Acid-Base Disorders

728-655
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Learning Objectives

- Differentiate between respiratory and metabolic causes of acidosis and alkalosis
- Identify causes of metabolic acidosis and alkalosis
- Choose treatment strategies for acute and chronic metabolic or respiratory acidosis or alkalosis

Reading Assignment

Pharmacotherapy. A Pathophysiologic Approach,
11th edition. Chapter 69. Acid-Base Disorders. Pp 813-832

Paraldehyde—medication used as an anticonvulsant, sedative
Phenformin—biguanide withdrawn from the market in 1970s because it caused lactic acidosis

Study questions
Calculate patient's anion gap

How does acetazolamide work to prevent altitude sickness?

Which acid-base disorder does this person have?

55 year old male with history of type 2 diabetes and alcohol abuse admitted for acute diarrhea which started two days ago.
Na 142, K 3.2, Cl 110, HCO3 20, Glucose 200, BUN 25, Cr 1.1
pH 7.30; PaCO2 22

25 year old male seen in ED for confusion and non-specific abdominal pain
Na 128, K 5, Cl 92, HCO3 8, Glucose 200, BUN 45, Cr 2
pH 7.22; PaCO2 20

22 year old unresponsive female brought to ED by ambulance with respiratory rate 6 breaths per minute.
Na 135, K 4.5, Cl 110, HCO3 35, Glucose 68, BUN 25, Cr 1.2
pH 7.22; PaCO2 58

Overview

- Acid-base disturbances common, cause significant morbidity and mortality
- Organs involved in homeostasis
    - Lungs
    - Kidneys
- Primary therapy: ELIMINATE THE CAUSE

Acid-base chemistry

$HCl \rightarrow H^+ + \text{Chloride ion } (Cl^-)$
(acid)

$NH_3 + H^+ \rightarrow NH_4^+$
(ammonia) (base)

Acid donates a proton
Base accepts a proton

Acidity of body fluids measured in hydrogen ion concentration or pH

$$pH = pK + \log \frac{[base]}{[acid]}$$

Henderson-Hasselbalch equation

Buffer

Renal regulation

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

Respiratory regulation

- Carbonic acid-bicarbonate buffer system critical for homeostasis
- Carbonic acid equilibrium with carbon dioxide
    - pCO_2 regulated by lungs
    - Increasing ventilation volume and rate decreases pCO_2
- Carbonic acid equilibrium with bicarbonate
    - HCO_3 regulated by kidneys
    - HCO_3 freely filtered at the glomerulus
    - Carbonic anhydrase activity regulates carbonic acid and water + CO_2
    - Secretion and reabsorption in the renal tubule maintains homeostasis

Definitions

- Acidic alteration in blood pH <7.35
- Alkalemia alteration in blood pH >7.45

Acid-Base Disorder	**pH**	**Primary Disturbance**	**Compensation**
Acidosis			
Respiratory	Decrease	Increase $PaCO_2$	Increase HCO_3^-
Metabolic	Decrease	Decrease HCO_3^-	Decrease $PaCO_2$
Alkalosis			
Respiratory	Increase	Decrease $PaCO_2$	Decrease HCO_3^-
Metabolic	Increase	Increase HCO_3^-	Increase $PaCO_2$

Steps in Acid-Base Disorder Evaluation

1. Obtain ABGs and electrolytes simultaneously
2. Compare HCO_3^- on ABGs to electrolytes
3. Calculate SAG (serum anion gap)
   - SAG = Na^+ – Cl^- – $HCO3^-$
4. Is acidemia or alkalemia present?
5. Is the primary abnormality respiratory or metabolic?
6. Estimate the compensatory response
7. Compare change in Cl^- with change in Na^+

Evaluation of acid-base disorders

1. Look at the pH

- pH > 7.4 → alkalemia
- pH < 7.4 → acidemia

2. Identify the Primary Acid-Base Disorder

- pH & PaCO2 change in the same direction → metabolic
- pH & PaCO2 change in the opposite direction → respiratory

3. Identify the compensation

Serum anion gap

- SAG = Na^{+} – Cl^{-} – $HCO3^{-}$
  - Some equations may include K+
- Normal SAG = 9mEq/L
- AG >17-20 mEq/L indicative of unmeasured anions

