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Review

Review of Hypoglycemia in the Older Adult: Clinical Implications and Management

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ABSTRACT

The aging of the population is a worldwide phenomenon. The prevalence of diabetes rises with increasing age, so the personal and financial costs of diabetes in the aging population have become significant burdens. In 2012, 104 billion (59%) of the estimated $176 billion in United States healthcare expenditures attributable to diabetes were utilized by patients older than 65 years of age [American Diabetes Association (1)]. With improvement in diabetes management and better glycemic control in the general population, there is an increase in the prevalence of hypoglycemia, which is the complication of the treatment of diabetes. Older adults with diabetes have a higher risk for hypoglycemia due to altered adaptive physiologic responses to low glucose levels. These patients also have comorbidities, such as cognitive and functional loss, that interfere with prompt identification and/or appropriate treatment of hypoglycemia. Older adults who suffer from hypoglycemia also have increased risk for falls, fall-related fractures, seizures and comas and exacerbation of chronic conditions, such as cognitive dysfunction and cardiac events. Thus, hypoglycemia in the older adult must be proactively avoided to decrease significant morbidity and mortality. Education of the patients and caregivers is important in prevention and treatment of hypoglycemia. In this article, we discuss the important aspects and unique challenges pertaining to hypoglycemia in older population. We also highlight the risks, consequences and prevention and management strategies for hypoglycemia that can be used by healthcare providers caring for older populations.

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RÉSUMÉ

Le vieillissement de la population constitue un phénomène mondial. La prévalence du diabète augmente en fonction de l'âge, de sorte que les coûts personnels et financiers du diabète liés à la population vieillissante sont devenus d'importants fardeaux. En 2012, les 104 milliards de dollars (G$) (59%) en soins de santé attribuables au diabète que les É.–U. ont dépensés par rapport à l'estimation prévue de 176 G$ ont servi aux patients de plus de 65 ans [American Diabetes Association (1)]. En raison de l'amélioration de la prise en charge du diabète et de la meilleure régulation de la glycémie de la population générale, on observe une augmentation de la prévalence de l'hypoglycémie, qui est la complication liée au traitement du diabète. Les personnes âgées souffrant de diabète sont exposées à un risque plus élevé d'hypoglycémie en raison de l'altération des réponses physiologiques adaptatives aux faibles taux de glycémie. Ces patients ont également des comorbidités comme des pertes cognitives et fonctionnelles qui interfèrent avec l'identification prompte et/ou le traitement approprié de l'hypoglycémie. Les personnes âgées qui souffrent d'hypoglycémie sont également exposées à l'augmentation du risque de chutes, de fractures liées aux chutes, de crises épileptiques et de comas et à l'exacerbation de maladies chroniques comme le dysfonctionnement cognitif et les événements cardiaques. Par conséquent, l'hypoglycémie chez la personne âgée doit être évitée de manière proactive pour diminuer significativement la morbidité et la mortalité. L'éducation des patients et la formation des soignants sont importantes pour la prévention et le traitement de l'hypoglycémie. Dans le présent article, nous traitons des aspects importants et des défis particuliers de l'hypoglycémie

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dans la population âgée. Nous mettons également l'accent sur les risques, les conséquences et les stratégies de prévention et de prise en charge de l'hypoglycémie que les prestataires de soins de santé peuvent utiliser pour intervenir auprès des populations âgées.

Definition and Classification of Hypoglycemia

It is difficult to know the exact prevalence of hypoglycemia (usually defined as blood glucose levels less than 70 mg/dL or 3.9 mmol/L) because many different classifications have been used in studies over the years. In addition, developments in new technologic methods over the past decades have made changes in how hypoglycemia is determined. Traditionally, hypoglycemia was defined as the presence of the Whipple triad, which included 1) low blood glucose; 2) symptoms and signs associated with low blood glucose levels; and 3) resolution of these symptoms and signs by carbohydrate ingestion. Some studies categorize hypoglycemia as major or minor episodes. Major hypoglycemia typically suggests life-threatening levels requiring third-party assistance. Minor hypoglycemia, presenting with symptoms such as tachycardia, sweating and dizziness can be treated with simple sugars. Minor hypoglycemic episodes frequently go unrecognized in older adults because they may present with nonspecific symptoms such as brief episodes of lightheadedness or vertigo. However, in frail older patients, they can lead to dangerous falls with fractures, decline in quality of life and increased mortality. Symptomatic vs. silent are other ways of classifying hypoglycemia (2). Hypoglycemic unawareness is a common cause of silent hypoglycemia and is highly prevalent in older adults. Thus, it is important to look carefully for the possibility of unrecognized hypoglycemia in older patients.

