REVIEW ARTICLE KERALA MEDICAL JOURNAL

Fluid, Electrolytes and Acid-Base-Regulation

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ABSTRACT

Published on 30th June 2011

Problems with fluid, electrolyte, and Acid-Base Balance occur in the young, reflecting: low residual lung volume, high rate of fluid intake and output, high metabolic rate yielding more metabolic wastes, high rate of insensible water loss and Inefficiency of kidneys in infants. The very young and the very old are the most frequent victims of fluid, acid-base, and electrolyte imbalances.

The disorders of water balance, sodium metabolism, potassium metabolism and acid base balance are discussed in detail.

Keywords: Dehydration, Hypokalemia, Hyponatremia, Acid Base Balance

*See End Note for complete author details

Body Water Content: Developmental Aspects

Water content of the body is greatest at birth (70-80%) and declines until adulthood, when it is about 58%.At puberty, sexual differences in body water content arise as males develop greater muscle mass. Homeostatic mechanisms slow down with age. Elders may be unresponsive to thirst clues and are at risk of dehydration.

Problems with fluid, electrolyte, and Acid-Base Balance occur in the young, reflecting: low residual lung volume, high rate of fluid intake and output, high metabolic rate yielding more metabolic wastes, high rate of insensible water loss and Inefficiency of kidneys in infants. The very young and the very old are the most frequent victims of fluid, acid-base, and electrolyte imbalances.

As the age advances, total body water content gradually declines throughout life. Infants have low body fat, low bone mass, and are 73% or more water. Healthy males have about 60% water; in healthy females around 50% body weight is water. This difference reflects females' higher body fat and smaller amount of skeletal muscle. In old age, only about 45% of body weight is water.

Fluid Compartments:

Water occupies two main fluid compartments (Figure 1)

- Intracellular fluid (ICF) –
  - about two thirds of total body fluid volume contained in cells,
  - Make up to 40% of total body weight.
- Extra cellular fluid (ECF) – consists of two major subdivisions, (Figure 2)
  - Plasma – the fluid portion of the blood, covers around 25%,
  - Interstitial fluid (IF) – fluid in spaces between cells, covers the remaining75% of ECF,
  - Other ECF components are–lymph, cerebrospinal fluid, eye humors, synovial fluid, serous fluid, and gastrointestinal secretions.

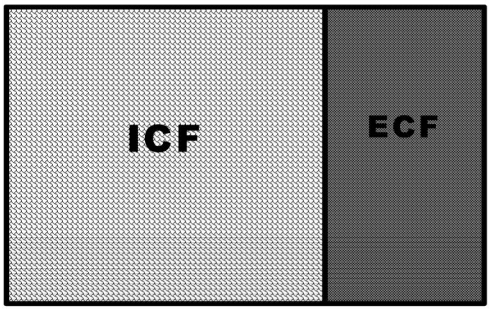

Figure 1. **Two main fluid compartments**

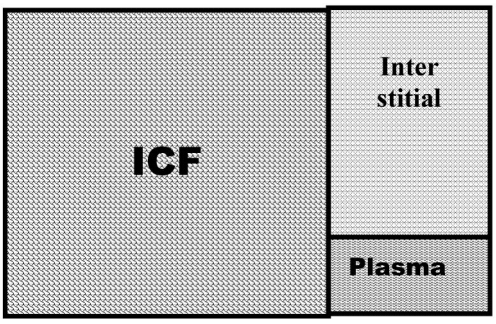

Figure 2. **Extra cellular fluid compartments**

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Fluid Compartments and composition:

Body Fluids consist of various components with fixed concentrations.

- Water is the universal solvent of body fluids
- Solutes are broadly classified into
  1. Electrolytes – consisting of inorganic salts, acids and bases,
  2. Non-electrolytes- which are mainly glucose, lipids, creatinine, and urea.

Electrolytes mainly contribute for the osmotic pressure than nonelectrolytes.

The osmotically active particles and the osmotic pressure exerted by them decide the movement of water according to osmotic gradients.

