

Nutritional therapy for the management of diabetic gastroparesis: clinical review

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Abstract: Diabetic gastroparesis (DGP), or slow emptying of the stomach, is a well-established complication of diabetes mellitus and is typically considered to occur in individuals with long-standing type 1 and type 2 diabetes mellitus. Clinical consequences of DGP include induction of gastrointestinal (GI) symptoms (early satiety, abdominal distension, reflux, stomach spasm, postprandial nausea, vomiting), alteration in drug absorption, and destabilization of glycemic control (due to mismatched postprandial glycemic and insulin peaks). Effective nutritional management not only helps in alleviating the symptoms, but also in facilitating better glycemic control. Although there have been no evidence-based guidelines pertaining to the nutrition care process of the DGP, the current dietary recommendations are based on expert opinions or observational studies. The dietary management of gastroparesis needs to be tailored according to the severity of malnutrition and kind of upper GI symptom by changing the volume, consistency, frequency, fiber, fat, and carbohydrates in the meal. Small frequent meals, using more liquid calories, reducing high fat or high fiber, consuming bezoar forming foods, and adjusting meal carbohydrates based on medications or insulin helps in improving the upper GI symptoms and glycemic control. Enteral nutrition can be an option for patients who fail to stabilize their weight loss, or for those who cannot gain weight with oral feedings, while total parenteral nutrition is rarely necessary for the patient with gastroparesis.

Keywords: diabetic gastroparesis, delayed gastric emptying, diabetes mellitus, bezoar, GI symptoms, glycemic control

Introduction

Gastroparesis is a syndrome characterized by delayed gastric emptying in the absence of mechanical obstruction of the stomach. Disturbances in gastrointestinal motility with associated symptoms have long been recognized as a complication of diabetes mellitus, and were reported for the first time in 1945 by Rundles.¹ Diabetic gastroparesis (DGP) is a well-established complication of diabetes mellitus and is typically considered to occur in those individuals with long-standing type 1 and type 2 diabetes mellitus. Longitudinal studies suggest that delayed gastric emptying is present in 25%–55% of individuals with type 1 diabetes mellitus and 30% of type 2 diabetes mellitus patients.^{2,3} Gastric emptying requires interactions between smooth muscle, enteric and extrinsic autonomic nerves, and specialized pacemaker cells (the interstitial cells of Cajal). Several abnormalities in diabetes might result in gastric motor dysfunction including autonomic neuropathy, enteric neuropathy involving excitatory and inhibitory nerves, abnormalities of the interstitial cells of Cajal, acute fluctuations in blood glucose, incretin-based medications, and psychosomatic factors.⁴

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Diabetes mellitus is associated with an increased prevalence of symptoms in the upper and lower gastrointestinal tract. Upper gastrointestinal symptoms associated with DGP are early satiety, abdominal distension, reflux, stomach spasm, erratic glycemic control, decreased appetite, postprandial nausea, vomiting, and sometimes weight loss.⁵ The relationship between abnormal gastric emptying and abdominal symptoms is an area of considerable discussion. Gastric retention might be asymptomatic,⁶ and it may possibly be a result of the afferent dysfunction associated with vagal denervation.⁷ Moreover, in addition to delayed gastric emptying, other mechanisms (eg, impaired gastric accommodation, visceral hypersensitivity) also contribute to upper gastrointestinal (GI) symptoms. However, these findings should not imply that delayed gastric emptying is not relevant to symptom generation, or that it is not useful to document delayed gastric emptying in patients with upper GI symptoms.⁸ To the contrary, fullness, upper abdominal pain, and reduced hunger correlate better with delayed gastric emptying than with nausea and vomiting.⁹

Clinical consequences of DGP include induction of gastrointestinal symptoms, alteration in drug absorption, and destabilization of glycemic control.¹⁰ Changes in gastric emptying may affect postprandial blood glucose concentrations, which can contribute to poor glycemic control because of unpredictable delivery of food into the duodenum.¹¹ Impaired gastric emptying with continued administration of exogenous insulin may produce hypoglycemia.¹² Conversely, acceleration of emptying has been reported to cause hyperglycemia. Problems with blood glucose control may be the first indication that a diabetic patient is developing DGP.^{13,14} Patients with type 1 or 2 diabetes mellitus who present with the classic symptoms of gastroparesis and demonstrated documented delay in gastric emptying are more likely to have cardiovascular disease, hypertension, and retinopathy, suggesting that the underlying complication might be related to microangiopathies or macroangiopathies, which are known complications of poor diabetic control.¹⁵