Physiologic Responses to Hypoglycemia

In healthy adults, when blood glucose levels fall (usually below 70 mg/dL or 3.9 mmol/L), multiple responses are triggered, and euglycemia is quickly restored. In response to hypoglycemia, insulin secretion from the pancreas will first decrease as the initial response. Next, the pancreas will increase glucagon production as counter-regulation. The liver then detects the decrease in insulin and the increase in glucagon and responds by increasing both glycogenolysis and gluconeogenesis. The adrenal glands next produce epinephrine, which acts on muscle, fat and kidney to decrease glucose clearance. Should glucagon be deficient, this epinephrine response becomes particularly significant. The adrenals, along with the peripheral nervous system, which detects hypoglycemia, then mediate an autonomic response via neurotransmitters. Acetylcholine triggers hunger and diaphoresis while norepinephrine triggers arousal with tremor and palpitations. These are the primary life-saving responses to hypoglycemia. As secondary responses, cortisol and growth hormone are also released, but these are less critical in terms of adaptive responses to hypoglycemia.

Age-Related Compromise of the Adaptive Responsive to Hypoglycemia

The responses of a healthy adult to hypoglycemia are lost to varying degrees in the adult patient with diabetes and are critically lost in the older population (3,4). Increased duration of diabetes, as well as the effect of aging on the endocrine, neurologic and cardiovascular systems is additive to the consequences of hypoglycemia in older patients.

Aging has an impact on counter-regulation (5,6). In healthy older adults without diabetes, glucose counter-regulation by glucagon as well as growth hormone and epinephrine responses to hypoglycemia are impaired through the physiology of aging, effectively muting the autonomic process, which would have produced symptoms in the patient (3,5). Glucose is not properly secreted when its levels fall, which represents loss in pancreatic, renal and hepatic processes. This is additive with the autonomic compromise present in all patients with diabetes. The brain depends upon renal, hepatic and endocrine regulation of glucose levels and becomes an unfortunate victim of dysregulation. When deprived of glucose, which is its primary fuel, the particular tasks that are lost are those requiring quick response, multitasking and sustained attention. Even in a cognitively intact patient, an hour may elapse after hypoglycemia resolves before the brain is restored to full function (4).

Last, aging physiology also changes the pharmacokinetics of oral medications and insulin, particularly in regard to drug absorption and distribution as well as renal elimination (2). These changes are not necessarily predictable due to the differing spectra of renal-function losses with the physiology of aging, in addition to differences in body fat and gender.

The age-related compromise in response is detailed in Table 1.

Considering the age-related changes on the neurologic, endocrine, cardiac, renal and hepatic responses to hypoglycemia, it is clear that signs and symptoms may not be relied upon in these patients. Therefore, a warning may not be provided before a sentinel event such as a fall.

Consequences of Hypoglycemia in Older Adults

Consequences of hypoglycemia in older adults can be catastrophic. Hypoglycemia can increase the risk for cardiovascular

Table 1
Age-related compromise of the adaptive response to blood glucose <70 mg/dL (3.9 mmol/L)

	Normal physiologic response	Age-related changes
Glucagon	Increased release triggers hepatic increase in glycogenolysis and gluconeogenesis	Decreased secretion
Neurologic/autonomic glucose level 50-70 mg/dL (2.8-3.9 mmol/L)	Adrenal release of epinephrine, peripheral nervous system-mediated increase in acetylcholine producing hunger and norepinephrine producing tremor/diaphoresis and arousal	Decreased epinephrine secretion, decreased ACh/NE release, possible loss of hunger, tremor, diaphoresis/arousal Decreased ability to recognize and/or treat hypoglycemic symptoms
Glucose level <50 mg/dL (2.8 mmol/L)		Relatively increased epinephrine secretion
Vascular	Increase in arterial elasticity resulting in adaptive cardiac perfusion during diastole	Loss of arterial elasticity, resulting in compromise of perfusion to both cardiac and neurologic tissue (possibly resulting emiplegia/coma)

ACh, acetylcholine; *NE,* norepinephrine.