Acute Hypoglycemia in Emergency Room: A Review

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Authors' contributions

*This work was carried out in collaboration among all authors. All authors read and approved the final
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Review Article

ABSTRACT

Hypoglycemia is frequently encountered in the emergency department (ED) and has potential for
serious morbidity. The incidence and causes of iatrogenic hypoglycemia are not known. We aim to
describe how often the cause of ED hypoglycemia is iatrogenic and to identify its specific causes.
Adult patients with a chief complaint or ED diagnosis of hypoglycemia, or an ED glucose value of
≤70 milligrams per deciliter (mg/dL) between 2009–2014. Two independent abstractors each

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reviewed charts of patients with an initial glucose ≤ 50 mg/dL, or initial glucose ≥ 70 mg/dL with a subsequent glucose ≤ 50 mg/dL, to determine if the hypoglycemia was caused by iatrogenesis.

In ED patients with hypoglycemia, iatrogenic causes are relatively common. The most frequent cause was insulin administration for hyperkalemia and uncomplicated hyperglycemia. Additionally, patients at risk of hypoglycemia in the absence of insulin, including those with alcohol intoxication or poor nutritional status, should be monitored closely in the ED.

1. INTRODUCTION

Hypoglycemia is a serious and prevalent illness that can result in seizures, coma, and death, this condition is frequently treated in emergency rooms (EDs). According to a longitudinal study, EDs handle more than 95,000 hypoglycemic patients each year, accounting for 3.4 percent of the diabetic population, with 25% requiring hospitalization [1].

Hypoglycemia is the commonest side-effect of insulin treatment for diabetes. Hypoglycemia is frequently associated with diabetes therapy, although it can also be caused by a range of medicines and diseases, many of which are uncommon. In type 1 diabetes, severe hypoglycemia crises have been reported to occur anywhere from 62 to 320 times per 100 patient-years [2].

It was discovered that patients over the age of 65 on admission were 50% more likely to suffer an episode of hypoglycemia. Insulinoma has a reported incidence of 0.4 per 100,000 person-years, with a female preponderance of 59 percent and an average age of 47 years at surgery. Hypoglycemia is a well-known complication of bariatric surgery, particularly Roux-en-Y gastric bypass [3]. A population-based study found that individuals who underwent bariatric surgery had a 2 to 7-fold increase in hospitalization owing to hypoglycemia. However, the absolute risk of hospitalization with hypoglycemia after gastric bypass surgery is quite low (about 0.2 percent). In comparison, the risk in the overall population was 0.04 percent. Severe hypoglycemia over an extended period can result in multiple organ failure, cardiac arrhythmias, cardiac arrest, and lifelong neurological impairment [4].

2. DEFINITION OF HYPOGLYCEMIA

Clinically significant hypoglycemia is defined by the American Diabetes Association and the International Hypoglycemia Study Group as a blood glucose of 54 mg/dl (3.0 mmol/L) detected by self-monitoring blood glucose (SMBG), continuous glucose monitoring (CGM), glucose values of 54 mg/dl (3.0 mmol/L) for at least 20 minutes, or laboratory measurement of plasma glucose that is sufficiently low to indicate clinically significant hypoglycemia [5].

Severe hypoglycemia is characterized as a low glucose level along with severe cognitive impairment that necessitates the help of another person to recover. However, in population-based and clinical research, these definitions are challenging to operationalize. Most hypoglycemia incidents occur outside of the hospital system. The accuracy of patient memory, which can be poor, has an impact on self-reporting of hypoglycemia, especially for non-severe incidents [6].

Moreover, well almost 95% of hypoglycemia occurrences are handled outside of the hospital system, by the patient, careers, or emergency medical services. Several factors influence the likelihood that a hypoglycemic event will be brought to medical attention, such as patient healthcare coverage, the resource availability (e.g., food, medications, and third-party assistance) to manage hypoglycemia, and the ability to recognise and effectively treat hypoglycemic events when they occur. In one study of hypoglycemia ambulance calls, 13.5 percent of hypoglycemia patients (blood glucose 60 mg/dL [3.3 mmol/L]) were handled on the spot rather than being transferred to the emergency room [7].

