Diarrhoea and diabetes

Rowan Hillson

People with diabetes are more likely to have gastrointestinal symptoms than those without diabetes. An Australian study reported diarrhoea in 10.0% of people without diabetes and 15.6% of those with diabetes (adjusted odds ratio 2.06 [1.56–2.74]). WHO states: ‘Diarrhoea is defined as the passage of three or more loose or liquid stools per day (or more frequent passage than is normal for the individual). Frequent passing of formed stools is not diarrhoea.’ Check what your patient means by diarrhoea. Diarrhoea has myriad causes — only a few are considered here.

Colon and rectum cancer

Colon and rectum cancer may be missed when health care professionals wearing ‘diabetic blinkers’ assume all symptoms in someone with diabetes are due to diabetes. Diarrhoea is a frequent symptom.

‘Analysis of 15 studies… including 2,593,935 participants, found that diabetes was associated with an increased risk of colorectal cancer, compared with no diabetes (summary RR of colorectal cancer incidence 1.30, 95% CI 1.20 to 1.40).’

Glucose-lowering drugs

Metformin is first-line treatment for type 2 diabetes and was prescribed to 83.6% of people with diabetes in the UK THIN database in 2013. Diarrhoea is a common side effect, reported by 23.7% of patients on metformin in ADIPT, for example. A review found that 1.2–5% of patients discontinued immediate-release metformin. Symptoms may be more likely on first use of metformin, increasing with increasing dose.

Metformin reduces liver glucose production and acts within the gut increasing intestinal glucose uptake and changing the gut microbiome. Metformin also increases fluorodeoxyglucose (FDG) uptake in the guts, especially the colon, so patients needing a PET scan should stop their metformin beforehand. Hyperglycaemia may reduce FDG uptake. Talk with the PET team first — see Suriasi et al.

To reduce side effects, start with low dose immediate-release metformin with gradual increments and advise taking the drug with or after food. Extended-release metformin appears less likely to cause adverse effects.

GLP-1 agonists like exenatide also cause gastrointestinal side effects. Nausea is commonest. Diarrhoea was reported in 10.0% with once-weekly exenatide and 7.8% with twice-daily dosage. In a comparison, 6.1% of patients on once-weekly exenatide had diarrhoea compared with 13.6% of those on liraglutide.

Acarbose inhibits intestinal sucrose breakdown and often causes diarrhoea and flatulence, especially with high sugar intake. Treat hypoglycaemia with glucose, not sucrose.

Diet

People newly diagnosed with diabetes are encouraged to eat a healthy diet, including ‘5 a day’ fruit and vegetable portions. As fewer than a third of the population do this, a sudden increase to ‘5 a day’ may cause diarrhoea.

‘A 21 year old woman had experienced diarrhoea and diffuse abdominal pain for eight months. She had four to 12 bowel movements with watery stools daily… A 46 year old man [had] diarrhoea and a weight loss of 22 kg.’ No cause was found until both admitted chewing a lot of sugar-free gum — the man 20 sticks a day with additional sugar-free sweets — a massive sorbitol intake. Sorbitol is added to ‘diabetic’ sweets and other products. In large doses it acts as an osmotic laxative.

Gastroenteritis

When I was a junior doctor, a teenager with type 1 diabetes was admitted with gastroenteritis. He arrived clutching a sugar bowl which he was frantically emptying with a spoon. Someone had told him that because he had vomited, he must eat as much sugar as he could ‘to use up his insulin’. The overpowering aroma of ketones strongly suggested that his insulin had already been ‘used up’ so I removed the sugar. He made a full recovery after ketoacidosis treatment.

Gastroenteritis is a common precipitant of diabetic ketoacidosis. Diabetic ketoacidosis itself can cause vomiting and diarrhoea. Teach patients and families sick day rules. Insulin-treated patients (and many on non-insulin treatments) should learn blood-glucose monitoring, and, if they have type 1 diabetes, how to check blood ketones. They must have adequate supplies of test strips and know what to do about results — so must health care professionals. Staff still stop insulin in people with type 1 diabetes who are vomiting! Teaching resources are available.

Malabsorption

Coeliac disease

While the condition may be silent or cause tiredness, malaise, failure to grow or weight loss, many patients have abdominal discomfort and bloating with altered bowel habit. In more severe cases there is diarrhoea, often at night with incontinence, and loose, greasy, frothy faeces that are difficult to flush.

