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Question

GROUP 2 CATEGORY (MBBS)

1.DEFINE THE FOLLOWING TERMS

A. KETOGENESIS: Ketogenesis is the biochemical process through which organisms produce ketone bodies through breakdown of fatty acids and ketogenic amino acids. This process supplies energy under circumstances such as fasting or caloric restriction to certain organs, particularly the brain, heart and skeletal muscle. Insufficient gluconeogenesis can cause hypoglycemia and excessive production of ketone bodies, ultimately leading to a life-threatening condition known as ketoacidosis.

Ketone bodies are produced mainly in the mitochondria of liver cells, and synthesis can occur in response to an unavailability of blood glucose, such as during fasting. Other cells, e.g. human astrocytes, are capable of carrying out ketogenesis, but they are not as effective at doing so. Ketogenesis occurs constantly in a healthy individual. Ketogenesis in healthy individuals is ultimately under the control of the master regulatory protein AMPK, which is activated during times of metabolic stress, such as carbohydrate insufficiency. Activation in the liver inhibits lipogenesis, promotes fatty

acid oxidation, switches off acetyl-CoA carboxylase, turns on malonyl-CoA decarboxylase, and consequently induces ketogenesis. Ethanol is a powerful AMPK inhibitor and therefore can cause profound disruptions in the metabolic state of the liver, including halting of ketogenesis, even in the context of severe glucose shortage.

Ketogenesis takes place in the setting of low glucose levels in the blood, after exhaustion of other cellular carbohydrate stores, such as glycogen. It can also take place when there is insufficient insulin (e.g. in type 1 (but not 2) diabetes), particularly during periods of "ketogenic stress" such as intercurrent illness.

B. KETONAEMIA: This refers to the presence of an abnormally high concentration of ketone bodies in the blood.

Seriously ill patients are easy to detect clinically, but well-appearing diabetic patients who present with vague symptoms such as malaise, nausea and hyperglycemia with ketonemia are more difficult to identify.

C. KETONURIA: Ketonuria is a medical condition in which ketone bodies are present in the urine.It is seen in conditions in which the body produces excess ketones as an indication that it is using an alternative source of energy. It is seen during starvation or more commonly in type 1 diabetes mellitus.

Causes include:

-Metabolic abnormalities such as diabetes, renal glycosuria, or glycogen storage disease.

-Dietary conditions such as starvation, fasting, low-carbohydrate diets, prolonged vomiting, and anorexia.

-Conditions in which metabolism is increased, such as hyperthyroidism, fever, pregnancy or lactation.

D. KETOGENESIS : As seen in the definition of ketogenesis in 1a above

2. WHAT ARE THE CONSEQUENCES OF KETOSIS

Ketosis is a metabolic state characterized by elevated levels of ketone bodies in the blood or urine. Physiologic ketosis is a normal response to low glucose availability, such as low-carbohydrate diets or fasting, that provides an additional energy source for the brain in the form of ketones. In physiologic ketosis, ketones in the blood are elevated above baseline levels, but the body's acid-base homeostasis is maintained. This contrasts with ketoacidosis, an uncontrolled production of ketones that occurs in pathologic states and causes a metabolic acidosis, which is a medical emergency.

CONSEQUENCES OF KETOSIS

During ketosis, many parts of the body are burning ketones for energy instead of carbs. This includes a large part of the brain. During this adaptation phase, you may experience some temporary side effects.

In the beginning of ketosis, you may experience a range of negative symptoms. They are often referred to as "low-carb flu" or "keto flu" because they resemble symptoms of the flu.

These may include:

-Headache.

-Fatigue.

-Brain fog.

-Increased hunger.

-Poor sleep.

-Nausea.

-Decreased physical performance

-Bad breath is also common, often described as fruity and slightly sweet.

However, the "low-carb flu" is usually over within a few days.

- Leg Muscles May Cramp: In ketosis, some people may experience leg cramps. Leg cramps in ketosis are usually connected to dehydration and loss of minerals. This is because ketosis causes a reduction in water weight. Glycogen, the storage form of glucose in muscles and liver, binds water. This gets flushed out when you reduce carb

intake, and is one of the main reasons why people lose weight rapidly in the first week of a very low-carb diet.

-Ketosis May Cause Digestive Problems: Dietary changes can sometimes lead to digestive issues. This is also true for ketogenic diets, and constipation is a common side effect in the beginning. This is most commonly due to not eating enough fiber and not drinking enough fluids. Some people may also get diarrhea, but it's less common.

