

What Do You Need to Know About Diabetic Hypoglycemia?

Kim A. Carmichael, MD—Series Editor

Q How important is hypoglycemia among persons with diabetes?

A Hypoglycemia is the most important factor limiting safe glycemic management of persons with type 1 and type 2 diabetes.¹ Level 1 hypoglycemia (glucose, < 70 mg/dL) is clinically important because, at this level, persons usually develop neuroendocrine responses. However, since many individuals have impaired counterregulation and awareness, they lose these early physiologic triggers to prevent more serious events. Level 2 hypoglycemia (glucose, < 54 mg/dL) is when persons are likely to show clinical signs of neuroglycopenia, and level 3 is when there is a severe event with clinical alterations in mental or physical functioning requiring third-party assistance.

Before common use of continuous glucose monitoring (CGM) technology, the average person with type 1 diabetes would experience symptomatic hypoglycemia about twice per week and 1 severe episode per year.² More recent data show a risk of 0.98 to 3.2 serious events per person per year for persons with type 1

diabetes and 1 to 1.05 events per person per year for persons with type 2 diabetes.³ Hypoglycemia has been identified as the cause of death for 2% to 4% of individuals with type 1 diabetes.²

The Standards of Care from the American Diabetes Association indicate that the occurrence and risks for hypoglycemia, as well as cognitive function, be addressed at every patient encounter.^{1,3}

Q What are the potential complications of hypoglycemia?

A Severe hypoglycemia can be associated with confusion, falls, arrhythmia, and seizures. Persons with type 1 diabetes may have a mortality rate up to 10%.⁴ It can cause brain death and prolongation of the corrected QT interval, which are often associated with nocturnal hypoglycemia.² Hypoglycemia is the second-most frequent medication-associated cause of emergency hospitalization⁴ and is also a risk factor for motor vehicle accidents.⁴⁻⁶ Among older individuals, level 3 hypoglycemia increases the risk of dementia.¹

Patients with a history of hypoglycemia often fear intensive management, thereby limiting optimal glycemic control.⁷ They often will not discuss these fears with their health care providers, sometimes resulting in medication adjustments that further increase the risk of hypoglycemia.^{3,7}

Q What are the risk factors for developing diabetic hypoglycemia?

A The most common risk factor is use of insulin or sulfonylurea therapy, alone or in combination with other medications for diabetes.^{1,4} Persons who are more at risk for level 3 hypoglycemia include those older than 60 years of age, those of African American descent, those with poor to moderate glycemic control/variability, those with albuminuria, and those with diminished cognitive function.^{1,8} Other risk factors include peripheral neuropathy,⁷ chronic kidney disease,^{4,9} high insulin dose, low hemoglobin A1c (HbA1c), and long duration of diabetes.¹⁰ Recent changes in insulin dose after HbA1c measurements also increase the risk of hypoglycemia resulting in visits to the emergency department.⁹

Asymptomatic hypoglycemia is the most common risk factor for severe events among persons with type 1 diabetes.¹⁰ The most common cause of hypoglycemia unawareness is a generally reversible metabolic adaptation to frequent hypoglycemia, known as hypoglycemia-associated autonomic failure (HAAF).^{11,12} This adaptation has been shown to develop rapidly after as few as three 2-hour periods of hypoglycemia within 30 hours.¹³ Generalized autonomic neuropathy may also manifest similarly

AFFILIATIONS:

Professor of Medicine, Department of Internal Medicine, Division of Endocrinology, Diabetes, and Lipid Research, Washington University School of Medicine, St. Louis, Missouri

CITATION:

Carmichael KA. What do you need to know about diabetic hypoglycemia? *Consultant*. 2021;61(5):e23-e25. doi:10.25270/con.2021.05.00002

DISCLOSURES:

The authors report no relevant financial relationships.

CORRESPONDENCE:

Kim A. Carmichael, MD, Professor of Medicine, John T. Milliken Department of Medicine, Washington University School of Medicine, 660 S Euclid Ave, St Louis, MO 63110-1010 (carmichaelk@wustl.edu)

but often has other signs of autonomic dysfunction and may or may not be reversible.

Q How can our patients prevent hypoglycemia?

A First and foremost, patients should be educated about diet and lifestyle and should understand general risk factors. Patients need to be attentive to self-glucose monitoring, particularly related to dietary and medication changes, as well as physical activity or exercise.^{1,5,6} Persons at increased risk should always check their glucose levels before driving and eat a snack if they have any concern. Additional times of risk include during sleep or after consumption of ethanol.¹ Tools for patients and caregivers to stratify hypoglycemia risk, along with targeted risk-reduction strategies, are also available.³

Health care providers should counsel patients who are at risk to increase the preprandial minimum target (eg, from 70 mg/dL to 80 mg/dL).¹

Insulin pump therapy may also reduce the frequency of hypoglycemia.³ Patients already on insulin pump therapy may need to adjust their insulin infusion rates associated with exercise, changes in dietary timing, or prompts given by CGM devices.

CGM has increasingly become a useful intervention to reduce hypoglycemia risk, particularly in the setting of unawareness and impaired counterregulatory hormone responses.^{1,3,14} CGM is also effective in detecting nocturnal hypoglycemia¹⁴ and reducing time spent in level 1 hypoglycemia.¹ However, there are no studies to date demonstrating a decreased rate of level 3 hypoglycemia using CGM.¹

Dogs trained to identify hypoglycemia may also be helpful for patients with impaired awareness.³

Q How should patients with diabetes treat hypoglycemia?