Electrolyte concentration is expressed in milliequivalents per liter (mEq/L).It is a measure of the number of electrical charges in one liter of solution. mEq/L = (concentration of ion in [mg/L]the atomic weight of ion) ´ number of electrical charges on one ion). Every solute dissolved in a solvent undergoes rapid ionization and hence doesn't exist as a compound any more in a solution. Both radicals thus, exert independent osmolality in a solution.

- For single charged ions, 1 mEq = 1 mOsm
- For bivalent ions, 1 mEq = 1/2 mOsm

Extra cellular and Intracellular Fluids composition:-

- Each fluid compartment of the body has a distinctive pattern of electrolytes.
- Extra cellular fluids are similar in contents. (Except for the high protein content of plasma). Sodium is the chief extra cellular cation and Chloride is the major extra cellular anion and conversely, intracellular fluids have low sodium and chloride. Potassium is the chief intracellular cation, with Magnesium next in concentration. Phosphate is the chief anion inside the cell.
- As mentioned, Sodium and Potassium are the major cations of the extra- and intracellular fluids respectively and their concentrations are mutually opposite and this is maintained by the constant activity of cellular, ATP-dependent sodium-potassium pumps. Electrolytes determine the chemical and physical reactions of fluids, related to internal environment and cellular metabolism .Proteins, phospholipids, cholesterol, and neutral fats account for: 90% of the mass of solutes in plasma and 60% of the mass of solutes in interstitial fluid and 97% of the mass of solutes in the intracellular compartment.

Fluid Movement Among Compartments

Compartmental exchange is regulated by osmotic and hydrostatic pressure of either compartments and net leakage of fluid from the blood is picked up by lymphatic vessels and returned to the bloodstream. Exchanges between interstitial and intracellular fluids are complex due to the selective permeability of the cellular membranes.

Two-way water flow is substantial .Ion fluxes into the cells are restricted, and move selectively by active transport. Nutrients, respiratory gases, and wastes move unidirectional. Plasma is the only fluid that circulates throughout the body and links external and internal environments. Osmolalities of all body fluids are equal; changes in solute concentrations are quickly followed by osmotic changes and are rectified by the immediate resetting.

Regulation of Water Intake and output

To remain properly hydrated, water intake must equal water output.

- Water input is mainly ingested fluid (60%) and solid food (30%). Metabolic water or water of oxidation (10%).
- Water output is mainly through, Urine (60%) and feces (4%) Insensible losses (28%) sweat (8%). Increases in plasma osmolality trigger thirst and release of antidiuretic hormone (ADH).

Water Intake and Output Regulation

The hypothalamic thirst center is stimulated by a decline in plasma volume of 10%–15%, by increases in plasma osmolality of 1–2%, mediated through baro-receptor input, angiotensin II, and other receptors sensing the reduced plasma volume

Thirst is quenched as soon as we begin to drink water. Feedback signals that inhibit the thirst centers include; moistening of the mucosa of the mouth and throat and activation of stomach and intestinal stretch receptors.

Obligatory water losses include: Insensible water losses from lungs and skin and the water that accompanies undigested food residues in feces. Obligatory water loss reflects the fact that: Kidneys excrete 900-1200 mOsm of solutes to maintain blood homeostasis and urine solutes must be flushed out of the body in water

Regulation of ADH

Water reabsorption in collecting ducts is proportional to ADH release and low ADH level produce dilute urine and reduces volume of body fluids and high ADH level produce concentrated urine. Hypothalamic osmoreceptors trigger or inhibit ADH release.

Factors that specifically trigger ADH release include prolonged fever; excessive sweating, vomiting, or diarrhea; severe blood loss; and traumatic burns.

Disorders of Water Balance:

Dehydration is a situation, in which water loss exceeds water intake and the body is in negative fluid balance .Its causes include: hemorrhage, severe burns, prolonged vomiting or diarrhea, profuse sweating, water deprivation, and diuretic abuse. Dehydration is characterized by: dry mouth, thirst, dry flushed skin, and oliguria.

And prolonged dehydration may lead to weight loss, fever, and mental confusion which can proceed into further consequences including hypovolemic shock and loss of electrolytes.

