Few Questions from the Chapter – **Acid Base Balance** of the book
FirsTest Series – Biochemistry
Author – **Dr.M.Amali Bruno** Publisher **Kalam Books**.
Book Available Online at www.first-test-series.com and www.targetpg.com

Question 107
Which of the following is more appropriate for a 17 year old Female suffering from IDDM
pH: 7.05
PO2 : 108
PCO2 : 12
HCO3 : 5
Base Excess : -30
Choices
A) Metabolic Acidosis
B) Respiratory Acidosis
C) Metabolic Alkalosis
D) None of the above
Answer
A) Metabolic Acidosis
Reference:
Harrison
Discussion
Arterial Blood Gas (ABG), an investigation which plays an important role in therapeutic decision making requires proper interpretation. A proper understanding of various components that are analysed is vital. As a detailed discussion of acid base disturbances is out of scope of this article; few basic facts are discussed in the following paragraph.
Drawing blood for ABG:
- A plastic / glass syringe is used.
- 0.1ml of Heparin is used for 1ml of blood drawn, as an anticoagulant. (Heparin is withdrawn into the syringe and pushed back, thus allowing heparin to just coat the syringe)
- The safest place to draw blood for ABG **is radial artery** at the wrist. Femoral artery also can be used.
- The syringe should be sealed immediately with cap (or needle tip inserted to a cork) to avoid air bubbles.
- Blood drawn should be analysed within 10mts. Otherwise it should be cooled to **4°C** with ice slush when a delay of up to one hour is acceptable. (Usually the syringe is sent in a flask with ice).
- Routine practice of temperature correction for blood gas measurements is not required.

Analysis :
The parameters analysed are
- PO_2,
- PCO_2
- HCO_3^-

PO_2

Accepted **Arterial O_2 tension** at room are as below.

Criteria		mmHg
Adults & Children	Normal	97
	Acceptable	>80
New born		40-70

Old individuals (Age in yrs)	60	> 80
	70	> 70
	80	> 60
	90	> 50

The relationship between PaO_2 and SaO_2 are

	PaO_2	**O_2 Saturation**
Hypoxemia	< 80	<95
Mild	60-79	90-94
Moderate	40-59	75-89
Severe	< 40	<75

pH:
The first step in an ABG interpretation is to look whether there is acidemic or alkalemic

Normal	:	7:4 (7.35 to 7.45)
Acidemia	:	<7.35
Alkalemia	:	>7.45

- Acidemic, Alkalemic refer to the pH change only
- Acidosis, Alkalosis refer to the entire clinical & Biochemical picture.

HCO_3^-
The second step is to look into HCO3. The primary change in HCO3 is called as ***Metabolic'***

Normal	:	24 mmol/L. (22-26)
Metabolic acidosis	:	< 22 mEq/L
Metabolic alkalosis	:	> 26 mEq/L

PCO_2
The third step in an ABG interpretation is to look into the PCO2.The primary change is PCO2 is refered to as ***'Respiratory'***

Normal	:	40 mmHg (35-45)
Respiratory acidosis	:	> 45mm Hg
Respiratory alkalosis	:	< 35mm Hg

Wherever there is a change in PH, compensation occurs. Respiratory Compensation occurs for a metabolic acid-base disturbance and vice versa and in such cases ***PCO2 & HCO3 move in the same direction***

- If HCO3 decreases (Metabolic acidosis) then PCO2 also decreases (Respiratory compensation)
- If PCO2 increases (Respiratory acidosis), HCO3 also increases (Metabolic compensation)

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The normal expected rates of compensation are as follows: Please note that the unit of HCO_3^- is mEq/L (milliequivalent per litre) and the unit of $PaCO_2$ is mm Hg (millimeter of Mercury)

Primary Disorder	Defect	Effect on pH	Compensatory Response	Expected Response	Limit of Compensation
Metabolic Acidosis HCO_3^- Decreased	Gain in H^+ or loss of HCO_3^-	Decrease	Respiratory Alkalosis $PaCO_2$ Decreased	$\Delta PaCO_2 = \Delta HCO_3^-$ x 1.2 (1 to 1.5)	PCO_2 = 12mmHg
Metabolic Alkalosis HCO_3^- Increased	Gain in HCO_3^- or loss of H^+	Increase	Respiratory Acidosis $PaCO_2$ Increased	$\Delta PaCO_2 = \Delta HCO_3^-$ x 0.7 (0.25 to 1.0)	PCO_2 = 55mmHg
Respiratory Acidosis $PaCO_2$ Increased	CO_2 Retention	Decrease	Metabolic Alkalosis HCO_3^- Increased	Acute: $\Delta HCO_3^- = \Delta PaCO_2$ x 1.0 (0.7 to 1.3)	HCO_3^- = 32 mmol/L
				Chronic: $\Delta HCO_3^- = \Delta PaCO_2$ x 0.35 (0.1 to 0.8)	HCO_3^- = 45 mmol/L
Respiratory Alkalosis $PaCO_2$ Decreased	CO_2 Washout	Increase	Metabolic Acidosis HCO_3^- Decreased	Acute: $\Delta HCO_3^- = \Delta PaCO_2$ x 0.2 (0.1 to 0.3)	HCO_3^- = 12-20 mmol/L
				Chronic: $\Delta HCO_3^- = \Delta PaCO_2$ x 0.4 (0.3 to 0.5)	HCO_3^- = 12-15 mmol/L

