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**PHARMACOLOGY**

**18/MHS07/019**

**BCH 204**

**Question**

1. Outline the toxicity values and deficiency manifestation of the following minerals:

- Potassium
- Calcium
- Magnesium
- Chloride
- Iron

### **◆POTASSIUM**

#### **DEFICIENCY MANIFESTATION**

##### **A. Hyperkalemia**

Hyperkalemia is a clinical condition associated with elevated plasma potassium above the normal range (3.5–5 mEq/L).

##### **Causes of hyperkalemia**

- Renal failure: The kidney may not be able to excrete a potassium load when GFR is very low.
- Mineralocorticoid deficiency: For example, in Addison's disease.
- Cell damage: For example, in trauma and malignancy.

##### **Symptoms of hyperkalemia**

First manifestation is cardiac arrest, changes in electro- cardiogram, cardiac arrhythmia, muscle weakness which may be preceded by parasthesia (abnormal tingling sensation).

##### **Treatment for Hyperkalemia**

Treatment may include:

- Going on a low-potassium diet
- Stopping or changing meds that are contributing to the hyperkalemia
- Taking medicine to lower the potassium in your body. Water pills (diuretics) remove potassium via the urinary tract.
- Treating your kidney disease, which may include dialysis, which filters potassium from your blood

##### **B.Hypokalemia (low plasma concentration)**

In hypokalemia, the level of potassium in blood is too low.

##### **Causes of hypokalemia**

- Gastrointestinal losses: Potassium may be lost from the intestine due to vomiting, diarrhea.
- Renal losses: Due to renal disease, administration of diuretics.
- Drinking too much alcohol
- Sweating a lot
- Folic acid deficiency
- Certain antibiotics
- Diabetic ketoacidosis (high levels of acids called ketones in your blood)
- Laxatives taken over a long period of time
- Certain types of tobacco

- Some asthma medications
- Low magnesium

**Several syndromes can be associated with low potassium, such as:**

- Cushing's syndrome
- Gitelman syndrome
- Liddle syndrome
- Bartter syndrome
- Fanconi syndrome

### **Symptoms of hypokalemia**

Muscular weakness, tachycardia, electrocardiographic (ECG) changes (flattering of ECG waves), lethargy, and confusion.

- Fatigue
- Muscle cramps or twitching
- Constipation
- Arrhythmia (abnormal heart rhythms)

### **Treatment**

#### **Potassium supplements**

If a disorder is causing hypokalemia, it is treated. Usually, potassium can be replaced by taking potassium supplements by mouth. Because potassium can irritate the digestive tract, supplements should be taken in small doses with food several times a day rather than in a single large dose. Special types of potassium supplements, such as wax-impregnated or microencapsulated potassium chloride, are much less likely to irritate the digestive tract.

To treat hypokalemia more rapidly, potassium is given by vein (intravenously) in the following situations:

- The potassium level is dangerously low.
- The low level causes abnormal heart rhythms.
- Supplements taken by mouth are ineffective.
- People continue to lose more potassium than can be replaced using supplements taken by mouth.

Most people who take diuretics do not need to take potassium supplements. Nevertheless, doctors periodically check the potassium level in blood so that supplements can be given if necessary. Alternatively, diuretics that help the kidneys conserve potassium (potassium-sparing diuretics), such as amiloride, eplerenone, spironolactone, or triamterene can be used, but these drugs are used only if the kidneys are functioning normally.

When hypomagnesemia occurs with hypokalemia, it too is treated.

### **POTASSIUM TOXICITY**

**The normal serum potassium levels are between 3.5 and 5.0mmol/L (3.5 and 5.0 mEq/L). Any value above this range is referred to as toxic.**

## **◆IRON**

### **DEFICIENCY MANIFESTATION**

Disorders of iron metabolism

Iron deficiency and iron overload are the major disorders of iron metabolism.

#### **A. Iron deficiency**

A deficiency of iron causes a reduction in the rate of hemoglobin synthesis and erythropoiesis, and can result in iron deficiency anemia.