A All persons should carry some form of medical alert identification. Patients should be educated about how

to recognize early symptoms of hypoglycemia, as well as know the risk factors for this to occur. People should check glucose levels before operating motor vehicles, maintaining glucose levels of greater than 100 mg/dL.⁵

The most important factor in managing HAAF is to avoid hypoglycemia in order to facilitate the normal compensatory metabolic responses to recover.⁴ This may take 2 weeks for initial responsiveness and up to 3 months for full recovery.

For mild hypoglycemia, patients should consume food with fast-acting simple carbohydrates (eg, glucose) without high fat or protein content.¹ Once the glucose is normalized, then eating a meal or snack would be indicated.

In persons unable or unwilling to take oral glucose, parenteral glucose (in a health care environment) or glucagon would need to be given. A prescription for glucagon should be given for all patients at risk of level 2 or 3 hypoglycemia.^{1,3}

Historically, glucagon was only available as a brand-name powder that required reconstitution before injection. A generic for this has recently been approved by the US Food and Drug Administration. The powdered formulations require education for patients and their families/caregivers/friends/coworkers regarding preparation, reconstitution, dosing, and injection technique and may then take several minutes to administer. During the stress of a hypoglycemic event, many caregivers may be hesitant or unable to provide this form of glucagon. Since 2019, newer forms of glucagon, including prefilled liquid pens and nasal powder devices, have become available to adults in the United States to treat persons with hypoglycemia.³ These have proven to be effective and well-tolerated by patients.

REFERENCES

1. American Diabetes Association. 6. Glycemic targets: standards of medical care in diabetes-2021. *Diabetes Care*. 2021;44(Suppl 1):S73-S84. <https://doi.org/10.2337/dc21-s006>
2. Cryer PE, Axelrod L, Grossman AB, et al. Evaluation and management of adult hypoglycemic disorders: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2009;94(3):709-728. <https://doi.org/10.1210/jc.2008-1410>
3. Thieu VT, Mitchell BD, Varnado OJ, Frier BM. Treatment and prevention of severe hypoglycaemia in people with diabetes: current and new formulations of glucagon. *Diabetes Obes Metab*. 2020;22(4):469-479. <https://doi.org/10.1111/dom.13941>
4. Best C, Carmichael KA. Iatrogenic hypoglycemia: identification, troubleshooting, and precautions. *Consultant*. 2015;55(7):541-542. <https://www.consultant360.com/articles/iatrogenic-hypoglycemia-identification-troubleshooting-and-precautions>
5. Carmichael KA. What do doctors need to teach their patients with diabetes about driving their vehicles? *Consultant*. 2014;54(4):271-272. <https://www.consultant360.com/articles/what-do-doctors-need-teach-their-patients-diabetes-about-driving-their-vehicles>
6. American Diabetes Association. Diabetes and driving. *Diabetes Care*. 2014;37(Suppl 1):S97-S102. <https://doi.org/10.2337/dc14-S097>
7. Flatt AJS, Little SA, Speight J, et al. Predictors of recurrent severe hypoglycemia in adults with type 1 diabetes and impaired awareness of hypoglycemia during the HypoCOMPaSS study. *Diabetes Care*. 2020;43(1):44-52. <https://doi.org/10.2337/dc19-0630>
8. Lee AK, Lee CJ, Huang ES, Sharrett AR, Coresh J, Selvin E. Risk factors for severe hypoglycemia in black and white adults with diabetes: the Atherosclerosis Risk in Communities (ARIC) study. *Diabetes Care*. 2017;40(12):1661-1667. <https://doi.org/10.2337/dc17-0819>
9. Lacy ME, Whitmer RA, Lee SJ, Rushakoff RJ, Pletcher MJ. Identifying potential intervention points for acute hypoglycemic events in patients with type 2 diabetes using retrospective clinical data. *Clin Diabetes*. Published online March 1, 2021. <https://doi.org/10.2337/cd20-0057>
10. Henriksen MM, Andersen HU, Thorsteins-son B, Pedersen-Bjergaard U. Asymptom-

atic hypoglycaemia in type 1 diabetes: incidence and risk factors. *Diabet Med.* 2019;36(1):62-69. <https://doi.org/10.1111/dme.13848>

11. Cryer PE. Mechanisms of hypoglycemia-associated autonomic failure in diabetes. *N Engl J Med.* 2013;369(4):362-372. <https://doi.org/10.1056/nejmra1215228>
12. Seaquist ER, Anderson J, Childs B, et al. Hypoglycemia and diabetes: a report of a workgroup of the American Diabetes Association and the Endocrine Society. *Diabetes Care.* 2013;36(5):1384-1395. <https://doi.org/10.2337/dc12-2480>
13. Moheet A, Kumar A, Eberly LE, Kim J, Roberts R, Seaquist ER. Hypoglycemia-associated autonomic failure in healthy humans: comparison of two vs three periods of hypoglycemia on hypoglycemia-induced counterregulatory and symptom response 5 days later. *J Clin Endocrinol Metab.* 2014;99(2):664-670. <https://doi.org/10.1210/jc.2013-3493>
14. Wei W, Zhao S, Fu SL, et al. The association of hypoglycemia assessed by continuous glucose monitoring with cardiovascular outcomes and mortality in patients with type 2 diabetes. *Front Endocrinol (Lausanne).* 2019;10:536. <https://doi.org/10.3389/fendo.2019.00536>