DGP is diagnosed by demonstrating delayed gastric emptying in a symptomatic patient after the exclusion of other potential etiologies of symptoms followed by exclusion of mechanical obstruction using abdominal radiography, computed tomography, and magnetic resonance imaging. An upper endoscopy is necessary to exclude the presence of stricture, mass, or ulcer. Laboratory tests are conducted to exclude infectious, metabolic, and immunologic causes of upper GI symptoms.^{16,17} After the exclusion of the above

factors, DGP is diagnosed by demonstrating delayed gastric emptying through scintigraphy, breath tests, ultrasound, manometry, or electrogastrography.¹⁸ Once established, DGP tends to persist, despite amelioration of glycemic control.¹⁹ Talley et al have reported that DGP impairs mean quality of life independently of other comorbid factors such as age, tobacco and/or alcohol use, and type of diabetes mellitus.¹⁵

The increasing availability of noninvasive tools to measure gastric emptying has not only increased our ability to diagnose the disease, but it has also uncovered significant gaps in our understanding of the pathophysiology of the disease and effectiveness of current therapies.²⁰

The goal of managing patients with DGP is to maintain adequate glycemic control; reduce the upper GI symptoms; and to correct fluid, electrolyte, and nutritional deficiencies and provide medical management to improve gastric emptying.²⁰ In addition, patient education and explanation of the condition is an integral part of treatment.

Nutritional support is often overlooked in patients with DGP, and there is a lack of randomized controlled trials assessing the effect of nutritional interventions on outcomes. Dietary modifications play a vital role in reducing symptoms and improving glycemic control. There have been no evidence-based guidelines pertaining to the nutrition care process of gastroparesis patients; however, many of the current dietary and nutrition recommendations are based on expert opinions or observational studies.²¹ In the present clinical review, we will focus on the nutritional interventions for the management of diabetic gastroparesis.

The nutritional management of patients diagnosed with DGP can be individualized based on the severity of the condition. There are three main steps in nutritional management, which include:

1. Conducting a nutritional assessment of the patient;
2. Selecting an intervention based on the patient's nutritional status and upper GI symptoms;
3. Individualizing the selected dietary intervention based on the patient's dietary habits.

The first step towards nutritional therapy is the nutritional assessment of the patient in order to help identify those who need aggressive nutritional support early on versus those who might benefit from some initial adjustments in oral food selections.

Unintentional weight loss over time is one of the most important parameters to assess regardless of the patient's overall appearance. The guidelines for the identification of patients at nutritional risk are:²²

1. A body mass index $< 20 \text{ kg/m}^2$.
2. Unintentional weight loss of 5%–10% over 3–6 months.

A patient with diabetes mellitus who presents with vomiting, diarrhea, and poor glucose control may have a falsely low actual weight due to dehydration. Failure to use the patient's euvoletic actual weight might overestimate the amount of weight loss over time, thereby suggesting significant malnutrition rather than identifying the fact that the patient is merely dehydrated. It is also imperative to remember that those patients who are clinically overweight or obese, yet have unintentionally lost a significant amount of weight over a short time interval, may carry the same risk profile as a chronically undernourished patient.

If a patient with diabetes has a declining target weight and complains of early satiety, especially in the morning, gastroparesis could be suspected. If unintentional weight loss has occurred in any patient with gastroparesis, it is important for the clinician and patient to set a goal weight. If the patient falls below the goal weight or fails to achieve an agreed upon weight, nutrition support should be seriously considered.²³

When obtaining a diet history, the dietitian should be sure to evaluate for early satiety; changes in appetite; problems with nausea, vomiting, or diarrhea; problems with chewing and/or swallowing, which can affect a patient's ability to ingest certain foods; the patient's typical daily dietary intake; the use of supplemental nutrition (oral, enteral, or parenteral); food intolerances or allergies; use of supplements such as vitamins, minerals, herbs, or protein powders; and use of stool bulking agents or laxatives. The nutritional intervention is selected based on the severity of the GI symptoms (mild, moderate, or severe) and individualized depending on the patient's eating habits.

