كلية المستقبل الجامعة الاهلية
قسم الصيدلة

Lecture: 2 of Pharmaceutical Chemistry

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Electrolyte and Electrolyte Replacement Therapy

2. Potassium (K^+) (Normal value 3.5-5.2 mmol/L)

Potassium is a major ICF cation (only 2 % of potassium is in the plasma). It necessary for transmission and conduction of nerve impulses, maintenance of normal cardiac rhythm and necessary for smooth and skeletal muscle contraction.

Hypokalemia

Hypokalemia represents a decrease in plasma potassium concentration below 3.5 mmol/L.

Causes of hypokalemia

a. Primary hyperaldosteronism (Conn's syndrome) and secondary hyperaldosteronism (the increase in aldosterone secretion promote Na^+ reabsorption and K^+ is excreted in its place).
b. Increase potassium losses from GI tract (vomiting and diarrhea)
c. Inadequate potassium intake
d. Increase potassium losses from kidneys, skin and dialysis
e. Excess IV insulin (insulin promote rapid cellular potassium uptake)
f. Prolonged potassium losing diuretic therapy

Symptoms of hypokalemia

- Abdominal pain (low K^+ can cause nausea and diarrhea)
- Acute skeletal weakness resulting in paralysis
- Hypotension
- Irregular pulse

Treatment of hypokalemia

Potassium chloride: Most patients with hypokalemia and acidosis are also chloride depleted. Available as liquid, slow release tablet or capsule, and IV.

Potassium bicarbonate: It can be used in patients with hypokalemia and metabolic acidosis.

Hyperkalemia

Hyperkalemia represents an increase in plasma potassium concentration above 5.2 mmol/L.

Causes of hyperkalemia

a. Hypoaldosteronism (Addison's disease)
b. Increased dietary intake
c. Excessive IV administration of K^+
d. Renal failure (impaired excretion)
e. Acidosis (H^+ competes with K^+ to get into cells & to be excreted kidneys)
f. Diabetes mellitus (decreased insulin promotes cellular K loss)
g. Drugs such as ACEI and spironolactone

Symptoms of hyperkalemia

- Tiredness or weakness
- Nausea or vomiting
- Chest pain/dyspnea
- Palpitations and arrhythmias

3. Calcium (Ca^{++}) (Normal value 2.15-2.55 mmol/L)

Ninety-eight per cent of body calcium is found in the skeleton (major cation in teeth and bones), although the amount of calcium in ECF is only two per cent of the total calcium, this per cent is essential because of its functions in nerve impulse transmission, neuromuscular excitability and cardiac muscle contractions, as an enzyme co-factor in blood clotting and necessary for structure of bone and teeth. The regulation of calcium level depend on calcium intake and calcium loss.

Factors affecting calcium intake

1. The amount of calcium in diet.
2. The active metabolite of vitamin D, 1,25-dihydroxycholecalciferol (1,25-$(OH)_2$ D_3, also called calcitriol), is needed for calcium absorption.
3. Calcium in the intestine may form insoluble complexes (poorly absorbed) with oxalate and phosphate.
4. An excess of fatty acids in the intestinal lumen in steatorrhoea may contribute to calcium malabsorption.

Factors affecting calcium loss

1. Urinary calcium excretion depends on:
    a. The amount of calcium reaching the glomeruli
    b. The glomerular filtration rate
    c. Renal tubular function
2. Parathyroid hormone and 1,25-dihydroxycholecalciferol (vitamin D) increase urinary calcium reabsorption.

The plasma calcium is present in two main forms:

A. Calcium **bound** to proteins, mainly albumin: this accounts for a little less than half the total calcium concentration and is the physiologically inactive form.

B. Free **ionized** calcium, which comprises most of the rest. This is the physiologically active fraction.

Control of plasma calcium

1. Parathyroid hormone (PTH) (increase Ca^{++} concentration)

Parathyroid hormone produced in the parathyroid gland. The biological actions of this hormone include:

a. Stimulation of osteoclastic bone resorption, so releasing both free ionized calcium and phosphate into the ECF, this action increases the plasma concentrations of both calcium and phosphate.

b. Decreased renal tubular reabsorption of phosphate, causing phosphaturia and increased reabsorption of calcium; this action tends to increase the plasma calcium concentration but to decrease the phosphate.

