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Impact of Percutaneous Endoscopic Gastrostomy on Gastroesophageal Reflux and Gastric Emptying in Pediatric Patients GER and Gastric Emptying after PEG

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Abstract:- Background/Aims. Percutaneous endoscopic gastrostomy (PEG) is frequently indicated in patients with global developmental delay (GDD) with dysphagia. The present study aims at evaluating the influence of PEG on the GER and the gastric emptying of liquids in children with GDD.

Methods. 16 children with GDD (6M/10F, median age 9 yrs [1 - 17]) with clinically indicated PEG were evaluated with intraluminal impedance and pH monitoring and 13 C- acetate breath test (gastric emptying). Baseline and 5-month values for esophageal acid exposure, bolus contact time, number of reflux episodes and the gastric emptying half- time were compared with paired t-test.

Results. The number of total reflux episodes raised after PEG (mean 18.8, 95% CI 1 to 36.3, P = 0.038), mainly due to an increase in weakly acid reflux episodes (mean difference 16.7, 95% CI 6.5 - 27, P = 0.004). The variation of the gastric emptying half- time was not significant at five months (+7.9 min (95% CI -9.9 to 25.7), P = 0.348).

Conclusions. PEG placement did not affect the reflux index, the bolus contact time, and the gastric emptying. A slight increase in weakly acid reflux episodes without clinical repercussion was observed.

Keywords:- *Gastric Emptying; Breath Test; Cerebral Palsy; Gastrostomy;*

I. INTRODUCTION

Dysphagia occurs in 30 to 40% of patients with cerebral palsy and other causes of neurodevelopmental delay (1). Although some patients may be treated with speech therapy, percutaneous endoscopic gastrostomy (PEG) is the standard of care for providing long-term nutritional support among those patients (2), (3). Gastroesophageal reflux disease (GERD) is frequent in this clinical context, and some health care providers prefer to surgically install the gastrostomy tube, along with anti-reflux surgery. However, there is no systematic requirement for prophylactic fundoplication in a child with clinical GERD that is well controlled by medical treatment (4) . Also, the anti- reflux surgery fundoplication in neurologically impaired patients is associated with higher rates of failure and significant morbidity (5).

Persistent vomiting after gastrostomy is a great concern for parents and health care providers, as it may contribute to food intolerance and leaking after gastrostomy, particularly among neurologically impaired patients. However, it is known if the persistent vomiting is related to gastroesophageal reflux or gastric dysmotility (6, 7, 8). Recently, it has been reported that 16% of children undergoing PEG will require a fundoplication after up to 10 years follow-up. In the multivariate analysis, the only significant risk factor for a fundoplication was neurological impairment (OR 1.98, 95% confidence interval 1.98; 1.1 to 3.86) as compared to the whole set of patients submitted to PEG (9). At this time, how PEG affects gastroesophageal reflux (GER) parameters and the gastric emptying is not well-known. The aim of the present study is to evaluate the gastroesophageal reflux and the gastric emptying in patients with global developmental delay (GDD) at baseline and after PEG.

II. MATERIAL AND METHODS

Patients. 16 patients (6M/10F, 2 to 17 yrs, median 9) with GDD-associated dysphagia and PEG indicated by the assistant physician were prospectively evaluated. Demographic and clinical baseline data are displayed in table 1. Exclusion criteria included age less than 1 year or more than 18 years, previous abdominal surgery, ventriculoperitoneal shunt, gastroesophageal reflux disease refractory to clinical treatment, moderate to severe erosive esophagitis (Los Angeles grade C or D), progressive neurological disease (as defined by the assistant physician), congenital anomalies of upper digestive tract, blood dyscrasia, esophageal stricture, portal hypertension, peritonitis, chronic hepatic disease, previous peritoneal dialysis, and ascites. Also, patients presenting major complications after PEG placement, requiring surgical intervention, were excluded.

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The study was approved by the Institutional Review Board at the Universidade Federal de São Paulo (number 473.473). Informed consent was requested from all parents or legal guardians. Patients older than 7 years-old also provided informed assent whenever possible.