Laboratory values are a useful adjunct in the initial evaluation and continued management of the patient with gastroparesis (ie, glucose [fasting], glycated hemoglobin, Ferritin, vitamin B12, and 25-OH vitamin D), particularly among patients with longstanding gastroparesis.²³

Although there are many factors that can theoretically slow gastric emptying, there have been no controlled clinical trials conducted among patients with DGP. However, dietitians may successfully manipulate these factors in an effort to improve gastric emptying after the nutritional assessment. Altering one or more of them in combination with prokinetic therapy may help to restore nutritional status. A trial of evaluating one factor at a time helps to identify what is most important to the individual patient in terms of relieving symptoms.^{21,23} The suggested dietary options need to be individualized based on the patient's eating patterns and preferences. Frequent follow-up with regular intervention not only helps in improving the

patient's nutritional status, but also improves glycemic control. The selection of the nutritional intervention is based on the factors affecting gastric emptying as discussed in Table 1.

Factors affecting gastric emptying Volume

Large meals not only slow gastric emptying, but can decrease the lower esophageal sphincter pressure, which enhances reflux of gastric contents. Small frequent meals (six to eight meals or more, if necessary) may enable patients to tolerate food and achieve adequate calorie intake.

Liquids versus solids

If decreasing the meal size and increasing the frequency of the meals does not work, the next step is to switch over to more liquid-based calories. Several cross-sectional studies report that gastric emptying of solid and/or nutrient liquid meals is delayed in about 30%–50% of randomly selected patients with long-standing type 1 or 2 diabetes.^{24,25} Liquids empty by gravity and do not require antral contraction to leave the stomach; therefore liquids, even those that are highly caloric, will empty from the stomach. Pureed foods become liquefied after mixing with saliva and gastric secretions, and may be more easily tolerated than solid foods. A trial diet consisting primarily of pureed food or liquids can be designed to meet a patient's nutritional requirements. Transitioning to more liquid calories towards the end of the day may be useful in alleviating a patient's symptoms while continuing to provide appropriate nutrition. Patient positioning is also important given that supine position emptying is most likely delayed due to both the antigravity effects of lying down and duodenal compression by the spine. It is advisable that patients sit up after meals for ~1 hour and elevate the head of the bed 6–8 inches to prevent reflux when sleeping.²⁶

Fiber

Dietary fiber (found in many fruits, vegetables, beans, and grains) may act to slow stomach emptying in some patients who may feel early satiety. Patients with gastroparesis are prone to bezoar formation (an indigestible concretion of foods), and thus low-fiber foods are recommended. Some of the bezoar formation foods are berries, apple, sauerkraut, fig, coconut, legumes, oranges, and potato peels; however, there have been no controlled trials that have been conducted to date (Tables 2 and 3).²⁶

Although the avoidance of high fiber foods is recommended in patients with gastroparesis, what is not known is the type of fiber and the quantity of fiber that should be

withheld. Over-the-counter fiber or bulking laxatives (acacia fiber [Benefiber®; Novartis Consumer Health, Inc, Parsippany, NJ]; isabgol [Citrucel®; GlaxoSmithKline Inc, Middlesex, UK]; FiberChoice®; Prestige Brands Inc, Irvington, NY) should probably be discontinued.

Fat

Fat is a potent inhibitor of gastric emptying, and fatty foods take a longer time to digest. Many patients are not affected by dietary fat if it is present in liquid form (eg, whole milk, milkshakes, nutritional supplements, etc). Approximately 25%–30% of calories can be provided from unsaturated fats. Small meals at frequent intervals that consist of low-fat and complex carbohydrates are advised, and sometimes high-calorie liquid supplements may be required to fulfill daily calorie requirements.²⁷ Alternatives to saturated fat and trans fat sources needs to be encouraged.

Hyperglycemia

Hyperglycemia (glucose > 200 mg/dL) is known to worsen the symptoms of DGP. In the patient with diabetes mellitus, it is often unclear whether the gastroparesis leads

to poor glucose control or vice versa. Wide fluctuations in blood glucose (hyperglycemia and postprandial hypoglycemia) impair gastric emptying more than a continuous glucose elevation; hence, subsequent monitoring of the glycated hemoglobin assures optimal glycemic control. Hyperglycemia is a catabolic process resulting in unintentional weight loss, and this could ultimately thwart the efforts of nutrition repletion.^{3,28}

Medications

Medications may cause delayed gastric emptying, mimicking the symptoms of gastroparesis. Delayed gastric emptying is common with narcotic pain medications, calcium channel blockers, certain antidepressants, aluminum containing antacids, glucagon, and glucagon-like peptide-1 analogs.²⁹ The patient's medication list should be reviewed regularly, and health care professionals should avoid prescribing drugs that aggravate gastroparesis.