Iron deficiency anemia is the commonest of all single nutrient deficiencies. **The main causes are:**

- Deficient intake:**Including reduced bioavailability of iron due to dietary fiber, phytates, oxalates, etc.

- Impaired absorption:**For example, intestinal malabsorptive disease and abdominal surgery.

- Excessive iron: In terms of blood values, iron levels above 350–500 µg/dL are considered toxic, and levels over 1000 µg/dL indicate severe iron poisoning.**

**loss: For example, menstrual blood loss in women and in men from gastrointestinal bleeding(in peptic ulcer, diverticulosis or malignancy).**

Iron deficiency causes low hemoglobin resulting in hypo-chromic microcytic anemia in which the size of the red blood cells are much smaller than normal and have much reduced hemoglobin content.

Clinical features of anemia: Weakness, fatigue, dizziness and palpitation. Nonspecific symptoms are nausea, anorexia, constipation, and menstrual irregularities. Some individuals develop pica, a craving for unnatural articles of food such as clay or chalk.

## **B. Iron overload**

Hemosiderosis and hemochromatosis are the conditions associated with iron overload.

- Hemosiderosis:** Hemosiderosis is a term that has been used to imply an increase in iron stores as hemosiderin without associated tissue injury. Hemosiderosis is an initial stage of iron overload.

- Hemochromatosis:** Hemochromatosis is a clinical condition in which excessive deposits of iron in the form of hemosiderin are present in the tissues, with injury to involved organs as follows:

Liver: Leading to cirrhosis

Pancreas: Leading to fibrotic damage to pancreas with diabetes mellitus

Skin: Skin pigmentation, bronzed diabetes

Endocrine organ: leading to hypothyroidism, testicular atrophy

Joints: Leading to arthritis

Heart: Leading to arrhythmia and heart failure.

## **IRON TOXICITY**

Toxic effects begin to occur at doses above 10–20 mg/kg of elemental iron. Ingestions of more than 50 mg/kg of elemental iron are associated with severe toxicity. **In terms of blood values, iron levels above 350–500 µg/dL are considered toxic, and levels over 100µg/dL indicate severe iron poisoning.**

## **◆CHLORIDE**

### **DEFICIENCY MANIFESTATION**

#### **A. Hyperchloremia**

An increased chloride concentration occurs in dehydration, metabolic acidosis and Cushing's syndrome.

Hyperchloremia is a disorder in which a person has too much chloride in their blood. Chloride is an electrolyte, and changes in electrolyte levels can cause dehydration.

**Symptoms include:**

- fluid retention
- high blood pressure
- muscle weakness, spasms, or twitches
- irregular heart rate
- confusion, difficulty concentrating, and personality changes
- numbness or tingling
- seizures and convulsions

### **Causes of hyperchloremia**

- Gastrointestinal problems, such as vomiting or diarrhea. These issues can cause dehydration.
- A high fever that causes sweating and dehydration.
- Dehydration due to medications, intense exercise, heat exposure, or not drinking enough fluids.
- High sodium levels in the blood. Chloride tends to rise when sodium does.
- Too much salt intake. Chloride is an ingredient in sodium chloride, which is table salt.
- Diabetes insipidus, which causes the kidneys to pass large amounts of fluid.
- Diabetic coma.
- Some medications, particularly hormones, diuretics, and corticosteroids, such as hydrocortisone.
- Starvation due to eating disorders, severe malnourishment, or problems absorbing nutrients from food.
- Addison ' s disease, a disorder that occurs when the adrenal glands cannot produce enough hormones.

### **Treatment**

- taking medications to prevent nausea, vomiting, or diarrhea
- changing drugs if they are a factor in the electrolyte imbalance
- drinking 2–3 quarts of fluid every day
- receiving intravenous fluids
- eating a better, more balanced diet
- treating underlying mental health problems if an eating disorder is the culprit
- avoiding alcohol, caffeine, and aspirin
- gaining better control over blood glucose levels, since uncontrolled diabetes can cause electrolyte imbalances

## **B. Hypochloremia**

A decreased chloride concentration is seen in severe vomiting, metabolic alkalosis, excessive sweating and Addison's disease.