Study protocol. At baseline and 5 months after PEG placement, eligible patients were clinically evaluated with standardized clinical and demographic questionnaires, assessing gastrointestinal symptoms, medications in use, nutritional and anthropometric data. In addition, at the same moment, a multichannel intraluminal impedance and pH monitoring (MII-pH) and a 13 C-acetate breath test (13 C-ABT) were performed. Thereafter, patients were followed-up in the outpatient clinic of the university hospital, and outcomes were reviewed at one year follow-up. PEG placement was done with standard pull technique in all patients, using 15Fr tube for infants with less than 10kg, and 20Fr for those with more than 10kg. One patient presented a gastrocolic fistula and was excluded from the study.

Multichannel intraluminal impedance and pH monitoring (MII-pH). It was performed with a reusable probe with 6 impedance channels and one distal antimony pH sensor (MMS, Enschede, Netherlands), with infant catheter for patients with less than 75 cm height, and child probe for those between 75 and 150 cm. Briefly, after 4 hours fasting, the polyvinyl 6.4 F probe was calibrated and passed gently through the nostril after topical anesthesia with 10% lidocaine. The initial positioning was determined by Strobel formula 10 and confirmed with a chest radiograph. The exam was performed off medications - proton pump inhibitors, H 2 receptor blockers and prokinetics were stopped, respectively, 7, 5 and 2 days before the exam.

Impedance signs are digitized at 50Hz frequency and stored in a portable device (MMS, Enschede, Netherlands) during the exam duration (24 hours). Meanwhile, a responsible adult recorded symptoms, events, meals, and positioning (upright, recumbent) pressing the appropriated button in the device and filling a specific form. After finishing the exam, data was downloaded and the tracings were manually analyzed by one of the authors (RSM) at least twice. The variables of interest for the study were the number of reflux episodes (acidic, weakly acidic and weakly alkaline), the number of proximal reflux events (up to esophageal upper third, i.e., the first two channels), the acid exposure (% time under pH 4) and the bolus contact time. Normal values were defined according to previously published data (11).

13 C-acetate breath test (13 C-ABT). This test allows indirect evaluation of the gastric emptying of a liquid meal (12). After a minimum fasting of 8 hours, a baseline air sample was collected by mask and a liquid meal (200 mL polymeric formula with 1kcal/mL, protein 2.5 g/ 100 mL, carbohydrates 12 g/ 100 mL and lipids 4.4g/100mL) 6 containing 100 mg of sodium 13 C-acetate (Eurisotop, Paris). Then, further breath samples were collected at 15, 30, 45, 60, 75, 90, 105, 120, 150, 180, 210, and 240 minutes post test meal. The breath samples were then analyzed with the non-dispersive infrared spectrometer IRIS (Wagner Analysen, Bremen, Germany), using the protocol “gastric emptying of liquids”, which provides an estimate for gastric emptying half-time (normal values 49-142 minutes) (12).

- *Statistics*.

Qualitative variables were described by its proportion, whereas continuous variables by their median and range. The primary outcome measure was bolus clearance time. Secondary outcome measures were other MII-pH parameters and the gastric emptying half time. Values at baseline and after 5 months were compared using the paired t-test, and mean difference and its 95% confidence interval (95% CI) were displayed for these comparisons. Spearman`s correlation coefficient were calculated between the variation in the Z score for weight and the variation in the number of weakly acid episodes, and between the variation in the number of weakly acid reflux episodes and the baseline gastric emptying half-time Finally, discordance between reporting of symptoms (such as vomiting) pre and post procedure was tested using McNemar’;s test. A P <0.05 was considered significant in all tests.

III. RESULTS

Baseline symptoms are depicted in table 1. Median (range) Z scores for weight for age and for height for age were, respectively, -3.6 (-5.04 to -1.29) and -2.32 (-4.2 to -0.6). Complications happened in three patients: one major complication (gastrocolic fistula - requiring surgery), and two minor complications (local infections, successfully treated with antibiotics). Only one patient required hospital admission during the first five months after PEG placement (due to gastrocolic fistula). This patient was thereafter diagnosed with a neurologically progressive disease and he was excluded from the study.