Causes of metabolic acidosis

- M: Methanol
- U: Uremia
- D: DKA
- P: paraldehyde/phenformin (biguanide)
- I: Iron/ isoniazide
- L: Lactic acidosis
- E: Ethylene glycol
- S: Salicylates

More recently proposed GOLDMARK

Causes of Anion Gap Metabolic Acidosis

knowmedge

Mnemonic: "GOLDMARK"

G	Glycols (ethylene glycol and propylene glycol)
O	Oxoproline
L	L-Lactate
D	D-Lactate
M	Methanol
A	Aspirin
R	Renal Failure (Uremia)
K	Ketoacidosis

- Paraldehyde use is exceedingly rare
- Many drugs besides iron and isoniazid cause lactic acidosis
- Oxyproline from chronic acetaminophen use
- D-lactic acid-short bowel syndrome
- Propylene glycol is a solvent used in some parenteral medications

Mehta AN, Emmett JB, Emmett M. GOLD MARK: an anion gap mnemonic for the 21st century. *Lancet*. 2008;372(9642):892. doi:10.1016/S0140-6736(08)61398-7

Clinical presentation

- Asymptomatic if mild and acute
- Range of signs depending on cause, severity, duration

Chronic metabolic acidosis

- Severe acidemia is rare
- COMPENSATION
- Increase CO_2 excretion by increasing respiratory rate

Acid disorders--compensation

Acidosis	**Compensation**
Metabolic	$PaCO_2$ mmHg should decrease by 1.3 x the fall in plasma HCO_3 mEq/L
Acute respiratory	Plasma HCO_3 should increase by 0.1 x the increase in $PaCO_2 \pm 3$ mmHg
Chronic respiratory	Plasma HCO_3 should increase by 0.35 x the increase in $PaCO_2 \pm 4$ mmHg

Expected $PaCO_2$ in patient with metabolic acidosis
$PaCO_2 = (1.5 \times HCO_3 + 8) \pm 2$ mmHg

Example: Plasma HCO_3 16 mEq/L. Expect compensation of $PaCO_2$ about 30-34mmHg

Non-anion gap metabolic acidosis

- GI bicarbonate losses—diarrhea
- Renal tubular acidosis
    - Failure to reabsorb filtered bicarbonate

Treatment of mild to moderate

- Plasma bicarbonate 12-20mEq/L; pH 7.2-7.4
- Fix underlying problem
    - GI losses
    - Minimize effects of renal tubular acidosis (DC nephrotoxic meds, hydration)
- Replace deficit over several days
    - Loading dose = (Vd HCO_3 x body weight) x (goal HCO_3 – current HCO_3)

Vd HCO_3 = 0.5L/kg

Example:
LD = (0.5L/kg x 60 kg) x (24-15 mEq/L)
LD = 270 mEq
Replace over 3-5 days
Consider ongoing losses, estimate 2mEq/kg/day. Needs 120 mEq/day
Needs 70mEq (to replace deficit) + 120 mEq (to keep up with daily losses) so
Regimen: Alkali product 60 mEq three times daily for 3 days
See Table 69-8 for oral replacement products

Alkalosis

Acid-Base Disorder	pH	Primary Disturbance	Compensation
Acidosis			
Respiratory	Decrease	Increase $PaCO_2$	Increase HCO_3^-
Metabolic	Decrease	Decrease HCO_3^-	Decrease $PaCO_2$
Alkalosis			
Respiratory	Increase	Decrease $PaCO_2$	Decrease HCO_3^-
Metabolic	Increase	Increase HCO_3^-	Increase $PaCO_2$

Alkalosis	Compensation
Metabolic	PaCO2 increase by 0.4-0.6 x the rise in plasma HCO3
Acute respiratory	Plasma HCO3 decrease by 0.2 x the PaCO2 decrease but usually not to <18 mEq/L
Chronic respiratory	Plasma HCO3 decrease 0.35 x the PaCO2 decrease but usually not to < 14 mEq/L

Metabolic alkalosis

- Typically due to renal dysfunction as kidney usually able to excrete excess bicarbonate
- Identify precipitating factor