3. RISK FACTORS OF HYPOGLYCEMIA IN ED

Insulin delivery has previously been implicated as a major cause of iatrogenic hypoglycemia. Hyperkalemia is most common in patients with end-stage renal failure on chronic dialysis, and insulin is frequently given to hyperkalemic patients in the emergency department to transfer potassium to the intracellular space until dialysis

is available. Renal insufficiency reduces insulin clearance, increasing the risk of hypoglycemia [8].

According to a recent study, 17% of ED patients who get insulin for hyperkalemia develop hypoglycemia within three hours. Furthermore, iatrogenic hypoglycemia has been reported following ED insulin therapy for uncomplicated hyperglycemia; ED glucose reduction for uncomplicated hyperglycemia may be ineffective and wastes time and resources. Patients with chronic alcoholism or acute alcohol intoxication are more likely to have reduced glycogen stores with simultaneous gluconeogenesis inhibition due to inadequate nutrition and relative thiamine shortage, putting them at greater risk for hypoglycemia [9].

Care for acute intoxication and accompanying conditions may divert attention away from routine glucose monitoring, which is especially necessary when oral intake is restricted due to intoxication or parenteral sedation. Hypoglycemia was recently discovered to be an independent predictor of eventual critical disease in this patient population. Hypoglycemia prevention is critical for patient safety because hypoglycemia has been linked to poor outcomes [10].

Dietary factors include: delayed meals (29%), irregular or insufficient carbohydrates (25%), and skipped meals or snacks (20 percent). Excessive physical activity (16%) and stress (13%) were also frequently cited factors. Drug errors were blamed less frequently; 10% of patients blamed an incorrect insulin dose, and 5% blamed a newly started glucose-lowering medication [11]. Participants in the ACCORD trial mentioned similar factors, such as delayed or missed meals (31% of patients in the intensive treatment arm and 44% of patients in the standard treatment arm), eating fewer carbohydrates than usual (26% and 25%, respectively), more or unplanned exercise (15% and 12%, respectively), and using more insulin than prescribed or usually administered (5% and 7%, respectively) (4 percent and 3 percent, respectively) [12].

In type 2 diabetes, many patient- and treatment-related factors increase the risk of hypoglycemia. Prior hypoglycemia, both severe and mild, is one of the best predictors of future hypoglycemia. According to a large claims-based case control study of people with type 2 diabetes in the United States, an emergency room visit for hypoglycemia within the previous 180 days increased the likelihood of subsequent

hypoglycemia hospitalization by 9.5 times. Over a 6.4-year period, having a prior history of severe hypoglycemic incidents increased the likelihood of calling an ambulance, going to the emergency room, or being hospitalized for hypoglycemia by more than 6-fold [13].

Regarding complications of hypoglycemia, randomized controlled studies reported that patients with T2DM who received more aggressive glucose-lowering medication compared to those who received less aggressive glucose-lowering therapy had a higher mortality rate, and in patients in intensive care units with hypoglycemia [14]. Hypoglycemia has also been linked to aberrant cardiac repolarization and a lengthening of QTc, which can lead to life-threatening cardiac arrhythmias [15].

Acute hypoglycemia has also been shown to cause an increase in pro-coagulant activity, the production of inflammatory cytokines, and eventually endothelial dysfunction and vascular damage. Hypoglycemia and cognitive performance appear to have a more convoluted relationship, A history of severe hypoglycemia was linked to a higher incidence of dementia in older people with type 2 diabetes. Severe hypoglycemic coma is defined as the subgroup of severe hypoglycemia related to a convulsion or unconsciousness [16]. Severe hypoglycemia is still lethal and is reported to be the cause of death in 4% to 10%. It may be linked to cognitive problems and brain structure abnormalities in young children with type 1 diabetes, and it may be linked to irreversible brain damage [17].

Severe hypoglycemia is likely to result in poor psychological consequences as well as undesired compensatory responses. In fact, individuals who encounter an episode of severe hypoglycemia have a 3.4-fold risk in death over the next 5 years. The neurological repercussions of a hypoglycemic episode include transitory focal impairments, such as Todd's paresis, which occurs when a person awakens from an undiscovered nocturnal hypoglycemia with symptoms and signs resembling a stroke [18].