At the 5-month follow-up, 6/15 (40%) patients were asymptomatic - the most common symptom was vomiting (7/15, 46.7%), gagging (1/15, 6.7%) and stridor (1/15, 6.7%). Of those seven patients with vomiting at follow-up, four presented the symptom at baseline, and three developed it (P = 1). Weight for age Z-scores increased significantly (mean difference 1.36, 95% CI 0.7 a 2, P < 0.001), but there was no significant change in the height for age z-scores (mean difference 0.32, 95% CI -0.28 a 0.93, P = 0.267).

MII-pH and Gastric emptying. In the first assessment, the median reflux index was 8.2 (2.5 to 48.3), with 10 (62.5%) abnormal results, while the median bolus contact time was 1.5% (0.12 to 8.14), with just 3 (18.8%) abnormal results. The median total number of reflux episodes was 46.5 (5 to 94) at baseline. No patient presented abnormal gastric emptying at baseline, and the variation of the gastric emptying half- time was not significant at five months. However, one patient developed an abnormal gastric emptying half-time (157 min); nonetheless, this patient remained asymptomatic during follow-up.

After PEG, a significant rise in the amount of reflux episodes was observed (18.8 (95% CI 1 to 36.3), P = 0.038), mainly due to an increase in weakly acid reflux episodes (Table 2). There was no correlation between the variation in the Z score for weight and the variation in the number of weakly acid episodes (Spearman's rho -0.11; P = 0.706). Also, there was no correlation between this difference and the baseline gastric emptying half-time (rho = -0.13; P = 0.671). At 1 year follow-up, none of the patients required anti-reflux surgery.

IV. DISCUSSION

MII-pH and gastric emptying for liquids were evaluated at baseline and 5 months after PEG placement in a group of patients with GDD and no increase in the esophageal acid exposure was observed as well as it did not affect the gastric emptying of liquids in neurologically impaired patients with poor nutritional status at baseline. On the other hand, there was a higher number of weakly acidic GER episodes, along with higher weight-for-age z-score. Although nutritional recovery was not a primary outcome in the present study, this is the most relevant clinical outcome for those patients as it results in better quality of life (for patients and caregivers), as well as reduced overall morbidity and health system utilization (13).

The increase in the number of GER episodes, mainly due to greater number of weakly acid GER episodes, was not associated with worsening symptoms and/or increasing feeding difficulties, as demonstrated by the non-significative variation in the number of patients reporting vomiting and the improvement in the nutritional status. Furthermore, no patient required anti-reflux surgery at one year follow-up. Thomson et al. reported non-significative increase in the number of reflux episodes after PEG (14). Another group reported an increase in acid GER episodes after PEG, but without significant increase in the reflux index (15). In adult patients, a higher incidence of aspiration pneumonia is observed after PEG placement, and the inspissated diet has been shown effective in reducing its incidence, particularly among patients with clinical GERD (16). We hypothesize that increasing feeding volume may have increased the number of weakly-acidic GER episodes. Possibly, as patients with moderate to severe peptic esophagitis were not included in the study, the study group tolerated well the mild increase in weakly acidic reflux frequency.

Even though abnormally high esophageal acid exposure was frequent at baseline, PEG placement had no significant impact on the overall acid esophageal exposure. It is important to notice that high reflux indices were observed at baseline in this study, as other authors (17, 18) have reported it. Çaltepe et al. reported large prevalence of abnormal esophageal acid exposure among patients with cerebral palsy, with a mean reflux index of 16% (up to 48.3%), regardless the type of cerebral palsy (spastic, hypotonic or mixed), in a group of 29 subjects (7/29 [24.3%] on tube feeding) (18). Among the factors associated with the high prevalence of reflux among neurologically impaired patients are abnormal gastrointestinal motility with hypotonic lower esophageal sphincter, straining (due to spasticity, frequent cough, seizures) and gastroparesis (13, 19, 20).

