Review

Type 2 Diabetes, Hypoglycemia, and Basal Insulins: Ongoing Challenges

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ABSTRACT

Hypoglycemia in people with insulin-treated type 2 diabetes can be a limiting factor for management and a barrier to optimizing glycemic control. Even mild episodes of hypoglycemia can affect an individual's quality of life, and fear of hypoglycemia can lead to underinsulinization. This article explores the prevalence and consequences of hypoglycemia in people with type 2 diabetes with a focus on those who use basal insulins, offering strategies for prevention and management. It also discusses the benefits and challenges associated with new basal insulins, and their potential role in reducing hypoglycemia risk. (*Clin Ther.* 2017;39:S1–S11) © 2017 Elsevier HS Journals, Inc. All rights reserved.

Key words: basal insulin, hypoglycemia, management, type 2 diabetes.

INTRODUCTION

In people with insulin-treated type 2 diabetes, hypoglycemia can be a limiting factor in the management of, and a barrier to the optimization of, glucose control. Even mild episodes of hypoglycemia can affect an individual's quality of life, and fear of hypoglycemia can lead to underinsulinization.[1]

Clinicians may not always inquire about hypoglycemia, and as a result, there can be missed opportunities to address issues surrounding its prevention and management.[2,3] This article addresses key issues related to the recognition, consequences, and management of hypoglycemia in people with type 2 diabetes —particularly as a result of basal insulin use.

What Is Hypoglycemia and How Is It Recognized?

The diagnostic criterion for hypoglycemia varies depending on the definition and guideline used; it ranges between <4.0 and <3.0 mmol/L.[4–6] Because of these different thresholds, it is often difficult to quantify the overall prevalence of hypoglycemia or to make meaningful comparisons of hypoglycemia rates between trials in people with type 2 diabetes (thresholds have varied from <3.1 to 3.9 mmol/L in basal insulin trials[7,8]).

Hypoglycemia is generally defined as a triad of an abnormally low blood glucose level, the presence of autonomic or neuroglycopenic symptoms (Table I), and symptoms of response to the administration of carbohydrates.[4–6] The severity of hypoglycemia is defined by its clinical manifestations (Table II).[4,9]

It is important for clinicians to inquiry about hypoglycemia in people with type 2 diabetes treated with insulin; a patient care flow sheet can serve as a helpful reminder in this regard.[4,10] Moreover, questions as to the timing, antecedent events, and patterns can help to determine the etiology of the hypoglycemia and whether it is related to prandial or basal insulin use, and whether there are additional factors involved (Figure).

Physicians need to ensure that patients and their families are educated about hypoglycemia avoidance, treatment, and harm reduction. Harm reduction in hypoglycemia includes: (1) reviewing the need for medical alert identification; (2) reviewing the proper treatment of hypoglycemia; (3) prescribing glucagon and discussing the training of an at-home supportive caregiver; and (4) reviewing guidelines for driving.

It is also important for health care providers to determine the blood glucose level at which a patient first

Table I. Symptoms of hypoglycemia.[*]

Autonomic	Neuroglycopenic
Trembling	Difficulty concentrating
Palpitations	Confusion
Sweating	Weakness
Anxiety	Drowsiness
Hunger	Vision changes
Nausea	Difficulty speaking
Tingling	Headache
	Dizziness

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recognizes the symptoms of hypoglycemia. This level can vary by individual, based on his or her overall level of glycemic control, frequency of antecedent hypoglycemia, and other factors. If neuroglycopenic manifestations occur before autonomic symptoms (*hypoglycemia unawareness*), then the patient may be unable to self-treat his or her hypoglycemia, increasing the risk for harm. Hypoglycemia unawareness has been found in up to 10% of insulin-treated people with type 2 diabetes.[11] Patients with hypoglycemia unawareness may need to have their glycemic target adjusted and their insulin regimen reassessed.

Hypoglycemia unawareness is generally caused by repeated episodes of hypoglycemia, leading to the loss of related counter-regulatory hormonal responses.[4,12] However, hypoglycemia unawareness may also be related to decreased cognitive ability: In a subgroup of almost 3000 participants in the ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial,[13] poor cognitive function was associated with an increased risk for severe hypoglycemia. Cognitive testing can help to identify patients who may have difficulty taking insulin properly and who are at risk for hypoglycemia unawareness.[14]

How Common Is Hypoglycemia in People with 2 Diabetes?

The rate of hypoglycemia in people with type 2 diabetes is difficult to define. In clinical practice, for example, it was found that only 15% of people with type 2 diabetes had spoken to their doctors about mild or moderate events.[2] Less than 10% of people on basal insulin who experienced a hypoglycemic episode in the preceding 30 days had consulted their physicians.[3]

In the clinical trial setting, determining hypoglycemia rates can be challenging. Study investigators define and quantify hypoglycemia in different ways, which can lead to variable findings.[15] Other methodologic factors may also affect results. For example, shorter studies may

Table II. Severity of hypoglycemia.[*]

Severity	Definition
Mild	Autonomic symptoms are present. The individual is able to self-treat.
Moderate	Autonomic and neuroglycopenic symptoms are present. The individual is able to self-treat.
Severe	Individual requires assistance of another person. Unconsciousness may occur. Plasma glucose is typically <2.8 mmol/L.

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