

Motto Vision; The Dream/Tomorrow



- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine





Renal Module 2nd Year MBBS (LGIS) Sodium & Chloride Metabolism - 1

Department of Biochemistry Rawalpindi Medinal University Rawalpindi

Presenter: Dr Nayab Ramzan Deptt of Biochemistry RMU Date: 12-02-25



Professor Umar Model of Integrated Lecture



Learning Objectives

At the end of the session, students will be able to



- 1. Describe the sources, functions & daily requirements of sodium.
- 2. Explain causes & effects of hyponatremia and hypernatremia
- 3. Discuss Sources functions requirements of chloride with deficiency and toxic effects on body
- 4. Practice the principles of bioethics & apply strategic use of A.I in the related clinical condition.
- 5. Read relevant research articles related to the Core Knowledge.

Dietary Recommendations & Sources

- Sodium is the chief cation of the Extracellular fluid.
- No RDA for sodium as we rarely eat too little in fact most of us eat substantially more than we need, (10 -15 grams)
- Maximum of 5 g is required per day in persons having no family Hx of hypertension
- If there is history of Hypertension then only 1gram NaCl/day
- <u>SOURCES:</u>
- Main dietary source is table salt. 40% sodium
- Good sources of sodium include bread, whole grains, leafy vegetables, nuts, eggs, milk meat & processed foods



Sodium Absorption & Metabolism

Consumption

- 5-15 gram of NaCl is consumed per day but most of it is lost in urine.
- If less Na⁺ is taken or plasma Na⁺ falls due to any reason the Na⁺ may totally disappear from urine.
- Mainly regulated by aldosterone.
- Na⁺ is readily absorbed in ileum and little is lost in feces.
- Kidneys conserve Na⁺ at the expense of K⁺ or H⁺.



Sodium Metabolism

Ingestion of Na+ stimulates:

- Thirst centres in the brain
- Secretion of ADH from the pituitary
- This leads to water retention & increase in BP.



Sodium Metabolism

Na+ K+ ATPase PUMP:

- Present in cell membranes, is responsible for maintaining physiological distribution of Na⁺ and K⁺ within & outside cells.
- Na⁺ ions are capable of entering the cell interior but are extruded actively by this mechanism.
- This pump depends upon availability of energy provided by ATP.
- An enzyme named Na⁺, K⁺ activated triphosphatase (Na+ K+ ATPase) hydrolyzes ATP & is an essential component of this pump.
- 3Na+ out ,2K+ in hence electrogenic pump.



Functions of Sodium in the Body

1. Maintenance of osmotic pressure of plasma and plasma volume:

- From 85-90% of all Na+ is extracellular & is responsible for maintaining the normal volume of the extracellular fluid.
- A low Na⁺ plasma level →decreased plasma volume-→ decreases the cardiac output → fall in blood pressure.
- Severe deficiency of Na may lead to circulatory collapse with renal failure

FUNCTIONS OF SODIUM IN THE BODY

- 2. <u>Regulation of nerve</u> <u>excitability.</u> Na⁺ & K⁺ antagonize action of Ca⁺⁺ and Mg⁺⁺ so play an important role in regulation of nerve excitability
- Sodium ions have role in depolarisation phase of action potential in neurons and muscles.
- An action potential is a predictable change in membrane potential that occurs due to the open and closing of voltage gated ion channels on the cell membrane.



Functions of Sodium in the Body

3. <u>CO2 Transport &</u> <u>blood pH regulation:</u>

Being closely associated with Cl^{-} and HCO_{3}^{-} it takes part in carriage of CO_{2} in blood and in regulation of blood pH



Functions of Sodium in the Body

4. <u>Regulation of acid</u> base balance:

It is the MAJOR CATION OF EXTRA CELLULAR FLUID and is largely associated with chloride and bicarbonate in the regulation of acid base balance.



Functions of Sodium in the Body

5. <u>Formation of HCl of</u> <u>gastric juice:</u>

Cl⁻ ions used for forming HCl are derived from NaCl so it helps in **formation of HCl of gastric juice**

6. Maintenance of viscosity of blood: Salts Na⁺ of Na with globulins are soluble and further Na & K both regulate in maintaining the degree of hydration of the plasma proteins



Functions of Sodium in the Body

• 7. Acid base balance:

Na+ H+ exchange in renal tubule to acidify urine

 8. Absorption of glucose: Na ions also help in absorption of glucose, from small intestine + reabsorbtion of glucose, lactate, water and amino acids from PCT (Secondary active transport).