Improving glycemic control

The most important goal for the nutritional intervention of DGP is to achieve or maintain optimal glucose control and to

Table 1 Summary of nutritional interventions for diabetic gastroparesis

1. Decrease volume of meals
 - Eat smaller, more frequent meals
2. Prefer liquid vs solid meals
 - Chew the food thoroughly and take 20–30 minutes to finish your meal
 - Try solid meals in the morning, switch to semi-liquid and liquid meals over the course of the day
 - Any food can be blended with water, vegetable juice, or broth to make a puree
3. Glycemic control
 - Monitor the need to change the meal timing, form of carbohydrate (simple, complex) according to the anti-diabetic medications/insulin
4. Fat
 - Fat in liquid is well-tolerated; maintain the intake of 20%–30% of calories from fat
 - Implement #1–3 before fat restriction
5. Fiber
 - Identify the high fiber foods increasing the upper gastrointestinal symptoms and individualize the sources of fiber
 - Delayed gastric emptying in the gut could lead to fermentation and alleviate the symptoms
 - If bezoar formation is a concern, avoid foods causing bezoar like oranges, berries, coconut, legumes, fiber supplement
 - Treat bacterial overgrowth if suspected/symptomatic
6. Monitor and replace micronutrients as needed: iron, B₁₂, vitamin D and calcium
 - Avoid caffeine, alcohol, tobacco and stress
 - Eat nutritious foods first before filling up on “empty calories”
 - High fiber foods should be avoided as they may be more difficult on the stomach and may cause bezoar formation
 - Avoid chewing gum, which increases air swallowing
 - Avoid foods that lower oesophageal sphincter pressure: pepper-mint, chocolate, fat, and caffeine
 - Chew well and eat slowly (30 minute meals)
 - Do not lie down immediately after eating
 - Lose weight if you are overweight
 - On days when symptoms are worse; try taking just liquids to let the stomach rest
 - Any food can be blenderized with water, vegetable juice or broth to make a puree
 - Check weight twice a week, if the weight is decreasing increase the amount of liquid supplements

Table 2 Foods high in fiber

➤ Whole grains and whole grain products
• Bran cereals, oat bran, wheat bran, multigrain breads, granola, high-fiber bread.
➤ Beans and legumes
• Whole beans, dried beans, fava beans, kidney beans, baked beans, black beans, peas.
➤ Nuts and seeds
• Almond, flaxseed, sunflower seeds, pumpkin seeds.
➤ Fruits
• Berries, dried fruits (figs, dates, apricot, prunes), guava, apples.
➤ Vegetables
• Green leafy vegetables, green beans, broccoli, Brussels sprouts, squash.

relieve symptoms. This is achieved more easily by frequent monitoring of blood glucose levels and self-adjustment of insulin administration throughout the day. Nutritional intake is often variable due to the symptoms of early satiety, bloating, anorexia, and vomiting and it can often be inconsistent from meal to meal and day to day, leading to swinging glucose levels throughout the day.

Hyperglycemia in the absence of neuropathy or myopathy disrupts normal antral motor complexes at plasma glucose levels as low as 140 mg/dL in healthy humans.³⁰ In type 1 and type 2 diabetes, gastric emptying of liquids is delayed when blood glucose levels exceed 270 mg/dL.¹³ Likewise, in type 1 diabetes, delays in solid emptying are observed during hyperglycemia, which improves during euglycemia. Hyperglycemia also blunts motor responses to prokinetic drug treatment of DGP.^{31,32}

The American Diabetic Association recommends that 55%–60% of calories be contributed by carbohydrates, 15% from protein, and 25%–30% from fat.³³ The amount of carbohydrates ingested is usually the primary determinant of postprandial response, but the type of carbohydrate also affects this response. Intrinsic variables that influence the

effect of carbohydrate-containing foods on blood glucose response include the specific type of food ingested, type of starch (amylose versus amylopectin), style of preparation (cooking method and time, amount of heat or moisture used), ripeness, and degree of processing. Extrinsic variables that may influence glucose response include fasting or preprandial blood glucose level, macronutrient distribution of the meal in which the food is consumed, available insulin, and degree of insulin resistance.³⁴

