

Management of adult diabetic ketoacidosis

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Dear editor

In the article “Management of adult diabetic ketoacidosis” by Gosmanov et al¹ there are some discrepancies with the literature. The authors write, “Insulin deficiency [...] which underlie the pathophysiology of DKA [diabetic ketoacidosis]”, and on page 258, they write, “Insulin administration is essential in DKA treatment [...]”.¹ Since the Nobel prize was awarded in 1977 to Rosalyn S Yalow for the development of new methods of biochemical analysis that make it possible to measure insulin concentration in human plasma, these methods have been used worldwide. In 1981, the monograph *Diabetic Coma: Ketoacidotic and Hyperosmolar* was published,² and on page 67, Figure 6.3 has the names of 12 authors who have reported sufficient amounts of plasmatic insulin in patients with DKA. In contrast, absolute deficiency of plasmatic insulin has been reported in diabetic patients with hyperglycemic hyperosmolar syndrome,³ as well as in diabetic patients on routine control without subjective complaints.⁴ Where are published concrete reports on the deficiency of plasmatic insulin in patients with DKA? What is the “safe level” of plasmatic insulin concentration that makes development of DKA impossible?

On page 259, the authors write, “The use of bicarbonate in severe DKA is controversial [...]”. On the same page, the authors also write that “severe acidosis [...] can lead to impairment in sensorium [...]”. Severe “impairment in sensorium” is a life-threatening coma. If intravenous sodium bicarbonate is also included in the treatment, however, the lethality of coma in DKA is zero.⁵ In contrast, without sodium bicarbonate, lethality can be up to 100%.⁶ What here is controversial? The glycolytic enzyme phosphofructokinase is pH-dependent, as its activity is decreasing with decreasing pH, and thus, glucose use in brain cells is impaired.⁷ This is the explanation of the life-saving effects of sodium bicarbonate in the treatment of coma in DKA.

Disclosure

The author reports no conflicts of interest in this communication.

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Authors' reply

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Dear editor

We appreciate Dr Rosival's interest and comments raised after reading the review "Management of adult diabetic ketoacidosis".¹ The author raises several interesting points that warrant further discussion. Insulin has two important metabolic roles: suppression of lipolysis, ketogenesis, and unrestrained hepatic glucose production via inhibition of gluconeogenesis and glycogenolysis; and activation of glucose uptake and metabolism by insulin-sensitive tissues.² When these insulin-mediated processes are active, diabetic patients do not develop ketoacidosis and severe hyperglycemia. When we stated that patients with diabetic ketoacidosis (DKA) have absolute insulin deficiency, we referred to the functional inability or deficiency of insulin to inhibit ketone body formation, suppress endogenous glucose production, and activate glucose utilization by peripheral tissues. Indeed, patients with DKA may not have an absolute deficiency of the hormone; previous studies have shown that development of a ketotic state is possible in subjects with a plasma insulin level of 5 $\mu\text{U}/\text{mL}$.³

Bicarbonate therapy is not indicated in mild and moderate forms of DKA because metabolic acidosis will correct with insulin therapy.^{2,4} Clinicians should exercise clinical

judgment in deciding to use bicarbonate therapy in patients with severe DKA.⁵ We agree that it is tempting to use bicarbonate infusion in patients with DKA who are comatose and have severe acidosis. However, in the absence of randomized trials we should be cautious in that decision because while treating acidosis as a symptom, we may inadvertently cause harm through the development of peripheral hypoxemia, worsening of hypokalemia, paradoxical central nervous system acidosis, cerebral edema, and an increase in intracellular acidosis. We believe that in DKA patients with severe acidosis and a pH <7.0, it may be prudent to administer two ampules of bicarbonate in parallel with ongoing efforts to provide insulin and fluids, followed by repeated measurement of metabolic parameters and clinical reassessment of the patient. It is unclear if the provision of bicarbonate to the DKA patients with a pH >7.0 could offer any clinical advantage over routine DKA therapy.⁶

Disclosure

The authors report no conflicts of interest in this communication.

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