Hypotonic Hydration

Renal insufficiency or an extraordinary amount of water ingested quickly can lead to cellular over hydration, or water intoxication. When ECF is diluted – sodium content is normal but excess water is present and the resulting hyponatremia promotes net osmosis into tissue cells, causing cellular swelling. These events must be quickly reversed to prevent severe metabolic disturbances, particularly in neurons.

Edema

- Atypical accumulation of fluid in the interstitial space, leading to tissue swelling is caused by anything that increases flow of fluids out of the bloodstream or hinders their return. Factors that accelerate fluid outflow include: Increased blood pressure, capillary permeability, incompetent venous valves, localized blood vessel blockage, congestive heart failure, hypertension and high blood volume.
- Hindered fluid return usually reflects an imbalance in colloid osmotic pressure like hypoproteinemia – which may be the result of protein malnutrition, liver disease, or glomerulonephritis, in which the reduced osmotic pressure, forces fluids out of capillary beds at the arterial ends which fail to return at the venous ends.
- Edema may also be the result of blocked (or surgically removed) lymph vessels, enhancing the leaked proteins to accumulate in interstitial fluid and exert increasing colloid osmotic pressure, which draws fluid from the blood resulting in interstitial fluid accumulation, effective blood pressure fall and impaired circulation.

Electrolyte Balance

- Electrolytes are salts, acids, and bases, but electrolyte balance usually refers only to salt balance. Salts are important for: Neuromuscular excitability, secretory activity, membrane permeability and controlling fluid movements. Salts enter the body by ingestion and are lost via perspiration, feces, and urine.

Sodium in Fluid and Electrolyte Balance

- Sodium holds a central position in fluid and electrolyte balance. Sodium salts account for 90-95% of all solutes in the ECF, and contribute 280 mOsm of the total 300 mOsm ECF solute concentration, Sodium is the single most abundant cation in the ECF.
- The role of sodium in controlling ECF volume and water distribution in the body is a result of sodium being the only cation to exert significant osmotic pressure, Sodium ions leaking into cells are being pumped out against their electrochemical gradient and sodium concentration in the ECF normally remains stable.
- Changes in plasma sodium levels affect plasma volume, blood pressure, ICF and interstitial fluid volumes. Renal acid-base control mechanisms are coupled to sodium ion transport.

Regulation of Sodium Balance:
Role of Aldosterone:

- Sodium reabsorption 65% of sodium in filtrate is reabsorbed in the proximal tubules, 25% is reclaimed in the loops of Henle. When Aldosterone levels are high, all remaining Na^+ is actively reabsorbed. Water follows sodium if tubule permeability has been increased with ADH.
- The renin-angiotensin mechanism triggers the release of Aldosterone; this is mediated by the juxtaglomerular apparatus, which releases renin in response to sympathetic nervous system stimulation, decreased filtrate osmolality and decreased stretch (due to decreased blood pressure). Renin catalyzes the production of angiotensin II, which triggers Aldosterone release.

- Adrenal cortical cells are directly stimulated to release Aldosterone by elevated K^+ levels in the ECF. Aldosterone brings about its effects (diminished urine output and increased blood volume) slowly.

Cardiovascular System Baroreceptors:-

- Baroreceptors alert the brain of increases in blood volume (hence increased blood pressure) then sympathetic nervous system impulses to the kidneys decline, afferent arterioles dilate, glomerular filtration rate rises, and sodium and water output increases.
- This phenomenon, called pressure diuresis, decreases blood pressure. Drops in systemic blood pressure lead to opposite actions and systemic blood pressure increases. Since sodium ion concentration determines fluid volume, Baroreceptors can be viewed as "sodium receptors".

Maintenance of Blood Pressure Homeostasis:-

Atrial Natriuretic Peptide (ANP) reduces blood pressure and blood volume by inhibiting the events that promote vasoconstriction, Na^+ and water retention. It is released in the heart atria as a response to stretch (elevated blood pressure). ANP has potent diuretic and natriuretic effects and it promotes excretion of sodium and water and inhibits angiotensin II production.