Functions of Sodium in the Body

 9. Sodium ions also take part in working of Na+K+2Cl- co transporter in thick ascending loop of Henle.



Factors Affecting Urinary Excretion of Sodium:

- Normally, about 2/3rd of filtered Na+ is reabsorbed in PCT
- 30% reabsorption in thick ascending loop of Henle by Na+K+2Cl- co transporter.
- 5% reabsorption In DCT by Na+Cl- co transporter sensitive to Thiazides
- Na+ reabsorption occurs in cortical and medullary CDs.



Na⁺ HANDLING IN THE NEPHRON

Factors Affecting Urinary Excretion of Sodium:

- Normally 90-95% of filtered Na⁺ is reabsorbed in the kidneys.
- Factors affecting urinary excretion of Na⁺ are as follows:
- Glomerular filtration. In glomerulonephritis amount of Na⁺ filtered is small and all the Na⁺ filtered is reabsorbed.→ hypernatremia
- 2. Tubular reabsorption is decreased in chronic renal diseases→excess urinary Na+ loss—> hyponatremia



Core Knowledge Factors Affecting Urinary Excretion of Sodium:

3. Severe acidosis:

- It aggravates Na⁺ loss in urine as NH₃ production from the renal tubules is insufficient to buffer H⁺ ions in the tubular lumen.
- Thus there arises a deficiency of NH₄⁺ ions which could otherwise be excreted in the urine in exchange for Na⁺.
- Due to deficient NH₄⁺ formation Na⁺ is lost.



Factors Affecting Urinary Excretion of Sodium:

4. Diuresis:- Most Na⁺ is lost in diuretic conditions as in uncontrolled diabetes mellitus or after administration of mannitol or urea, which cause osmotic diuresis. **Thiazide diuretics inhibit** Na⁺ reabsorption & increase its urinary excretion. Acetazolamide increases urinary Na+ excretion



Factors Affecting Urinary Excretion of Sodium:

•5. Hormones:

- i. Adrenal cortical hormone. Aldosterone and deoxy corticosterone increase Na⁺ reabsorption and eliminate more K⁺ and H⁺ in urine. Aldosteronism is associated with more Na⁺ retention.
- Conditions such as Conn's syndrome →greater formation of Aldosterone— i.e hypernatremia, hypertension along with hypokalemia and metabolic alkalosis. CCF +liver cirrhosis → more aldosterone formation.
- ii. ACTH. It affects through its stimulant action on adrenal cortex → cortisol, a weak mineralocorticoid released, causing Na⁺ retention.
- iii. Sex hormones(weak mineralocorticoid). They slightly increase Na⁺ reabsorption.
- iv. Placental hormones: Certain hormones during pregnancy cause Na⁺ retention
- V. ANP:

ANP (Atrial Natriuretic Peptide)

- ANP is released from atrial muscle fibers in response to increased blood volume, elevated blood pressure and high salt intake.
- ANP acts on kidneys to increase sodium excretion and urine output.
- It has actions opposite to that of Renin & Aldosterone (Renin & Aldosterone increase salt retention & blood pressure).
- Increases urine loss of sodium by inhibition of aldosterone and the stimulus for its secretion is increase in volume of ECF/plasma



Horizontal Integration

Renin-Angiotensin System



Vertical Integration

Clinical Correlates

- Excessive Na⁺ intake may lead to or aggravate preexisting hypertension
- HYPERTENSION: (HTN or HT), [high blood pressure (HBP)] -A long-term medical condition in which the blood pressure in the arteries is persistently elevated.
- Long-term high blood pressure is a major risk factor for <u>stroke, coronary artery</u> <u>disease, heart failure, atrial</u> <u>fibrillation, peripheral arterial</u> <u>disease, vision loss, chronic kidney</u> <u>disease, and dementia.</u>
- Hypertension is a major cause of premature death worldwide.

High Blood Pressure

High blood pressure is a sign that the heart and blood vessels are being overworked

Untreated, the disease can lead to atherosclerosis and congestive heart failure.