Hypochloremia is an electrolyte imbalance that occurs when there's a low amount of chloride in your body.

Chloride is an electrolyte. It functions with other electrolytes in your system, such as sodium and potassium, to regulate the amount of fluid and the pH balance in your body. Chloride is most commonly consumed as table salt (sodium chloride).

Hypochloremia occurs when there's a low level of chloride in your body. It can be caused by fluid loss through nausea or vomiting.

### **Symptoms include:**

- fluid loss
- dehydration

- weakness or fatigue
- difficulty breathing
- diarrhea or vomiting, caused by fluid loss

**Hypochloremia can also be caused by any of the following conditions:**

- congestive heart failure
- prolonged diarrhea or vomiting
- chronic lung disease, such as emphysema
- metabolic alkalosis, when your blood pH is higher than normal

### **Treatment of hypochloremia**

If your doctor detects an electrolyte imbalance such as hypochloremia, they'll investigate whether a condition, disease, or medication you're taking is causing the imbalance to occur. Your doctor will work with you to treat the underlying problem that's causing the electrolyte imbalance.

If your hypochloremia is due to a medication or drug that you're taking, then your doctor may adjust the dosage, if possible. If your hypochloremia is due to problems with your kidneys or an endocrine disorder, your doctor may refer you to a specialist.

You may receive intravenous (IV) fluids, such as normal saline solution, to restore electrolytes to normal levels.

Your doctor may also request that you have your electrolyte levels tested regularly for monitoring purposes.

If your hypochloremia is mild, then it can sometimes be corrected by an adjustment to your diet. This could be as simple as consuming more sodium chloride (salt). Here's what you need to know about daily salt intake.

### **CHLORIDE TOXICITY**

**Chloride toxicity has not been observed in humans except in the special case of impaired sodium chloride metabolism, e.g. in congestive heart failure (13). Healthy individuals can tolerate the intake of large quantities of chloride provided that there is a concomitant intake of fresh water. If Chloride is higher than the values below then there would be toxicity.**

## **◆MAGNESIUM**

### **DEFICIENCY MANIFESTATION**

#### **A. Hypomagnesemia**

Hypomagnesemia is an abnormally low serum magnesium level. It is usually associated with magnesium deficiency. Since magnesium is present in most common food stuffs, low dietary intakes of magnesium are associated with general nutritional insufficiency, accompanied by intestinal malabsorption, severe vomiting, diarrhea or other causes of intestinal loss.

#### **Symptoms of low magnesium**

The symptoms of hypomagnesemia are very similar to those of hypocalcemia, impaired neuromuscular function such as tetany, hyper-irritability, tremor, convulsions and muscle weakness.

**Early signs of low magnesium include:**

- nausea
- vomiting
- weakness

- decreased appetite

As magnesium deficiency worsens, symptoms may include:

- numbness
- tingling
- muscle cramps
- seizures
- muscle spasticity
- personality changes
- abnormal heart rhythms

**Common causes of low magnesium include:**

- Alcohol use
- Burns that affect a large area of the body
- Chronic diarrhea
- Excessive urination (polyuria), such as in uncontrolled diabetes and during recovery from acute kidney failure
- Hyperaldosteronism** (disorder in which the adrenal gland releases too much of the hormone aldosterone into the blood)
- Kidney tubule disorders
- Malabsorption syndromes, such as celiac disease and inflammatory bowel disease
- Malnutrition
- Medicines including amphotericin, cisplatin, cyclosporine, diuretics, proton pump inhibitors, and amino glycoside antibiotics
- Pancreatitis (swelling and inflammation of the pancreas)
- Excessive sweating

**Treatment of low magnesium**

Hypomagnesemia is typically treated with oral magnesium supplements and increased intake of dietary magnesium.

Examples of magnesium-rich foods include:

- spinach
- almonds
- cashews
- peanuts
- whole grain cereal
- soymilk
- black beans
- whole wheat bread
- avocado
- banana
- halibut
- salmon
- baked potato with the skin

**Treatment**

If your hypomagnesemia is severe and includes symptoms such as seizures, you may receive magnesium intravenously, or by IV.