Influence of Other Hormones on Sodium Balance:

- Estrogens are known to enhance Na Cl reabsorption by renal tubules and cause water retention during menstrual cycles and edema during pregnancy. Conversely, progesterone decreases sodium reabsorption and acts as a diuretic, promoting sodium and water loss whereas glucocorticoids enhance reabsorption of sodium and promote edema.

Regulation of Potassium Balance

- Relative ICF-ECF potassium ion concentration:- Relative ICF-ECF potassium ion concentration affects a cell's resting membrane potential. Excessive ECF potassium decreases membrane potential, too little K^+ causes hyperpolarization and non-responsiveness. Hyperkalemia and hypokalemia can disrupt electrical conduction in the heart, leading to sudden death. Hydrogen ions shift in and out of cells, leading to corresponding shifts in potassium in the opposite direction. This interferes with activity of excitable cells.

Regulatory Site of Potassium is Cortical Collecting Ducts:

- Less than 15% of filtered K^+ is lost to urine regardless of need. K^+ balance is controlled in the cortical collecting ducts by changing the amount of potassium secreted into filtrate. Excessive K^+ is excreted over basal levels by cortical collecting ducts. When K^+ levels are low, the amount of secretion and excretion is kept to a minimum. Type A intercalated cells can reabsorb some K^+ left in the filtrate.

Influence of Plasma Potassium Concentration:

- High K^+ content of ECF favors principal cells to secrete K^+. Low K^+ or accelerated K^+ loss depresses its secretion by the collecting ducts.

Influence of Aldosterone:

- Aldosterone stimulates potassium ion secretion by principal cells. In cortical collecting ducts, for each Na+ reabsorbed, a K^+ is secreted. Increased K^+ in the ECF around the adrenal cortex causes, release of aldosterone and Potassium secretion. Potassium controls its own ECF concentration via feedback regulation of aldosterone release.

Regulation of Calcium

Ionic calcium in ECF is important for blood clotting, cell membrane permeability, and secretory behavior. Hypocalcaemia increases neuronal excitability and, causes muscle tetany, whereas hypercalcemia inhibits neurons and muscle cells and may cause cardiac arrhythmias.

Calcium balance is controlled by parathyroid hormone (PTH) and calcitonin.

Influence of PTH:

- PTH promotes increase in calcium levels by targeting bones – PTH activates osteoclasts to break down bone matrix and enhances intestinal absorption of calcium from small intestine.
- PTH enhances calcium reabsorption and decreases phosphate reabsorption in the kidneys. Calcium reabsorption and phosphate excretion go hand in hand. Filtered phosphate is actively reabsorbed in the proximal tubules. In the absence of PTH, phosphate reabsorption is regulated by its transport maximum and excesses are excreted in urine, high or normal ECF calcium levels inhibit PTH secretion

and release of calcium from bone is inhibited and hence, larger amounts of calcium are lost in feces and urine and more phosphate is retained.

Influence of Calcitonin:

Calcitonin is released in response to rising blood calcium levels. Calcitonin is a PTH antagonist, but its contribution to calcium and phosphate homeostasis is minor to negligible.

Regulation of Anions

- Chloride is the major anion accompanying sodium as a rule in the ECF and 99% of chloride is reabsorbed under normal pH conditions. When acidosis occurs, fewer chloride ions are reabsorbed. Other anions have transportmaximums and excesses are excreted in urine.

Acid-Base Balance

Normal pH of body fluids:

- Arterial blood pH is 7.4 ,
- Venous blood and interstitial fluid pH is 7.35 ,
- Intracellular fluid pH is 7.0
- Alkalosis or alkalemia is a condition where–arterial blood pH rises above 7.45
- Acidosis or acidemia is a condition where arterial pH drops below 7.35 (physiologicalacidosis).

Sources of Hydrogen Ions:

Most hydrogen ions originate from cellular metabolism, breakdown of phosphorus-containing proteins releases phosphoric acid into the ECF, anaerobic respiration of glucose produces lactic acid, and fat metabolism yields organic acids and ketone bodies and transporting carbon dioxide as bicarbonate releases hydrogen ions.

