ACUTE METABOLIC COMPLICATIONS OF DIABETES MELLITUS

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The article of this issue is:

Diabetes-related emergencies are:
1- Ketoacidosis
2- Hyperosmolar non-ketotic state.
3- Lactic acidosis
4- Hypoglycemia

DIABETIC KETOACIDOSIS

Diabetic ketoacidosis is a medical emergency characterized by the triad of hyperglycemia, ketosis and acidosis.

Essential Laboratory Criteria
• Blood glucose >250 mg/dL
• PH <7.30
• Serum bicarbonate <18 mmol/L
• Anion gap >15
• Ketonemia and ketonuria

Pathogenesis

Diabetes is a state of starvation despite the abundance of glucose. This state of starvation is caused by absolute or relative insulin deficiency. Hyperglycemia causes osmotic diuresis leading to dehydration and loss of sodium and potassium (Figures 1, 2). Potassium losses are also aggravated by secondary hyperaldosteronism. Insulin deficiency, elevated glucagon and adrenalin result in unrestrained lipolysis and increased supply of FFA’s for hepatic ketogenesis. In the presence of even little amounts of insulin, formation of ketocids in the liver is inhibited (figure 3). Insulin stimulates the enzyme co-carboxylase and increases malonyl Co A formation from acetyl CoA, the exact opposite effect of glucagon. Malonyl CoA inhibits carnitine palmitoyl transferase, the key enzyme that carries fatty acids into mitochondria for ß- oxidation.

Susceptibility

In type 1 diabetes; DKA is the initial presentation in up to 25% of children and adolescents. Inter-current infection, stress caused by trauma or surgery, and/or missed insulin
Acute Metabolic…….

**Figure 4**: Biochemical features of diabetic ketoacidosis (DK), hyperosmolar nonketotic state (HNK) and lactic acidosis (LA) can be present in the same patient.

**CLINICAL MANIFESTATIONS**

**Symptoms**
- Polyuria, thirst and polydipsia.
- Abdominal pain may be severe and unnecessary laparotomy performed.
- Weight loss and marked weakness.
- Blurred vision, nausea, vomiting and leg cramps are recognized symptoms.

**Physical Signs**
- Dehydration, hypotension, and tachycardia (caused by contraction of intra- and extracellular fluid volumes).
- Air-hunger and acetone smell (ketones).
- Hypothermia, confusion or coma occurs in less than 10% of cases.

**LABORATORY FINDINGS**

In DKA, common laboratory test results are:
- Glucose ≥ 250 mg/dL.
- Sodium: normal or reduced.
- Potassium: serum K normal, reduced or elevated, but total body potassium is always reduced.
- Bicarbonate: reduced to less than 18 mmol/L.
- Ketones: ++ (in serum and urine).
- Lactate (in blood): N or slightly increased.
- Osmolarity: N or +
- PH: reduced to less than 7.3.
- Anion gap which is the difference between the sum of measured cations (sodium + potassium) and the sum of anions (chloride + bicarbonate). Normally the difference is <12. In DKA the AG is >15. AG = [Na + K - (Cl + HCO3)]

**CLINICAL ASSESSMENT**

In ketoacidosis of moderate severity the average amount of fluid and electrolyte losses in an adult patient are usually as shown below:
1. Water 6 L (3L extracellular: replace with saline and 3L intracellular: replace with dextrose 5%).
2. Sodium 500 m.mol.
3. Chloride 400 m.mol.
4. Potassium 350 m.mol.

**INVESTIGATIONS**

Important but should not delay fluid replacement and insulin treatment.
1. Venous blood: urea & electrolytes, glucose, bicarbonate.
2. ABG’s: are performed in severe acidosis (plasma bicarb. < 12 mmol/L).
3. Urine for ketones by test strip.
4. ECG.
5. Infection screen: CBC, urine and blood culture, C-reactive protein and CXR.

**DIFFERENTIAL DIAGNOSIS**

The diagnosis of DKA is usually straightforward in patients with known diabetes. DKA must be differentiated from acidosis and coma due to other causes:
- Hypoglycemia
- Uremia
- Gastroenteritis with metabolic acidosis
- Lactic acidosis
- Salicylate intoxication
- Encephalitis.

**LABORATORY MONITORING**

Regular monitoring is crucial in management of patients with ketoacidosis.
- Glucose, urea & electrolytes and HCO3 are measured at: baseline, 1hr, 2hr, 3hr, 6hr, 12hr, 24hr
- Creatinine is measured at baseline, 6, 12 and 24hr
- Arterial blood gases at baseline are not necessary if venous plasma bicarbonate is > 15 m.mol/L. With severe acidosis (serum HCO3 is < 12 m.mol/L) measure at baseline, 2 and 6 hrs.

**CLINICAL MONITORING**

- Close monitoring and recording of vital signs (HR, BP and RR) is important.
- Consciousness level monitoring: important to diagnose hypoglycemia and brain edema during treatment, if deterioration in consciousness occurs.
- Fluid balance chart with accurate recording.
- CVP line insertion: especially if cardiovascular and/or renal compromise is present.

**MANAGEMENT**: Diabetic ketoacidosis is a medical emergency that should be treated in a hospital ICU.
However, mild cases can be treated in the ward. Principal components of treatment are:
1. Fluid repletion.
2. Soluble (short acting) insulin.
4. Antibiotics if infection is present or suspected

**Fluid Replacement:** is started with 0.9% saline I.V. as follows:
- 1L over 30 minutes.
- 1L over 1 hr.
- 1L over 2 hrs.
- 1L over next 2 to 4 hrs.
- This replenishes most of the extracellular fluid compartment (6L in first 24 hrs).
Additional fluid replacement should be based on clinical response and urine output.
- When blood glucose is < 15 mmol/L (270 mg/dL), start 5% dextrose 1L / 8 hourly I.V.
- If still dehydrated continue 0.9% saline.

**Insulin treatment**
- 50u soluble insulin in 50mL 0.9% saline I.V. by an infusion pump:
  - 6u /hr initially.
  - 3u /hr when blood glucose is 15 mmol/L (270 mg/dL).
  - 2u /hr if blood glucose is < 10 mmol/L (180 mg/dL).
- Check blood glucose hourly initially; if no reduction in the first hour, increase the insulin rate.
- Aim for fall in blood glucose is 3 to 6 mmol /L (55 to 110 mg/dL) per hour.
- Soluble insulin can be given I.M. (loading 20 to 30 unit followed by 5u hourly).
- A fast acting insulin analogue can be given by S.C. injection (0.3u/kg then 0.1u/kg, hourly).
- No place for long acting or premixed insulin in the treatment of ketoacidosis.

**COMPLICATIONS**
- Cerebral edema Is common in young children and causes unexplained loss of consciousness and high mortality.
  - May be caused by rapid lowering of blood glucose or Use of hypotonic fluids and/or bicarbonate.
  - Treatment: mannitol i.v. and oxygen.
- Other complications include: Hypoglycemia, ARDS, thromboembolism, DIC, acute circulatory failure and sudden death from hypo- or hyper-kalemia.