HYPOGLYCEMIA in Diabetes Mellitus

Hypoglycemia is a serious acute complication of diabetes treatment. Recognizing the risk factors and taking steps to prevent low blood glucose should be a part of self-management education for all people taking glucoselowering medications. It is important for home care clinicians to evaluate their patient's understanding of hypoglycemia and the appropriate treatment options.

CASE STUDY

Bob, a 72-year-old man with a 20-year history of type 2 diabetes takes metformin and glyburide. Two weeks ago, he began taking 20 units of insulin glargine at bedtime. He checks his glucose every night before bed although last night he forgot. Bob also has hypertension and coronary artery disease, having had a coronary artery bypass graft 5 years ago. He has some peripheral neuropathy but walks every afternoon for exercise. This morning his wife said he was slow to awaken and seemed 'a little confused.' His forehead was cool and clammy. She left him in bed and waited for the doctor's office to open before calling. The office staff told her to call emergency services, fearing he was suffering a stroke or cardiac event. When emergency personnel arrived, he was evaluated and found to be even less responsive and somewhat combative. After learning he had diabetes, his capillary glucose was checked and found to be 38 mg/dL. Bob was taken to the emergency department for further evaluation.

ypoglycemia is an acute complication of diabetes treatment and is regarded as the main limiting factor in tight glucose control. It has been linked to adverse outcomes including ischemic events, arrhythmias, and neurological damage and can lead to increased morbidity and mortality (McCall, 2014). It has also been identified as a reason for emergency department (ED) visits accounting for more than 9% of adverse drug events in one study (Geller et al., 2014), and noted as the primary reason for approximately 300,000 adult ED visits in 2009 (Centers for Disease Control and Prevention, 2014a, 2014b). It is the most common and serious adverse event of insulin therapy (Lee, 2014). The American Diabetes Association (ADA) defines hypoglycemia as a plasma blood glucose ≤70 mg/dL (ADA, 2017a, 2017b) and it is classified depending on the degree of debilitating symptoms rather than the absolute value of blood glucose.

In people without diabetes, glucose homeostasis is maintained by the interplay of various hormones. Glucose is the body's primary source of energy and must always be available in the blood. Excess glucose is stored in the liver as glycogen that can be converted to glucose if needed for energy. Two hormones produced by the islets of Langerhans in the pancreas, glucagon produced by the α (alpha) cells, and insulin produced by the β (beta) cells, maintain glucose normally between 70 and 100 mg/dL (Lilley et al., 2017). Over time with a diagnosis of diabetes, the interplay between these hormones becomes dysfunctional and increases the risk of hypoglycemia (Unger, 2013).

In a study by Hsu et al. (2013), people with symptoms of hypoglycemia whether mild or severe had increased risk of cardiovascular events, all-cause hospitalization and all-cause mortality. It was suggested that the surge of sympathetic activity during hypoglycemia is the underlying mechanism that can lead to destabilization of atherosclerotic plaque, arrhythmias, and cardiac and cerebral ischemia (Hsu et al.).

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Risk Factors

Insulin and other glucose-lowering drugs, especially insulin secretagogues like glyburide and glipizide, contribute to hypoglycemia by elevating insulin levels. Irregular meal times and intake, skipped meals, excess of glucose-lowering medication, or strenuous exercise can cause low blood glucose. In a review of ED visits by people taking insulin, the top two precipitating factors were neglecting to eat and taking the wrong insulin (rapid acting vs. long acting). Patients ≥80 years old had the highest rate of ED visits and subsequent hospital admission for hypoglycemia (Geller et al., 2014).

People with other conditions including impaired renal function or congestive heart failure are at the highest risk (Pathak et al., 2016). Poor renal function can delay the clearance of insulin and other glucose-lowering drugs, potentially leading to excess blood levels and increased glucose-lowering effect. Patients taking betablockers for heart failure may not experience early symptoms of hypoglycemia that can significantly delay recognition and treatment (Lilley et al., 2017). The risk of hypoglycemia increases as endogenous insulin decreases and the patient must rely on insulin injections (McCall, 2014) making those with type 1 diabetes much more likely to experience hypoglycemia than their type 2 counterparts.

Older adults are particularly at risk, not only because of changes in drug metabolism, renal clearance, and polypharmacy, but also because of potential deficits in self-care. Even mild-to-moderate hypoglycemia can lead to falls, fractures, cognitive dysfunction, and hospitalization (Munshi, 2014). It is important to note that glyburide in particular increases the risk of hypoglycemia in the elderly and should be avoided (Munshi).

