after removal of the nasogastric tube, a flexible guidewire is inserted through the lubricated (9 Fr) jejunal feeding tube. The jejunal tube is inserted into the lumen of the (16 Fr) gastric tube. The assembly is then passed nasally into the stomach and advanced until its tip lies in the distal antrum. After air injection, the pylorus is cannulated with the guidewire, then the jejunal tube is advanced over the guidewire. The same maneuver is used to cross the angle between the first and second portions of the duodenum. By maintaining the straightest possible path in the stomach, the tube is then advanced beyond Treitz's ligament. The position of the gastric tube is adjusted so that aspiration ports are located in the gastric antrum.

The study was reviewed and approved by the local ethics commitee and informed consent was obtained from the patient's relatives or guardians.

Intragastric pH

Intragastric pH was continuously monitored during two successive periods of fasting (240 min) and nasojejunal feeding (240 min). During the feeding period, a liquid diet (Nutrison standard; Nutricia, Zoetemeer, The Netherlands; 1 kcal/ml, pH 6.5) was infused at a rate of 100 ml/h through the distal port of the nasogastrojejunal tube. Intragastric pH was measured by means of a glass pH electrode (InMedical gastroesophageal probe, Mettler-Toledo, Switzerland), positioned in the gastric antrum under bedside fluoroscopy immediately before the study. The intragastric pH probe was connected to a pH meter (Knick 761 pHmeter, Elscolab, Kruisbeke, Belgium) through an isolation module. The pH electrodes were calibrated in two different buffer solutions (pH 4.1 and 7.0, respectively) before each experiment. The pH values were downloaded onto a personal computer (one measurement per min) for mathematical and statistical analysis.

Bile and nutrient reflux

In a subgroup of patients, the liquid diet was additionally labeled with [^{111}In] DTPA (pentetic acid) (300 to 500 μCi in 500 ml) immediately before infusion. The gastric contents were aspirated every 30 min for determination of volume, glucose, and bile acid concentration (during fasting and feeding) as well as for the radioactivity count (during feeding). Bile acid concentrations in the gastric contents were measured on a Cobas Fara (Roche, Switzerland) by a quantitative enzymatic assay at 530 nm based on the procedure described by Mashige [13].

Radioactivity of the gastric contents was measured using a gamma counter (1282 Compugamma CS, LKB, Turku, Finland) and the results expressed in disintegrations/min per ml. To ensure that gastric activity was not secondary to gastric inflammation, a blood sample was also drawn and its radioactivity was compared to that of gastric aspirates. Under physiological conditions no [^{111}In] DTPA is absorbed, so that no significant blood activity should be present.

Data analysis

For each patient and each phase, we computed the mean pH value, the length of time that pH was above 4.0, the number of episodes of acute gastric alkalinization defined as an increase in more than one pH unit in 3 min, and the coefficient of variation (standard deviation/mean) as an expression of the variability of the parameter. Variables are expressed by medians and interquartile range and were compared between the fasting and feeding periods by the Wilcoxon signed rank test. This test was also used to compare mean bile acid and mean glucose concentrations.

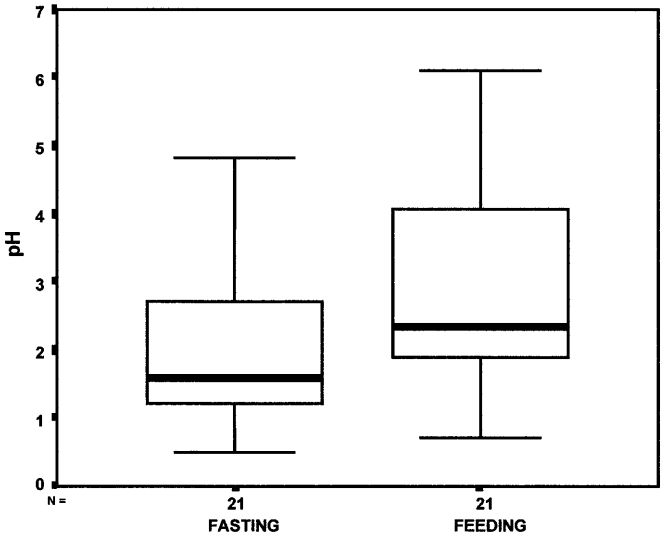

Fig. 1 Box-plots showing the range of intragastric pH during fasting and nasojejunal tube feeding periods. The *lower* and *upper boundaries* of the boxes are the 25th and 75th percentiles. The *thick horizontal lines* inside the boxes represent medians. Statistical analysis: Wilcoxon's signed rank test

