Complications of DM.

ACUTE COMPLICATIONS

- **Diabetic Ketoacidosis.**
- **Hyperosmolar Nonketotic Syndrome (*Hyperglycemic Hyperosmolar State*).**
- **Lactic Acidosis.**
- **Hypoglycemia.**

Diabetic ketoacidosis;-

Diabetic ketoacidosis (DKA) is a medical emergency and remains a serious cause of morbidity, principally in people with type 1 diabetes. It is a potentially life-threatening condition that has an overall mortality rate of approximately 2.5%, with most deaths resulting from complicating or precipitating medical conditions rather than the metabolic disturbances of DKA itself.

In established diabetes a common course of events is that patients develop an intercurrent infection, lose their appetite, and either stop or reduce their dose of insulin in the mistaken belief that under these circumstances less insulin is required.

DKA is characteristic of type 1 diabetes and is often the presenting problem in newly diagnosed patients (approximately 25% of T1DM patients at diagnosis) and otherwise most often develops when patients with known T1DM stop taking prescribed insulin.

However, an increasing number of patients presenting with DKA have underlying type 2 diabetes.

In established type 1 diabetes, DKA may be precipitated by an intercurrent illness because of failure to increase insulin dose appropriately to compensate for the stress response. No obvious precipitating cause can be found in many cases.

Pathogenesis

A clear understanding of the biochemical basis and pathophysiology of DKA is essential for its efficient treatment. The cardinal biochemical features are:

•*hyperketonemia* (≥ 3.0 mmol/L) or ketonuria (more than 2+ on standard urine sticks)

•*hyperglycemia* (blood glucose ≥ 11 mmol/L (approximately 200 mg/dL))

•*metabolic acidosis* (venous bicarbonate **<** 15 mmol/L and/or venous pH < 7.3 (H+ > 50 nmol/L)).

The hyperglycaemia causes a profound osmotic diuresis leading to dehydration and electrolyte loss, particularly of sodium and potassium. Potassium loss is exacerbated by secondary hyperaldosteronism as a result of reduced renal perfusion. Ketosis results from insulin deficiency,

exacerbated by elevated catecholamines and other stress hormones, resulting in unrestrained lipolysis and supply of FFAs for hepatic ketogenesis. When this exceeds the capacity to metabolise acidic ketones, these accumulate in blood. The resulting metabolic acidosis forces hydrogen ions into cells, displacing potassium ions.

About half the deficit of total body water is derived from the intracellular compartment and occurs comparatively early in the development of acidosis with relatively few clinical features

Average loss of fluid and electrolytes in adult diabetic ketoacidosis of moderate severity

- Water: 6 L
- Sodium: 500 mmol
- Chloride: 400 mmol
- Potassium: 350 mmol

3 L extracellular -replace with saline 3 L intracellular -replace with dextrose

Every patient in diabetic ketoacidosis is potassium-depleted, but the plasma concentration of potassium gives very little indication of the total body deficit. However, soon after insulin treatment is started there is likely to be a precipitous fall in the plasma potassium due to dilution of extracellular potassium by administration of intravenous fluids, the movement of potassium into cells induced by insulin, and the continuing renal loss of potassium.

The magnitude of the hyperglycaemia does not correlate with the severity of the metabolic acidosis; moderate elevation of blood glucose may be associated with life-threatening ketoacidosis.

Clinical assessment

Clinical features of diabetic ketoacidosis

- Polyuria, thirst, Weight loss , Weakness, Nausea, vomiting, Leg cramps, Blurred vision, Abd.pain.
    - Dehydration , Hypotension (postural or supine)
    - Cold extremities/peripheral cyanosis, Tachycardia.
- Air hunger (Kussmaul breathing)
- Smell of acetone , Hypothermia .
- Confusion, drowsiness, coma (10%)

In the fulminating case the striking features are those of salt and water depletion, with loss of skin turgor, furred tongue and cracked lips, tachycardia, hypotension and reduced intra-ocular pressure. Breathing may be deep and sighing, the breath is usually fetid, and the sickly-sweet smell of acetone may be apparent. Mental apathy, confusion or a reduced conscious level may be present. The state of consciousness is very variable in patients with diabetic ketoacidosis; coma is uncommon.

