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COURSE: Medical Biochemistry IV (BCH 313)

ASSIGNMENT (Group 2):

1. Define the following terms: a. Ketogenesis b. Ketonaemia c. Ketonuria d. Ketogenesis
2. What are the consequences of Ketosis?
3. Write concisely on the management of ketoacidosis.

**ANSWERS**

1a. **Ketogenesis**: Ketogenesis is a metabolic pathway that produces ketone bodies, which provide an alternative form of energy for the body. Ketone bodies are produced by breaking down fatty acids and ketogenic amino acids. Ketogenesis supplies our organs, especially the brain, with needed energy under circumstances (such as fasting). Insufficient ketogenesis can lead to hypoglycemia, also known as low blood sugar. On the other hand, excessive production of ketone bodies can lead to ketoacidosis, a life-threatening condition that is the result of extremely high levels of ketones and blood sugar.

b. **Ketonaemia**: It is the condition of having excess ketone bodies in the blood stream.

c. **Ketonuria**: It is a condition in which ketone bodies are present in the urine. It is seen in conditions in which the body produces excess ketones; it is most common in individuals who have diabetes, particularly type 1 diabetes mellitus. It can also occur in women who are pregnant or breastfeeding.

2. **Consequences** **of** **Ketosis**.

Ketosis refers to the metabolic state in which the body converts fat stores into energy, releasing ketones in the process and thereby causing the buildup of ketones in the body.

* Excess ketones in the body lead to ketoacidosis. **Diabetic** **ketoacidosis** (DKA) is an example involving the overproduction of ketone bodies. It takes place when there is a lack of, or resistance to, insulin. This usually occurs in people with type I diabetes, although it can happen to people with advanced type II diabetes as well.
* Once carbohydrate stores are depleted and gluconeogenesis cannot occur anymore, ketogenesis is substantially increased, and there are larger amounts of ketone bodies produced. Due to the acidic nature of beta-hydroxybutyrate and acetoacetate, this causes an anion gap **metabolic** **acidosis**.
* On presentation, patients are usually very dehydrated from being hyperglycemic. Along with being dehydrated, patients typically present with **confusion**, **nausea**, **vomiting**, and **abdominal** **pain**.
* Because of the acidosis, patients often breathe very deeply and rapidly to eliminate carbon dioxide and cause a **respiratory** **alkalosis**.

3. **Management** **of** **Ketoacidosis**.

Diabetic ketoacidosis (DKA) is a rare yet potentially fatal hyperglycemic crisis that can occur in patients with both types 1 and 2 diabetes mellitus. Due to its increasing incidence and economic impact related to the treatment and associated morbidity, effective management and prevention is important.

The management of patients with diabetic ketoacidosis includes obtaining a thorough but rapid history and performing a physical examination in an attempt to identify possible precipitating factors. The major treatment of this condition is initial rehydration (using isotonic saline) with subsequent potassium replacement and low-dose insulin therapy. The use of bicarbonate is not recommended in most patients.

The therapeutic goals for diabetic ketoacidosis consist of improving circulatory volume and tissue perfusion, reducing blood glucose and serum osmolality toward normal levels, clearing ketones from serum and urine at a steady rate, correcting electrolyte imbalances and identifying precipitating factors.

**FLUID REPLACEMENT**

The severity of fluid and sodium deficits is determined primarily by the duration of hyperglycemia, the level of renal function and the patient's fluid intake. Dehydration can be estimated by clinical examination and by calculating total serum osmolality and the corrected serum sodium concentration.

The initial priority in the treatment of diabetic ketoacidosis is the restoration of extra-cellular fluid volume through the intravenous administration of a normal saline (0.9 percent sodium chloride) solution. This step will restore intravascular volume, decrease counter regulatory hormones and lower the blood glucose level. As a result, insulin sensitivity may be augmented.

**INSULIN THERAPY**

Modern management of diabetic ketoacidosis has emphasized the use of lower doses of insulin. This has been shown to be the most efficacious treatment in both children and adults with diabetic ketoacidosis. The current recommendation is to give low-dose (short-acting regular) insulin after the diagnosis of diabetic ketoacidosis has been confirmed by laboratory tests and fluid replacement has been initiated.

It is prudent to withhold insulin therapy until the serum potassium concentration has been determined. In the rare patient who presents with hypokalemia, insulin therapy may worsen the hypokalemia and precipitate life-threatening cardiac arrhythmias.

**POTASSIUM** **THERAPY**

Although the typical potassium deficit in diabetic ketoacidosis is 500 to 700 mEq (500 to 700 mmol), most patients are hyperkalemic at the time of diagnosis because of the effects of insulinopenia, hyperosmolality and acidemia. During rehydration and insulin therapies for diabetic ketoacidosis, the serum potassium concentration typically declines rapidly as potassium reenters the intracellular compartment.

One protocol entails using insulin and intravenous fluids until the serum potassium concentration is less than 5.5 mEq per L (5.5 mmol per L). At this time, potassium chloride is added to intravenous fluids in the amount of 20 to 40 mEq per L. The exact amount of potassium that is administered depends on the serum potassium concentration. When the serum potassium level is less than 3.3 mEq per L (3.3 mmol per L), the administration of 40 mEq per L of potassium is appropriate. If the serum potassium is greater than 3.3 mEq per L but less than 5.5 mEq per L, 20 to 30 mEq per L of potassium can be administered. The goal is to maintain the serum potassium concentration in the range of 4 to 5 mEq per L (4 to 5 mmol per L).

**BICARBONATE** **THERAPY**

In general, supplemental bicarbonate therapy is no longer recommended for patients with diabetic ketoacidosis, because the plasma bicarbonate concentration increases with insulin therapy. Insulin administration inhibits ongoing lipolysis and ketone production and also promotes the regeneration of bicarbonate.

**PHOSPHATE** **THERAPY**

Osmotic diuresis leads to increased urinary phosphate losses. During insulin therapy, phosphate reenters the intracellular compartment, leading to mild to moderate reductions in the serum phosphate concentration. Adverse complications of hypophosphatemia are uncommon and occur primarily in patients with severe hypophosphatemia (a serum phosphate concentration of less than 1.0 mg per dL [0.32 mmol per L]).

Prospective studies have indicated no clinical benefit for phosphate replacement in the treatment of diabetic ketoacidosis, and excessive phosphate replacement may contribute to hypocalcaemia and soft tissue metastatic calcification. Although the replacement of phosphate per se is not routinely recommended, it may be useful to replace some potassium as potassium phosphate. One protocol is to administer two thirds of the potassium as potassium chloride and one third as potassium phosphate. The use of phosphate for this purpose reduces the chloride load that might contribute to hyperchloremic acidosis and decreases the likelihood that the patient will develop severe hypophosphatemia during insulin therapy.

When diabetic ketoacidosis has been controlled, subcutaneous insulin therapy can be started. The half-life of regular insulin is less than 10 minutes. Therefore, to avoid relapse of diabetic ketoacidosis, the first subcutaneous dose of regular insulin should be given at least one hour before intravenous insulin is discontinued.

Successful outpatient therapy requires the absence of severe intercurrent illness, an alert patient who is able to resume oral intake and the presence of mild diabetic ketoacidosis (pH of greater than 7.2 and a plasma bicarbonate concentration of greater than 10 mEq per L).