Results

Study population

A total of 21 patients (age 61 ± 12 years; Acute Physiology and Chronic Health Evaluation II score on admission 20 ± 9) were studied. Their main characteristics are given in Table 1. The nasogastrojejunal feeding tube was placed without any technical problems and without endoscopic guidance in all investigated patients. Patients were investigated 4.4 ± 2.6 days after admission, while they were being ventilated mechanically for 3.9 ± 2.0 days. They received various medications adapted to their medical condition, including sedative agents (mainly propofol), sufentanil ($n = 13$), and vasoactive agents ($n = 7$). The volume of gastric aspirates was 151 ± 211 ml (mean ± SD) the day before the experiment, and intragastric pH was 2.2 ± 1.3 (mean ± SD) at the start of the study. Hemodynamic (mean arterial pressure) and respiratory (arterial oxygen tension/fractional inspired oxygen ratio) parameters recorded at the start are given in Table 1.

pH

During fasting, median intragastric pH was 1.59 (1.20–2.73); (mean ± SD: 2.1 ± 1.2). During nasojejunal feeding it increased slightly but significantly to 2.33 (1.65–4.64) ($p = 0.013$) (Fig. 1) (mean ± SD: 2.9 ± 1.8). The length of time that the pH was 4 or above increased from 1 (0–24) to 9 (0–142) min ($p = 0.026$). A large variability in pH values with time was usually found in an individual whatever the period (fasting or feeding), as illustrated by the data from a representative patient in Fig. 2. The variability of pH values, however, did not change significantly between the two phases [coefficient of variation 0.30 (0.25–0.41) during fasting vs 0.30 (0.17–0.42) during feeding]. Similarly, we did not find any difference in the number of acute alkalinization episodes during either phase [fasting 1 (0–6), feeding 1 (0–5)].

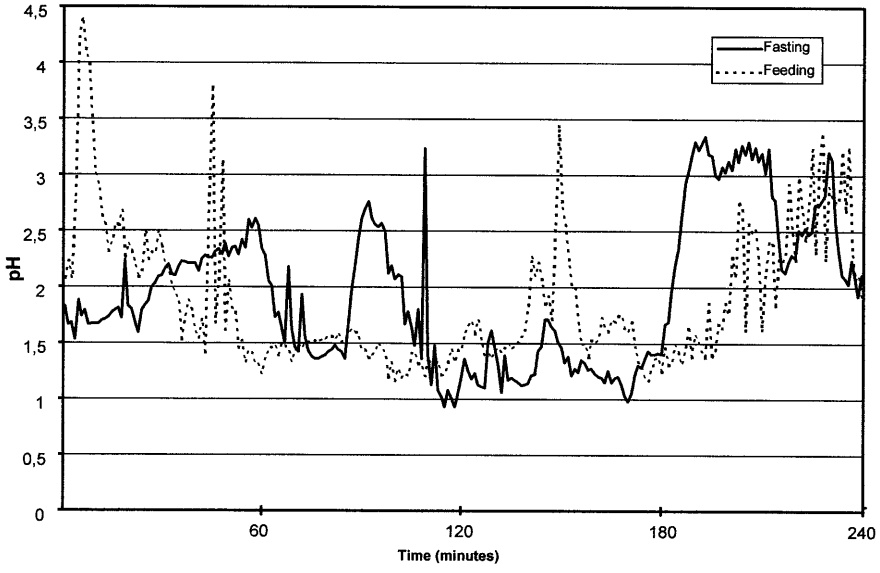

Fig. 2 Variation of intragastric pH in a study patient. Intragastric pH was measured by continuous pHmetry during fasting *continuous line* and during nasojejunal tube feeding *dotted line*. Considerable variability in pH values was usually found in the same patient