C: chloride deficit; gastric losses
R: renal perfusion reduced
A: aldosterone increased or high dose steroid treatment
P: potassium deficit

found in Prof Sorkness's presentation from 2019

Diuretics

- Loop and thiazide diuretics promote excretion of Na and K in association with Cl
- No appropriate increase in HCO3 excretion
- Along with the decreased intravascular volume, RAAS activated and hyperaldosteronism results

Other causes

- Alkali intake
  - Antacids in individuals with peptic ulcer disease
- High dose penicillins
  - Act as nonreabsorbable anions and enhance excretion of K and H

Treatment

- Metabolic alkalosis not well-tolerated
- Correct the precipitating factor
    - Vomiting—antiemetic
    - Use H2 antagonist or PPI to decrease NG tube losses
    - Discontinue the diuretic
    - Correct hypovolemia to restore renal perfusion
- Decrease corticosteroids or switch to one with lower mineralocorticoid activity
- Replace electrolytes (potassium) if needed

Treatment for severe

- Acidifying agents if pH > 7.6
    - Hydrochloric acid
    - Ammonium chloride
    - Arginine monohydrochloride

Respiratory alkalosis

- Decrease in $PaCO_2$ that leads to increase in pH
- Occurs in normal pregnancy and at high altitudes

- Ventilatory excretion exceeds metabolic production of CO_2

Presentation

- Often asymptomatic
- May cause light-headedness, syncope
- Nausea, vomiting
- Respiratory alkalosis can alter serum electrolytes
    - Decrease K
    - Slight increase Cl
    - Reduction in ionized Ca which might lead to muscle cramps

Treatment

- Most have few or no symptoms and pH<7.5
- Eliminate underlying cause—pain, anxiety, hypovolemia
- Oxygen if hypoxemia

- If severe, pH>7.6, mechanical ventilation with sedation, paralysis

Respiratory acidosis

- Lungs fail to excrete CO2 which lowers pH
- Acute respiratory acidosis caused by
    - Inhibition of respiratory center (drugs, head injury)
    - Low pulmonary perfusion (PE, cardiac arrest)
    - Neuromuscular abnormalities (spinal cord injury, neuromuscular disease)
    - Airway, pulmonary disorders (COPD, asthma, obstruction)
- Chronic respiratory acidosis caused by
    - Neuromuscular abnormalities (spinal cord injury, neuromuscular disease)
    - Pulmonary disorders (COPD, interstitial pulmonary disease)
    - Overfeeding –parenteral nutrition

Treatment

- Eliminate the cause
- Consider that hypoxemia might be the cause
    - Supplemental oxygen
- Mechanical ventilation
- Aggressive use of narcotic or benzodiazepine antagonists
- Bronchodilators if severe bronchospasm
- Rare bicarbonate administration
- Close monitoring—frequent ABGs

Treatment of severe

- Plasma bicarbonate 8 mEq or lower; pH <7.2
- Depends on underlying cause
- May require emergent hemodialysis
- Alkali therapy may be useful for some renal tubular acidosis, hyperchloremia secondary to diarrhea, specific intoxications (salicylates)
- Alkali therapy should not be used in
    - Hypernatremia
    - Hypervolemia
    - Acute kidney injury
    - Congestive heart failure
    - Pulmonary disease with decreased ventilation
    - Diabetic ketoacidosis

Sodium bicarbonate

- Use should be judicious
- Goal is to increase pH and plasma bicarbonate, not normalize

Question

Brian is climbing Pike's Peak as fast as he can as this is his last day of vacation. Which of the following is he likely to have?

a) Metabolic acidosis
b) Metabolic alkalosis
c) Respiratory acidosis
d) Respiratory alkalosis

Question

Jim has type 2 diabetes and stage 3 chronic kidney disease. He presents to the clinic complaining of diarrhea for past 2 days.

Labs: Na 134 mEq/L; K 3.6 mEq/L; Cl 110 mEq/L; HCO3 20 mEq/L; BUN 38 mg/dl; Scr 2.8 mg/dl

Blood gas: pH 7.3; $PaCO_2$ 30 mmHg

Calculate his anion gap