Gastrointestinal Manifestations in Diabetes Mellitus

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Introduction

Gastrointestinal (GI) complications have become increasingly common with the rising prevalence of diabetes. These complications include gastroparesis and enteropathy, which are primarily attributed to abnormal GI motility resulting from diabetic autonomic neuropathy affecting the GI tract.[1]

Up to 75% of individuals with diabetes may experience GI symptoms, significantly impacting their quality of life and increasing healthcare costs. The hallmark GI symptoms associated with diabetes include postprandial fullness, nausea, bloating, abdominal pain, diarrhea, and constipation.[1]

Gastroparesis is a well-known gastrointestinal complication of diabetes, commonly reported in women. Studies have shown delayed gastric emptying in 27% to 65% of individuals with type 1 diabetes mellitus (T1DM) and up to 30% of those with type 2 diabetes mellitus (T2DM). Even though international literature highlights a broad range of prevalence rates, data from India remain scarce, with only a few studies reporting a prevalence of up to 29% among Indian diabetics with a disease duration of more than five years. This suggests that diabetic gastroparesis may be underreported in the Indian population, emphasizing the need for increased awareness and systematic evaluation of this condition.[1,2]

Pathogenesis of GI Symptoms in Diabetes[3]

Disordered Gut-Brain Axis

Gastrointestinal symptoms in diabetes can broadly be attributed to disruptions in the gut-brain axis. Key pathogenic factors include autonomic (vagal and myenteric) neuropathy, peripheral neuropathy, structural and functional changes in the central nervous system (CNS) such as diabetic encephalopathy, acute and chronic dysglycemia, psychological dysfunction, and the effects of pharmacotherapy.

Autonomic Neuropathy

The long-standing hypothesis associates GI symptoms with disordered GI motility caused by irreversible autonomic neuropathy. Autonomic neuropathy identified through these methods correlates with peripheral neuropathy in diabetes, but its relationship with GI symptoms is relatively weak.

CNS Involvement

Evidence suggests that diabetic patients may experience gastric hypersensitivity and rectosigmoid hyposensitivity.

Dysglycemia and GI Symptoms

Acute blood glucose fluctuations significantly impact GI motor function and symptom perception. Acute hyperglycemia increases proximal gastric compliance, slows gastric emptying, and enhances fullness, nausea, and bloating sensations. Even modest increases in blood glucose within the physiological postprandial range (around 140 mg/dL) can slow gastric emptying and alter gut sensations.

Impact of Ketosis and Ketoacidosis

Ketosis and diabetic ketoacidosis may contribute to abdominal pain, often due to severe gastric emptying delays or ileus resulting from metabolic acidosis and electrolyte imbalances.

Clinical Features of Diabetic Enteropathy and Associated GI Symptom[1]

- Diarrhea affects up to 20% of diabetic enteropathy patients, often nocturnally, and is linked to poorly controlled diabetes with neuropathy.

- Nocturnal fecal incontinence arises from sphincter dysfunction, with hyperglycemia reducing rectal compliance.
- Metformin causes GI issues like diarrhea, constipation, and bloating in up to 10% of users, which are manageable through dose adjustment.

GI Effects of Anti-Diabetic Medications and Their Implications[4]

GI adverse effects are common in individuals with type 2 diabetes treated with glucose-lowering medications, such as alpha-glucosidase inhibitors, metformin, and GLP-1 receptor agonists. These drugs can cause symptoms like diarrhea, nausea, bloating, and abdominal pain.

Alpha-Glucosidase Inhibitors

- Medications like acarbose and miglitol cause malabsorption of carbohydrates, leading to predictable GI side effects like diarrhea and abdominal distention.

Metformin

- As a first-line treatment, metformin can cause GI symptoms, particularly diarrhea and nausea, in up to 25% of users.
- It works by blocking gluconeogenesis, acting as an insulin sensitizer, and slowing gastric emptying. To reduce side effects, clinicians often start with a low dose and gradually increase it.

GLP-1 Receptor Agonists

- Drugs like liraglutide and semaglutide can delay gastric emptying, leading to nausea, vomiting, diarrhea, and abdominal discomfort.
- The discontinuation rate due to GI effects ranges from 4.5% to 13%, with nausea being the most common symptom.
- Long-acting GLP-1 agonists cause less nausea and vomiting but are more likely to induce diarrhea.

Gastric Emptying and GLP-1 Receptor Agonists

- Both long- and short-acting GLP-1 receptor agonists delay gastric emptying, with short-acting ones causing a more significant delay.

Preoperative Considerations

- Guidelines suggest withholding long-acting GLP-1 agents one week before surgery due to delayed gastric emptying, though evidence supporting this is weak.
- When insulin is co-prescribed, delayed gastric emptying may increase the risk of hypoglycemia, especially in those with impaired gastric motility.

Management of GI Symptoms in Diabetes

GI symptoms are common in people with diabetes and significantly affect their quality of life. These symptoms are often not reported spontaneously and should be actively identified and assessed using validated tools. The underlying pathophysiology is complex and poorly understood, causing accurate diagnosis and effective management challenges.[3]

Dietary and pharmacological approaches for glucose control in T2DM are mostly used, but several drugs are associated with GI symptoms, which may need discontinuation in some cases.[3]

For patients where abdominal pain is a predominant symptom of enteropathy, medications such as tricyclic and tetracyclic antidepressants, gabapentin, and pregabalin may offer varying levels of benefit.[1]

Improving overall glucose control, particularly reducing glucose variability, is essential in managing diabetic enteropathy, especially in cases where diarrhea is the main symptom. Therapeutic options include multiple daily insulin dosing, insulin pump therapy, and continuous glucose monitoring.[1]

References

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