Uncontrolled diabetes mellitus due to gastroparesis diabetorum: treatment with metoclopramide

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Summary

A case is reported of uncontrolled diabetes mellitus due to gastroparesis diabetorum in which treatment with metoclopramide restored diabetic control. Diagnostic, pathological and therapeutic aspects of diabetic gastroparesis, which is thought to reflect autonomic neuropathy involving the gastrointestinal tract, are discussed.

Introduction

Uncontrolled diabetes mellitus may be caused by diabetic gastroparesis, i.e. gastric atony and delayed emptying. This can occur without obvious alimentary symptoms. A patient is described in whom metoclopramide treatment improved gastric emptying and restored diabetic control.

Case report

A 78-year-old woman with a maturity-onset diabetes of 21 years' duration was admitted to the hospital after a fortnight of severe daily hypoglycaemic episodes. She had lost 30 kg in one year. Gastrointestinal complaints were absent except for one episode of watery diarrhoea on the day before admission. On examination the abdomen was normal. She had postural hypotension and resting tachycardia (100 beats/min). Signs of peripheral sensorimotor neuropathy were present. She had no retinopathy, nephropathy, sweating abnormalities, or urinary bladder dysfunction. The insulin dosage was reduced from 36 to 22 units daily, but her diabetes was still poorly controlled and hypoglycaemic episodes recurred.

A radiological examination of the gastrointestinal tract showed diminished oesophageal peristaltic waves, gastric food residues, dilatation of the stomach with decreased peristalsis and with barium retention for more than 24 hr (Fig. 1). The transit time of the contrast medium through the small intestine was prolonged. Gastroduodenoscopy revealed no pyloro-duodenal obstruction. Electro-

myography showed the presence of peripheral neuropathy. The postural hypotension and the resting tachycardia had suggested autonomic neuropathy involving the cardiovascular system. This was confirmed by measuring the immediate heart rate response to standing as described by Ewing *et al.* (1978): the electrocardiographic R-R interval ratio at beat 30 v. beat 15 after standing was 0.95 in the patient, whereas diabetics without autonomic neuropathy have a 30 : 15 R-R interval ratio of ≥ 1.03 .

These data led to the diagnosis of gastroparesis diabetorum causing the worsening of diabetic control in a patient with peripheral and autonomic neuropathy. Treatment was instituted with oral metoclopramide in a dosage of 10 mg, 30 min before each meal. The insulin regimen of 22 units daily was not changed. Diabetic control improved and no further hypoglycaemic episode occurred during the following months.

X-ray control (Fig. 2) during the fifth week of metoclopramide therapy showed considerable improvement, although complete gastric emptying of the barium still required 7 hr (compared with more than 24 hr before treatment).

Discussion

Uncontrolled diabetes mellitus may be due to irregular food absorption caused by gastric atony and delayed emptying of the stomach (gastroparesis diabetorum). This worsening of diabetic control can occur in the absence of gastrointestinal complaints. The usual clinical manifestations are nausea, vomiting, vague abdominal complaints or anorexia. Bezoar formation can occur. Gastroparesis should also be suspected in the diabetic with unexplained weight loss, particularly if neuropathy involving other systems exists.

Radiological investigation is a readily available but relatively insensitive diagnostic method. Solid residue in the stomach at the beginning of the

FIG. 1. Before the administration of metoclopramide, gastrointestinal radiological examination shows marked barium retention after 5 hr (a) and after 24 hr (b).

examination, decreased peristalsis with delayed gastric emptying and duodenal bulb atony are the principal radiological signs (Gramm, Reuter and Costello, 1978). Endoscopy should be done to exclude pyloro-duodenal obstruction. Gastric scintiscanning is a more accurate way to study gastric emptying. Using a double isotope scintiscanning technique, which differentiates between solid and liquid emptying, Campbell *et al.* (1977) showed gastric stasis to be present in all 3 patients with diabetic autonomic neuropathy and symptoms of gastroparesis although impaired gastric emptying was recognized radiologically in only one patient.

The delay in gastric emptying has been attributed to vagal damage occurring as part of a more generalized autonomic neuropathy (Wooten and Meriwether, 1961). Diabetics with symptoms of autonomic neuropathy have an impaired vagally-mediated acid secretion in response to insulin-induced hypoglycaemia but they have normal parietal cell function (Hosking *et al.*, 1975). Surgical vagotomy, however, has no effect on the pattern of gastric emptying in non-diabetics when measured

with the scintiscanning technique (Heading *et al.* 1975).

Pathological data concerning diabetics with gastroparesis are scarce. Duchen *et al.* (1980) recently reported post-mortem studies of the autonomic nervous system in 5 insulin-dependent diabetics with peripheral and autonomic neuropathy involving the gastrointestinal tract. There was a severe loss of myelinated axons and a marked excess of collagen in the vagus nerve of all patients studied. This confirms the earlier observation of myelin degeneration in the vagal nerves as well as in the peripheral nerves of diabetics by Kristensson *et al.* (1971). However, several other pathological lesions were found in these patients such as distension and vacuolization of neurones in coeliac and other sympathetic ganglia, inflammatory changes in the autonomic ganglia and in or around unmyelinated nerve fibres, and focal hyaline degeneration in the visceral smooth muscle. These findings suggested to Duchen *et al.* that several different pathogenetic mechanisms may be involved in the development of autonomic neuropathy in diabetes. The ultrastructural analysis

FIG. 2. Following metoclopramide therapy gastric emptying improved considerably, as shown 3 hr after the barium ingestion.

Auerbach's myenteric plexuses of the small intestine in ketonuric diabetic Chinese hamsters with radiological abnormalities comparable to those found in human gastroparesis diabetorum showed degeneration of the distal unmyelinated axons (Diani *et al.*, 1979).

Treatment of diabetic gastroparesis with pyloroplasty or partial gastrectomy, cholinergic agents or cholinesterase inhibitors has been disappointing (Wooten and Meriwether, 1961; Zitomer, Gramm and Kozak, 1968). More recently, however, a limited number of reports about metoclopramide therapy for diabetic gastroparesis have suggested an improvement in gastric emptying and diabetic control as evidenced in the present patient (Berkowitz, Metzger and Sturdevant, 1976; Campbell *et al.*, 1977; Longstreth, Malagelada and Kelly, 1977; Braverman

and Bogoch, 1978). The dopamine antagonist metoclopramide increases the frequency of type II gastric peristaltic contractions, speeding up the rate of gastric emptying (Longstreth *et al.*, 1977). Metoclopramide may act by increasing the amount of acetylcholine released at the postganglionic nerve endings (Hay, 1977).

The authors conclude that gastroparesis diabetorum should be considered in the patient with uncontrolled diabetes mellitus, even in the absence of abdominal symptoms, and that metoclopramide can be helpful in its treatment.

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