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Diabetic ketoacidosis (DKA), also known as diabetic acidosis or diabetic coma, is a severe complication of diabetes mellitus (DM; Michel, 2011). More commonly seen in patients with type 1 diabetes (T1D), DKA results when lipid breakdown generates a surplus of acidic ketone bodies (Guven, Matfin, & Kuenzi, 2009). According to Dods (2013), DKA can be defined as a condition with "blood glucose greater than 250 mg/dL, blood bicarbonate less than 15 mEq/L, pH less than 7.35, ketonemia, and increased anion gap" (p. 266). The pathophysiology of DKA in patients with T1D will first be addressed, followed by a discussion of proper emergency treatment for this life-threatening condition.

The three main abnormalities of DKA patients include hyperglycemia, ketosis, and metabolic acidosis (Guven et al., 2009). An episode of DKA is precipitated by insulin deficiency with hyperglycemia. Insulin deficiency may develop in a patient following illness or infection, an insufficient insulin dose, ignorance of the condition of T1D, neglect of the medication regimen, and defective self-health maintenance (Michel, 2011). When insulin fails to provide adequate glucose, the cells tap into the fat stores for fuel (Petit & Adamee, 2011). It is the acidic products of fat metabolism that account for the acidosis. Normally, pancreatic beta cells release a bolus of insulin in response to rising blood glucose levels; however, in T1D the beta cells are destroyed through autoimmune process and the result is an absolute insulin deficiency (Michel, 2011). Without insulin secretion, hyperglycemia persists, and the cells starve for energy.

The energy-hungry cells stimulate adipose tissue lipolysis, releasing free fatty acids into the blood stream. Increased breakdown of adipose tissue into glycerol and fatty acids is related to the increased availability of tissue lipase, an enzyme that is suppressed by insulin. Low insulin levels also correlate with low lipoprotein lipase activity, which leads to lipolysis. Free fatty acids

circulate until they reach the liver and are transported into mitochondria for oxidation by carnitine palmitoyl transferase (CPT1). It is pertinent to note that CPT1 is usually inhibited when insulin levels are normal. Acetyl Coenzyme A (CoA) is an enzyme that responds to the presence of insulin by catalyzing the transformation of acetyl CoA into malonyl CoA. Malonyl CoA is the molecule that inhibits CPT1 and, therefore, fatty acid oxidation. When CPT1 is unhindered by insulin, it shuttles fatty acids into the hepatic mitochondria where they undergo oxidation and form ketone bodies, namely, beta-hydroxybutyrate, acetoacetate, and acetone (Casteels & Mathieu, 2003; Marieb, 2004).

Ketones can be used as an alternate fuel source by cells lacking mitochondria and by brain cells, but in a state of insulin deficiency ketone utilization by the peripheral tissues is diminished (Harvey, 2010; Casteels & Mathieu, 2003). An overproduction and an under-utilization of ketoacids results in ketosis (Casteels & Mathieu, 2003). Bicarbonate ions buffer the increased hydrogen ions by forming water and carbon dioxide; nevertheless, as ketosis progresses bicarbonate cannot keep up, and a metabolic acidosis ensues (Casteels & Mathieu, 2003). In a state of ketosis, beta-hydroxybutyrate and acetoacetate are eliminated by the kidneys along with their counter ions, potassium, and sodium (Dods, 2013). This ketonuria contributes to the acidosis by causing the hydrogen ion concentration to rise (2013).

Besides increased lipolysis, the body responds to the glucose-hungry cells by increasing serum glucose levels even though hypoglycemia is not the problem (Beard, 2011). Hyperglycemia is further exacerbated by the release of counter regulatory hormones (Casteels & Mathieu, 2003). Low insulin levels cause the secretion of hormones that increase hepatic formation of new glucose molecules and hepatic breakdown of stored glycogen into glucose molecules (Koul, 2009). Hormones such as glucagon, catecholamines, cortisol, and growth

hormone are released; they not only increase the blood glucose but also have an antagonistic effect toward insulin (Beard, 2011). Glucagon is a hormone secreted by the alpha cells of the islets of Langerhans that increases proteolysis, transports the resulting amino acids into liver cells, and converts these amino acids into glucose precursors during the process of gluconeogenesis (Guven et al., 2009). Insulin promotes the active transport of amino acids into the cells and prevents protein breakdown (Guven et al., 2009). Catacholamines respond to stress by stimulating lypolysis in adipose tissue, decreasing insulin secretion, and increasing hepatic glycogenolysis and gluconeogenesis (Michal, 2012). Corticotropin-releasing hormone is released from the hypothalamus and stimulates the pituitary gland to synthesize and secrete adrenocorticotropic hormone (ACTH), which induces the adrenal cortex to secrete cortisol into the blood (Michal, 2012). Cortisol acts as an antagonist to insulin by promoting gene transcription of catabolic enzymes in extrahepatic cells (Michal, 2010). Cortisol also stimulates gluconeogenesis in the liver (Michal, 2012). Growth hormone (GH) mobilizes fatty acids to be used as fuel and inhibits glucose uptake by insulin in the peripheral cells (Guven et al., 2009). With these in place, GH increases protein synthesis and sustains hyperglycemia (Guven et al., 2009).