Table 1 Characteristics of the patients (*ARDS* adult respiratory distress syndrome, *IPPV* intermittent positive pressure ventilation, *ASB* assisted spontaneous breathing, *Pr* propofol, *Mi* midazolam, *S* sufentanil, *Dp* dopamine, *N* noradrenaline, *Db* dobutamine, *Ad* adrenaline, PaO_2/FIO_2 arterial oxygen tension/fractional inspired oxygen ratio)

Patient No.	Sex/age (years)	Diagnosis	Study day	Gastric aspirates (ml/24 h)	Gastric pH	Mean arterial pressure (mm Hg)	Mechanical ventilation			Medications		
							Duration	Ventilatory mode	PaO_2/FIO_2[a]	Sedative agents	Analgesics	Vasoactive agents
1	M/60	Aspiration pneumonia	5	55	1.8	89	3	IPPV	2	Pr	S	Dp, N
2	M/66	Pulmonary infection Cardiac and renal failure	6	5	2.2	71	6	IPPV	3	Pr, Mi	S	Dp, Db, N
3	F/56	*Pseudomonas* pneumonia Ischemic left ventricular failure	6	170	3.0	102	6	IPPV	3	Pr	S	–
4	F/74	Aortic valvulopathy Cardiopulmonary arrest Cerebral anoxia	6	0	1.4	98	6	ASB	1	–	–	Db
5	F/53	Cerebral hemorrhage Coma	4	0	1.1	86	4	ASB	2	–	–	–
6	F/56	Cerebral hemorrhage Congenital coagulopathy Neurogenic pulmonary edema	2	300	4.5	79	2	IPPV	3	Pr	S	–
7	M/31	Head injury (road traffic accident) Cerebral edema	5	380	1.4	124	5	IPPV	2	Pr, Mi	S	–
8	M/51	ARDS Pulmonary tuberculosis	3	580	0.4	85	3	IPPV	2	Pr	S	–
9	F/73	Ischemic cardiomyopathy Pulmonary sepsis Acute renal failure	6	0	1.1	100	6	IPPV	1	–	–	Db
10	M/44	Pulmonary infection Peripheral arterial occlusion disease – aortic aneurysm	2	40	2.8	67	2	IPPV	3	Pr	S	N, Ad
11	F/42	Pulmonary infection Valvular heart disease	8	105	1.8	82	6	IPPV	2	Mi	S	Db
12	M/65	Chronic obstructive airway disease – cerebral anoxia (suspected aspiration)	9	200	2.5	102	9	ASB	1	–	–	–
13	M/69	Bronchopneumonia Chronic obstructive airway disease	2	0	1.9	89	2	IPPV	2	Pr	S	–
14	M/61	Nosocomial *(Proteus)* pneumonia – chronic lung disease	2	5	1.8	95	2	IPPV	2	Pr	–	–
15	M/59	Pneumonia Ischemic heart disease Atrial fibrillation	3	0	0.9	77	3	IPPV	2	Pr	–	Dp
16	M/69	*Pseudomonas* pneumonia Aortic valvulopathy Renal failure	11	200	3.8	64	4	IPPV	2	Pr	–	Dp, Db, N
17	F/84	Head injury Aspiration pneumonia	4	0	2.6	85	4	IPPV	3	Pr	–	–
18	F/67	Pneumonia Chronic lung disease Diabetes mellitus	4	430	1.0	93	3	IPPV	2	Pr	S	–

Table 1 Continued

Patient No.	Sex/age (years)	Diagnosis	Study day	Gastric aspirates (ml/24 h)	Gastric pH	Mean arterial pressure (mm Hg)	Mechanical ventilation			Medications		
							Duration	Ventilatory mode	PaO_2/FIO_2[a]	Sedative agents	Analgesics	Vasoactive agents
19	M/57	Aspiration pneumonia Multiple sclerosis	1	700	1.3	96	1	IPPV	1	Pr	–	–
20	F/67	Pancoast's tumor Bronchorrhea Atrial fibrillation	2	0	5.6	70	2	IPPV	1	Pr	S	–
21	M/71	Chronic lung disease Pneumothorax Hypercapnia	2	0	2.6	103	2	IPPV	2	Pr	S	–

