How to Approach Acid Base Disorders

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The pH in the body is maintained within a narrow range for the adequate metabolic functions and enzymatic processes. Timely and accurate diagnosis of acid base disorder can be life saving. For proper diagnosis and treatment of acid base disorders you need clinical data, laboratory data, correlation of clinical and laboratory data to see if the laboratory diagnosis fits in clinical scenario and then treatment of acid base disorder and the underlying disease.

Clinical data

History and physical examination of the patient provides important information and usually give an idea about the acid base disorder that might be present.

Acid base disorder	Clinical conditions
Metabolic acidosis with high anion gap (AGMA)	**G**lycols intoxication, acetoaminophen (**O**xooprolone) overdose, **L** lactic acidosis, **D** lactic acidosis, **M**ethanol, **A**cetosalicylic acid , **R**enal failure, Diabetic **K**etoacidosis, (GOLD MARK)
Metabolic acidosis normal anion gap (NAGMA)	Diarrhea, Ureteral diversion, Renal tubular acidosis, Hyperalimentation aldosterone inhibitors, carbonic anhydrase inhibitors, early renal failure
Metabolic alkalosis	Vomiting, nasogastric suction, diuretic use, posthypercapnia state, excess mineralocorticoid activity or primary hyperaldosteronism, licorice intake, exogenous steroids, Cushing's disease, Bartter's syndrome, current diuretic use, excessive alkali administration and refeeding
Respiratory acidosis	Acute central nervous system depression, drugs, cerebrovascular event, neuromuscular disease, myasthenia gravis, acute airway obstruction Severe pneumonia, LLung injury- flail chest Ventilator malfunction Chronic obstructive lung disease Chronic respiratory center depression-Pickwician Chronic neuromuscular disorders
Respiratory alkalosis	Acute Anxiety , Drug use-salicylate, catecholamines, progesterone Hypoxia Pregnancy Sepsis, Mechanical ventilation Hepatic encephalopathy CNS system disease

Symptoms and signs of metabolic disorders:

Mostly symptoms and signs are due to underlying disease. Nonspecific symptoms and signs may be associated with different acid base disorders.

CNS symptoms: headache, confusion, or decreased level of consciousness, anorexia, nausea and vomiting, warm, flushed skin; decreased cardiac output and increased respiratory depth and rate call Kussmaul breathing may be seen in metabolic acidosis.

Dizziness, paresthesias (around mouth and fingers and toes) positive Trousseau's sign , hyperactive deep tendon reflexes and depressed respirations is often present in metabolic alkalosis.

Acute respiratory acidosis may be associated with feeling of fullness in head, mental cloudiness, decreasing level of consciousness, dizziness, muscle twitching, seizures, warm, flushed skin and cardiac dysrhythmias. Weakness and dull headache may be seen in chronic respiratory acidosis.

Light-headedness and inability to concentrate, paresthesias around mouth and distal extremities. palpitations, shortness of breath, chest tightness, feeling of panic, sweating, dry mouth, trembling, loss of consciousness, seizures may occur in respiratory alkalosis.

Laboratory data

After good history and physical examination laboratory investigations and their correct interpretation is required. Main investigations for the diagnosis of acid base disorders are the arterial blood gases (ABG) and serum electrolytes. Ancillary laboratory data will be needed to find out the cause.

Interpretation of ABG

Arterial blood gas report includes pO_2, pCO_2, pH. These three parameters are measured. In addition two values bicarbonate level and base excess are calculated. Check for the consistency of the report using Kassirer Bliech equation. Convert pH into H^+. Multiply 40 by 1.25 for every 0.1 unit decrease in pH and multiply 40 by 0.8 for every 0.1 unit increase in pH. Then check if the values of H^+, bicarbonate and pCO_2 fit in the equation. $H^+ = 24 \times pCO_2 \div HCO_3$. If the calculation is correct then proceed further.

