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Case Report

Impaired Awareness of Hypoglycaemia in an Obese Woman with Type 2 Diabetes Mellitus

Gilles Plourde[1, 2*]

[1*]Associate Professor at the Faculty of Health Sciences, University of Ottawa, Ontario, Canada

[2] Faculty of Medicine, University of Montreal, Montreal, Quebec Canada

Correspondence to: Gilles Plourde, Drug Safety Unit – Director's Office, Health Canada, Ontario, Canada; **E-mail:** gilles.plourde@hc-sc.gc.ca; drgplourde@gmail.com

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Case Report

Jane is a 46 year-old obese woman with a 28 year history of type 2 diabetes (T2DM) presented to the clinic following a loss of consciousness the previous day. Her loss of consciousness took place at home and the patient was awake at the time of the incident. This was witnessed by her husband, who administered intramuscular glucagon immediately. After regaining consciousness, the patient consumed a meal consisting of complex carbohydrates. Her blood glucose was not checked at the time of the unconsciousness, but was normal after treatment (glucagon + orange juice). Her T2DM was managed with 32 units of rapid-acting insulin glulisine (Apidra) accompanying each meal and 52 units of long-acting insulin glargine (Lantus) at bedtime. She was also treated with LSI but she was always irregular in the follow-up of her diet and physical activity regimens. She denied having any recent problems with hypoglycaemia and reported that she measured her blood glucose at least once a day and it was 'always normal'. She is a bus driver and had a traffic accident 2 years ago but she was unable to recall the details. Nobody was injured during the accident which occurred at a very low speed but was witnessed by a client.

What should you ask on medical history?

HCPs should follow the '6As model of counselling and assess about the frequency and timing of severe hypoglycaemia, individual awareness of hypoglycemia, hypoglycaemia detected by others, and hypoglycaemia detected only because of monitoring [1-3]. The HCPs should also asses for risk factors for impaired awareness of hypoglycaemia (IAH) (see definition below) that includes age over 50, infrequent self-monitoring of blood glucose (SMBG), duration of diabetes longer than 10 years, glycemic control with glycated hemoglobin (A1C) less than 0.070 (Optimal control is < 0.070, Sub optimal 0.070 – 0.084; inadequate > 0.084) and episodes of hypoglycemia where assistance was required or where there was a loss of consciousness. Then the HCPs assess about drugs used including beta-blockers (non-selective), hypnotics, tranquillisers and alcohol. The HCPs should also assess for the social support including the fear of hypoglycemia, and the impact or anxiety on other family members. He should assess her daily routine for insulin administration, eating patterns, exercise routine, the frequency of SMBG and the distribution of hypoglycemia [1-6].

Finally, the HCP complete the following questionnaire with the patient by asking specific questions related to hypoglycemia according to the Clarke's questionnaire (5) aims to quantify the degree of IAH. Each response is rated R for 'reduced awareness' or A for 'aware'. A patient who provides four or more R responses is considered to have IAH. The questions are as follows:

1) Do you always have symptoms when your blood sugar is low (A) Do you sometimes have symptoms when your blood sugar is low R.

   Response: I do not always have symptoms when my blood sugar is low (1).

2) Have you lost some of the symptoms that used to occur when your blood sugar was low?
   Yes (R) No (A);

   Response: Yes sometimes (1).

3) In the past six months how often have you had moderate hypoglycemia episodes? (Episodes where you might feel confused, disoriented, or lethargic and were unable to treat yourself)
   Never (A) Once or twice (R) Every other month (R) Once a month (R) More than once a month (R)

   Response: Yes it happened once or twice (1).

4) In the past year how often have you had severe hypoglycemic episodes?
   (Episodes where you were unconscious or had a seizure and needed glucagon or intravenous glucose) Never (A) 1 time (R) 2 times (R) 3 times (R) 5 times (R) 6 times (R) 7 times (R) 8 times (R) 9 times (R) 10 times (R) 11 times (R) 12 or more times (U)

   Response: I had one episode last year and one yesterday (1).

5) How often in the last month have you had readings <70 mg/dl (<3.9 mmol/L) with symptoms?
   Never 1 to 3 times 1 time/week 2 to 3 times/week 4 to 5 times/week Almost daily (R = answer to 5 < answer to 6, A = answer to 6 > answer to 5)

   Response: Maybe 1–2 times per week.

6) How often in the last month have you had readings <70 mg/dl (<3.9 mmol/L) without any symptoms? Never 1 to 3 times 1 time/week 2 to 3 times/week 4 to 5 times/week, Almost daily (R = answer to 5 < answer to 6, A = answer to 6 > answer to 5)

   Response: Maybe 1–2 times per week.

