

DECISIONS

Impaired awareness of hypoglycemia in a man with type 1 diabetes

Gilles Plourde MD PhD, Agnes V. Klein MD, Robert Dent MDCM

Competing interests: None declared.

This article has been peer reviewed.

Correspondence to: Gilles Plourde, gilles.plourde@hc-sc.gc.ca

CMAJ 2014, DOI:10.1503/cmaj.131391

A 32-year-old man with a 22-year history of type 1 diabetes presented to the diabetes clinic following a loss of consciousness at home the previous evening. The incident, which occurred when the patient was awake, was witnessed by his wife. She administered intramuscular glucagon within minutes. After regaining consciousness, the patient drank some orange juice and then consumed a meal consisting of complex carbohydrates. His blood glucose was not checked at the time of the loss of consciousness, but it was normal after initial treatment with glucagon and orange juice. His diabetes is managed with 38 units of rapid-acting insulin glulisine with each meal and 62 units of long-acting insulin glargine at bedtime. The patient stated that he had not had any recent problems with hypoglycemia. He reported that he measures his blood glucose level at least once a day and that it is “always normal.” He drives a car as part of his job and was injured in a traffic collision within the past year, but he is unable to recall the details of the collision.

What questions should the patient be asked?

Physicians should ask about the frequency and timing of severe hypoglycemia, personal awareness of hypoglycemia, signs of hypoglycemia detected by others and hypoglycemia detected only because of monitoring.¹⁻³ Risk factors for impaired awareness of hypoglycemia include age greater than 50 years, infrequent self-monitoring of blood glucose, duration of diabetes longer than 10 years, glycemic control with glycated hemoglobin (HbA_{1c}) less than 7.0% (optimal control: < 7.0%; suboptimal: 7.0%–8.4%; inadequate: > 8.4%) and episodes of hypoglycemia where assistance was required or where there was a loss of consciousness (Box 1).¹⁻⁶

Clarke's hypoglycemia awareness questionnaire⁵ aims to quantify the degree of impaired awareness of hypoglycemia. Each response is rated as “R” (reduced awareness) or “A” (aware). A patient who provides four or more “R” responses is considered to have impaired awareness of hypoglycemia.

What is the most likely diagnosis?

The patient scored 5 on the Clarke questionnaire, which is consistent with a diagnosis of impaired awareness of hypoglycemia. Hypoglycemia is a risk associated with insulin therapy; impaired awareness has a physiologic basis related to the impact of hypoglycemia on the brain and an impaired response of counter-regulatory mechanisms in the setting of long-standing type 1 diabetes and insulin-treated type 2 diabetes.

In patients with impaired awareness of hypoglycemia, the ability to perceive the onset of hypoglycemia becomes diminished or absent. Symptoms are insidious and include difficulty concentrating, confusion, reduced consciousness, coma or seizures that occur before autonomic activation (tremor, sweating, palpitation and nausea).⁴ Impaired awareness is believed to affect about 20%–25% of people with type 1 diabetes and up to 10% of people with insulin-treated type 2 diabetes.⁴ The condition increases the risk of severe hypoglycemia by three- to sixfold compared with people with normal awareness.⁴ It should be differentiated from “hypoglycemia unawareness,” which suggests a rare but total loss of symptomatic response to low glucose.⁴ The differential diagnosis also includes a number of rare conditions, including all of the causes of syncope, with the two broad categories being cardiac and neurologic. The latter includes seizure disorders.

How can awareness of hypoglycemia be restored for this patient?

The key to reversing impaired awareness of hypoglycemia is relaxing glycemic control to avoid episodes of hypoglycemia (Box 1).⁴ To achieve this, experts recommend frequent self-monitoring of blood glucose, including preprandial and nocturnal measurements, avoiding blood glucose values less than 4 mmol/L, raising blood glucose targets (e.g., preprandial target 6.0–12 mmol/L and bedtime > 8 mmol/L), preventing an HbA_{1c} level of less than 6.0%, and including regular snacks between meals and at bedtime.¹⁻⁴

Box 1: Factors in the diagnosis and management of impaired awareness of hypoglycemia¹⁻⁶

Factors to address during medical history-taking

- Drugs that may increase risk: β -blockers (nonselective), hypnotics, tranquilizers and alcohol
- Social support: fear of hypoglycemia and its impact on other family members (e.g., anxiety)
- Daily routine: insulin administration, eating patterns and exercise
- Blood glucose self-monitoring diary: frequency and distribution of hypoglycemia