[a] PaO_2/FIO_2: 1 > 250; 2: 150–250; 3: < 150

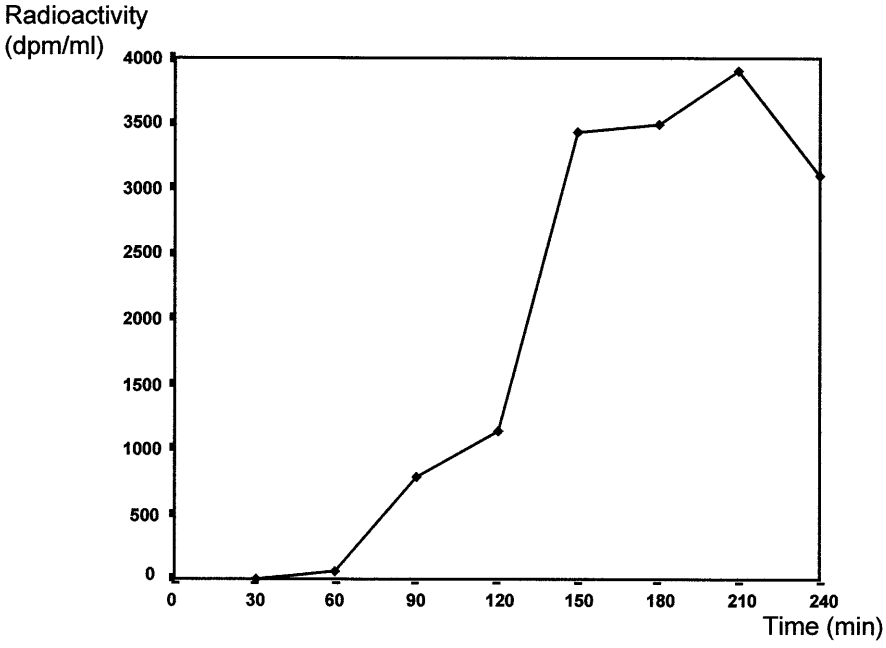

Fig. 3 Time course of median radioactivity of the gastric contents in the 11 patients fed with a [^{111}In] DTPA (500 μci in 500 ml) labeled diet. The gastric contents were aspirated every 30 min during nasojejunal tube feeding, at 100 kcal/h. A sharp increase in gastric contents radioactivity was observed after initiation of jejunal feeding

Bile and nutrient reflux

Reflux of bile and nutrients was assessed in 11 patients (patients 1 to 11 in Table 1). During feeding, 10 of 11 patients demonstrated a significant increase in radioactivity in the gastric contents (no increase in radioactivity in patient 9). Among these, only 1 (patient 3) had possible bowel inflammation, as demonstrated by the presence of significant blood activity. The time course of gastric content radioactivity is shown in Fig. 3. In these 11 patients, bile acid concentrations in the gastric contents increased from 392 (61–1076) μmol/l during fasting to 1446 (320–2770) μmol/l during feeding ($p = 0.010$). Mean glucose concentrations in the stomach increased from 59 (28–95) mg/dl (fasting) to 164 (104–449) mg/dl (feeding) ($p = 0.006$). The volume of gastric aspirates tended to rise during feeding, although it did not reach a formal significant statistical level [fasting 82 (52–92) ml vs feeding 89 (67–107) ml; $p = 0.091$].

Discussion

Aspiration of bacteriologically contaminated gastric contents is one of the most important complications associated with tube feeding in critically ill patients. Nutrients administered via a nasogastric tube have a relatively high pH and promote gastric colonization [14, 15]. Since gastric emptying is also frequently impaired in

these patients, aspiration of gastric contents is thought to occur regularly during nasogastric feeding, and this may contribute to the pathogenesis of ventilator associated pneumonia [15].

In order to maintain the stomach acid during nasogastric feeding, several methods have been proposed, including acidification of enteral feed [16] and intermittent administration of nutrients [17]. Although these methods may have some efficacy in decreasing the bacterial growth in the stomach, they do not decrease the risk of aspiration of gastric contents. Therefore, some authors have suggested using the nasojejunal rather than the nasogastric route for feeding these patients [10], especially since intestinal motility, as opposed to gastric motility, is frequently preserved during critical illness [18]. This may offer the theoretical advantage of keeping the stomach empty and acid, provided that sucralfate rather than H_2-blockers are used as stress ulcer prophylaxis when indicated.

