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Short Article

Diabetic Gastroparesis: Diagnosis, Management, and Future Perspectives

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Abstract

Gastroparesis, a complication of diabetes, is characterized by delayed gastric emptying without obstruction. It arises from chronic hyperglycemia-induced damage to the autonomic and enteric nervous systems, manifesting primarily as nausea, vomiting, early satiety, and bloating. This condition severely impacts quality of life and glycemic control, increasing the risk of further diabetes-related complications. Early diagnosis and treatment are essential, involving stringent glycemic control, lifestyle changes, pharmacological therapy, and sometimes surgical interventions. Diagnostic approaches include ruling out other causes, followed by tests like scintigraphy, radiological examination, and breath tests. Treatment begins with dietary modifications and, if necessary, progresses to enteral or parenteral nutrition. Glycemic management is crucial, with specific medications either recommended or contraindicated. Pharmacological treatments include metoclopramide and domperidone, though both have significant side effects. Emerging therapies involve ghrelin and motilin agonists, and antidepressants like mirtazapine. Gastric electrical stimulation, endoscopic, and surgical procedures offer additional treatment avenues for severe cases. Effective management of gastroparesis can substantially improve patient outcomes and long-term diabetes management.

Keywords

Gastroparesis, diabetes mellitus, glycemic control, diet, scintigraphy, NaSSAs, metoclopramide

Introduction

Gastroparesis is one of the complications of diabetes, defined as a disorder of gastric emptying without any accompanying obstruction in stomach [1]. This condition stems from consistently high blood sugar levels, which harm the autonomic and enteric nervous systems, resulting in slowed gastric emptying [4]. The symptoms of this condition are non-specific but primarily include nausea, vomiting, early satiety, and bloating [2]. Individuals suffering from diabetic gastroparesis experience a reduced quality of life and significantly poorer glycemic control despite ongoing treatment, which in turn raises the risk of developing other diabetes-related complications in the future. Thus, early diagnosis and appropriate treatment of gastroparesis are crucial [1,2,3]. Effective management involves strict glycemic control, lifestyle modifications, pharmacological treatment, and sometimes surgical intervention [2,5].

Diagnosis

The symptoms of gastroparesis are nonspecific and can appear in many conditions such as gastroesophageal reflux disease, peptic ulcer disease, and gastric cancer. Furthermore, typical signs of DG, including delayed gastric emptying and episodes of hypoglycemia, are present in 50% of patients [6]. Therefore, diagnostic testing should begin with ruling out other potential causes of the symptoms. Also, preferably endoscopically, gastric outlet obstruction should be excluded. Subsequently, the diagnostic process should focus on documenting delayed gastric emptying [7]. Before this evaluation, several general principles should be followed, including abstaining from tests in cases of severe hyperglycemia (above 275 mg/dl). Additionally, 48-72 hours before the examination, medications that may affect gastric emptying should be discontinued, both those that inhibit it (e.g., opioids, GLP-1 analogs, drugs used in Parkinson's disease) and those that accelerate it (e.g., erythromycin, metoclopramide) [8].

The gold standard is scintigraphy with evaluation of food passage using technetium-99 isotope. In this examination, the rate of gastric emptying of a standardized meal containing the isotope is assessed. The meal consists of two soft-boiled eggs, one slice of whole-grain bread, and a glass of skimmed milk, totaling 296 kcal [9]. The normal time should not exceed 4 hours. A result indicating delayed gastric emptying is obtained when >23% retention of food is demonstrated after 4 hours in males and >24% in females [10].

Radiological examination of the upper gastrointestinal tract using barium is also utilized – inactive symptoms of gastroparesis include slow peristaltic activity and gastric dilation [6]. Other available tests include ultrasound examination, which assesses changes in the antral segment of the stomach after consuming liquid food, manometry, characterized by the absence of proper peristalsis between meals and reduced contraction strength after a meal, and capsule endoscopy, determining gastric emptying based on pH changes from acidic (present in the stomach) to alkaline pH in the duodenum [11,12]. Electrogastrography, allowing differentiation between neuropathy and myopathy in evaluating gastrointestinal motility, is primarily used as a research tool. Dominant electrical activities from other organs combined with low-amplitude gastric waves, along with a lack of standardization and low specificity, significantly limit the usefulness of this method in clinical practice [7,13,14].

There have been many discussions about using breath tests in diagnosing gastroparesis, where the assessment of labelled CO_2 content in exhaled air is related to the rate of gastric emptying. In this test, the patient consumes a meal containing acetic acid or Spirulina platensis algae with the 13-C isotope, which, after absorption in the intestines and catabolism in the liver, is excreted as labelled CO_2 in exhaled air. Currently, this test is approved by the FDA, with sensitivity and specificity of 89% and 90% respectively [7]. However, its use is questionable in cases of concurrent liver, pancreatic, and lung diseases, as well as in cases of short bowel syndrome or severe gastroparesis [6].

An interesting aspect of the diagnostic process of gastroparesis is the role of gastroscopy. In addition to its previously mentioned application of excluding gastric outlet obstruction, upper gastrointestinal endoscopy may reveal retained food despite overnight fasting, and even the presence of gastric bezoars [15].

Treatment

DG can lead to compromised food intake, insufficient calorie intake, and deficiencies in vitamins, carbohydrates, proteins, and minerals [16]. Affected patients experience impaired absorption of various nutrients including vitamin B12, vitamin C, folic acid, thiamine, niacin, magnesium, phosphorus, and zinc [17]. Management in affected individuals is typically gradual. The treatment of gastroparesis begins with dietary modifications, in this case, implementing a small-particle (<2 mm), low-fat, and low-fiber, while ensuring adequate hydration [18].