Principles of treatment

- Structured patient education should include discussion of the symptoms of hypoglycemia and hypoglycemia avoidance, self-monitoring of blood glucose, the adequate use of insulin and a discussion of management strategies (carbohydrate intake and insulin dose) for exercise training, alcohol intake and the appropriate selection of food for meals and snacks.²
- Strategies to increase compliance to therapy should be emphasized to restore awareness of hypoglycemia and to protect patients from severe hypoglycemia.¹⁻⁴
- Patients may require psychological counselling to help them modify management of diabetes and to address problems of "low concern" or "denial" regarding hypoglycemia unawareness, which are often seen in these patients.⁶
- Impaired awareness of hypoglycemia poses a potential risk to safety, not only when patients are driving but also when they are exposed to heights, under water, operating machinery and other activities, and justifies the recommendation to perform self-monitoring of blood glucose in relation to such activities, even if it seems inconvenient.^{1,3}
- Relatives should be taught about impaired awareness of hypoglycemia and how to administer glucagon (subcutaneous or intramuscular injection).³

Helping patients identify subtle cues to their low blood glucose level is also recommended.¹⁻⁴ Although guidelines from the Canadian Diabetes Association give some recommendations about hypoglycemia and driving,³ this patient requires special consideration for two reasons: part of his job requires that he drive a car, and he has had both a period of unconsciousness and a motor vehicle collision where impaired awareness of hypoglycemia was a plausible explanation.

Case revisited

We recommended that our patient decrease all of his insulin doses by 30% and perform regular self-monitoring of blood glucose at least four times daily (preprandial and at bed time). Because he was injured in a motor vehicle accident for which impaired awareness of hypoglycemia played a plausible role, we notified the ministry of transportation, who then investigated his suitability for driving, according to provincial law.⁷

Regular self-monitoring of blood glucose showed frequent asymptomatic hypoglycemia, requiring further reductions in his insulin dose. With our recommended treatment, the patient was able to avoid hypoglycemia completely and to reduce his total daily insulin dose by another 20% over a period of two months. Simultaneously, he began to regain warning symptoms when his blood glucose fell into the hypoglycemic range. He was allowed to drive again with a noncommercial licence, provided that he self-monitor his blood glucose before driving and periodically during every driving exposure.⁷ He was able to organize a change in his work functions, which permitted him to keep his job.

Box 2 includes resources for both physicians and patients.

Box 2: Resources for physicians and patients

- Canadian Diabetes Association. *The Canadian Diabetes Association 2013 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada*. *Can J Diabetes* 2013;37:S1-S212. http://guidelines.diabetes.ca/App_Themes/CDACPG/resources/cpg_2013_full_en.pdf
- Joslin Diabetes Center. Managing diabetes: www.joslin.org/info/managing-diabetes.html
- Canadian Medical Association. 2012. *CMA Driver's Guide: Determining Medical Fitness to Operate Motor Vehicles, 8th edition*. www.cma.ca/driversguide
- Canadian Diabetes Association. *Clinical Practice Guidelines for Diabetes and Private and Commercial Driving*. *Can J Diabetes*. 2003;27:128-140. www.diabetes.ca/files/DrivingGuidelinesBeggJune03.pdf

References

1. Frier BM. How hypoglycemia can affect the life of a person with diabetes. *Diabetes Metab Res Rev* 2008;24:87-92.
2. Choudhary P, Amiel SA. Hypoglycemia: current management and controversies. *Postgrad Med J* 2011;87:298-306.
3. Clayton D, Woo V, Yale J-F. Hypoglycemia. Canadian Diabetes Association clinical practice guidelines. *Can J Diabetes* 2013; 37:S69-71. Available: <http://guidelines.diabetes.ca/browse/chapter14> (accessed 2013 July 10).
4. Graveling AJ, Frier BM. Impaired awareness of hypoglycemia: a review. *Diabetes Metab* 2010;36:S64-74.
5. Clarke WL, Cox DJ, Gonder-Frederick LA, et al. Reduced awareness of hypoglycemia in adults with IDDM. A prospective study of hypoglycemia frequency and associated symptoms. *Diabetes Care* 1995;18:517-22. Available: <http://care.diabetesjournals.org/content/18/4/517.full.pdf> (accessed 2014 Jan. 29).
6. Rogers HA, de Zoysa N, Amiel A. Patients experience of hypoglycemia unawareness in type 1 diabetes: Are patients appropriately concerned? *Diabet Med* 2012;29:321-7.
7. Begg IS, Yale J-F, Houlden RL, et al. Canadian Diabetes Association's clinical practice guidelines for diabetes and private and commercial driving. *Can J Diabetes*. 2003;27:128-40.

Affiliations: Centre for the Evaluation of Radiopharmaceuticals and Biotherapeutics, Biologic and Genetic Therapies Directorate (Plourde, Klein), Health Canada; School of Human Kinetics (Plourde), Faculty of Health Sciences, University of Ottawa; Weight Management Clinic (Dent), Ottawa Hospital, University of Ottawa, Ottawa, Ont.

Contributors: All authors participated in the planning, writing and revision of the manuscript and approved the final version submitted for publication.