1. Look at three components of ABG, pH, pCO_2, HCO_3
    a. What is pH? Normal – euphemia
    b. High – alkalemia – can be due to respiratory or metabolic alkalosis
    c. Low – academia – can be due to metabolic or respirator acidosis
2. Look at pCO_2
    a. Raised - primary respiratory acidosis or compensatory to metabolic alkalosis.
    b. Low - primary respiratory alkalosis or compensatory to metabolic acidosis.
3. Look at HCO_3
    a. Raised – primary metabolic alkalosis or compensatory to respiratory acidosis.
    b. Low - primary metabolic acidosis or compensatory to respiratory alkalosis.
4. Determine primary process
    a. Look at pH. Primary process will be one which is in the same direction as pH. Example: pH 7.3, HCO_3 15 meq/l and pCO_2 31 mmHg. There is academia, metabolic acidosis and respiratory alkalosis. Primary process is metabolic acidosis since the pH is acidotic.
    b. Compensatory or secondary process is in opposite direction. Such as respiratory alkalosis in the above example
    c. If both components are in the same direction then both are primary and it is a mixed disorder
5. Determine if the acid base disorder is simple or mixed. Check the compensatory response if it is as predicted on the basis of physiological response.
    a. If it is within physiological range then it is simple disorder
        i. $FiO_2 \times$ (barometric pressure If metabolic acidosis, HCO_3 is decreased. Predicted pCO_2 = 40 - 1.25 x ΔHCO_3 or Winter's formula PCO_2 = observed HCO_3 x 1.5 + 8 +2
        ii. If metabolic alkalosis, predicted pCO2 = 40 + 0.6 x ΔHCO3
        iii. For acute respiratory acidosis predicted HCO_3 = 24 + (0.1 x ΔpCO_2)
        iv. For chronic respiratory acidosis predicted HCO_3 = 24+ (0.35 x ΔpCO_2)
        v. For acute respiratory alkalosis predicted HCO_3 = 24 - (0.2 x ΔpCO_2)
        vi. For chronic respiratory alkalosis predicted HCO_3 = 24 - (0.5 x ΔCO_2)

    b. If there is no compensatory response or the response is less than predicted or more than expected then it is a mixed disorder.
6. If primary process is respiratory then decide if it is acute or chronic. Look at predicted HCO_3 response. For chronic respiratory process acidosis or alkalosis full compensatory metabolic response takes 2 to 5 days. Patient has respiratory problem of one day duration, PCO_2 is 30 mmHg and HCO_3 is 22 mEq/l, it is acute respiratory alkalosis. If this patient has HCO_3 19 or below then additional metabolic acidosis is present. Similarly a patient with chronic obstructive pulmonary disease has pCO_2 60 mmHg and HCO_3 31 meq/l, it is chronic respiratory acidosis. If this patient has HCO_3 26 meq/l then additional metabolic acidosis could be present
7. If respiratory alkalosis then determine the cause whether it is intrinsic lung disease or external problem like chest wall pathology or central.

    Calculate A-aO_2 gradient as: – water-vapor pressure) – PaO_2 – ($PaCO_2 \div$ gas-exchange ratio).

    The fraction of inspired oxygen (FiO_2) is 0.21 in ambient air, the barometric pressure is 760 mm Hg at sea level, and the water- fat. At sea level and a body temperature of 37°C, the alveolar– arterial gradient is: vapor pressure is 47 mm Hg at 37°C. The gas-exchange ratio, which is approximately 0.8 at steady-state levels, varies according to the relative utilization of carbohydrate, protein, and

$[0.21 \times (760 - 47)] - (Paco_2 \div 0.8)$ - pO2 or 150 – 1.25 x $PaCO_2$.
Normal A-aO_2 gradient is 5 to 10 mm Hg in healthy young persons and 15 to 20 mm Hg in elderly. If change in PCO_2 is due to intrinsic lung disease or ventilation perfusion mismatch then this gradient is increased. In case of chest wall (neuromusculoskeletal) or central nervous system problem then this gradient is normal.

8. If metabolic acidosis is present then what is the type. Calculate anion gap as:
   $AG = Na^+ - (Cl^- + HCO_3^-)$
   Normal anion gap is 8-12 with average 10. Metabolic acidosis is divided into two types based on anion Gap
   a. High anion gap metabolic acidosis
      Usual causes include glycols ingestion, acitoaminophen ingestion, L lactic acidosis, D lactic acidosis, methanol, aspirin, renal failure, ketoacidosis (GOLD MARK)
      i. Calculate osmolal gap if high anion gap metabolic acidosis is present

Osmolal gap = measured serum osmolality – calculated serum osmolality. Where calculated osmolality is = 2 (serum Na^+) + Blood sugar in mg/dl + BUN in mg/dl /2.8 or Blood urea in :mg/dl/6

   b. If osmolol gap is high with anion gap metabolic acidosis suspect methanol or ethylene glycol poisoing
      1. If visual symptoms present– methanol poisoning
      2. Calcium oxalate crystals in urine present – ethylene glycol poisoning

      Blood level of methanol or ethylene glycol per dl can be estimated by multiplying the osmolal gap with the molecular weight and dividing by 10
      If osmolal gap is 20. Then the methanol concentration will be 20 x 32 (mol wt of methanol) ÷ 10 = 320 mg/dl. For ethylene glycol multiply osmolal gap by 62 and divide by 10.