Enlarged heart (heart failure)

Atherosclerosis

Clinical Correlates

Hyponatremia

✓[Na⁺ < 135 mEq/L; Normal = 135-145 mEq/L]</p>

Causes:

- Chronic renal insufficiency (damage to tubules lead to sodium wasting nephropathy).
- In Addison's disease, the Adrenal cortex doesn't make sufficient Aldosterone, this also has the same action.
- Diuretics
- Excessive ADH secretion --> H2O retention in the body --> low plasma sodium
- Psychogenic polydipsia (excess H2O intake)
- Severe vomiting, diarrhea, sweating

Clinical Correlates

Hyponatremia

Cerebral Edema

HypoNa+ \rightarrow slow shift of water into intracellular fluid specifically in BRAIN --> Cerebral Edema

Symptoms are malaise, headache, seizures, coma in severe cases

Treatment is that of primary cause and administer NaCl

Central Pontine Myelinolysis (CPM)

- Neurological disorder
- Most frequently occurs after too rapid medical correction of sodium deficiency (Hyponatremia).
- Rapid rise in sodium concentration is accompanied by movement of small molecules & pulls water from brain cells

Clinical Correlates

Hypernatremia

- [Na+ >145 mEq/L; Normal = 135-145 mEq/L]
- Majority of cases of hypernatremia result from an increased loss of water than Na+ ions.

Causes:

- Excessive, rapid IV adm'n of NSS (Normal saline soln)
- Conn syndrome, Cushing syndrome (Primary Aldosteronism)
- Administering high solute artificial milk to infants
- Post operatively due to excessive secretion of corticosteroids
- Head injury causing Diabetes Inspidus (leading to hypernatremia due to relatively more loss of water in urine)
- Heart failure, renal failure, hypoproteinemia. (Secondary Aldosteronism showing excessive retention of Na+ & water.
- Inadequate water intake
- Kidney disease
- Deficiency of antidiuretic hormones.

Hypernatremia

<u>Clinically</u> patients of Na+ excess show a raised venous pressure, peripheral edema (which indicates a high body sodium & becomes apparent when the volume of extracellular fluid has increased by >10%) and pulmonary edema with eventual resp failure.

<u>Cerebral Symptoms</u>: Altered mental status, weakness, neuromuscular irritability etc may be seen due to hyperosmolarity of plasma causing decreased brain cell volume.

Dietary Requirement & Sources of Chloride

 On an average 3,400 mgs are required per day mostly as part of sodium chloride

Sources:

- Common salt as cooking medium, whole grains, leafy vegetables, eggs and milk
- **Absorption/Reabsorption:**
- Chloride is absorbed through the Small and Large Intestine by the intestinal mucosa.
- 70 80% of Cl is reabsorbed in the Proximal Convoluted Tubule
- 20 25% is reabsorbed in the Loop of Henle.
- Surplus excreted in Urine

foods that contain chloride



Chloride Metabolism

- Component of table salt and other salts
- Helps in regulation of body's fluid/acid base balance, osmotic pressure.
- Readily moves in and out of the cells, it mainly remains in extra cellular fluid.
- Important in transmission of nerve impulses
- Cl- also a component of HCl produced (independent of Na+) by the stomach.



Chloride Shift / Hamburger phenomenon

- Chloride shift is v imp in transport of CO2 in blood (Hamburger's phenomenon)
- This process occurs in the cardiovascular system and refers to the exchange of bicarbonate (HCO₃⁻) and chloride (Cl⁻) across the membrane of red blood cells (RBCs).



Vertical Integration

Clinical Correlates

- Excess of chloride is excreted by the kidneys and some chloride is also lost in sweat.
- Severe dehydration is the only cause of high blood chloride levels.
- Cushing syndrome: Low Cl-, Low K+, metabolic alkalosis (Cushing's syndrome is characterized by excess cortisol secretion resulting from excess ACTH by the pituitary)
- Excessive chloride loss is the most common cause of chloride deficiency, vomiting being the most common cause→ compensatory increase in plasma HCO3-→Hypochloremic Alkalosis.
- Low blood chloride level slows blood flow to brain and oxygen delivery to the tissues, it also disrupts acid base balance and may cause Arrhythmias.
- Untreated low blood chloride level can be life threatening.



