Diabetes and the gastrointestinal tract

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Abstract

The range of gastrointestinal complications of diabetes extends from the mouth to the anus. In some cases the resulting conditions are familiar — such as gastro-oesophageal reflux and constipation — and the relevance of the diabetes is little more than that these conditions are seen more frequently in diabetic patients than in the general population. Indeed, the range of treatments and their effectiveness are the same in both groups irrespective of the presence of diabetes. But there are two unusual gastrointestinal complications that are peculiar to diabetes: gastroparesis and diabetic diarrhoea. The management of patients with these problems can be extremely challenging; apart from the sheer unpleasantness of chronic vomiting and diarrhoea to the point of incontinence, fluid depletion and loss of diabetic control may necessitate hospital admission. Both vomiting and diarrhoea can be intractable, and the disappointing response of both conditions to the existing range of treatments is often frustrating for patient and physician. Much of the difficulty stems from the fact that their aetiology is poorly understood. The skills involved in looking after such patients extend far beyond the prescribing manual.

Keywords Botulinum toxin; candidiasis; constipation; diabetes mellitus; diabetic diarrhoea; electrical gastric stimulation; gastro-oesophageal reflux; gastroparesis; serotonin antagonists

What's new?

- Rigorous attention to diet and judicious use of prokinetic drugs remain the cornerstone of treatment for most patients with gastroparesis
- Botulinum toxin injection to the pylorus is no longer recommended in refractory gastroparesis
- Electrical gastric stimulation ('gastric pacing') may rapidly improve symptoms in severe otherwise unresponsive gastroparesis
- Treating diabetic diarrhoea remains challenging but serotonin receptors and ghrelin receptors appear promising targets for future therapeutic intervention

Introduction

Although the gastrointestinal complications of diabetes mellitus (Figure 1) are clearly not as life threatening as those that affect some other systems, their consequences for a patient's quality of life can be profound. It is naïve to conclude that most of the more serious gastrointestinal complications of diabetes are simply a result of autonomic neuropathy. The correlation between severity of symptoms and degree of autonomic dysfunction is often poor. The control of the enteric nervous system is complex and the neurohumoral interactions extend beyond the sympathetic—parasympathetic system. A rational approach to diagnosis and therapy of the disturbances of the gut in diabetes would require much more understanding of its neurophysiology than has yet been revealed. Treatment is largely empirical and not always satisfactory — as this review will demonstrate.

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Oesophageal problems

The classical symptoms of gastro-oesophageal reflux — heartburn and regurgitation — are more common in patients with diabetes than in the population at large. There is no difference in the prevalence of risk factors for reflux, such as hiatal hernia or reduced lower oesophageal sphincter function; the major defect in diabetes is that oesophageal peristalsis is impaired. At least in part, this is the result of neuropathy in the motor rather than the autonomic system, which leads to less effective clearance of refluxed acid from the oesophagus.[1,2] Fortunately, diabetic patients with gastro-oesophageal reflux respond well to proton pump inhibitors (and other conventional treatments).

Dysphagia due to impaired peristalsis is unusual but patients with diabetes, especially when glucose control is poor, are prone to odynophagia as a result of candida infection. Absence of oral thrush does not preclude fungal oesophagitis as only half of all patients with candida in the oesophagus have signs of infection in the mouth. The diagnosis is obvious at endoscopy, where creamy plaques on a reddish base are characteristic (Figure 2). Treatment with oral anti-fungal agents, such a fluconazole, is very effective and does not need to await mycological confirmation.

Diabetic gastroparesis

Acute hyperglycaemia itself can lead to short-term inhibition of gastric emptying in both diabetic and healthy subjects, but diabetic gastroparesis usually occurs in the setting of long-standing diabetes where there is evidence of end-organ damage, such as neuropathy, retinopathy and nephropathy.[3,4] The associated unreliability of gastric emptying may complicate the management of the blood glucose. In addition, the recurring symptoms can have a deleterious effect on fluid balance and nutrition, as well as on the bioavailability of oral hypoglycaemic agents, which can result in multiple hospital admissions.

The pathogenesis of diabetic gastroparesis is not well understood, but is related to abnormalities in both neuronal and humoral mechanisms. It is generally accepted that chronic hyperglycaemia contributes to neuropathic changes and dysfunctional innervation of the stomach. The resultant alterations in gastric myo-electrical function result in gastric dilatation, reduced peristalsis and delayed gastric emptying. Apart

