Diabetic Ketoacidiosis

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Objectives

- Introduction and awareness of the pathophysiology of Diabetic Ketoacidosis
- Clinical recognition,establishing a diagnosis and assessment of co-morbidities
- Clinical Management of DKA and recognition of complications

Introduction:

- State of absolute or relative insulin deficiency aggravated by ensuing hyperglycemia, dehydration, and acidosis-producing derangements in intermediary metabolism.

Characterized by

- Hyperglycemia over 300 mg/dL
- Low bicarbonate (<15 mEq/L)
- Acidosis (pH <7.30)
- Ketonemia and ketonuria.

Pathophsiology

Path physiology

- Insulin deficiency
- Increased counter-regulatory hormones (ie, glucagon, cortisol, growth hormone, epinephrine).
- Enhanced hepatic gluconeogenesis, glycogenolysis, and lipolysis

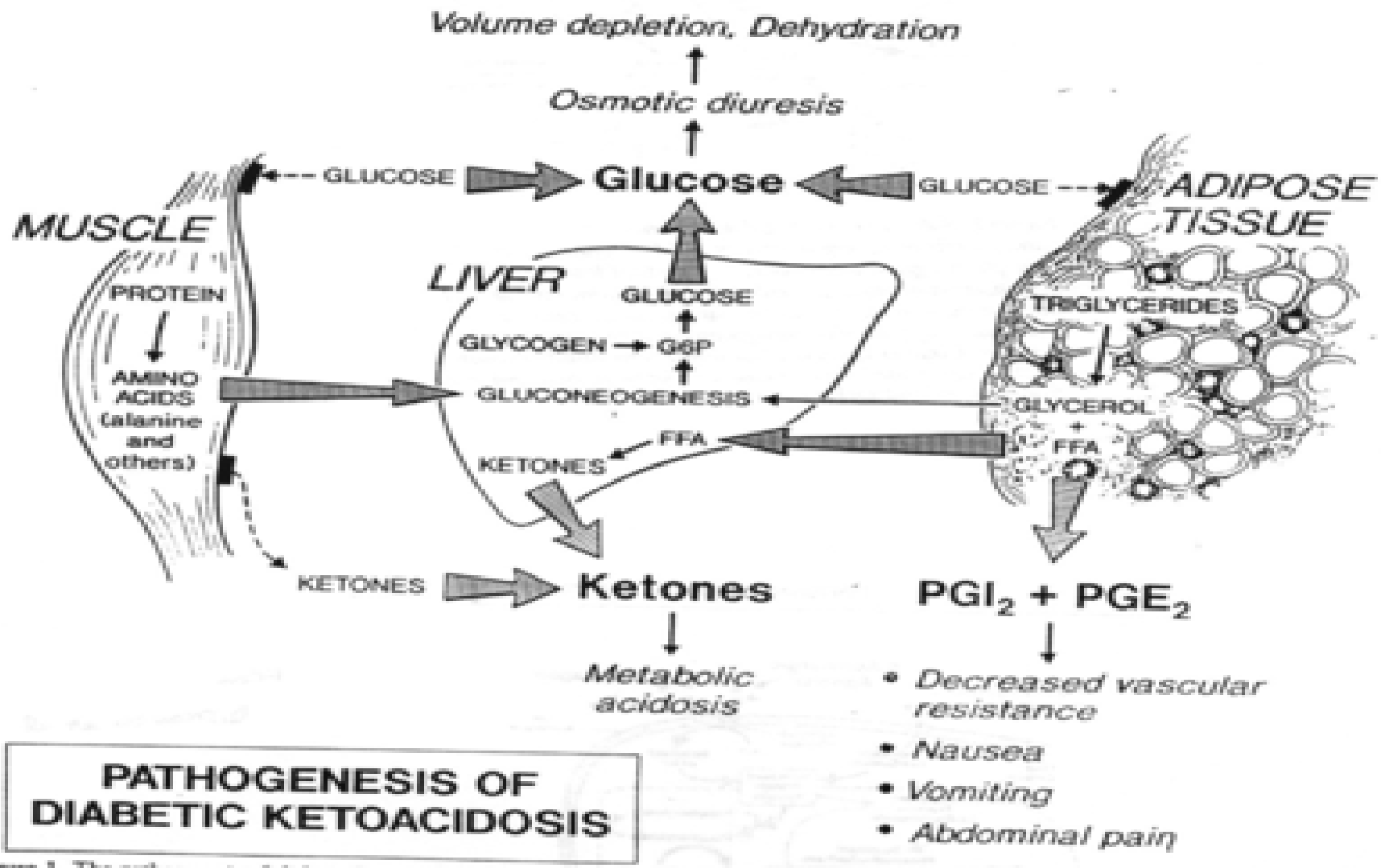
Consequences of hyperglycemia

- Uncontrolled hyperglycemia
- Osmotic diuresis
- Dehydration
- Renal shutdown

Excessive lipolysis

- Increased flux of FFA into the liver
- Increased oxidation
- Accumulation of end products
- When metabolites exceed buffering capacity then acidosis


Increased lipolysis and triglyceride breakdown
Decreased glucose uptake
Increased proteolysis
Increased FFA in plasma
Increased plasma amino acids
Increased FFA to liver
Hyperglycemia
Increased amino acids to liver
Glycosuria
Increased ketogenesis
Increased gluconeogenesis
Osmotic diuresis
Ketonuria
Loss of electrolytes
Cellular dehydration
Decreased alkali reserve
Hyperglycemia
Volume depletion
Acidosis
Impaired renal function
Osmotic diuresis



PATHOGENESIS OF DIABETIC KETOACIDOSIS

Figure 1. The pathogenesis of diabetic ketoacidosis. Severe insulin deficiency causes hyperglycemia, ketosis, and increased production of PGI_2 and PGE_2. Hyperglycemia is due to increased gluconeogenesis from amino acids, glycerol, and lactate and to decreased peripheral utilization of glucose. Ketosis is due to increased triglyceride lipolysis and increased FFA release from adipose tissue, to preferential utilization of FFAs for ketogenesis in the liver, and to decreased peripheral utilization of ketones. Increased PGI_2 and PGE_2 production by adipose tissue is due to accelerated triglyceride lipolysis and enhanced production of PGI_2 and PGE_2 in adipose tissue. Hyperglycemia causes an osmotic diuresis, volume