Hypoclycaemia unawareness and falls in older adults with type 2 diabetes

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Introduction

Hypoglycaemia unawareness is the lowering of plasma glucose level below that needed to initiate adrenergic symptomatic response, thereby obliterating the gap between the onset of a symptomatic protective response and of cognitive impairment.

Case report

A 65-year-old female, known to have diabetes for 24 years, was brought into the accident and emergency ward unconscious after taking her insulin injection and breakfast several hours earlier. She was not hypertensive and did not take alcohol. No history of fever, headaches, vomiting, or visual impairment was obtained. There was a history of similar episodes of loss of consciousness in the past. She was on Mixtard 30/70 insulin, 34 units in the morning, and 16 units in the evening. Her weight, height and body mass index (BMI) were 52 kg, 1.58 m, and 21.0 kg/m^2 respectively. Glasgow Coma Score (GCS) was 6/15, pulse rate 117 per minute and regular, and blood pressure 130/80 mmHg. Plasma glucose at presentation was 1.9 mmol/l. Other routine investigations were normal. After resuscitation she complained of pain in the right ankle. The ankle was swollen, tender and an X-ray revealed a fracture of the fibula. After reducing her insulin to 20 units morning and 10 units evening, her fasting glucose has been between 96 mg/dl and 130 mg/dl, with no hypoglycaemic symptoms for over 6 months of follow-up.

Discussion

Hypoglycaemia unawareness is the onset of neuroglycopenia before the appearance of autonomic warning symptoms,[1] and persons with diabetes are more vulnerable because of both exogenous insulin excess and counter-regulatory failure. In individuals without diabetes when blood glucose declines to hypoglycaemic levels, insulin secretion is suppressed.[1] This suppression leads to reduced peripheral glucose uptake and increased hepatic glucose output, which typically terminates the episode. However, if glucose continues to decline glucagon and adrenaline secretion are stimulated.[1] This promotes hepatic glucose production via gluconeogenesis and glycogenolysis.

Persons with type 1 diabetes of over 5 years' duration may lose their glucagon response to hypoglycemia.[2] The pancreatic alpha cells fail to recognise hypoglycaemia as a stimulus for release of glucagon, but it is secreted normally in response to alanine.[3] Therefore, the thrust of the acute counter-regulatory response is carried by adrenaline. Unfortunately, the counter-regulatory response is blunted in many patients. Adrenaline response to other stimuli, (e.g. exercise) appears normal, which is therefore also a selective failure of hypoglycaemia recognition.[3] Frequent hypoglycaemia can reduce the counter-regulatory response to hypoglycaemia by ≥50%.[4] Chronic hypoglycaemia in particular appears to increase the expression of glucose transporters localised in the micro-vessels of the blood–brain barrier (GLUT-1) as well as the neuron-specific glucose transporters (GLUT-3).[5] Thus during subsequent hypoglycaemia, the brain is less neuroglycopenic than normal and does not need to generate the counter-regulatory responses and the autonomic symptoms to defend and alert the subject about hypoglycaemia. This is the mechanism of cerebral adaptation causing impaired awareness of hypoglycaemia in chronic hypoglycaemia.

In type 2 diabetes, patients early in the course of their disease probably retain most of their alpha-cell response (glucagon) to hypoglycaemia, whereas patients with advanced type 2 disease have virtually no such response to hypoglycemia.[6] These patients, like those with type 1 diabetes, also develop a blunting of their adrenaline response (see Table 1), that is proportional to antecedent hypoglycemia[2].

Older adults with type 2 diabetes have an increased risk of falls; factors of particular concern include diabetes-related complications such as peripheral neuropathy, reduced vision, and renal function. Insulin therapy is associated with increased falls,[7,8] possibly because of more severe disease and/or hypoglycaemic episodes. Fractures are one of the most serious fall-related injuries, and diabetes appears to increase the risk for fracture.[9,10]

Hypoglycaemia unawareness is preventable and treated by frequent blood glucose monitoring and avoiding blood glucose values <3.5 mmol/l. Over-tight glycaemic control should be avoided, and regular intake maintained. Patients should be educated about subtle neuroglycopenic symptoms, and counselled regarding alcohol and exercise schedules.[3]

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Table 1 Glucose counter-regulation during early stages of hypoglycaemia

	Glucose	Insulin	Glucagon	Adrenaline
Non-diabetic	Reduced	Reduced	Increased	Increased
Type 1 diabetic	Reduced	No reduction	No increase	Attenuated increase
Type 2 diabetic	Reduced	Reduced	Increased	Increased
Advanced type 2 diabetic	Reduced	No reduction	No increase	Attenuated increase

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