Abdominal pain is sometimes a feature of diabetic ketoacidosis, particularly in children. Serum amylase may be elevated but rarely indicates coexisting pancreatitis. In infected patients, pyrexia may not be present initially because of vasodilatation secondary to acidosis.

Investigations

The following are important but should not delay the institution of intravenous fluid and insulin replacement:

- Venous blood: for urea and electrolytes, glucose, bicarbonate.
- Arterial blood gases to assess the severity of acidosis. (The severity of ketoacidosis can be assessed rapidly by measuring the venous plasma bicarbonate; less than 12 mmol/L indicates severe acidosis. The hydrogen ion concentration gives a more precise measure but requires arterial blood.)
- Urinalysis for ketones.
- ECG.
- Infection screen: full blood count, blood and urine culture, C-reactive protein, chest X-ray. Although leucocytosis invariably occurs, this represents a stress response and does not necessarily indicate infection.

Management

Diabetic ketoacidosis is a medical emergency which should be treated in hospital, preferably in a high-dependency area. Regular clinical and biochemical review is essential, particularly during the first 24 hours of treatment.

The principal components of treatment are:

- the administration of short-acting (soluble) insulin
- fluid replacement
- potassium replacement
- the administration of antibiotics if infection is present.

Monitoring in diabetic ketoacidosis1

Laboratory	Baseline	1 hr	2 hr	3 hr	6 hr	12 hr	24 hr
Glucose2	√	√	√	√	√	√	√
Urea, electrolytes	√	√	√	√	√		√
Creatinine	√				√	√	√
Bicarbonate	√	√	√	√	√	√	√
Blood gases	(√)		√3		√3		

Management of diabetic ketoacidosis

Fluid replacement

The aim is to replace the fluid deficit (average 6 l) over approximately 24 h, but the rate of replacement depends on medical co-morbidity. Rehydration should initially be with intravenous 0.9% saline at a rate of the order of 1 litre over 30 min followed by 1 litre over 2 h, 1 litre over 4 h, 1 litre over 6 h and then 1 litre 6-hourly. An accurate record of fluid balance is essential. As the glucose falls, intravenous dextrose (5–10%) may be required. With prolonged use of dextrose, there is potential for hyponatraemia and if the sliding scale needs to be continued for several days after the biochemistry has corrected (e.g. if patient is not eating), then it may be appropriate to switch to using 5% dextrose alternating with 0.9% saline.

Insulin

- 50 U soluble insulin in 50 mL 0.9% saline i.v. via infusion pump
    - 6 U/hr initially
    - 3 U/hr when blood glucose < 15 mmol/L (270 mg/dL)
    - 2 U/hr if blood glucose < 10 mmol/L (180 mg/dL)
- Check blood glucose hourly initially; if no reduction in first hour, rate of insulin infusion should be increased
- Aim for fall in blood glucose of 3-6 mmol/L (approximately 55-110 mg/dL) per hour

Potassium

- None in first L of i.v fluid unless plasma potassium < 3.0 mmol/L
- When < 3.5 mmol/L, give 20 mmol/hr
- When plasma potassium is 3.5-5.0 mmol/L, give 10 mmol/hr

As the plasma potassium is often high at presentation, treatment with intravenous potassium chloride should be started cautiously and carefully monitored. Sufficient should be given to maintain a normal plasma concentration and large amounts may be required (100-300 mmol in the first 24 hours). Cardiac rhythm should be monitored in severe cases because of the risk of electrolyte-induced cardiac arrhythmia.

Bicarbonate

In patients who are severely acidotic ([H+] > 100 nmol/L, pH < 7.0) the infusion of sodium bicarbonate (300 mL 1.26% over 30 mins into a large vein) should be considered, with the simultaneous administration of potassium. Its use is controversial, however, and should only be considered in exceptional circumstances. Complete correction of the acidosis should not be attempted.

