Acid-base Balance and its Disorders

PHARMACEUTICAL CHEMISTRY 1
UNIT II (SECTION -A)

FOR OPTIMAL FUNCTIONING OF CELLS..

- Acids and bases in the body must be in balance.
- We all consume every day food and drinks which contain acids, metabolism produces also acids...

BODY PH BALANCE

- Chemical blood buffers:
- Lungs,
- Cells,
- Kidneys

- Defences against changes in hydrogen concentration (getting acidotic..)

YOU GET ACIDOTIC EVERY DAY…….

- While living, eating and drinking…there is-
  Production of 1 mmol of fixed acid/kg body weight per day (60 kg=60 mmol/day)

BUFFERS

- Extracellular….
- Hemoglobin

  ('Chloride shift'-for each chloride leaving the cell-one bicarbonate ion enters)
- Plasma protein

  (with the liver, varying the amount of H-ions in the protein structure)
- Bicarbonate system:

  Normal acid to base ratio is 20:1

  20 parts bicarbonate to 1 part carbonic acid (H_2CO_3=CO_2),

  Neutralizing a strong acid bicarb. will be lost

Human Acid-base Homeostasis

- Tight regulation:
- CO_2 tension

  by respiratory excretion (of volatile acids)
- Plasma bicarbonate [HCO_3^-]

  By renal HCO_3^- reabsorption and

  Elimination of protons produced by metabolism
- pH is determined by CO_2 tension and [HCO_3^-]
- Human Acid-base Homeostasis

PHYSIOLOGY OF BUFFERING

- Ability of a solution containing a weak or poorly dissociated acid and its anion (a base) to resist change in pH when strong acid or alkali is added

- 1 ml of 0.1 M HCl to 9 ml distilled water =
- $[H^+]$ from 10^{-7} M to 10^{-2} M= **pH from 7 to 2**
- 1 ml of 0.1 M HCl to 9 ml of **phosphate buffer**: dissoc. H^+ combines with $[HPO_4^{2-}]$ = $(H_2PO_4^-)$
- **pH** fall **of only 0.1**= to **6.9**

BICARBONATE BUFFER

- Extracellular most important buffer
- Proteins and phosphate buffer less important
- Intracellular phosphate- most important b.
- Equilibrium conditions because abundant carbonic anhydrase in blood
- $H^+ + HCO_3^- \Leftrightarrow H_2CO_3 \Leftrightarrow H_2O + CO_2$
- $[H^+] = Keq \times [H_2CO_3]/[HCO_3^-]$

ACIDOSIS

- Clinical effects of severe acidosis: pH <7.2
- Cardiovascular system effects:
- Decreased myocardial contractility
- Decreased cardiac output
- Cardiac failure
- Hypotension
- Decreased hepatic and renal blood flow
- Centralization of effective blood volume
- Tissue hypoxia
- Pulmonary edema

METABOLIC ACIDOSIS

- Hallmark is ⇓$[HCO_3^-]$
- Acid production ↑ net acid intake ↑
  above net renal excretion
- (ketoacidosis, lactic acidosis, ammonium chloride loading)
- failure of renal net excretion
  (chronic renal failure, renal tubular acidosis)
- Bicarbonate loss via the gastroinestinal tract (diarrhea, gastrointestinal fistula)
- Nonbicarbonate solutions added to ECF (dilutional acidosis)

RESPIRATORY ACIDOSIS

- Acute increase in pCO_2
- Buffered primarily by intracellular buffers
- Chronic state:
- Kidneys compensation:
- Increase net acid excretion,
- (48 hours for fully development)
- Underlying cause:
- Central nervous system disease,
- lung (COPD)and heart disease,
- sedatives and opiates depressing the respiratory center
- Hypercapnic encephalopathy can develop

METABOLIC ALKALOSIS

- Plasma bicarbonate **$[HCO_3^-]$ ⇑ = pH ⇑**
- **H^+** GI **loss** or shift into cells
- Excess **HCO_3^-**
  - Administration of ⇑ bicarbonate, or precursors: ⇑ lactate, acetate, citrate or
  - Failure to excrete: mineralocorticoid effect
- **Loss of fluid** with
  - Diuretic therapy
  - $[Cl^-]$, $[K^+]$ and $[H^+]$ loss from plasma-extracellular volume contraction

ALKALOSIS

Table 11.11 Major adverse consequences of severe alkalemia

Cardiovascular
- Arteriolar constriction
- Reduction in coronary blood flow
- Reduction in angina treshold
- Predisposition to refractory arrhythmias

Respiratory
- Hypoventilation with attendant hypercapnia and hypoxemia

Metabolic
- Stimulation of anaerobic glycolysis and lactic acid production
- Hypokalemia, hypomagnesia, and hypophosphatemia
- Decreased plasma ionized calcium concentration

Cerebral
- Reduction of cerebral blood flow
- Tetany, seizures, lethargy, delirium, and stupor

RESPIRATORY ALKALOSIS

pCO_2 ⇓, pH ⇑ due to:

Hypoxia (compensatory hyperventilation)

- Acute: pulmonary edema or emboli, pneumonia,
- Chronic: severe anemia, high altitude, hypotension

Respiratory center stimulation

- Pregnancy, Anxiety, Fever, heat stroke, sepsis, salisylate intox., cerebral disease, hepatic cirrhosis,

Increased mechanical ventilation

RESPIRATORY ALKALOSIS

- **Most common acid-base disorder**

  Physiologic in pregnancy and high altitude
- **Bad prognosis** in critically ill patients

  (the higher hypocapnia, the higher mortality)
- Hyperventilation,
- Perioral and extremity paresthesias,
- Light-headedness,
- Muscle cramps,
- **Hyperreflexia**, seizures, ⇓ **ionized Ca** ⇒ tetany

THANKING YOU