-Elevated Heart Rate: Some people also experience increased heart rate as a side effect of ketosis. This is also called heart palpitations or a racing heart, and can happen during the first few weeks of a ketogenic diet.

Other, less common side effects may include:

-Ketoacidosis: A few cases of ketoacidosis (a serious condition that occurs in uncontrolled diabetes) have been reported in breastfeeding women, likely triggered by a very low-carb diet. However, this is extremely rare.

-Kidney stones: Although uncommon, some epileptic children have developed kidney stones on a ketogenic diet.

-Raised cholesterol levels: Some people get increased total and low-density lipoprotein (LDL) cholesterol levels.

3. WRITE CONCISELY ON THE MANAGEMENT OF KETOACIDOSIS.

Attacks of ketoacidosis can be prevented in those known to have diabetes to an extent by adherence to these clear-cut instructions on how to treat themselves when unwell. These instructions include advice on how much extra insulin to take when sugar levels appear uncontrolled, an easily digestible diet rich in salt and carbohydrates, means to suppress fever and treat infection, and recommendations when to call for medical help

People with diabetes can monitor their own ketone levels when unwell and seek help if they are elevated. The main aims in the treatment of ketoacidosis are replacing the lost fluids and electrolytes while suppressing the high blood sugars and ketone production with insulin. Admission to an intensive care unit (ICU) or similar high-dependency area or ward for close observation may be necessary.

Management of ketoacidosis includes the following:

1. **Fluid replacement:** The amount of fluid replaced depends on the estimated degree of dehydration. If dehydration is so severe as to cause shock (severely decreased blood pressure with insufficient blood supply to the body's organs), or a depressed level of consciousness, rapid infusion of saline (1 liter for adults, 10 ml/kg in repeated doses for children) is recommended to restore circulating volume. Slower rehydration based on calculated water and sodium shortage may be possible if the dehydration is moderate, and again saline is the recommended fluid. Very mild ketoacidosis with no associated vomiting and mild dehydration may be treated with oral rehydration and subcutaneous rather than intravenous insulin under observation for signs of deterioration.

2. **Insulin:** Some guidelines recommend a bolus (initial large dose) of insulin of 0.1 unit of insulin per kilogram of body weight. This can be administered immediately after the potassium level is known to be higher than 3.3 mmol/l; if the level is any lower, administering insulin could lead to a dangerously low potassium level. Other guidelines recommend delaying the initiation of insulin until fluids have been administered. It is possible to use rapid acting insulin analogs injections under the skin for mild or moderate cases.

3. **Potassium:** Potassium levels can fluctuate severely during the treatment of ketoacidosis, because insulin decreases potassium levels in the blood by redistributing it into cells via increased sodium-potassium pump activity. A large part of the shifted extracellular potassium would have been lost in urine because of osmotic diuresis. Hypokalemia (low blood potassium concentration) often follows treatment. This increases the risk of dangerous irregularities in the heart rate. Therefore, continuous observation of the heart rate is recommended, as well as repeated measurement of the potassium levels and addition of potassium to the intravenous fluids once levels fall below 5.3 mmol/l. If potassium levels fall below 3.3 mmol/l, insulin administration may need to be interrupted to allow correction of the hypokalemia.

4. **Sodium bicarbonate:** The administration of sodium bicarbonate solution to rapidly improve the acid levels in the blood is controversial. Some guidelines recommend it for extreme acidosis (pH<6.9), and smaller amounts for severe acidosis (pH 6.9–7.0). While it may improve the acidity of the blood, it may actually worsen acidity inside the body's cells and increase the risk of certain complications.

5. **Cerebral edema:** Cerebral edema, if associated with coma, often necessitates admission to intensive care, artificial ventilation, and close observation. The

administration of fluids is slowed. Intravenous mannitol and hypertonic saline (3%) are used—as in some other forms of cerebral edema—in an attempt to reduce the swelling.

6. **Resolution:** Resolution of DKA is defined as general improvement in the symptoms, such as the ability to tolerate oral nutrition and fluids, normalization of blood acidity (pH>7.3), and absence of ketones in blood (<1 mmol/l) or urine. Once this has been achieved, insulin may be switched to the usual subcutaneously administered regimen, one hour after which the intravenous administration can be discontinued.