2. Calcitonin (decrease Ca^{++} concentration)

Calcitonin (produced in the C cells of the thyroid gland) decreases osteoclastic activity, slows calcium release from bone and has the opposite effect on plasma concentrations of PTH.

3. Vitamin D (increase Ca^{++} concentration)

The biological actions of vitamin D include:

1. Increases calcium absorption by intestinal mucosal cells.
2. In conjunction with PTH, it increases osteoclastic activity, releasing calcium from bone
3. Increase urinary calcium reabsorption.

Hypocalcemia

Hypocalcemia represents a decrease in plasma calcium concentration less than 2.15 mmol/L.

Causes of hypocalcemia

a. Vitamin D deficiencies
b. Hypoparathyroidism
c. Decrease in total body calcium from chronic renal failure
d. Loop diuretics

Symptoms of hypocalcemia

- Neurologic: tetany (from paresthesias to seizures and bronchospasm)
- Cardiac (prolonged QT, hypotension, heart failure, arrhythmia)

Treatment of hypocalcemia

Symptomatic or acute case: IV calcium gluconate

Asymptomatic case: Oral therapy, calcium carbonate or citrate

Vitamin D deficiency: Vitamin D

Hypercalcemia

Hypercalcemia represents an increase in plasma calcium concentration above 2.55 mmol/L.

Causes of hypercalcemia

a. Increased calcium intake
b. Increase intestinal absorption (vitamin D overdose)
c. Hyperparathyroidism
d. Bone malignancies
e. Decreased excretion (thiazide diuretics)

Symptoms of hypercalcemia

- Fatigue
- Muscle weakness
- Constipation
- ECG changes (short QT interval, AV Block and arrhythmias)

4. Magnesium (Mg^{++}) (Normal value 0.65-1.05 mmol/L)

Magnesium is an intracellular cation which distributed as follow ~55% in bone, ~44% in cells, ~1% in ECF (~2/3 ionized (physiologically important) while ~1/3 bound to protein, contributes to enzyme and metabolic processes, particularly protein synthesis. It plays an important role in the relaxation of smooth muscle and stabilizes cardiac muscle cells.

Hypomagnesemia

The causes of hypomagnesemia include decreased intake, decreased in absorption (malnutrition and malabsorption) and increased GIT loss (vomiting and diarrhea).

Hypermagnesemia

The causes of hypermagnesemia include renal failure and increased magnesium intake (Mg-containing antacids or laxatives).

5. Chloride (Cl^-) (Normal value 96-106 mmol/L)

Chloride is the main ECF anion. It help to maintain ECF osmolality and acid-base balance. It associated directly with Na^+ and inversely with HCO_3^-.

Hypochloremia

Hypochloremia represents a decrease in plasma chloride concentration. The causes include hypochloremic alkalosis, losses through skin, GI tract and kidneys.

Hyperchloremia

Hyperchloremia represents an increase in plasma chloride concentration. The causes include increased intake and drugs (ammonium chloride).

6. Phosphate ($PO4^{-3}$)

Important ICF anions, about 85% is stored in bone as calcium salts, 14% in cell membranes as phospholipids and 1% in extracellular fluid. Phosphate combined with lipids, proteins, carbohydrates, nucleic acids (DNA and RNA), and high energy phosphate transport compound and it important acid-base buffer in body fluids. Phosphate regulated in an inverse relationship with Ca^{2+} by PTH and calcitonin. Phosphate concentrations shift oppositely from calcium concentrations and symptoms are usually due to the related calcium excess or deficit.

7. Bicarbonate(HCO_3^-)

Bicarbonate is the principle buffer of body pH (extracellular). It plays an important role in acid-base balance by neutralizing the acids.