The choice of nutritional therapy administration route primarily depends on the severity of the disease. In mild gastroparesis, oral nutrition is sufficient, whereas in severe cases, enteral or parenteral nutrition may be required. Indications for enteral nutrition include unintentional loss of 10% or more body weight over a period of 3-6 months and/or multiple hospitalizations due to treatment-resistant symptoms [19]. One of the most effective methods of enteral nutrition, capable of alleviating symptoms and reducing hospitalizations, is the placement of a jejunal tube (J-tube), bypassing the affected stomach [20]. Enteral nutrition, in combination with parenteral therapy, is always the preferred treatment method due to low cost, low risk of complications, and ease of nutrient delivery [19].

Undoubtedly, glycemic control is a crucial aspect of therapy. Acute hyperglycemia slows gastric emptying, leading to impaired nutrient absorption in both those with type 1 diabetes and healthy individuals [21]. A similar mechanism has been observed in patients with type 2 diabetes, where acute hyperglycemia also played a significant role in prolonging gastric emptying [22]. It is worth noting that daily fluctuations in glycemic levels, not induced by therapeutic actions, have minimal or no effect on gastric emptying [23]. The impact of both chronic hyperglycemia and improved glycemic control in individuals with chronic hyperglycemia on gastric emptying remains unclear [24,25,26]. Nevertheless, in the case of DG, both short-term and long-term glycemic control are effective therapeutic methods, improving long-term diabetes management [19].

Some medications used in glycemic control can prolong gastric emptying and should not be used in individuals with gastroparesis. Among such medications are glucagon-like peptide-1 (GLP-1) analogs [27,28]. Amylin analogs (e.g., pramlintide) may also exacerbate symptoms of gastroparesis [29]. On the other hand, dipeptidyl peptidase-4 (DPP-4) inhibitors do not have a negative impact on gastric emptying and thus are not contraindicated in patients with gastroparesis [30].

Both nutritional therapy and glycemic control alone are rarely sufficient solutions for controlling symptoms associated with DG. For a large group of individuals, targeted pharmacological or surgical treatment is required [31].

Metoclopramide, an antagonist of the dopamine receptor, is used in pharmacological treatment of gastroparesis. Its action is based on accelerating gastric emptying and alleviating symptoms of the disease [32]. However, there is a lack of evidence for its effectiveness in long-term treatment [33]. Additionally, chronic use (>12 weeks) of metoclopramide is associated with an increased risk of adverse effects on the central nervous system, such as drowsiness, fatigue, akathisia, anxiety, depression, or tardive dyskinesia [34,35]. A viable alternative comes in the form of domperidone. Domperidone is another prokinetic agent used in the treatment of DG. Its action is associated with similar efficacy and fewer adverse effects on the central nervous system compared to metoclopramide, as it penetrates the blood-brain barrier to a minimal extent [34,36]. However, its use carries an increased risk of cardiac arrhythmias and sudden cardiac death by 70%, causing its unavailability in many countries [37].

Some drugs potentially applicable in patients with gastroparesis are currently under clinical investigation. Ghrelin and motilin, along with their receptors, are associated with gastric emptying acceleration. Administering agonists of these hormones may bring benefits to patients. These include, among others, relamorelin and erythromycin [38,39]. Clinical trials are currently underway to assess their efficacy and safety [40,41,42]. Noradrenergic and specific serotonergic antidepressants (NaSSAs), such as mirtazapine, also show promising results in alleviating nausea and vomiting and may be utilized in selected patients in the future [43,44].

Another available and currently used solution is gastric electrical stimulation [GES) with high-frequency and low-energy current, which significantly reduces the frequency of vomiting and nausea in patients, especially when gastroparesis occurs in the context of diabetes [45]. Unfortunately, this method has not been shown to affect gastric emptying time [46].

Selected patients also undergo endoscopic and surgical procedures. One of them is injecting botulinum toxin in the proximity of the pyloric sphincter, which allows to alleviate nausea and vomiting in more than half of the patients [47,48]. In cases of severe gastroparesis, endoscopic pyloromyotomy yields positive results: it accelerates gastric emptying and alleviates symptoms of the disease [49].

Conclusions

Diabetic gastroparesis (DG) presents significant diagnostic and therapeutic challenges. Current diagnostic methods, while effective, are often cumbersome, underscoring the need for more accessible and precise tools. Effective management should emphasize dietary modifications and strict glycemic control, with careful selection of medications to avoid exacerbating symptoms.

Emerging treatments like ghrelin and motilin agonists show promise, but their efficacy needs further validation. Gastric electrical stimulation and surgical interventions offer symptom relief but require refinement to improve overall outcomes.

Future research should aim to better understand DG's pathophysiology, particularly in asymptomatic patients, and develop innovative diagnostic and therapeutic approaches. A multidisciplinary strategy is essential to enhance patient outcomes and quality of life in DG management.

Disclosure

Author's Contribution:

Conceptualization, MD, OD and PG; methodology, OD and DM; check, DM; formal analysis, MD, JG and AS; resources, OD, PG, DM and JM; data curation, MD; writing - rough preparation, MD, OD, PG and DM; writing - review and editing, MD, OD, PG, DM, JG, JM and AS; visualization, PG and JM; supervision, MD; project administration, MD; All authors have read and agreed with the published version of the manuscript.

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