Hydrogen Ion Regulation:

Concentration of hydrogen ions is regulated sequentially by:

- Chemical buffer systems which act within seconds,
- The respiratory center in the brain stem – acts within 1-3 minutes,
- Renal mechanisms – require hours to days to effect pH changes

Chemical Buffer Systems:

Strong acids – all their H^+ is dissociated completely in water , weak acids – dissociate partially in water and are efficient at preventing pH changes, strong bases – dissociate easily in water and quickly tie up H^+, weak bases – accept H^+ more slowly (e.g.,HCO_3^- and NH_3)

Chemical Buffer Systems have one or two molecules that act to resist pH changes when strong acid or base is added. Any drifts in pH are resisted by the entire chemical buffering system.

Three major chemical buffer systems are:

- Bicarbonate buffer system
- Phosphate buffer system
- Protein buffer system

Bicarbonate Buffer System:

- A mixture of carbonic acid (H_2CO_2) and its salt, sodium bicarbonate ($NaHCO_3$) (potassium or magnesium bicarbonates work as well). This system is the only important ECF buffer.
- If strong acid is added: hydrogen ions released combine with the bicarbonate ions and form carbonic acid (a weak acid) and stabilizes the pH of the solution.
- If strong base is added: it reacts with the carbonic acid to form sodium bicarbonate (a weak base), the pH of the solution rises only slightly.

Phosphate Buffer System:

Nearly identical to the bicarbonate system. Its components are: Sodium salts of dihydrogen phosphate ($H_2PO_4^-$), a weak acid, Monohydrogen phosphate ($H_2PO_4^-$), a weak base. This system is an effective buffer in urine and intracellular fluid; rather it is the most potent stabilizer in the ICF.

Protein Buffer System:

Plasma and intracellular proteins are the body's most plentiful and powerful buffers. Some amino acids of proteins have free organic acid groups (weak acids), and groups that act as weak bases (e.g., amino groups), and these are the amphoteric molecules.

Physiological Buffer Systems

The respiratory system regulation of acid-base balance is a physiological buffering system. There is a reversible equilibrium between dissolved carbon dioxide and water. Carbonic acid and the hydrogenand bicarbonate ions.

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

During carbon dioxide unloading, hydrogen ions are incorporated into water. When hypercapnia or rising

plasma H^+ occurs, deeper and more rapid breathing expels more carbon dioxide, hydrogen ion concentration is reduced, alkalosis occurs and this causes slower, more shallow breathing, causing H^+ to increase.

Hence, a functional impairment of the respiratory system brings forth an acid-base imbalance (respiratory acidosis or respiratory alkalosis).

Renal Mechanisms of Acid-Base Balance

Chemical buffers can tie up excess acids or bases, but they cannot eliminate them from the body. The lungs can eliminate carbonic acid by eliminating carbon dioxide. Only the kidneys can rid the body of metabolic acids (phosphoric, uric, and lactic acids and to some extent, ketones) and prevent metabolic acidosis. The ultimate acid-base regulatory organs are the kidneys.

The most important renal mechanisms for regulating acid-base balance are:

- Conserving (reabsorbing) or generating new bicarbonate ions;
- Excreting bicarbonate ions.

Losing a bicarbonate ion is the same as gaining a hydrogen ion;

Reabsorbing a bicarbonate ion is the same as losing a hydrogen ion.

Hydrogen ion secretion occurs in the PCT and in type A intercalated cells, hydrogen ions come from the dissociation of carbonic acid into bicarbonate and H^+ ions.

Reabsorption of Bicarbonate

Carbon dioxide combines with water in tubule cells, forming carbonic acid, Carbonic acid splits into hydrogen ions and bicarbonate ions. For each hydrogen ion secreted, a sodium ion and a bicarbonate ion are reabsorbed by the PCT cells. Secreted hydrogen ions form carbonic acid; thus, bicarbonate disappears from filtrate at the same rate that it enters the peritubular capillary blood.

Carbonic acid formed in filtrate dissociates to release carbon dioxide and water Carbon dioxide then diffuses into tubule cells, where it acts to trigger further hydrogen ion secretion.

