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Chronic Feeding Intolerance: Management in Geriatric Palliative Care

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Abstract:

Feeding intolerance, with symptoms of anorexia, esophageal reflux and pulmonary aspiration, is caused either by an anatomic obstruction of the stomach or jejunum, or by a neuromuscular dysfunction of the upper gastrointestinal tract. The materialization of feeding intolerance is an increased gastric residual volume. However, feeding intolerance expands beyond impaired gastric emptying; so jejunal feeding does not always eliminate the risk of aspiration of gastric content. Proper diagnosis of feeding intolerance and its mechanism is made by endoscopy, radio-scintigraphy for assessment of the gastric transit time and/or measurement of the gastric residual volume. Studies on feeding intolerance come from critical care medicine; few longitudinal studies have been published in the internal medicine and palliative medicine literature. Three case histories from our institution illustrate a spectrum of challenges in the management of chronic feeding intolerance. Remarkable are the following observations: a quick gastric transit by using a small volume of gastrographin does not exclude feeding intolerance, neurogenic feeding intolerance may be transient, and recovery of gastric emptying after pyloroplasty may be prolonged. Patience and perseveration may be worth.

Key words: Gastric Emptying, Gastrointestinal Diseases, Jejunum, Palliative Medicine, Stomach.

Introduction

Gastric emptying is often impaired during acute illness, and more so in mechanically ventilated patients in critical condition. Gastroparesis or 'delayed gastric emptying', is one of the well-known manifestations of diabetic autonomic neuropathy; it may occur in hypothyroid or hypoadrenal states, polymyositis, amyloidosis, brain stem tumors, spinal cord injury, paraneoplastic autonomic neuromyopathy, but more often as an adverse effect of medications, following viral illness, or under stressful situations [1-3].

Impaired gastric emptying and the broad spectrum of gastro-intestinal motility disorders are challenging for appropriate feeding the patient. The patient might not tolerate enteral feeding, either orally or by nasogastric or gastrostomy tube, due to nausea, vomiting, reflux, abdominal pain

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and pulmonary aspirations. Facing this problem the label 'feeding intolerance' (FI) is used; yet, there is no consensus on its definition [4]. With the aid of ultrasound, CT or endoscopy a mechanical obstruction is distinguished from the functional FI. The latter diagnosis is established by scintigraphic assessment of the gastric emptying time or the surrogate (13)C-octanoate breath test. In enteral fed patients assessment of the gastric residual volume (GRV) may be an acceptable substitute for this purpose [5,6].

In the recent literature, indications for withholding enteral feeding and initiating TPN were three consecutive GRV measurements >500 mL within a 24 hours [6] and, at variance, GRV >250 mL [7]. In practice is important to keep in mind that caloric and hyperosmotic liquids empty the stomach slower than noncaloric liquids and at an overall linear rate in response to the inhibitory feedback from small intestinal receptors. Volume and gravity are important driving forces in gastric emptying of noncaloric isotonic liquids which empty in a nonlinear pattern and are affected by posture [8,9]. The current first line treatment for FI is based on the prokinetic agents metoclopramide and erythromycin, alone or in combination, and domperidone; however, their use is limited by the risk of adverse effects and decreased efficiency over a few days [1].

Case Reports

Case 1

An 81-year-old woman was referred for palliative care. She had suffered for several years due to paroxysms of excruciating pain in the lips, gums and cheek typical for trigeminal neuralgia. Magnetic resonance imaging revealed compression of the trigeminal nerve root by the superior cerebellar artery. Therapy with carbamazepine, lamotrigen and phenytoin was of no avail, so microvascular decompression surgery was performed to alleviate neuralgia. The procedure was complicated by intracerebral bleeding. Decompression ventriculostomy was not followed by recovery of consciousness and the patient remained in unaware wakefulness state. She was weaned from mechanical ventilation. Laparoscopic gastrostomy was performed, but enteral feeding resulted in repeated pulmonary aspirations. In diagnosing functional FI a jejunostomy tube was placed, by which feeding was uneventful. The gastrostomy tube was left in place. Ten weeks after neurosurgery the patient was transferred to our institution for long-term palliative care. On physical examination the findings were within the normal range for an elderly person, except for unresponsiveness. The patient was breathing spontaneously through the tracheostomy. A gastrostomy tube was in attendance secured in place, but the jejunal feeding tube has been pulled out during the transfer. The repositioning of the tube under radiologic imaging failed. Before considering another invasive procedure feeding tolerance was assessed based on a modified protocol: 150 mL water was instilled through the gastrostomy tube; the gastric content aspirated 30 minutes later showed nil fluid (GRV = 0). Continuous drip feeding was instituted through the gastrostomy, and the allocation was gradually increased to 1400 Kcal/day comprising feeding formula (Jevity®) and water. Enteral feeding has been provided without complications till present (May 2016). On regular basis the patient receives phenytoin 300 mg/day, lansoprazole 60 mg/day and lactulose.