Patients with T1D exhibit polyuria and polydipsia. As the blood becomes increasingly overloaded with glucose, the kidneys' reabsorbing threshold is surpassed and glucose is excreted in the urine. Glucose is an osmotically active particle and pulls water out of the filtrate and into the urine. Polydipsia occurs because hyperglycemia causes fluid shifts in the cells resulting in dehydration. T1D patients may also experience polyphagia because their cells are starving for energy and their body's stores of carbohydrates, fats, and proteins are depleted. Because of this use of the body's stores of fat and protein and the loss of fluid, patients with T1D often

experience weight loss. Polyphagia is not present in all T1D patients because of the epigastric pain and vomiting that often accompanies their acidotic state (Koul, 2009; Guven et al., 2009).

The osmotic diuresis that results in the patient's experience of polyuria also has dramatic effects on electrolyte levels. Sodium, potassium, phosphate, and magnesium are lost in the urine which predisposes the DKA patient to dehydration and imbalanced electrolyte levels (Guven et al., 2009). Ketonemia leads to ketonuria; potassium and sodium are excreted with ketones as their counter ions (Dods, 2013). Despite the loss of potassium in the urine, potassium levels often stay normal due to potassium shifts from the intracellular compartment to the extracellular compartment (Grinslade & Buck, 1999). Circulating hydrogen ions move into the cells in an attempt to correct the acidosis (Casteels & Mathieu, 2003). Within the cells, the hydrogen cations are buffered and potassium cations leave the cell in order to maintain intracellular electrical balance (Casteels & Mathieu, 2003). Extracellular potassium may also be increased by proteolysis (Grinslade & Buck, 1999). Although the serum levels of potassium appear normal or even high, the total body potassium level is depleted in DKA patients (Casteels & Mathieu, 2003).

A patient with DKA may take rapid, deep breaths called Kussmaul respirations in an attempt to blow off carbon dioxide to normalize the blood pH. According to Nattrass (2002), "Spontaneous decarboxylation of acetoacetate allows excretion of acetone through the lungs" (p. 52), giving the breath a fruity odor. Tachycardia and hypotension may also manifest due to decreased blood volume, which will be further depleted by vomiting (Guven et al., 2009; Koul, 2009).

Proper treatment of DKA is focused on restoring blood volume, enhancing tissue perfusion, correcting hyperglycemia and acidosis, and normalizing electrolyte levels (Guven,

2009). Due to the emergent and life-threatening nature of DKA, the patient must be treated promptly. Intravenous (IV) access should be initiated to administer fluid and electrolyte replacement. Fluid replacement is necessary for expanding the blood volume so that the tissues can be perfused and receive insulin (Koul, 2009). Restored blood volume also diminishes the release of counter regulatory hormones especially catacholamines and cortisol (Casteels & Mathieu, 2003). When serum sodium is low, a solution of 0.9% NaCl should be infused at a rate of one liter per hour or at a rate that achieves a restored urine output of 30-60 mL/hr. and a stabilized blood pressure (Michel, 2011; Koul, 2009). If the sodium level is within or above the normal limits, 0.45% NaCl is used (Koul, 2009).

If fluid replacement dilutes the serum sodium concentration, cerebral edema may ensue especially in pediatric patients. DKA patients are often dehydrated before treatment because of the high concentration of osmotically active substances, such as glucose, in the extracellular fluid. According to Koul (2009), “Persistent glucose-induced hypertonicity is implicated in causing neural cells to produce osmotically active idiogenic molecules” (p. 140). Neural cells accumulate these molecules during dehydration to protect the brain from becoming too volume depleted. When IV fluids resolve the high serum osmolality, the brain cells draw water out of the extracellular fluid resulting in cerebral swelling. Monitoring for the manifestations of Cushing’s triad is useful for assessing increased intracranial pressure, and unequal pupil dilation may indicated herniation. Neurological assessments are key to identifying cerebral edema, and rapid intervention involves the administration of mannitol and an alteration of the IV fluid rate. If mannitol is not available, a hypertonic solution of three percent saline may be administered with careful observance of hypernatremia, hyperosmolality, and central pontine myelinolysis (Koul, 2009).

Because of the detrimental effects of cerebral edema, fluid replacement therapy should progress slowly. Since insulin draws potassium and glucose into the intracellular compartment, potassium levels should be ascertained before the administration of insulin to prevent hypokalemia. If the patient's potassium level is low before fluid administration then potassium should be given along with fluid replacement. The potassium level should be restored to 3.5 to 5.0 mg/dL to prevent cardiac dysrhythmias. Once the blood volume has been replenished and the potassium level is above 3.5 mg/dL, administration of insulin should begin (Michel, 2011). Insulin corrects hyperglycemia and hyperketonemia; a continuous IV infusion is initiated at a rate of 0.1 units/kg/hr. (Michel, 2011). The potassium level should be intensely monitored during insulin administration. Potassium should be added to the IV infusion if the level falls below 3.5 mg/dL (Guven et al., 2009). The blood sugar should also be monitored during insulin therapy. If glucose levels reach 250 mg/dL a solution of five percent dextrose is administered to prevent hypoglycemia (Michel, 2011). Insulin should be infused slowly because rapidly lowering serum glucose levels may also precipitate cerebral swelling (Michel, 2011). According to Guven et al. (2009), severe acidosis exerts inhibitory effects on insulin. The patient should be started on a loading dose of regular insulin and then continuously infused with low doses of insulin (Guven et al., 2009).

DKA therapy must be actively guided by the fluid and electrolyte levels that the patient manifests. Koul (2009) encourages having two qualified medical personnel separately calculating fluid management to avoid calculation errors. Emergency supplies such as mannitol and dextrose solution should be readily available (Koul, 2009). Prevention of DKA is achieved through adequate patient teaching on the insulin regimen and early diagnosis of T1D in patients who may be at risk.

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