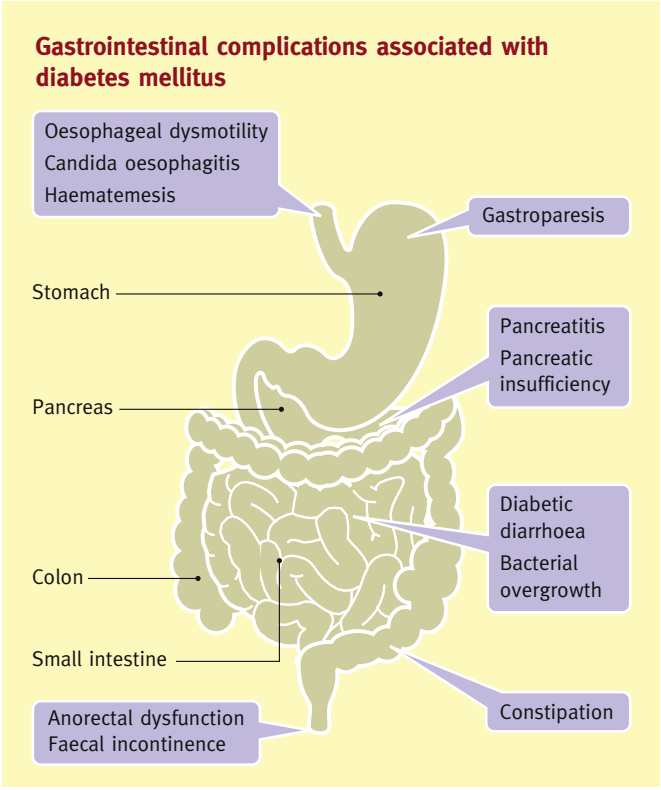

Figure 1

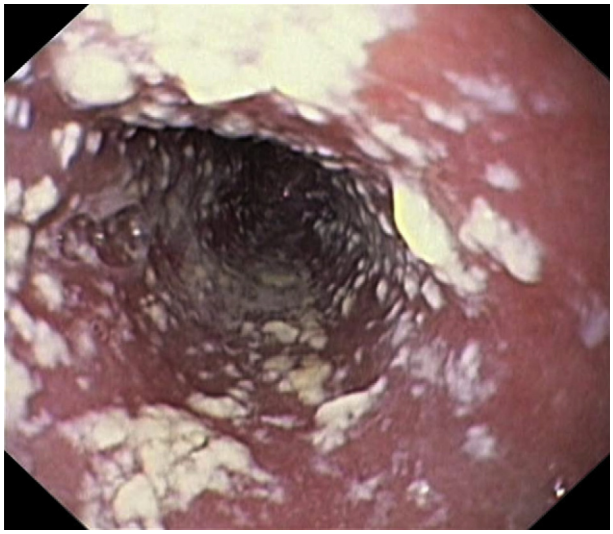

Figure 2 Candida oesophagitis seen at upper gastrointestinal endoscopy.

from disordered control of gastric motor function, it is clear that hyperglycaemia *per se* prolongs gastric emptying.

Symptoms of gastroparesis include post-prandial fullness, bloating and epigastric discomfort (though rarely pain). Early satiety, nausea and vomiting are frequent and the vomitus may contain food eaten many hours earlier. The severity of symptoms does not always correlate with the degree of gastroparesis.[5] Whereas a succussion splash can be demonstrated in severe disease, physical examination is often unhelpful. Although some patients are predisposed to the formation of gastric bezoars from indigestible food, many patients who have diabetes with measurable abnormalities of gastric emptying are asymptomatic.

The diagnosis of impaired gastric emptying is often apparent clinically but a dilated stomach may be seen on plain abdominal radiography. It is essential to consider other causes of delayed gastric emptying. A history of duodenal ulceration may suggest pyloric stenosis, whereas pain, anaemia and weight loss may indicate a distal gastric neoplasm. Upper gastrointestinal endoscopy is mandatory to exclude an anatomical cause for gastric outlet obstruction. A substantial gastric residue may be present despite prolonged fasting. There is an appreciable risk of aspiration during endoscopy, which is best performed after a prolonged (possibly 24-hour fast), so it may be safest to admit the patient to hospital for a day or so before endoscopy to allow IV fluids to be given. Other causes of gastroparesis (that may be more readily treatable) must be considered and excluded, and an accurate drug history is essential (Table 1).

Impaired gastric emptying may be seen with a barium meal examination but the value of this investigation in modern clinical practice is negligible. The most relevant investigation of gastric motor function that is widely available is radionuclide scintigraphy. Liquids and solids have differential rates of gastric emptying, and protocols for assessing emptying of the stomach vary between centres.[6] Data from radiolabelling of solid (as opposed to liquid) meals would seem likely to be helpful in clinical practice since, in diabetic gastroparesis, the impairment of emptying tends to be worse for solids. This technique might seem likely to offer valuable information but in practice its role is seriously limited by the lack of correlation between symptom severity and gastric emptying of the radiolabelled meal.

Treatment of diabetic gastroparesis is often a challenge. Selection of therapy is likely to depend on the frequency and severity of symptoms, the impact on diabetic control, the patient's state of nutrition, and the degree to which the condition interferes with their daily activities. Optimization of blood glucose with close control throughout the day and night is the cornerstone of treatment.[7] Even mild elevation of blood glucose is associated with altered antroduodenal motility and impaired gastric emptying. The range of subsequent treatment options includes dietary modification, pharmacotherapy and, ultimately, more invasive approaches where the condition proves refractory (Figure 3).

Foods high in lipids are known to reduce gastric emptying, so frequent small, low-fat meals are appropriate. Advising the patient to spread their daily food intake between four or five evenly spaced and evenly balanced meals is often helpful. Given that the rate of emptying of liquids in diabetic gastroparesis is usually less abnormal than that of solids, liquidized foods are worth a trial where solids are not tolerated. If neither solid nor liquid foods can be taken in sufficient quantity, enteral nutrients can be used to supplement standard meals.

While close attention to diabetic control and diet are essential, they are unlikely to be sufficient especially when symptoms are severe. Several drugs have prokinetic activity. The dopamine receptor antagonists, metoclopramide and domperidone, locally increase released acetylcholine at the myenteric plexus. Both drugs accelerate gastric emptying and improve symptoms of gastroparesis — at least in the short term. However, their efficacy over the longer term is less certain and there are issues of safety