C*omment:* FI occurred in the setting of a critical cerebral event. FI remitted spontaneously within two months, highlighting the unpredictable course of functional FI.

Case 2

An 84-year-old woman was admitted for hospice care with the diagnosis of terminal stage carcinoma.

Remarkable in the patient's medical history were bipolar disorder on long-term oral treatment by levomeprazine 18.75 mg/day, olanzapine 2.5 mg/day and lorazepam 1 mg/day. Cardiovascular disease, now in remission, included arterial hypertension, ischemic heart disease, and left heart failure with moderately reduced left ventricular ejection fraction. In 2013, left breast carcinoma estrogen receptor positive had been diagnosed and managed by mastectomy and radio-chemo-hormonal therapy. In 2014 the treatment had been discontinued because of poor patient compliance. During the subsequent 8 months the patient has lost about 20 kg in weight; abdominal pain and repeated vomiting had occurred. Gastroscopy in December 2014 showed diffuse infiltration of the gastric mucosa by tumor, narrowing of the antrum and severe pyloric stenosis; balloon pyloroplasty was performed. Biopsy samples from the gastric mucosa showed lobular carcinoma of mammary origin estrogen receptor positive. In May 2015, the patient has been readmitted to hospital because of recurrence of abdominal discomfort, early satiety and frequent vomiting. The decision was taken not to repeat pyloroplasty; stenting the pylorus was thought not to be feasible. Surgical jejunostomy was proposed for palliation but the patient refused to undergo the procedure. Eventually, she was referred for hospice care with the diagnosis "terminal stage cancer". Treatment was continued with fulvestrant (third-generation nonsteroidal aromatase inhibitor) 500 mg intramuscular 1/28 days. On admission the patient appeared in poor physical condition and poor mood. The vital signs were within the normal range. Wasting and sarcopenia were prominent. There was no palpable abdominal mass. Management was started with metoclopramide 10 x 3 before meals and transdermal fentanyl 12.5 µg/hour. A friendly and supporting patient/caregiver relationship was established and small volume feeding was started. The usual medications (listed above) were continued. Because of the poor response to metoclopramide the drug was replaced with tablet ondansetron 4 mg thrice daily. Over a period of 2 weeks acceptable tolerance to food was observed. Nausea and vomiting diminished. The patient's general condition has gradually improved. Within a few months the patient was able to sit, to walk with a rolling walker 20 - 30 meters, and participate in social activities. One year after referral to our institution with the diagnosis of end-stage carcinoma she is surprisingly well feeling and free of abdominal complaints; she gained 7 kg in lean body weight. She has mild normocytic anemia (hemoglobin 11 g/dL); the serum albumin increased to 2.9 g/dL. However, trials to discontinue ondasetron treatment resulted in recurrence of vomiting.

C*omment:* Gastric outlet stenosis by tumor was overcome by pyloroplasty, but functional FI remained. The latter improved under the combined effects of behavioral therapy, ondansetron, and nonsteroidal aromatase inhibitor.

Case 3

An 83-year-old woman was admitted for hospice care with the diagnosis of carcinoma pancreas, gastric outlet obstruction and FI. Remarkable in the patient history were type 2 diabetes mellitus, arterial hypertension and depressive disorder. Medications at the time of admission included transdermal fentanyl 50 µg/hour, enoxaparin 40 mg subcutaneous, and hydration with 0.9% saline. To assess the GRV a nasogastric tube was inserted in the morning in fasting state. Aspiration of the gastric content yielded 400 mL of fluid containing remnants of solid food ingested the day before. After emptying the stomach 200 mL water were slowly infused through the nasogastric tube. One hour later the gastric content was emptied: the GRV was 200 mL, equal to the instilled. Thereupon enteral feeding was discontinued, hydration with saline was provided, and treatment with intravenous metoclopramide 10 mg x 3/day was started. Two

days later a trial of small volume enteral feeding was commenced: through the nasogastric tube 100 mL of feeding formula Osmolite was provided followed by 100 mL water by slow drip. Two hours later the GRV was 200 mL. Veto was ordered to enteral feeding. The following morning in the fasting state aspiration of the gastric content yielded 600 mL fluid containing remnants of solid food, showing that the recommendation was not respected. On the 5th day on intravenous metoclopramide treatment another trial confirmed that FI persisted: 100 mL Osmolite were administered by slow drip through the nasogastric tube followed by 100 mL water; three 3 hours later the GRV was 300 mL. On insistence of the family the patient was referred to an acute care hospital for supplementary assessment. The examination consisted of diatrizoate meglumine/ diatrizoate sodium solution (Gastrographin®) follow-through. On imaging there was a slightly enlarged stomach that quickly emptied in the duodenum; there was no reflux. This examination excluded the presence of a mechanical obstruction of the stomach and jejunum. A diagnosis of 'transient gastroparesis' was advocated, whereupon the patient and proxies insisted on reinstitution of oral feeding. This provoked repeated vomiting, pulmonary aspiration and the patient died a few days later.