NICE advocates screening for coeliac disease in all patients with newly-diagnosed type 1 diabetes and in anyone with ‘persistent unexplained abdominal or gastrointestinal symptoms’.

Pancreatic disease

Lack of pancreatic digestive enzymes causes malabsorption with pale, malodorous, greasy stools that float and won’t flush. Causes include chronic pancreatitis, haemochromatosis, cystic fibrosis, and pancreatic cancer. Among people with cystic fibrosis, diabetes develops in about 20% of adolescents and 40–50% of adults. Pancreatic damage also causes malabsorption.

Hormones

Among French patients with thyroid over-activity, 32% had gastrointestinal signs — which can include diarrhoea or increased frequency of normal motions.
Glucagonoma is a rare islet-cell tumour causing diabetes and diarrhoea, often with a migratory skin rash.\textsuperscript{20}

**Ulcerative colitis**

Ulcerative colitis is an autoimmune disorder like type 1 diabetes. Among 488 children with ulcerative colitis more had diabetes (OR 2.7 [95% CI 1.1–6.6]) than did controls.\textsuperscript{21} Steroid treatment may cause diabetes in previously normoglycaemic people, or worsen glucose control in pre-existing diabetes.\textsuperscript{22}

**‘Diabetic diarrhea’**

Clark and Young said: ‘To justify the sobriquet of diabetic diarrhea the patient should experience intermittent episodes of diarrhea which at their worst are watery and voluminous with upwards of twenty or sometimes even more stools daily, these often being preceded by considerable urgency. Although more frequent during the night, the diarrhea also occurs during the day often shortly after meals suggesting, somewhat unexpectedly, an exaggerated gastro-colic reflex. The episodes will last for days or weeks and then remit spontaneously for a variable period. Between attacks the bowel habit returns to normal or the complaint may instead be constipation. The typical patient with diabetic diarrhea has long-standing insulin-dependent diabetes which has been poorly controlled. There are usually other complications, particularly somatic and autonomic neuropathy.’\textsuperscript{23}

Key causes are probably diabetic autonomic neuropathy affecting bowel function, especially motility, with or without accompanying bacterial overgrowth of the small bowel. However, diabetic diarrhea is a diagnosis that should be reached after excluding other more likely, and often more treatable causes.

Small intestinal bacterial overgrowth is diagnosed by jejunal aspirate, or by breath tests (usually hydrogen). The latter are subject to confounding factors and the methodology used affects the prevalence found among people with diabetes (26–62% for example). Treatment is with antibiotics, preferably those that are poorly absorbed from the gut.\textsuperscript{24}

Loperamide and codeine are used but neither is recommended for long-term treatment and they may not be very effective. Both octreotide and lanreotide have been tried to treat the autonomic component.\textsuperscript{25,26}

Aim to improve glucose control, bearing in mind that the person is likely to have autonomic neuropathic damage elsewhere, for example, cardiac, so hypoglycaemia is particularly dangerous.

**Summary**

- Diarrhoea is common among people with diabetes, as are other gastrointestinal problems.
- There are many reasons why people with diabetes are more likely to have diarrhea than the general population, but don’t assume that the diabetes is to blame.
- Remember cancer of the colon, rectum and pancreas.
- Introduce dietary changes slowly.
- Avoid ‘diabetic sweets’, especially those containing sorbitol.
- Glucose-lowering drugs, especially metformin, often cause diarrhoea.
- Gastroenteritis or associated diabetes mismanagement is a common cause of diabetic ketoacidosis. Diabetic ketoacidosis also causes vomiting and diarrhoea. Teach sick day rules. Ensure patients can monitor blood glucose and ketones and know how to use the results.
- Remember malabsorption, including coeliac disease and cystic fibrosis, and pancreatic disorders.
- Consider thyroid over-activity and rare endocrinopathies.
- Does your patient have ulcerative colitis?
- Is it ‘diabetic diarrhea’? While excluding other causes consider small intestinal bacterial overgrowth, and gastrointestinal autonomic neuropathy.
- Diarrhoea may be common but cause and treatment are often challenging in people with diabetes – so seek gastroenterological advice if there is no simple answer or if symptoms persist.

**Dr Rowan Hillson, MBE.**

Past National Clinical Director for Diabetes

**References**