Hypoglycemia is associated with changes in regional brain activation, not just in the region of the hypothalamic–pituitary axis, but also in brain regions involved in interception (relevant to symptom generation and perception) and in regions involved in emotional salience, aversion, executive function, and memory. Long-term type 1 diabetes might affect these regional brain responses, and it's been suggested that

increased thalamic activity in hypoglycemia in type 1 diabetes could help maintain subjective awareness despite diminished catecholamine responses [19]. There is evidence that the threshold for cognitive impairment changes less in response to antecedent hypoglycemia than the threshold for subjective awareness and neurohumoral responses, suggesting a potential mechanism for the increased risk of severe hypoglycemia as the person loses the ability to self-treat [20].

It has been demonstrated that hypoglycemia at night influences the identification of hypoglycemia the following day. Because the counter regulatory responses to hypoglycemia are muted during deep sleep, episodes may go undiagnosed and asymptomatic. Rare, unexpected nocturnal deaths in young people with type 1 diabetes have been documented, ascribed to hypoglycemia and accounting for 5% of all deaths in this cohort [21].

There is a growing body of research associating severe hypoglycemia to future mortality both in the hospital and in the community, with estimates ranging from 50% to 600%. Some of the reactions to acute hypoglycemia have been identified as underlying processes, particularly the proinflammatory and coagulopathy effects, but the data remain consistent with hypoglycemia being a sign of frailty and a high risk of death. Severe hypoglycemia has been associated with approximately a doubling in risk of subsequent cardiovascular events, including death, but the relationship is bi-directional [22].

4. CLINICAL SYMPTOMS AND RATE OF HYPOGLYCEMIA CONDITION

Clinical symptoms include sweating, shakiness, anxiety, nausea, dizziness, confusion, blurred vision, headache, and lethargy. Concurrent inflammatory processes, comorbidities, and low food intake are all contributors in the development of hypoglycemic episodes. Inadequate food intake is a prevalent risk factor for hypoglycemia, yet it is not the leading cause of death among hypoglycemic individuals [23]. Because hypoglycemia is a common illness among ED patients, differential diagnoses such as stroke, transient ischemic attack, and seizure disorder should be cleared out quickly and thoroughly. Every year, on average, 0.1/100 diet-treated patients, 0.4-0.6/100 sulfonylurea-treated patients, and 2.3/100 insulin-treated patients experienced severe hypoglycemia, as defined by the need for third-party intervention [24].

According to the Centers for Disease Control and Prevention, there were 245,000 emergency department visits for hypoglycemia in 2014, or 1.12 visits per 100 person-years, which is higher than the number of hyperglycemic crises treated in emergency rooms (0.95 occurrences per 100 person-years) Between 2007 and 2009, insulin and oral glucose-lowering medications were linked to 14% and 10.7% of emergency hospitalizations in diabetes patients aged 65 and older, respectively [25].

5. MANAGEMENT OF ACUTE HYPOGLYCEMIA IN ED

Treatment of hypoglycemia is still based on administration of carbohydrates or of glucagon [intramuscular (IM) or subcutaneous (SC) injection]. Glucagon is released by pancreatic islet cells in response to hypoglycemia, and it helps to correct low blood glucose levels by promoting glycogenolysis and, to a lesser extent, increasing gluconeogenesis. This action, which increases endogenous (mainly hepatic) glucose synthesis, acts as a counter-regulator to insulin in maintaining normal plasma glucose concentrations, and is used in the emergency treatment of insulin-induced hypoglycemia in type 1 diabetes (T1D) [26].

Hyperinsulinism and alimentary hypoglycemia. The volatility of glucagon in aqueous solution has limited its use outside of the emergency room, as fast reconstitution is essential. Even in its current role as an emergency treatment for insulin-induced hypoglycemia, this reconstitution technique can be difficult and mistake when conducted by non-healthcare practitioners in a stressed situation. In aqueous solution, glucagon is unstable, and spontaneous breakdown results in a loss of bioactivity [27].