Comment: Though attributed to mechanical obstruction by carcinoma of the head of pancreas, FI in this case was functional. It is remarkable that fast emptying the radiocontrast agent from the stomach and duodenum did not exclude FI for water and nutrients.

Discussion

In all three patients FI was functional in nature, either alone or added on an anatomic obstruction of the gastro-duodenal tract. Functional FI is a neuromuscular disorder involving different pathophysiologic mechanisms. Abnormalities in fundic tone, antroduodenal discoordination, weak antral pump, gastric dysrhythmias, and abnormal duodenal feedback are contributing to delays in gastric emptying. Moreover, the intestinal motility is also often disturbed. The triggers of functional FI are varied: the most frequently met are visceral pain, sepsis, toxins, medications, increased intracranial pressure and other disorders of the central nervous system [1]. Functional FI may coexist with an organic disease causing obstruction from inside the gastrointestinal tract or compression from outside. FI may be acute and rapidly remitting or may last for long periods of time, hindering oral administration of medications and oral nutrition [1-3]. In association with cancer functional FI may appear as a paraneoplastic syndrome, at a distance from the tumor and elicited through humoral mediators [10]. Cancer involving the stomach or duodenum, yet not occlusive, may trigger a dysfunctional peristalsis that causes FI. The latter is exemplified in case 2 in this presentation, in which successful pyloroplasty did not allow for oral feeding, and in case 3, in which quick gastric passage of radiocontrast agent contrasted with the retention in the stomach of solids, liquids and even water. Gastroparesis associated with pancreatic cancer is a well described phenomenon. Up to one-half of patients with advanced pancreatic cancer experience slowed gastric emptying in the absence of an anatomic obstruction. Pancreatic cancer may affect gut motility by direct infiltration of autonomic nerve fibers by tumoral tissue and by altering neurohormonal messengers within the bowel [11].

Management of chronic FI may be challenging. Present knowledge pertaining to FI mainly comes from intensive care medicine and acute hospital care [12]. A search of the literature revealed few data concerning the longterm course of FI in palliative medicine [13]. In practice, it is important to distinguish between obstructive and functional FI, and a combination of both. Some obstructions can be surmounted by stenting or can

be circumvented surgically. Functional FI as well as a functional element of obstructive FI can be palliated. There is no standard evidence-based treatment for functional FI [13].

At bedside, the simplest measures should be implemented first. Unnecessary medications should be discontinued, in particular those which may affect the gastric and intestinal motility. The patient should be positioned in Fowler's or semi-Fowler's position before feeding, during feeding and for one to two hours after feeding. This promotes gastric emptying. Left-sided lying during feeding, which alters emptying of the stomach into the duodenum, should be avoided. Less feeding formula or longer feeding times (controlling the feeding time) may reduce the risk of aspiration. Constipation, a cause of functional FI, should be treated. Pharmacologic treatment of chronic FI with prokinetic agents metoclopramide, domperidone and erythromycin is often disappointing [14]. Moreover, the risks of neurological adverse effects of metoclopramide, such as extrapyramidal disorders and tardive dyskinesia, outweigh the benefits in long term or high dose treatment [3]. Metoclopramide may be recommended for 5 days at maximum dose of 30 mg/24 hours, however, in palliative care it is sometimes used for longer durations and in higher doses. Domperidone due to small increased risk of serious cardiac side effects should be used at the lowest effective dose for the shortest possible duration. The maximum treatment duration for domperidone is one week. Domperidone is contra-indicated in conditions where cardiac conduction is, or could be, impaired, underlying cardiac disease, concomitant prescription of drugs that prolong the QTc interval, potent CYP3A4 inhibitors, or severe hepatic impairment [3]. There are promising techniques for palliation of impaired gastric emptying, either delivered endoscopically or via minimal invasive surgery [14,15]. Their utility may be narrowed by disorganized peristalsis and faulty nursing. Eventually, indications for withholding enteral feeding and initiating TPN are consecutive GRV measurements > 500 mL within a period of 24 hours [6] and, at variance, GRV >250 mL [7].

Conclusion

The three case histories presented illustrate the variety of etiologies of chronic FI, either pure functional FI or mixed obstructive and functional. The following observations deserve emphasis: First, in the presence of an anatomical obstruction, an associated functional element may be present and may be reversible. Second, the quick passage of gastrographin does not rule out gastroparesis. Third, recovery of gastric emptying after pyloroplasty can take several months. Fourth, gastroparesis, whether idiopathic or neurogenic, may be transient. Patience and perseverance can be rewarding.

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