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Signs and Symptoms

Symptoms are unique to individuals, can change with each episode, and may or may not be present. Both mood and memory may be impaired. People with diabetes often describe feeling shaky, hungry, or angry as well as being sweaty or anxious. Neuroglycopenic symptoms may occur when glucose levels fall below 50 mg/dL causing cognitive deterioration, fatigue, irritability, visual failure, and even coma and seizures (Unger, 2013). Patients who have chronically high glucose levels may experience symptoms at levels higher than 70 mg/dL. Recurrent episodes of low blood glucose lower the threshold at which people feel symptoms and can significantly delay treatment. A prolonged low glucose is likely to result in further episodes within a 24-hour period

Table 1. Oral Hypoglycemia Treatment Options Containing ~15 g of Carbohydrate

R	3-4 glucose tablets or liquid Follow package directions, dose may vary slightly	Monosaccharide: Commercially available over the counter. Contains pure glucose. 'Preferred treatment because of rapid absorption (ADA, 2017).
	½ cup of fruit juice 1 tablespoon honey	Monosaccharide: Contains fructose rather than glucose
	1 cup nonfat milk	Disaccharide: Contains lactose, rather than glucose
S	4–6 oz sweetened (nondiet) soda	Usually sucrose— disaccharide of glucose and fructose
	4–5 hard candies	Potential choking hazard and difficult to ingest rapidly. Not preferred treatment. "Fruit snacks" may contain fiber that delays absorption.

and may result in structural damage to the brain (Unger).

"Hypoglycemic unawareness" is a dangerous condition in which the patient experiences no symptoms of low blood glucose. This is most common in people with type 1 diabetes or longstanding type 2 diabetes. Hypoglycemia-associated autonomic failure results in an altered threshold of symptoms as well as a delay or loss of sufficient response from hormones such as glucagon, cortisol, and epinephrine that help regulate glucose. Symptoms such as sweating, hunger, and tremors may not occur until after mental confusion is evident (McCall, 2014). These patients often experience wide swings in glucose levels and should be encouraged to monitor their glucose more regularly. Family and friends should also be made aware to observe for subtle behavioral changes.

Treatment

The "rule of 15" or the "15-15 rule" is commonly followed in the treatment of hypoglycemia. It is a general starting point that includes the intake of 15 g of carbohydrate followed by a retest of blood glucose in 15 minutes. Within 15 minutes, 15 g of carbohydrate will raise the plasma glucose about 75 mg/dL (Unger, 2013). Pure glucose is the preferred method of treatment as foods with added fat can delay absorption of glucose (Table 1) (ADA, 2017a, 2017b). Plasma glucose or suspected glucose below 70 md/dL should be treated and retreated as necessary. Treatment should not be delayed while searching for a glucose meter. After the glucose has returned to normal, a meal or snack may be needed to avoid recurrence.

In cases of severe hypoglycemia where the person with diabetes is unable to swallow or otherwise help themselves, glucagon injection is necessary (it may be given subcutaneously, IM, or IV). Glucagon stimulates release of glucose by the liver thereby increasing blood glucose (Lilley et al., 2017); however, nausea and vomiting are common side effects. Family members must be instructed on how to use a glucagon kit as it requires not only injection but reconstitution of the powder into a solution. It is important to check the expiration date on the glucagon kit as it has a relatively short shelf life. A solution of 50% dextrose may be administered when intravenous access is available. Although both of these

treatments are effective, they are costly and are accompanied by side effects.

Fear of hypoglycemia can be intense and lead to underdosing of diabetes medication or overtreating low glucose levels (McCall, 2014). Because symptoms are so uncomfortable, it is easy to understand why someone might continue to treat with ingestion of carbohydrates until the symptoms have subsided that could take 15 minutes or more. This action and overtreatment leads to hyperglycemia. The addition of protein is not recommended for the treatment or prevention of hypoglycemia as it has little effect on glucose (Evert, 2014).

Hypoglycemia has been identified as a contributing factor in motor vehicle accidents. Having had low glucose levels increases the risk of recurrence for the following 24 hours. High-risk patients should be counseled to test their blood glucose before driving and at 1-hour intervals on long trips (Unger, 2013). Carbohydrates for hypoglycemia treatment should be available at all times for immediate treatment.

Assessment and Teaching

Prevention of hypoglycemia is best accomplished through knowledge of self-care and self-management. Patients who understand the interplay between diet, exercise, glucose monitoring, and medication are better able to anticipate changes in blood glucose levels based on their behavior and other factors. Attending a comprehensive diabetes education program is key early on after diagnosis with diabetes and when therapy changes, new complications arise, or for annual reassessment. Disappointingly less than 4% of Medicare patients with type 2 diabetes received diabetes education in the first 12 months after diagnosis (Duncan et al., 2009).

