Diabetic Gastroparesis

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KEYWORDS

• Type 1 and type 2 diabetes mellitus • Gastroparesis • Gastric dysrhythmias
• Prokinetic and antinauseant drugs • Gastric electric stimulation • Nausea • Vomiting

KEY POINTS

- Gastroparesis is delayed gastric emptying in the absence of obstruction, a complication that affects patients with type 2 as well as type 1 diabetes mellitus.
- Symptoms associated with gastroparesis are nonspecific, and the diagnoses should be confirmed with gastric emptying tests.
- Patients are often overweight and have nutritional deficiencies.
- Obstructive gastroparesis, a subset of gastroparesis, is caused by pyloric dysfunction, and botulinum toxin A injections may be helpful.
- Trending postprandial glucose excursions with continuous glucose monitoring aids in the dosing and timing of insulin administration in diabetic patients with gastroparesis.

INTRODUCTION

When gastroparesis afflicts patients with type 1 diabetes mellitus (T1DM) or type 2 diabetes mellitus (T2DM), the consequences are particularly severe. Symptoms associated with gastroparesis, such as early satiety, prolonged fullness, nausea, and vomiting of undigested food, not only reduce the quality of life but also compound difficulties in controlling blood glucose levels.

Gastroparesis is defined as a delay in the emptying of ingested food in the absence of mechanical obstruction of the stomach or duodenum.[1] Many patients with diabetes (as well as their physicians) do not appreciate that gastroparesis has developed. In diabetic patients with gastroparesis, ingested food is not emptied in a predictable period of time; thus, the anticipated nutrient absorption is not the reality. Consequently, the selected dose and timing of insulin therapy to control postprandial glucose may be inappropriate.

In many patients with gastroparesis, erratic postcibal glucose levels result in swings from hypoglycemia to severe hyperglycemia and even ketoacidosis.[2,3] Hyperglycemia

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itself elicits gastric dysrhythmias and slows gastric emptying.[4,5] Patients frequently are seen in emergency rooms for low glucose levels, severe hyperglycemia, or ketoacidosis. Gastroparesis as an underlying condition needs to be considered in these cases.

In addition to antinauseant and prokinetic drug therapies, patients with diabetic gastroparesis also need to change their diet and the timing and dosing of insulin to better match the slow emptying of ingested food. The epidemiology, pathophysiology, clinical presentation, diagnostic testing, and treatments for diabetic gastroparesis are reviewed in this article.

EPIDEMIOLOGY

A recent update reported that there are more than 36 million individuals with diabetes in North America and the Caribbean[6] and most are cases of T2DM. The estimates of prevalence of gastroparesis in T1DM vary widely. Although in tertiary centers, up to 40% of patients with T1DM have gastroparesis,[7] surveys in Olmsted County, Minnesota, indicated a prevalence of 5%.[8]

Similarly, in specialized centers, 10% to 30% of patients with T2DM have gastroparesis[9]; in Olmsted County, the prevalence was 1%.[10] These differences likely reflect a selection bias, because more patients with diabetes and complications are seen in tertiary medical centers compared with surveys of patients in the community. Nevertheless, because of the increasing numbers of patients with T2DM, this population represents the largest group of patients with gastroparesis.

The number of patients with diabetes worldwide continues to increase. The World Health Organization estimated that in 2013 almost 350 million individuals had diabetes (mainly T2DM), and predicted mortality from diabetes will double by 2030 (http://www.who.int/mediacentre/factsheets/fs312/es/). Assuming a low estimate of gastroparesis incidence in T2DM of 1%, at least 5 million individuals with diabetes complicated with gastroparesis will require specialized diagnosis and care.

Gastroparesis evolves over time, presumably as acute and chronic hyperglycemia and reduced insulin and insulinlike growth factor 1 (IGF-1) signaling results in damage to the interstitial cells of Cajal (ICCs) and enteric neurons of the stomach.[11,12] Over a 10-year period, approximately 5.2% of patients with T1DM developed gastroparesis, whereas 5 times fewer (1%) patients with T2DM developed gastroparesis over that same period.[8] Although good control of glycemia prevents or delays many of the chronic complications of T1DM,[13] the effect of good glucose control on the onset or progression of gastroparesis in T1DM is unknown. Diabetic patients with gastroparesis often have many of the chronic complications of diabetes (retinopathy, nephropathy) and increased hospital use. In a few patients, gastroparesis is the first diabetic, neuropathic complication.

Compared with T2DM, patients with T1DM with gastroparesis are younger, thinner, and tend to have more severe delays in gastric emptying.[14] Mortality is increased in diabetic patients when they develop gastroparesis and is usually related to cardiovascular events[15] when compared with diabetic patients without gastroparesis.

NORMAL POSTPRANDIAL GASTRIC NEUROMUSCULAR ACTIVITY

The normal stomach performs a series of complex neuromuscular activities in response to the ingestion of solid foods.[16] First, the fundus relaxes to accommodate the volume of ingested food (**Fig. 1**). Normal fundic relaxation requires an intact vagus nerve and is mediated by enteric neurons containing nitric oxide. The relaxation of the fundus allows food to be accommodated without excess stretch on the fundic walls.