depletion, hypotension, and dehydration. Ketosis causes an anion gap metabolic acidosis due to the dissociation of the ketoacids in the circulation and/or a hyperchloremic metabolic acidosis due to the loss of potential bicarbonate in the urine in the form of ketone bodies and the retention of chloride. Increased production of PGI_2 and PGE_2 causes decreased peripheral vascular resistance, hypotension, tachycardia, nausea, vomiting, and abdominal pain. Black rectangles denote impaired peripheral utilization of glucose and ketones, as indicated.

History:

- Insidious increased thirst (ie, polydipsia) and urination
- Nausea and vomiting
- Generalized weakness and fatigability
- Altered consciousness is common
- Symptoms of associated intercurrent illness

Physical:

- Signs of dehydration
- acetone odor
- Signs of acidosis
- Shallow rapid breathing or air hunger (Kussmaul or sighing respiration)
- Abdominal tenderness
- Disturbance of consciousness
- Signs of intercurrent illness

Diagnostic evaluation and lab studies

Urine

- highly positive for glucose and ketones by dipstick testing
- Rarely, urine is negative for ketones because most of the available laboratory tests can detect only acetoacetate, while the predominant ketone in severe untreated DKA is beta hydroxybutyrate.

Blood and plasma.

- Glucose: Levels may be as low as 250 mg/dL.

- Sodium: The osmotic effect of hyperglycemia moves extravascular water to the intravascular space. For each 100 mg/dL of glucose over 100 mg/dL, the serum sodium is lowered by approximately 1.6 mEq/L.

Blood and plasma

- Potassium: This needs to be checked frequently, as values drop very rapidly with treatment.
- Bicarbonate: Use in conjunction with the anion gap to assess degree of acidosis
- Complete blood count (CBC):

Osmolality

- Measured as 2(Na+) (mEq/L) + glucose (mg/dL)/18 + BUN(mg/dL)/2.8.
- Patients with DKA who are in a coma typically have osmolalities >330 mOsm/kg H20.
- If the osmolality is less than this in a comatose patient, search for another cause of obtundation.

Blood and plasma

- Arterial blood gases (ABG): pH is often <7.3. Venous pH may be used for repeat pH measurements.
- Phosphorous: If the patient is at risk for hypophosphatemia (eg, poor nutritional status, chronic alcoholism), then serum phosphorous should be determined
- Hyperamylasemia may be seen even in the absence of pancreatitis.