Additional procedures

- Catheterisation if no urine passed after 3 hrs
- Nasogastric tube to keep stomach empty in unconscious or semiconscious patients, or if vomiting is protracted
- Central venous line if cardiovascular system compromised, to allow fluid replacement to be adjusted accurately
- Plasma expander if systolic BP is < 90 mmHg or does not rise with i.v. saline
- Antibiotic if infection demonstrated or suspected
- ECG monitoring in severe cases .

Antibiotics

Infections must be carefully sought and vigorously treated since it may not be possible to abolish ketosis until they are controlled. The management of diabetic ketoacidosis may be complicated by the development of other conditions which require active therapy.

Complications of diabetic ketoacidosis

- **Cerebral oedema**
  - May be caused by very rapid reduction of blood glucose, use of hypotonic fluids and/or bicarbonate
  - High mortality
  - Treat with mannitol, oxygen
- **Acute respiratory distress syndrome.**
- **Thromboembolism**
- **Disseminated intravascular coagulation (rare)**
- **Acute circulatory failure**

Non-ketotic hyperosmolar diabetic coma;-

A hyperglycemic hyperosmolar state (HHS) occurs almost exclusively in patients with T2DM, one third of whom have not been previously diagnosed. Patients often are elderly and frequently have compromised renal function. Insulin deficiency, often exacerbated by insulin resistance resulting from the stress, leads to hyperglycemia, glucosuria, and an osmotic diuresis. However, the presence of some endogenous insulin secretion suppresses lipolysis and ketogenesis enough to prevent ketoacidosis. Patients with HHS typically develop more marked hyperglycemia, fluid and electrolyte deficits, and hyper osmolality compared to those with DKA.

HHS usually develops insidiously over days to weeks, and patients may be vulnerable to development of more severe hyperglycemia and volume deficits over this extended period.

HHS is associated with infections (40%), diuretic use (35% to 40%), and residency in nursing homes (25% to 30%). Other precipitating and complicating factors may include intestinal obstruction, mesenteric thrombosis, pulmonary embolism, peritoneal dialysis, subdural hematoma, and an extensive list of medications.

The overall mortality rate exceeds that of DKA (10% to 40%), with higher mortality rates associated with age older than 70 years, nursing home residency, and higher osmolality or serum Na+ concentration.

Clinically, patients have evidence of the marked fluid and electrolyte deficits and tend to have more prominent neurologic abnormalities than those with DKA, including confusion, obtundation, and coma.

Therapy for HHS follows the same general principles as that for DKA, with a greater volume replacement required (typically 8 to 12 L in fully developed HHS). Restoration of the fluid and electrolyte deficits should proceed more slowly than in DKA, ideally over 36 to 72 hours.

Insulin therapy should be started only after rehydration is in progress. There is a need for K+ replacement, but less than in DKA. Patients with HHS may be more sensitive to insulin than those with DKA and may require lower insulin doses.

In view of the severe dehydration and predisposition to vascular thrombosis, heparin prophylaxis usually should be provided. Despite the very marked hyperglycemia of HHS, patients may be able to return to oral treatment eventually.

Lactic acidosis;-

In coma due to lactic acidosis the patient is likely to be taking metformin for type 2 diabetes and is very ill and overbreathing but not as profoundly dehydrated as is usual in coma due to ketoacidosis. The patient's breath does not smell of acetone, and ketonuria is mild or even absent, yet plasma bicarbonate is reduced and the anion gap and H+ are increased. The diagnosis is confirmed by a high (usually > 5.0

mmol/L) concentration of lactic acid in the blood. Treatment is with intravenous sodium bicarbonate sufficient to reduce H+ below 60 nmol/L (pH 7.2), along with insulin and glucose. Despite energetic treatment, the mortality in this condition is over 50%. Sodium dichloroacetate may be given to lower blood lactate.