

New Options to Simplify the Treatment of Severe Hypoglycemia in Long-Term Care

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Margaret finished her rehabilitation session 30 minutes ago. She starts to sweat and reports that her heart is pounding, and she feels dizzy. She calls for a staff person, who enters with a lunch tray that was late arriving. He tries to get Margaret to eat. She refuses lunch and juice. She is combative by the time he tries to test her blood glucose. Her blood glucose is 39 mg/dL. The staff person runs out and returns with a glucagon emergency kit (GEK). He has seen the kit before, but it has been some time since he was trained on the multistep process to mix and inject it. Meanwhile, Margaret becomes confused, tries to stand up, and falls.

Severe hypoglycemia — characterized by altered mental and/or physical status and requiring assistance for the treatment of hypoglycemia — in a person with diabetes (PWD) is a potential occurrence in every long-term care (LTC) setting. One in four adults aged 65 or older are living with diabetes, and nearly 34% of long-term care residents have diabetes (*Diabetes Care* 2016;39:308–318; American Diabetes Association, “Fast Facts,” Feb. 2020, <https://bit.ly/3gKeMcj>). The risk of severe hypoglycemia is the most important factor determining glycemic goals and treatment in older patients with diabetes (*Diabetes Care* 2021;44[Suppl 1]:S168–S179). Optimal management of severe hypoglycemia can improve outcomes for patients, family, providers, staff, and the LTC facility or organization.

The presence of geriatric syndromes (especially decline in cognition, mobility, and function), existing diabetes-related complications, cardiovascular disease, and other comorbidities as well as the need for individualized medication management are primary challenges faced by LTC practitioners. Proactive and creative strategies are required at the institutional level to ensure consistent care practices, prompt assessment of unstable patients, adequate review and reporting of glucose monitoring data, and planning safe care transitions (*Diabetes Spectr* 2020;33:236–245).

Recent recommendations from the American Diabetes Association (ADA) suggest that different, simplified, and practical treatment approaches are needed for diabetes management in LTC because of the unique environmental challenges in various care settings (*Diabetes Care* 2021;44[Suppl 1]:S168–S179). Fortunately, major advances in blood glucose monitoring, insulin therapy, and most recently glucagon treatment can provide simplifications aimed at managing hypoglycemia in the LTC community.

The Problem of Severe Hypoglycemia in the Older Adult

People older than 70 years have reported more episodes of hypoglycemia than those under 60 years (*JAMA Intern Med*

2014;174:1116–1124). The average person with type 1 diabetes experiences a severe event two to four times annually, and more than 9% of persons with type 2 diabetes have a severe event as frequently as monthly (*Arch Intern Med* 2011;171:362–364; *JAMA Netw Open* 2020;3:e1919099; *Diabetes Technol Ther* 2019;21:66–72).

Several patient-specific factors exacerbate the problem of hypoglycemia and severe hypoglycemia in LTC facilities. The presence of multiple comorbidities; impaired cognitive function, intestinal absorption, and renal function; and variable appetite and food intake, undernutrition, and impaired swallowing all increase the risk for severe hypoglycemia. Careful assessment of individuals for the presence of these factors is essential to determining glycemic goals and treatment strategies.

In the institutional setting, hypoglycemia has several potential causes (American Medical Directors Association, *Diabetes Management in the Post-Acute and Long-Term Care Setting*, Clinical Practice Guideline, AMDA, 2015):

- Age and impaired counterregulation
- Unawareness of or prior severe hypoglycemia
- Inappropriately “tight control” of diabetes
- Fasting or erratic meal consumption and alcohol use
- Insulin administration errors (improper dose, timing, or type)
- Frequent or persistent use of sliding-scale insulin
- Concurrent use of sulfonylureas and insulin
- Polypharmacy (quinolones, angiotensin-converting enzyme inhibitors, angiotensin receptor blocker, and nonselective beta blockers)
- Chronic renal, hepatic, or cardiovascular disease
- Gastroparesis
- Increased insulin sensitivity (weight loss, increased activity)
- Endocrine deficiency (thyroid, adrenal, or pituitary)

Families of PWD have reported that they experience higher levels of diabetes distress and fear of hypoglycemia than the PWD (*Diabetes Ther* 2019;10:2305–2311). Surprisingly, two in three family members report being anxious and worried about the risk of hypoglycemia to their PWD. This concern is heightened for PWD who have moderate or advanced dementia because they may not be able to communicate their symptoms to first-line caregivers. Fear of hypoglycemia often results in potentially unhelpful strategies such as running glucose levels high or overconsuming food, which are counterproductive to optimal diabetes control.

The clinical challenges to providers include progressive cognitive decline in the PWD, frailty, and depression that can

compromise patient safety. Irregular and poor meal intake, refusal of glucose monitoring or medications, and falls are but a few challenges to staff caring for PWD in LTC. Furthermore, staff turnover issues in LTC amplify such challenges.

Finally, hypoglycemia poses a significant burden to the LTC facility and health care system. More than \$1.84 billion was spent on the direct costs of hypoglycemia in 2009 (*J Med Econ* 2016;19:852–857). Severe hypoglycemia is associated with a twofold increase in fall risk in older adults with type 2 diabetes. Not surprisingly, the exaggerated prevalence and severity of hypoglycemia in the elderly accounts for higher emergency department visits, cardiovascular events, hospitalizations, and mortality (*JAMA Netw Open* 2020;3:e1919099; *Diabetes Care* 2013;36:894–900).