Small frequent meals that are consistent in the amount of carbohydrates is the first modification that is suggested. The total amount of carbohydrates in the meal does not influence the glucose response if the pre-meal insulin is adjusted for the carbohydrate content of the meal; moreover, for patients receiving fixed doses of short and intermediate-acting insulin, day-to-day consistency in the amount of carbohydrates consumed is associated with lower glycated hemoglobin levels.²³

By switching the consistency of the meal from solid to puree or semi liquid, and by adjusting the insulin dose according to the blood glucose level and amount of carbohydrate in a given meal helps patients to relieve the symptoms and achieve glycemic control to a certain extent.

Patients with gastroparesis do not reflect those who reach the regular postprandial glycemic peak due to the delay in the transit time as a result of delayed gastric emptying. The time of the postprandial peak needs to be determined in order to coordinate it to the type of insulin used and the time of injection before and after a meal.

An insulin regimen including a basal dose of insulin (intermediate-acting NPH or long-acting Glargine® [Sanofi-aventis, Paris, France] or Levemir® [Novo Nordisk Inc, Princeton, NJ]) at bedtime or in the evening, and a short-acting regular or rapid-acting insulin administered before meals or sometimes ~30 minutes after their meal (based on the postprandial glycemic peak) would be most ideal in promoting optimal glycemic control.²³

Table 3 General guidelines for diabetic gastroparesis

➤ Avoid caffeine, alcohol, tobacco, and stress.
➤ Eat nutritious foods first before filling up on “empty calories.”
➤ Avoid chewing gum, which increases air swallowing.
➤ Avoid foods that lower esophageal sphincter pressure: pepper-mint, chocolate, fat, and caffeine.
➤ Chew well and eat slowly (30 min meals).
➤ Do not lie down immediately after eating.
➤ On days when symptoms are worse, try taking just liquids to let the stomach rest.
➤ Check weight twice a week. If the weight is decreasing, increase the amount of liquid supplements.

Total enteral and parenteral nutrition

Enteral nutrition can be an option for patients who fail to stabilize their weight loss or for those who cannot gain weight with oral feedings and have a severe weight loss of >5%–10% of usual body weight over 3–6 months. If the patient has repeated hospitalizations for refractory gastroparesis requiring intravenous hydration and/or medication delivery, and/or the patient has maintained his or her usual body weight but experiences significant clinical

manifestations such as diabetic ketoacidosis, cyclic nausea, and vomiting, enteral nutrition should be considered as a choice of therapy.

Enteral nutrition is less expensive and is associated with fewer infectious complications than total parenteral nutrition (TPN); it provides reliable delivery of nutrition and hydration, as well as medications. Enteral access provides better delivery and thus more consistent absorption of prokinetic and antiemetic medications; it also provides more consistent delivery of nutrients, enhances glucose control, and it is optimal in that it utilizes the gut. Endoscopically placed tubes can be easily removed when symptoms resolve, and patients can return to an oral diet since the goal is to ultimately get the patient back to oral feedings.^{13,35}

TPN is rarely necessary for the patient with gastroparesis; it should be reserved only for those who have a dysmobility that extends throughout much of the small bowel or colon, or those who fail enteral therapy. If TPN is required, close clinical and laboratory monitoring is imperative in preventing metabolic disarray.

Conclusion

Treating patients with DGP remains a very challenging task. Early satiety, upper abdominal pain, nausea, and vomiting impact the patient's quality of life and can result in significant medical problems, most notably malnutrition and poor glycemic control. Management of DGP consists of maintaining adequate glycemic control, hydration, and nutrition, and controlling symptoms of delayed gastric emptying. An accurate nutrition assessment is vital in the initial evaluation of a patient, as malnutrition contributes to significant morbidity and mortality in this patient population. Providing nutritional support, assuring excellent glucose control, and treating nutrient deficiencies can be extremely challenging in the patient with gastroparesis. Nutritional interventions can decrease symptoms, replenish nutrient stores, and improve an individual's overall quality of life; however, very few interventions used to manage the symptoms of DGP have been thoroughly studied. Therefore, well-designed randomized controlled trials are needed to determine the optimal nutritional management of this condition.

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