Generating New Bicarbonate Ions

Two mechanisms operate here for reversal to ionic equilibrium. Type A intercalated cells generate new bicarbonate ions and renal excretion of acid is carried out via secretion and excretion of hydrogen ions or ammonium ions (NH_4^+).

Hydrogen Ion Excretion

Dietary hydrogen ions must be counteracted by generating new bicarbonate. The excreted hydrogen ions must bind to buffers in the urine (phosphate buffer system). Intercalated cells actively secrete hydrogen ions into urine, which is buffered and excreted. Bicarbonate generated is moved into the interstitial space via a co-transport system, and passively moved into the peritubular capillary blood.

In response to acidosis, kidneys generate bicarbonate ions and add them to the blood and an equal amount of hydrogen ions are excreted in the urine.

Ammonium Ion Excretion

This method uses ammonium ions produced by the metabolism of glutamine in PCT cells and the glutamine when metabolized produces two bicarbonate ions, which moves to the blood and two ammonium ions which are excreted in urine.

Bicarbonate Ion Secretion

When the body is in alkalosis, type B intercalated cells secrete bicarbonate ions, reclaim hydrogen ions and acidify the blood. This mechanism is the opposite of type A intercalated cells and the bicarbonate ion reabsorption process. Even during alkalosis, the nephrons and collecting ducts excrete fewer bicarbonate ions than they conserve.

Acid-Base-Imbalance
Respiratory Acidosis and Alkalosis

This results from failure of the respiratory system to balance pH .P_{CO2} is the single most important indicator of respiratory inadequacy. Thenormal P_{CO2} fluctuates between 35 and 45 mm Hg, and values above 45 mm Hg signal respiratory acidosis and values below 35 mm Hg indicate respiratory alkalosis.

Respiratory acidosis is the most common cause of acid-base imbalance among all the discrepancies. This occurs during shallow breathing, or gas exchange is hampered by diseases such as pneumonia, cystic fibrosis, or emphysema .In contrast, respiratory alkalosis is a common result of hyperventilation.

Metabolic Acidosis

Broadly speaking, all pH imbalances except those

caused by abnormal blood carbon dioxide levels leads to, metabolic acid-base imbalance – bicarbonate ion levels above or below normal (22-26 mEq/L) The typical causes are ingestion of too much alcohol and excessive loss of bicarbonate ions. Other causes include accumulation of lactic acid, shock, ketosis in diabetic crisis, starvation, and kidney failure.

Metabolic Alkalosis

The rising blood pH and bicarbonate levels indicate metabolic alkalosis and the typical causes are; vomiting of the acid contents of the stomach, intake of excess base (e.g., from antacids), constipation, in which excessive bicarbonate is reabsorbed.

Respiratory and Renal Compensations

Acid-base imbalance due to inadequacy of a physiological buffer system is compensated for by the other systems. The respiratory system will attempt to correct metabolic acid-base imbalances and the kidneys will work to correct imbalances caused by respiratory disease.

Respiratory Compensation

The mechanism of respiratory compensation in metabolic acidosis is by elevation of the rate and depth of respiration and there by a gradual elimination of excess CO_2, whereupon the serum bicarbonate level returns to normal. In respiratory acidosis, the respiratory rate is often depressed and is the immediate cause of the acidosis.

In metabolic alkalosis, compensation exhibits slow, shallow breathing, allowing carbon dioxide to accumulate in the blood, and correction is necessitated in high pH (over 7.45) and elevated bicarbonate ion levels and rising P_{CO2}

Renal Compensation

To correct Respiratory acid-base imbalance, renal mechanisms are stepped up. Acidosis exhibits high P_{CO2} and high bicarbonate levels and the high P_{CO2} is the cause of acidosis and the high bicarbonate levels indicate the kidneys are retaining bicarbonate to offset the acidosis. Renal Compensation in respiratory alkalosis: Alkalosis has Low P_{CO2} and high pH .The kidneys eliminate bicarbonate from the body by failing to reclaim itor by actively secreting it.

END NOTE

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Conflict of Interest: None declared

Cite this article as: Jose John Kokad. Fluid, Electrolytes and Acid-Base-Regulation. Kerala Medical Journal. 2011 Jun 30;4(2):54-60

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