In the present study, we observed significant duodenogastric reflux in critically ill patients fed by the nasojejunal route. During fasting, duodenogastric reflux was already present, since significant amounts of bile were regularly recovered from the gastric aspirates. This likely contributed to the observed variability of intragastric pH and confirms the observations made by Inglis et al. [19] who demonstrated the frequent occurrence of duodenogastric reflux in critically ill patients by the detection of bilirubin in gastric aspirates.

During the feeding phase, we found an increase in gastric concentration of bile acids. This implies that stimulation of biliary secretions may still occur despite bypassing the duodenum during nasojejunal tube feeding; accordingly, the presence of nutrients in the stomach, a potent stimulus for gallbladder contraction, was detected in the vast majority of the patients. The persistence of a stimulus for biliary secretion may explain why most patients fed distally are able to absorb a polymeric diet adequately and do not require predigested nutrients. This also implies that complete inhibition of biliary and pancreatic secretions probably cannot be expected during jejunal nutrition.

To some extent, duodenogastric reflux is a physiologic event in humans; in the fasting state, it may occur in late phase II of the interdigestive migrating complex, but pancreaticobiliary secretions are then immediately cleared from the stomach during phase III activity [20, 21]. Antral phase III activity is altered in mechanically ventilated, critically ill patients [18], so that protection against duodenogastric reflux is expected to be disrupted in these patients. Also, reflux in our patients may have been exacerbated by the presence of the nasojejunal tube through the pyloric sphincter. In this regard, comparison of the incidence of duodenogastric reflux in patients with a nasogastric versus a nasojejunal tube would be valuable.

Although the method we used did not allow quantitation of the duodenogastric reflux during the feeding phase, we can approximate it by measuring the percentage of labeled nutrients that were aspirated. Despite probable incomplete sampling, less than 5 % of radioactivity was recovered. The limitation of the duodenogastric reflux is further supported by the fact that intragastric pH remained relatively acid (median pH 2.33) during high rate infusion of enteral feeding via the nasojejunal route.

To our knowledge, very few data are available in the literature on the incidence of gastric microbial colonization in patients fed by the nasojejunal route. In a subgroup of patients, Montecalvo et al. [10] found similar levels of gastric colonization with gram-negative bacilli in patients fed by either a gastric ($n = 7$) or a jejunal tube ($n = 5$), but gastric acidity may have been decreased in some of their study patients by administration of H_2-blockers or antacids. As far as bactericidal activity against gram-negative bacilli is concerned, the cutoff value of pH 4.0 is usually considered to be critical [22–25]. In vitro, gram-negative organisms were killed rapidly at a pH of 2.7 or lower [26]. In a more recent study, Prod'hom et al. [27] found colonization with high counts of gram-negative bacteria in only 3 of 46 patients with a median pH lower than 4.0. In the study by Bonten et al. [28], the percentage of time at a $pH < 4.0$ were 23.5 % in the patients colonized with *Enterobacteriaceae* and 59.1 % in noncolonized patients (the percentage of time at a $pH < 4.0$ in our patients during nasojejunal feeding was 73 %). In our study, we did not culture gastric aspirates and, therefore, we do not know the impact of nasojejunal nutrition on gastric microbial colonization. Although the gastric acid barrier may have been preserved in most of our patients, in view of the relatively low intragastric pH observed, a longer observation period may yield a greater duodenogastric reflux as well as higher gastric juice pH. Similarly, the nutrient infusion rate may also conceivably influence the results.

In conclusion, duodenogastric reflux is common in mechanically ventilated critically ill patients equipped with nasojejunal feeding tubes. It occurs both during fasting and during nasojejunal feeding. During nasojejunal feeding (100 ml/h over 4 h), a moderate alkalinization of the gastric contents occurs as a result of bile and nutrient reflux. Future studies should assess the impact of such reflux on gastric microbial colonization during long-term nasojejunal nutrition.

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