Management of Hyperglycemic Crises

Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar State

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KEYWORDS

- Hyperglycemic emergencies • Diabetic ketoacidosis
- Hyperglycemic hyperosmolar state • Management of hyperglycemic emergencies
- Diabetes

KEY POINTS

- Hyperglycemic emergencies are life-threatening complications of diabetes.
- This article reviews diabetic ketoacidosis and hyperglycemic hyperosmolar state addressing historical context, epidemiology, clinical features, and guidelines for management.

INTRODUCTION

Diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state (HHS) are the most serious and life-threatening hyperglycemic emergencies in patients with diabetes. Although DKA and HHS are often discussed as separate entities, they represent points along a spectrum of hyperglycemic emergencies owing to poorly controlled diabetes. Both DKA and HHS can occur in patients with type 1 diabetes (T1D) and type 2 diabetes (T2D); however, DKA is more common in young people with T1D and HHS is more frequently reported in adult and elderly patients with T2D. In many patients, features of the 2 disorders with ketoacidosis and hyperosmolality may also coexist. The frequency of DKA has increased by 30% during the past decade, with more than 140,000 hospital admissions per year in the United States.[1,2] The rate of hospital admissions for HHS is lower than for DKA, accounting for less than 1% of all diabetes-related admissions.[3,4] Both disorders are characterized by insulinopenia

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and severe hyperglycemia. Early diagnosis and management are paramount to improve patient outcomes. The mainstays of treatment in both DKA and HHS are aggressive rehydration, insulin therapy, electrolyte replacement, and discovery and treatment of underlying precipitating events. Herein we review the epidemiology, pathogenesis, diagnosis, and provide practical recommendations for the management of patients with hyperglycemic emergencies.

HISTORICAL REVIEW OF DIABETIC COMAS

The first detailed clinical description of diabetic coma in an adult patient with severe polydipsia, polyuria, and a large amount of glucose in the urine followed by progressive decline in mental status and death was reported by August W. von Stosch in 1828.[5] This publication was followed by several case reports describing young and adult patients with newly diagnosed or with established diabetes who presented with an abrupt clinical course of excessive polyuria, glycosuria, coma, and death.[6–8] In 1874, The German physician Adolf Kussmaul reported that many cases of diabetic coma were preceded by deep and frequent respiration and severe dyspnea.[9,10] Kussmaul breathing rapidly became one of the hallmarks of diabetic coma. Shortly after that, it was reported that in many of these patients, the urine contained large amounts of acetoacetic acid and β-hydroxybutyric acid.[11,12] Dr Julius Dreshfeld in 1886 was the first to provide a comprehensive description of the 2 different categories of diabetic coma,[13] one with Kussmaul breathing and positive ketones and the other, an unusual type of diabetic coma in older, well-nourished individuals, characterized by severe hyperglycemia and glycosuria but without Kussmaul breathing, fruity breath odor, or a positive urine acetone test.

Before the discovery of insulin in 1921, the mortality rate of patients with DKA was greater than 90%. The first successful case of DKA treated with insulin was reported by Banting and associates[14] in a 14-year-old boy who presented with a blood glucose of 580 mg/dL and strongly positive urinary ketones at the Toronto General Hospital in 1923. These authors reported a dramatic improvement in glycosuria along with disappearance of acetone bodies in the urine after a few doses of pancreatic extract injections.[14] After the discovery of insulin, the mortality rate associated with diabetic comas decreased dramatically to 60% in 1923 and 25% by the 1930s,[15] 7% to 10% in the 1970s[16,17] and is currently less than 2% in patients for DKA[1,18,19] and between 5% and 16% in patients with HHS.[20,21]

EPIDEMIOLOGY

Although DKA occurs more commonly in patients with autoimmune T1D, the cumulative number of cases of DKA reported in patients with T2D represents at least one-third of all cases.[22] Global epidemiologic studies have reported on the incidence of DKA among patients with T1D. An analysis from the Prospective Diabetes Registry in Germany including 31,330 patients reported a DKA admission rate of 4.81 per 100 patient-years (95% confidence interval [CI], 4.51–5.14).[23] Individuals with the highest risk included those with high hemoglobin A1c (HbA1c), longer diabetes duration, adolescents, and girls.[23] Multinational data from 49,859 children (<18 years) with T1D across 3 registries and 5 nations similarly found higher odds of DKA among females (odds ratio [OR], 1.23; 99% CI, 1.10–1.37), ethnic minorities (OR, 1.27; 99% CI, 1.11–1.44), and among those with an HbA1c of 7.5% or greater (OR, 2.54 [99% CI, 2.09–3.09] for an HbA1c from 7.5 to <9% and OR 8.74 [99% CI, 7.18–10.63] for an HbA1c of ≥9.0%).[24] Data from the T1D Exchange Clinic Network including 2561 patients, shows that young adults (18–25 years) have the highest occurrence of