- Check for urinary ketones, if present, possibility of ketoacidosis diabetic or starvation
- If normal anion gap metabolic acidosis, then causes may include diarrhea, renal tubular acidosis, hyperalimentation, ureterosigmoistomy, acetrazolamide intake, sodium chloride infusion

      ii. Calculate urinary anion gap by equation
      Urinary anion gap = (Urinary Na^+ + urinary K^+) – urinary Cl^-)
      Normal urinary anion gap is slightly positive.
      - In metabolic acidosis due to diarrhea urinary anion gap becomes highly negative as $NH4^+$ excretion along with Cl^- is increased
      - In case of distal renal tubular acidosis and type IV renal tubular acidosis when there is no ammonium excretion urinary anion gap remains positive
        a. Check serum potassium
           i. If low – Distal renal tubular acidosis
           ii. High – Type IV renal tubular acidosis.

      Note : If ammonium is being excreted with anions other than chloride like hippurate, benzoate in toluene toxicity or acetoacetate or □ hydroxylbutyrate in diabetic ketoacidosis urinary anion gap will remain positive even with increased ammonium excretion. To confirm presence of NH_4^+ calculate urine osmolal gap.

   c. Calculate urine osmolal gap
      i. Another indirect measure of H^+ excretion as NH_4^+ by kidneys is urinary osmolal gap is calculated as
         1. Urine osmolal gap = Measured urinary osmolality – calculated urine osmolality
         2. Calculated urinary osmolality =2 (Urinary Na^+ + Urinary K^+) + urinary urea in mg per deciliter/6+ urinary glucose in mg per deci literdl/18

ii. Normal urine osmolal gap is 60 to 100 (representing 2 x urinary NH_4^+). In metabolic acidosis it will be increased several folds due increase in NH_4^+ excretion.
Note : Urine osmolal gap will also increase if there is increased amount of unmeasured cations, or non dissociated acids in the urine.

9. Is there mixed acid base disorder when high anion gap metabolic acidosis is present
    a. Hyperchloremia with anion gap metabolic acidosis serum sodium: serum chloride < 1.27 will suggest – AGMA + NAGMA
    b. Hypochloremia serum sodium: serum chloride > 1.47 will suggest presence of additional hypochloremic metabolic alkalosis
    c. Delta delta gap
        i. Delta AG = Observed AG – 12
        ii. Delta bicarbonate = 24 -observed bicarbonate
    d. If delta delta gap or ratio >1, then additional NAGMA and if delta delta gap or ratio < 1 then there is additional metabolic alkalosis present

10. If metabolic alkalosis
    a. History? Recent alkali administration, □ lactams, cystic fibrosis, refeeding with carbohydrates, chronic alkali use. Check for alkali intake. If there is history of alkali ingestion – milk alkali syndrome
    b. If no alkali intake then check urinary chloride
        i. High – chloride resistant metabolic acidosis
        ii. Low – chloride sensitive metabolic alkalosis – vomiting, distant use of diuretics
    c. If urinary Cl is high the check for hypertension
        i. BP normal , think of Bartter Syndrome, Gittleman syndrome, active diuretic use, magnesium or potassium depletion
        ii. Hypertension present-Possibility of mineralcorticoid excess. Check plasma rennin activity
            1. Plasma rennin activity high. Consider renal artery stenosis, rennin secreting tumors, current diuretic use, malignant hypertension
            2. Plasma rennin activity low – check plama aldosterone level
                a. Plama aldosteron level low- Consider
                    i. Liddle's syndrome
                    ii. Cushing syndrome
                    iii. Exogenous steroids
                    iv. Licorice ingestion
                    v. 17 hydroxylase or 17 hydroxylase deficiency
                    vi. 11 □ hodroxy steroid dehydrogenase deficiency
                b. Plama aldosteron level high. Consider
                    i. Adrenal adenoma
                    ii. Bilateral adrenal hyperplasia,
                    iii. Adrenal carcinoma
                    iv. Glucocorticoid remediable hypertension

Further reading :

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