Recognizing Severe Hypoglycemia

Hypoglycemia is classified in three categories, which are helpful to document in the medical record to accurately indicate the severity and the interventions to minimize it:

- Level 1: Glucose < 70 mg/dL (3.9 mmol) and > 54 mg/dL (3.0 mmol/L)

- Level 2: Glucose < 54 mg/dL (3.0 mmol/dL)
- Level 3: A severe event characterized by altered mental and/or physical status requiring assistance for treatment of hypoglycemia

Clinically significant hypoglycemia results in neuroglycopenic symptoms that require immediate action with a quick-acting carbohydrate to resolve. A severe hypoglycemia event is characterized by an altered mental or physical status that requires assistance to treat. As with the case of Margaret, neuroglycopenic symptoms such as confusion, anxiety, and combative behavior may result. Coma and seizures are possible as well. Glucagon is the recommended treatment if a patient is obtunded and unable or unwilling to consume oral glucose.

It has long been believed that only individuals with tight glycemic control (glycated hemoglobin [A1C] levels < 7%) are at risk for severe hypoglycemia. However, the risk occurs across all levels of diabetes control, and it is prevalent even at A1C levels above 9% (*Arch Intern Med* 2011;171:362–364; *Diabetes Care* 2020;43:2060–2065).

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retirement home, a private elderly care institution, assisted living and independent living residents, and community dwelling and residential care facility residents.

The interventions were similar for community-dwelling individuals and for LTC residents. Only one study included participants with cognitive impairment. Eleven of the studies used the UCLA Loneliness Scale version 3 (score range: 20–80, with higher scores indicating more loneliness), two used the De Jong Gierveld Loneliness Scale, and two used researcher-created scales. The interventions were categorized into four types: (1) leisure/skill development (six studies); (2) psychological therapies (five studies); (3) social facilitation interventions (two studies); and (4) animal support interventions (two studies) (see the table).

The majority of the interventions improved loneliness scores over time, but the changes in most studies were modest. The interventions with the greatest reduction in loneliness were laughter therapy, reminiscence therapy, and horticultural therapy. Key components of these interventions were the focus on group activities and relationship formation over time. Interestingly, the most successful interventions did not rely on

significant physical activity or mobility, making them accessible to participants of diverse abilities.

The interventions with the smallest impact on loneliness were physical exercise, participation in general activities, and the reminiscence radio listening program. A major limitation of this review, which affects its generalizability, is the exclusion of residents with cognitive impairment in 14 of the 15 studies. Because cognitive impairment is associated with greater loneliness and may be a barrier to a successful loneliness intervention, additional studies including this population are needed.

These studies would need to use measurement scales that have been validated for people with dementia, such as the De Jong Gierveld Loneliness Scale, keeping in mind the limitations of self-reported measures in people with more advanced stages of dementia. Additional studies with computer or internet-based interventions for LTC residents, which have been shown to reduce loneliness in community-dwelling older adults, are also needed. 

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Treatment advances such as continuous glucose monitoring have reduced the frequency of severe hypoglycemia but not eliminated it (*Diabetes Technol Ther* 2019;21:66–72).

Any PWD who uses insulin or a sulfonyleurea is at high risk for hypoglycemia and severe hypoglycemia. The risk is highest with multiple basal and mealtime insulin combinations. However, in the elderly, using long-acting basal insulin alone is associated with severe hypoglycemia-related hospitalization and emergency department visits (*JAMA Netw Open* 2020;3:e1919099).

Sliding-scale insulin protocols are discouraged in LTC settings because of the hypoglycemia risk associated with stacking insulin, but unfortunately they are still used during situations such as acute hospitalization. This raises an important reminder that discharge orders must be carefully reviewed after a hospitalization, and sliding-scale regimens should be discontinued before or soon after LTC readmission.

Simplifying Severe Hypoglycemia Management

Because hypoglycemia treatment goals involve ensuring patient safety and reducing readmission rates after transitions of care, helping staff and families understand how to manage severe hypoglycemia is a reasonable expectation.

The ADA guidelines define specific actions to address severe hypoglycemia management in PWD (*Diabetes Care* 2021;44[Suppl 1]: S73–S84, S168–S179):

1. Older adults with diabetes are at higher risk of hypoglycemia than younger adults. Ascertain and address hypoglycemia episodes at routine visits.
2. Glucagon should be prescribed for all individuals who are at increased risk of blood glucose levels below 54 mg/dL. They should have a glucagon prescription available as needed, and caregivers should know where the glucagon is stored and how to administer it.

Glucagon, a pancreatic counterregulatory hormone responsible for raising blood glucose in the fasted state, is absent or dysfunctional in diabetes. Glucagon was first produced commercially 60 years ago and until recently was available only in a difficult-to-use multistep lyophilized powder glucagon emergency kit (GEK) that requires manual reconstitution at time of use. Further usability studies with GEKs have demonstrated that fewer than 13% of caregivers can successfully prepare and administer a full dose of glucagon during a simulated emergency (*Diabetes Technol Ther* 2017;19:423–432).

Innovations to simplify glucagon administration in an emergency outside

of the hospital setting are critically important to the health care system. As of 2019, new glucagon formulations are available that have simplified the ability to promptly deliver glucagon. Baqsimi (Eli Lilly) is glucagon in a powdered form that is delivered nasally, and Gvoke (Xeris) is a pre-mixed, solubilized liquid glucagon in an autoinjector or prefilled syringe that is administered subcutaneously. Each provides unique features for patients, families, staff, providers, and LTC

organizations to enhance both confidence and competency in the prompt, reliable management of a severe hypoglycemia event.

Because severe hypoglycemia is associated with significant morbidity in PWD in the post-acute and long-term care setting, prompt recognition of its symptoms and immediate treatment are essential. Newer formulations of glucagon will improve the treatment of hypoglycemia by family members, staff, and even untrained caregivers. 

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