The two FDA-approved formulations of standard glucagon are the Glucagon HypoKit® (Novo Nordisk, Copenhagen, Denmark) and the Glucagon Emergency Kit (Eli Lilly, Indianapolis, IN). Glucagon is reconstituted with sterile water, whereas the Glucagon Emergency Kit is reconstituted with a diluent containing glycerin, water for injection and hydrochloric acid) [28].

Injectable glucagon has been shown to help stabilise babies with hyperinsulinemic hypoglycemia and to reduce the need for continuous glucose infusions to prevent hypoglycemia. For three days, four infants received continuous subcutaneous NAS glucagon at 5 to 15 mg/kg/h, and the glucose

infusion rate was reduced from 10.8 4.9 mg/kg/min to an average of 4.9 1.2 mg/kg/min with no pump infusion set blockages [29].

Once severe hypoglycemia occurs, instant treatment is required, and it can be effectively reversed by injecting glucagon (which can be given intravenously, intramuscularly, or subcutaneously). When a hypoglycemic patient is unwilling or unable to take carbohydrates orally, parenteral therapy is required) [30]. In adults, the first line of defense against hypoglycemia is to administer 1 g/kg body weight dextrose as D50W. In some cases, this can be followed by a D5W or D10W infusion at a rate that keeps serum glucose above 100 mg/dL. Repeat bedside glucose assessment every 30 minutes for the first two hours to identify RH [31].

In patients with sulphonylurea-induced diabetes, glucose or glucagon administration These antidotal approaches are associated with further exacerbation of insulin release by glucose and glucagon, resulting in only temporary beneficial effects and later RH. Hypoglycemia may be unsatisfied because these antidotal approaches are associated with further exacerbation of insulin release by glucose and glucagon, resulting in only temporary beneficial effects and later RH [32].

Hypoglycemia treatment varies depending on the intensity and duration of the hypoglycemia incident and is represented by a therapeutic complexity range. For fully awake individuals with acute hypoglycemia, defined as a blood glucose concentration of 3.9 mmol/L (70 mg/dL), oral glucose (15–20 g) is the preferable treatment [11]. In most cases, treating hypoglycemia with 15–20 g of fast-acting carbs raises blood glucose levels within 15 minutes [33].

If self-monitored blood glucose shows persistent hypoglycemia 15 minutes after treatment, the treatment should be repeated until capillary blood glucose returns to normal, followed by a meal or snack containing complex carbohydrate (slow acting) to prevent hypoglycemia from returning [34]. When an individual is unconscious or unable to swallow, glucagon should be administered [3].

The International Society for Pediatric and Adolescent Diabetes (ISPAD) defines severe hypoglycemia in children and adolescents as an event associated with severe cognitive impairment (including coma and convulsions) that necessitates external assistance from another person to actively administer carbohydrates, glucagon, or other corrective actions [35]. Glucagon should be easily available to all parents and caregivers, according to ISPAD standards, especially when there is a significant risk of severe hypoglycemia [35].

In asymptomatic late preterm and term newborns, management of neonate hypoglycemia with Dextrose gel 200 mg/kg rubbed into the buccal mucosa is an effective therapy option. Dextrose gel is reasonably affordable, well tolerated, and has been demonstrated to reduce neonatal critical care unit admissions for intravenous dextrose. Corticosteroids or glucagon are used as second-line therapy for the treatment of persistent hypoglycemia [36].

Corticosteroids, which are given as hydroxycortisone 5 to 15 mg/kg per day or prednisone 2 mg/kg per day, increase blood glucose concentrations by decreasing peripheral glucose consumption. Glucagon is administered as a 30 mcg/kg bolus or as a 300 mcg/kg per minute continuous infusion. It is particularly effective in term newborns and infants born to diabetes moms [37].

6. CONCLUSION

Iatrogenic causes of hypoglycemia in ED patients are fairly common. Insulin treatment for hyperkalemia and simple hyperglycemia was the most common reason. Additionally, patients at risk of hypoglycemia in the absence of insulin, including those with alcohol intoxication or poor nutritional status, should be monitored closely in the ED. Due to the risk of complications, many conditions necessitate immediate interaction with an ED. Treatment is tailored to each disease.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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