Repeat labs are critical

- **Potassium needs to be checked every 1-2 hours during initial treatment. Glucose and other electrolytes should be checked every 2 hours or so during initial aggressive volume, glucose, and electrolyte management. If the initial phosphorous was low, it should be monitored every 4 hours during therapy**.

PITFALLS

- high serum glucose levels may lead to dilutional hyponatremia
- triglyceride levels may lead to factitious low glucose;
- high levels of ketone bodies may lead to factitious elevation of creatinine.

Other Tests:

- Electrocardiogram (ECG)
- Chest x-ray (CXR):
- Cultures
- Imaging

Co-morbidities

- concomitant infection (40%)
- Urinary tract infections (UTIs) are the single most common infection
- missed insulin treatments (25%)
- previously unknown diabetes (15%).
- Other associated causes make up roughly 20%

Other associated causes

- Myocardial infarction.
- Cerebrovascular accident.
- Complicated pregnancy.
- Trauma
- Stress
- Surgery

Clinical Management of DKA and recognition of complications

- Managing DKA in an ICU/acute care bed during the first 24-48 hours is always advisable.

Fluid resuscitation

- **Intravenous (IV) solutions replace extravascular and intravascular fluids and electrolyte losses. They also dilute both the glucose level and the levels of circulating counter-regulatory hormones.**

Fluid resuscitation

- Administer 1 liter over the first 30 minutes.
- Administer 1 liter over the second hour.
- Administer 1 liter over the following 2 hours.
- Administer 1 liter every 4 hours, depending on the degree of dehydration and central venous pressure (CVP) readings.

Fluid resuscitation

- When the patient becomes euvolemic, the physician may switch to half the isotonic sodium chloride solution, particularly if hypernatremia exists.
- When blood sugar decreases to less than 180 mg/dL, isotonic sodium chloride solution is replaced with 5-10% dextrose with half isotonic sodium chloride solution.

Insulin therapy

- A low-dose insulin regimen has the advantage of not inducing severe hypoglycemia or hypokalemia, as may be observed with a high-dose insulin regimen.
- Subcutaneous absorption of insulin is reduced in DKA because of dehydration; therefore, using IV or IM routes is always preferable.

Insulin therapy

- **The initial insulin dose is a continuous IV insulin infusion** using an infusion pump, if available, at a rate of 0.1 U/kg/h.
- Larger volumes may be easier in the absence of an intravenous infusion pump (eg, 60 U of insulin in 500 cc of isotonic sodium chloride solution at a rate of 50 cc/h with a micro-drip set).

Insulin therapy

- The optimal rate of glucose decline is 100 mg/dL/h.
- A common mistake is to allow blood glucose to drop to hypoglycemic levels. This mistake usually results in a rebound ketosis derived by counter-regulatory hormones. Rebound ketosis requires a longer duration of treatment

Potassium

- If the potassium level is greater than 6 mEq/L, do not administer potassium supplement.
- If the potassium level is 4.5-6 mEq/L, administer 10 mEq/h of potassium chloride.
- If the potassium level is 3-4.5 mEq/L, administer 20 mEq/h of potassium chloride.
- Monitor serum potassium levels hourly, and the infusion must stop if the potassium level is greater than 5 mEq/L.

Correction of acid-base balance

- Sodium bicarbonate only is infused if decompensated acidosis starts to threaten the patient's life, especially when associated with either sepsis or lactic acidosis.
- If sodium bicarbonate is indicated, 100-150 mL of 1.4% concentration is infused initially. This may be repeated every half hour if necessary

Treatment of concurrent infection

- In the presence of infection, administer proper antibiotics guided by the results of culture and sensitivity studies.
- Starting empiric antibiotics on suspicion of infection until culture results are available may be advisable.

Complications:

- The leading cause of DKA mortality in children is **cerebral edema**
- **Hypokalemia** is a complication that is precipitated by failing to rapidly address the total body potassium deficit brought out by rehydration

Complications:

- **Hypoglycemia** may result from inadequate monitoring of glucose levels during insulin therapy.
- **Acute pulmonary edema** potentially is related to aggressive or excessive fluid therapy.

Other complications

- CVT
- MI
- Acute gastric dilatation
- Erosive gastritis
- Late hypoglycemia
- Respiratory distress
- Infection

Prognosis:

- The presence of deep coma at the time of diagnosis, hypothermia, and oliguria are signs of poor prognosis

Thank You