It is essential that home care clinicians teach and use teach-back to determine patient's understanding of their glucose-lowering medication and hypoglycemia. This should be done regardless of their experience with this acute complication. The clinician can assess the patient by asking: Are they knowledgeable of their personal risk factors, symptom recognition, and treatment options? Do they carry diabetes identification and medication information on their person? Have they experienced hypoglycemia in the past and if so, how did they handle the situation? Every effort should be made to determine the contributing factors to each episode of hypoglycemia. As mentioned earlier, erratic intake or meal times and taking the wrong kind of insulin were the most common reasons noted in ED visits. The clinician can help patients evaluate contributing factors.

Some issues to explore with the patient are: might the diabetes medication dose have been inadvertently increased; can the patient accurately draw up or 'dial' a consistent insulin dose; do they use a pill box to help avoid double dosing? Does the patient follow a meal plan that is consistent with their medication regimen? Are they aware of the carbohydrate content of various foods? Is the carbohydrate content of meals consistent? Are they aware of when the insulin has peak action and they are most at risk? Do they understand the effect of exercise or timing of medications on glucose levels? Is alcohol intake a factor? Are family members or caregivers aware of the risks and symptoms of hypoglycemia? Is there an action plan in place if symptoms occur? Are treatment options readily available? Are they aware of when the provider should be contacted? Is there a pattern of hypoglycemia events? Are the glucose meter and related supplies in good condition and used correctly? Can they explain what the results mean and if action is needed based on monitoring results?

Some patients may benefit from continuous glucose monitoring (CGM) to retrospectively analyze glucose levels and to provide real-time tracking. Glucose values are displayed every 5 minutes along with trending information as well as high and low glucose alarms. CGM may be used in the short term as 'diagnostic' or by patients as an adjunct to capillary blood glucose monitoring (Vigersky, 2014). There are now insulin pumps that provide integrated CGM coming closer to a 'closed loop' system of insulin delivery based on real-time glucose monitoring (United States Food and Drug Administration, 2016).

Home care clinicians play an important role in assessing diabetes self-care knowledge and skills, and providing patients with important information and support as needed. Ideally, people taking glucose-lowering drugs have the necessary knowledge to prevent hypoglycemia. If low blood glucose does occur, they have treatment measures readily available. Clinicians should Brendan Delany / shutterstocl



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ensure that both patients and caregivers have the necessary self-care skills to remain safe. Glucose monitoring, food intake, medication taking, other chronic conditions, and exercise all play a role. A referral to a comprehensive diabetes education program should be considered if the patient is not already engaged with such a program. Programs can be found through the ADA (http://professional.diabetes.org/erp_list_zip) or the American Association of Diabetes Educators (https://www.diabeteseducator.org/patientresources/find-a-diabetes-educator). The National Diabetes Education Initiative, the Centers for Disease Control and Prevention, and the ADA have free printable pages on multiple diabetes education topics. After a thorough assessment, the home care clinician can use these preprinted sheets to reinforce hypoglycemia risk factors, signs and symptoms, and treatment.

Return to Case Study

Bob was clearly exhibiting signs of hypoglycemia upon awakening with diaphoresis and becoming progressively confused and combative. His wife was not attuned to recognizing these symptoms and therefore did not initiate treatment. While waiting for the provider's office to open, Bob's glucose continued to fall. The drama and expense of emergency services might have been avoided with prompt and appropriate treatment. In Bob's case, he had been to an early evening cocktail party with light snack foods and more than the usual alcohol intake. Being tired, he went to bed early without a full dinner. This lighter than usual dinner along with alcohol intake probably contributed to Bob's low blood glucose. Many alcoholic beverages have high carbohydrate content causing an initial spike in glucose followed by hypoglycemia. Additionally, taking glyburide increased his risk of hypoglycemia (McCall, 2014). The American Geriatrics Society recommends that glyburide should generally not be prescribed to older adults with type 2 diabetes (American Geriatrics Society, 2015). Bob's primary care provider and/or pharmacist should be contacted about an alternate oral agent. Although the body has mechanisms to respond to drops in blood glucose, aging can reduce the release of necessary stress hormones (Ballin, 2016). For Bob, hypoglycemia is especially dangerous given his cardiac history. A comprehensive assessment and targeted education would likely have saved Bob and his wife this traumatic experience. Depending on his overall glucose control and knowledge of selfcare, diabetes education and/or medication changes may be necessary. The home care clinician will be a valuable resource in helping Bob and his wife incorporate any changes into his diabetes regimen as well as serving as the bridge to his provider.

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