On average, the gastric emptying half-time for liquids increased 7.9min at follow-up, a non-significant variation. A recent study has reported an increase of 22 minutes in the gastric emptying half-time (measured with breath test) three months after laparoscopic gastrostomy placement (P = 0.03) in children with GDD (6). Also, the authors reported a significant correlation between the gastric emptying half time and esophageal acid exposure. In the present study, the gastric emptying half time was not correlated with the variation in the number of both acid and weakly acidic reflux episodes, and it was not related to a higher incidence of vomiting after PEG placement. Vomiting might be associated with oral sensitivity, GER, abnormal gastric emptying, food aversion and medications. Kakade et al. have also reported no increase in vomiting after PEG placement (21). Clinically relevant vomiting after PEG may warrant the evaluation of gastroparesis in selected patients, as upper gastrointestinal dysmotility may occur among GDD patients.

The present study presents some important limitations. The sample size was small, but it was appropriated for detecting clinically relevant differences between the two moments (baseline and 5-month follow-up). Furthermore, the follow-up may be regarded as short, as it was only 5 months. Recently, a large historical cohort of patients who underwent percutaneous gastrostomy (326 patients from 1 month to 25 years) has been reviewed (9), 56% with neurological disability. At the time of PEG, 242 (74%) presented GERD, which worsened in a third of them (82) and eventually leading to anti reflux surgery in 48, 42% of them during the first year of follow-up (9). It is possible that the worsening in GER severity may occur after one year in many patients. Finally, the evaluation of the gastric emptying was done with 13 C-ABT, a test that has been validated in children (12) but it has not been extensively used in patients with neurological impairment. The test has the advantage of using a non-radioactive marker and it does not need a gamma camera, being suitable for usage in clinical outpatient facilities. On the other hand, the need for mask collection in all our patients was a potential drawback. Also, as most of our patients could not eat a solid meal, we assessed the gastric emptying for a liquid meal, even though the gastric emptying of a solid meal is more sensitive for early abnormalities (22).

This study shows that PEG placement does not increase the reflux index, nor significantly affects the gastric emptying. Although an increase in weakly acid reflux episodes was detected, it probably reflected the facilitated access to appropriate nutrition, as demonstrated by the weight gain.

CONFLICTS OF INTEREST

Dr Rodrigo Strehl Machado, Dr Ygor Rocha Fernandes, Dr Regis Schander Ferrelli and Dr Silvio Kazuo Ogata have no conflicts of interest or financial ties to disclosure.

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Table 1. Baseline demographic data from 16 study subjects

Variable	N (%)
Gender	
Male	6 (37.5)
Female	10 (62.5)
Age	
1 - 6 yrs	5 (31.3)
7 - 12 yrs	7 (43.7)
13 - 18 yrs	4 (25.0)
Feeding at Baseline	
Oral	7 (43.8)
Nasogastric tube	9 (56.2)
Baseline diagnosis	
Cerebral palsy	11 (68.8)
Aicardi Syndrome	1 (6.2)
Mitochondrial Disease	1 (6.2)
Lafora Disease	1 (6.2)
Undefined	2 (12.4)
Symptoms	
Dysphagia	16 (100)
Vomiting	6 (37.5)
Gagging	2 (12.5)
Food refusal	2 (12.5)
Stridor	1 (6.2)
Asymptomatic **	6 (37.5)

* positive values mean increment over baseline values; ** except for dysphagia; GER: gastroesop reflux

Table 2. Mean difference (95% confidence interval) of reflux parameters and gastric emptying of 15 patients 5 months after PEG placement.

Variable	Mean difference* (95% CI)	*P*
Reflux index		
Total	-1.5 (-8.8 to 5.4)	0.650
Orthostatic	2.6 (-2.2 to 7.5)	0.255
Recumbent	-7 (-20.9 to 7)	0.298
Number of GER events		
Total	18.8 (1 to 36.3)	0.038
Acid	2 (-6.5 to 10.,4)	0.623
Weakly acid	16.7 (6.5 to 27)	0.004
Proximal Reflux		
Proportion of reflux episodes(%)	-6.5 (-14.7 to 1.8)	0.112
Gastric emptying		
Half-time	7.9 min (-9.9 to 25.7)	0.348

* positive values mean increment over baseline values; GER: gastroesophageal reflux

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