7) How low does your blood sugar need to go before you feel symptoms?
60-69 mg/dl (3.33 – 3.8 mmol/L) (A)
50-59 mg/dl (2.8 – 3.3 mmol/L) (A)
40-49 mg/dl (2.22 – 2.72 mmol/L) (R) < 40 mg/dl (< 2.2 mmol/L) (R)
Response: Between 2.22 – 2.72 mmol/L (1)

8) To what extent can you tell by your symptoms that your blood sugar is low?
Never (R) Rarely (R) Sometimes (R) Often (A) Always (A)
Response: Often.

What is the most likely diagnosis?

The patient scored "5" on the questionnaire, consistent with a diagnosis of IAH. Hypoglycemia is a risk associated with insulin therapy, while 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 longstanding T1DM and insulin-treated T2DM. In patients with IAH, the ability to perceive the onset of hypoglycaemia becomes diminished or absent. Symptoms are insidious and include difficulty concentrating, confusion, reduced consciousness, coma or seizures before autonomic activation (tremor, sweating, palpitation and nausea) [4]. Impaired awareness of hypoglycaemia is believed to affect approximately 20-25% of patients with T1DM and up to 10% of insulin-treated T2DM [4]. The condition increases the risk for severe hypoglycaemia by 3 to 6 fold compared to people with normal awareness [4]. It should be differentiated from "hypoglycaemia 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 neurological. The latter would include seizure disorders.

How will you treat this patient?

The key to reversing IAH is by adjusting the glucose target to avoid episodes of hypoglycaemia [4]. In order to achieve this goal, experts recommend frequent SMBG including pre-prandial and nocturnal measurements; avoidance of blood glucose values < 4 mmol/L, readjustment of blood glucose targets upwards (e.g., pre-prandial target 6.0 to 12 mmol/L and bedtime > 8 mmol/L), preventing A1C < 0.060 and inclusion of regular snacks between meals and at bedtime [1-4]. Helping patients identify subtle cues to their low blood glucose is also recommended [1-4]. While the CDA Clinical Practice Guidelines give some recommendations about hypoglycemia and driving [3], this patient requires special consideration because her job requires that she drives and because she has had both a period of unconsciousness and a motor vehicle accident where IAH was a plausible explanation.

The Case Revisited:

We published a similar case 2 years ago and we resolved the case by decreasing all of his insulin doses by 30% and perform regular SMBG at least four times daily (pre-prandial and at bed time) [7]. Since then, the approach has evolved largely with the use of the '6As model of counselling discussed in a previous article of this special issue. But for this specific patient instead of reducing insulin as a target we are now approaching these patients by individualising their glucose target by using the following graphic: graphical representation of individual physiologic and patient-centered aspects (https://durobojh7gocg.cloudfront.net/content/diacare/38/1/140/F1.large.jpg). Therefore, by simply personalising or adjusting her personal glucose target we were able to reduce her insulin doses and correct her IAH. I think that the HCP should now personalise more the treatment of patients with T2DM based on an individual glucose target rather than focusing on treatment target and I think it is the best lesson learn from this case. Because she was injured in a motor vehicle accident for which IAH played a plausible role, we notified the Ontario Ministry of Transportation who then investigated his suitability for driving, according to provincial law [8]. Regular SMBG demonstrated frequent asymptomatic hypoglycaemia requiring further reductions in her insulin dose. With our recommended treatment she was able to avoid hypoglycaemia completely and to reduce his total daily insulin dose by another 20% over a period of three months. Simultaneously, she began regaining warning symptoms when her blood glucose fell into the hypoglycaemic range. She was allowed to drive again with a non-commercial license provided that she does SMBG prior to driving and periodically during every driving exposure [8-10]. Our patient was able to organize a change in her work functions which permitted her to keep her job but not as a bus driver but as a road supervisor without clients. The present case emphasizes the importance of constantly personalising glucose target throughout treatment with insulin. The following points should also be considered [7]:

- Structured patient education program about symptoms of hypoglycaemia and hypoglycaemia avoidance, SMBG, the adequate use of insulin; 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 therapeutic modalities should be emphasized to restore hypoglycaemia awareness and to protect patients from severe hypoglycaemia [1-4].
- People with IAH may require psychological counseling to help them modify the management of their diabetes and to address the problems of "low concern" or "denial" regarding hypoglycaemia unawareness often seen in these patients [6].
- IAH poses a potential risk to safety, not only when driving, but also when exposed to heights or under water, operating machinery and other activities, and justifies the recommendation to perform SMBG in relation to such activities, even if this may seem inconvenient [1, 3].
- Relatives should be taught about IAH and learn on how to administer glucagon (1mg subcutaneously, or intramuscularly) [3].
- HCP should always remember to adjust treatment based on personalised glucose target throughout treatment with insulin.

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