Preventing Diabetic Ketoacidosis

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KEYWORDS

• Type 1 diabetes mellitus • Diabetic ketoacidosis • Prevention • Education • Recurrent • Noncompliance • Girls

KEY POINTS

- Diabetic ketoacidosis (DKA) is a complication of severe insulin deficiency leading to hyperglycemia, with its attendant glycosuria, dehydration, and ketogenesis, leading to acidosis.
- DKA is associated with significant morbidity, non-negligible mortality, and excessive health care expenditures.
- DKA is largely an avoidable and preventable complication of type 1 diabetes mellitus (T1DM).
- Risk factors associated with DKA at diagnosis of T1DM include age less than 5 years old, lack of private health insurance, lower socioeconomic status (SES), misdiagnosis, delayed diagnosis, and living in regions with a low background incidence of T1DM.
- Factors associated with increased DKA risk in children with established T1DM include age greater than 13 years, female gender, low SES, lack of private health insurance, poor family functioning, psychiatric disorders, higher reported insulin dose, and poor glycemic control.

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INTRODUCTION

T1DM is one of the most common chronic diseases of childhood with significant morbidity and non-negligible mortality.[1,2] The global incidence of T1DM is increasing by 3% per year in children and adolescents and by 5% per year in preschoolers.[3,4] Acute complications, such as DKA, are potentially avoidable causes of hospitalizations and mortality in children and adolescents with T1DM. DKA occurs in the presence of severe insulinopenia and is characterized by hyperglycemia, acidosis, and ketosis.

The early development of T1DM involves progressive insulin deficiency, leading to weeks of symptomatic hyperglycemia with polyuria, polydipsia, and weight loss.[5,6] If left untreated, the combination of insulin deficiency and stress (mediated through increased circulating levels of counter-regulatory hormones, including cortisol, catecholamines, growth hormone, and glucagon) leads to lipolysis. Hepatic metabolism of free fatty acids as an alternative energy source (ie, ketogenesis) results in accumulation of acidic intermediate and end metabolites (ie, ketones and ketoacids). The predominant ketones in the body are β-hydroxybutyrate, acetate, and acetoacetate.[5,6] In DKA, the ratio of β-hydroxybutyrate to acetoacetate increases from equimolar amounts (1:1) up to 1.3:1 to 5.5:1.[7] Accumulation of ketoacids is due to their rate-limiting metabolism. Diagnosis of DKA has been traditionally made with a combination of hyperglycemia (blood glucose >11 mmol/L or 200 mg/dL), venous pH less than 7.3 and bicarbonate levels less than 15 mmol/L.[8]

DKA at initial presentation is common, but rates vary strikingly between countries, ranging from approximately 13% to 80%.[9–11] The highest rates are typically seen in the developing world, not surprisingly given the resource constraints.[11] DKA in children previously diagnosed with T1DM is also unfortunately common, with highly variable rates between centers and countries.[11,12] DKA remains the most common cause of mortality in T1DM. The most devastating consequence of DKA is cerebral edema with an incidence of 0.5% to 0.9%.[13,14] The mortality rate from cerebral edema is 21% to 24%, and morbidity from serious neurologic sequelae occurs in 15% to 35% of cases.[11,12] Furthermore, DKA has a long-term impact on cognitive function, including a fall in IQ and persistent loss of short-term memory. The health care expenditures associated with 1 episode of DKA are substantial, estimated at more than $3500.[15]

EPIDEMIOLOGY AND CAUSES OF DIABETIC KETOACIDOSIS

DKA occurs generally under 2 circumstances and in a limited number of situations:

1. At diagnosis
2. In those with established diabetes
   a. As a result of accidental or deliberate insulin omission or
   b. Inappropriate management of intercurrent illness

Most, if not all, episodes of DKA can be prevented. These episodes generally represent a failure of timely diagnosis and/or management of T1DM. Understanding the epidemiology and factors associated with the onset of DKA is essential in developing measures to prevent these episodes.

DIABETIC KETOACIDOSIS AT DIAGNOSIS

Symptoms of new-onset T1DM typically develop over a few days to weeks before presentation, whereas DKA rapidly evolves once ketones accumulate[16]: 75% of patients with new cases of T1DM in the EURODIAB (the Epidemiology and Prevention of