Vertical Integration

Clinical Correlates

- <u>Hypochloremia</u>: A reduction in the serum Cl– level may occur due to vomiting, diarrhea, respiratory alkalosis, Addison's disease and excessive sweating.
- <u>Hyperchloremia</u>: An increase in serum Cl– concentration may be due to dehydration, respiratory acidosis and Cushing's syndrome
- Isotonic saline soln (0.9% NaCl) has more Cl than plasma and is acidic (NaCl soln having pH 7 vs plasma having pH 7.4). Hence when isotonic saline is infused, it is advisable to add KCl and NaHCO3 to the infusion to counteract the anticipated Hypochloremic Metabolic Acidosis

Family Medicine

Management of Hypertension

Lifestyle modifications:

- •Weight loss
- •Regular physical activity
- •Balanced diet (e.g., DASH diet)
- •Limit alcohol and salt intake

Pharmacologic treatment:

- •First-line agents: thiazide diuretics, ACE inhibitors, calcium channel blockers, ARBs
- Tailor medication based on patient needs and comorbidities

Monitoring:

- •Regular blood pressure checks
- •Ensure medication adherence

Patient education:

- Promote lifestyle changes
- •Manage comorbid conditions (e.g., diabetes, hyperlipidemia)

Spiral Integration

Role of AI in Management of Hypertension

- Al can potentially aid in **enhancing diagnostic** accuracy and efficiency.
- AI-powered decision support systems can also help clinicians in selecting appropriate treatment modalities
- Al-driven predictive models may help anticipate the risk of complications of the Disease in susceptible populations

Spiral Integration

Ethical Considerations

- From an ethical standpoint, the scenario raises considerations regarding patient autonomy, informed consent, and confidentiality
- The physician must ensure that patient fully understands her diagnosis, treatment options, and potential implications
- Discuss the necessity of a healthy lifestyle & treatment plan. This requires clear communication and understanding of risks and benefits.
- Additionally, the physician must respect patient's privacy and confidentiality throughout the diagnostic and treatment process

Spiral Integration

Research Article

Suggested Research Article

• Link:

https://www.researchgate.net/publi cation/387949986_THE_ROLE_OF_H EALTH_EDUCATION_IN_THE_PREVE NTION_AND_MANAGEMENT_OF_HY PERTENSION_IN_THE_ELDERLY_A_LI TERATURE_REVIEW

• Journal Name: January 2025

ResearchGate

- Title: THE ROLE OF HEALTH EDUCATION IN THE PREVENTION AND MANAGEMENT OF HYPERTENSION IN THE ELDERLY: A LITERATURE REVIEW
- Author Names: Nenden Lesmana, Putri Raningg, Dadang Rochman

Abstract:

- Introduction: Hypertension is a significant health problem that, if not properly managed, can lead to more severe complications. Hypertension requires proper and accurate treatment. Systolic blood pressure over 140 mmHg and diastolic blood pressure over 90 mmHg is known as hypertension. Objective: To understand the role of health education in the prevention and management of hypertension in the elderly.
- Methods : The method used in this study is a literature review. Academic articles were searched through online databases such as PubMed and Google Scholar from 2019-2024, resulting in 10 relevant articles.
- Results : Based on the review and analysis of the 10 selected articles, it was concluded that education can increase respondents' knowledge regarding the prevention and management of hypertension.
- Conclusion : The role of nurses in assisting patients can improve health by providing information about the care and medical treatments they receive, and by offering nursing care to meet the needs of hypertensive patients and provide the necessary treatment.

Learning Resources

- Essentials of Medical Biochemistry by Mushtaq Ahmed. Ninth edition, Vol 2, chapter 13, pages 196-201 & page 207.
- BIOCHEMISTRY Lippincott Illustrated Reviews, Eighth Edition, Page 448
- Harper's Illustrated Biochemistry 32nd Edition
- Google Scholar
- Google Images

How To Access Digital Library

1. Steps to Access HEC Digital Library

2.Go to the website of HEC National Digital Library.

3.On Home Page, click on the INSTITUTES.

- 4. A page will appear showing the universities from Public and Private Sector and other Institutes which have access to HEC National Digital Library HNDL.
- 5. Select your desired Institute.
- 6. A page will appear showing the resources of the institution
- 7. 6. Journals and Researches will appear
- 8. 7. You can find a Journal by clicking on JOURNALS AND DATABASE and enter a keyword to search for your desired journal.