## **B. Hypermagnesemia**

Hypermagnesemia is uncommon but is occasionally seen in renal failure. Depression of the neuromuscular system is the most common manifestation of hypermagnesemia.

Hypermagnesemia refers to an excess amount of magnesium in the bloodstream. It is rare and is usually caused by renal failure or poor kidney function.

### **Symptoms**

The symptoms of hypermagnesemia include:

- nausea
- vomiting
- neurological impairment
- abnormally low blood pressure (hypotension)
- flushing
- headache

### **Causes**

- lithium therapy
- hypothyroidism
- Addison's disease
- milk-alkali syndrome
- drugs containing magnesium, such as some laxatives and antacids
- familial hypocalciuric hypercalcemia

### **Treatment**

An intravenous (IV) calcium supply is then used to reduce symptoms such as impaired breathing, irregular heartbeat, and hypotension, as well as the neurological impact.

Intravenous calcium, diuretics, or water pills may also be used to help the body get rid of excess magnesium.

People with renal dysfunction or those who have had a severe magnesium overdose may require dialysis if they are experiencing kidney failure, or if magnesium levels are still rising after treatment.

**Acute clinical manifestations of Mg deficiency include** neuromuscular hyperexcitability, cardiac arrhythmias, and biochemical abnormalities of hypokalemia and hypocalcemia. Chronic Mg depletion may contribute to hypertension, atherosclerotic vascular disease, altered glucose homeostasis, and metabolic bone disease.

## **MAGNESIUM TOXICITY**

**Normal serum magnesium concentrations range between 0.75 and 0.95 millimoles (mmol)/L.**

**Toxicity value is seen when serum magnesium level is above 0.95mmol/L.**

## **◆CALCIUM**

### **DEFICIENCY MANIFESTATION**

#### **A. Hypocalcemia**

Hypocalcemia is characterized by lowered levels of plasma calcium.

The causes of hypocalcemia include:

- Hypoparathyroidism:** The commonest cause of hypoparathyroidism is neck surgery, or due to

magnesium deficiency.

•**Vitamin D deficiency:** This may be due to dietary deficiency, malabsorption or little exposure to sunlight. It may lead to bone disorders, osteomalacia in adults and rickets in children.

•**Renal disease:** The diseased kidneys fail to synthesize calcitriol due to impaired hydroxylation. Many people are at an increased risk for calcium deficiency as they age. This deficiency may be due to a variety of factors, including:

- poor calcium intake over a long period of time, especially in childhood
- medications that may decrease calcium absorption
- dietary intolerance to foods rich in calcium
- hormonal changes, especially in women
- certain genetic factors

It's important to ensure proper calcium intake at all ages.

Severe symptoms of hypocalcemia include:

- confusion or memory loss
- muscle spasms
- numbness and tingling in the hands, feet, and face
- depression
- hallucinations
- muscle cramps
- weak and brittle nails
- easy fracturing of the bones
- Neuromuscular irritability
- Cardiovascular signs such as an abnormal ECG.
- Cataracts

### **Treatment**

Calcium deficiency is usually easy to treat. It typically involves adding more calcium to your diet.

### **B. Hypercalcemia**

Hypercalcemia is characterized by increased plasma calcium level.

**The commonest causes of hypercalcemia are:**

- Hyperparathyroidism
- Malignant disease.

Clinical features of hypercalcemia

Neurological symptoms such as depression, confusion, inability to concentrate.

- Muscle weakness
- Gastrointestinal problems such as anorexia, abdominal pain, nausea and vomiting and constipation.
- Renal features such as polyuria and polydipsia.
- Cardiac arrhythmias.

### **CALCIUM TOXICITY**

**Calcium toxicity is rare, occurring in those with hyperparathyroidism or high calcium supplementation levels. Like vitamin D, toxicity can lead to calcification of soft tissues<sup>7</sup>. In addition, a very high intake of calcium can lead to kidney stone formation.**