If the compensation does not match, then a mixed acid base disorder is to be suspected.

Base Excess / Deficit is another parameter seen is any ABG report. The concept of base excess / deficit is found on the premise that the degree of deviation from the normal total buffer base availability can be calculated independent of compensatory CO2 changes. A negative base excess is refered to as deficit. An abnormal pH with a base excess within 5mmol./L denotes a relatively normal and balanced metabolic acid base status. An abnormal pH with a base excess outside 10mmol/L signifies significant metabolic acid base disturbance.

A few examples of acid base disturbances are interpreted below.

1. 17 yrs old F, IDDM

pH: 7.05 PCO2 : 12 PO2: 108

HCO3 : 5 BE: -30

Solution:

pH: 7.05 - Acidemic.

HCO3 : 5 Primary metabolic disturbance.

HCO3 deficit = 24 - 5 = 19

Expected PCO2 = 40-(19X1.2) = 40-22.8 = 17.2

Actual PCO2 >12

Interpretation:

Metabolic acidosis with respiratory alkalosis.

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2. Collapsed person, inttubated, given NaHco3

pH: 7.51, PCO2:35 PO2:62
HCO3:27 BE:+5

Solution:

pH: 7.51 - Alkalemia
HCO3: 27 - Primary metabolic problem.
HCO3 excess = 27-24 = 3
Excepted PCO2 = 40+(3X0.7) = 42.1
Actual PCO2 = 35
Interpretation: Metabolic alkalosis with respiratory acidosis

3. 24 yrs F Broken ankle.

pH: 7.55, PCO2: 27, PO2:105,
HCO3:23, BE:0,

Solution:

pH: 7.55 - Alkalemia.
PCO2: 27 Primary respiratory disturbance
PCO2 Deficit = 40-27 = 13
Expected HCO3 = 24-(13X0.2) = 21.4
Actual HCO3 = 23
Interpretation :
Respiratory alkalosis.

4. 45yrs Female.

pH:7.3, PCO2:46, PO2:55,
HCO3:24, BE: 0

Solution:

pH:7.3 Acidemia
PCO2 = 46 Primary respiratory problem
PCO2 Excess = 46-40 = 6
Expected HCO3 = 24+(6X0.1) = 24.6
Actual HCO3 = 24
Interpretation:
Acute Respiratory acidosis

5. 50 yrs Male

pH:7.43, PCO2:50, PO2:50,
HCO3:28, BE: +4

Solution:

pH:7.43 Normal range
PCO2:50 Excess:10
Expected HCO3 : 24+3.5 = 27.5

Actual HCO3 : 28
Interpretation :
Chronic respiratory acidosis.

6. 24 yrs Female, Unknown pill ingestion.
pH:7.1, PCO2: 55, PO2:42,
HCO3: 17, BE:-11
Solution:
pH:7.1 - Acidemia
HCO3:17 Primary metabolic disturbance
HCO3 deficit: 40-17=23
Expected PCO2 : 40 - (23X1.2)=40 - 27.6 = 12.4
Actual PCO2 : 55
Interpretation:
Metabolic and respiratory acidosis.

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Question
108. Normal anion gap metabolic acidosis is caused by: (AIPG 2003)
1.Cholera.
2.Starvation
3.Ethylene glycol poisoning.
4.Lactic acidosis.
Answer
1.Cholera.
Reference
Harrison 15th Edition Chapter 50 and Page 285
About Anion Gap : Fundamental Points
Blood has Anions and Blood has Cations. It is a simple fact that the net charges of Anions should be equal to Net charges of Cations. The Anions are Chloride, Bicarbonate, Phosphate, Sulphate, Albumin, lactate, uremic anions, salicylates, ethylene glycol, formate etc. Sodium is the predominant cation and other cations are Potassium, Calcium, Magnesium, Globulin etc.

So

Total Charges of Anion	=	**Total Charge of Cation**
Cl^- + $HCO3^-$ + Other Anions which are not measured	=	**Na^+ + Other Cations which are not measured**

Upon Re arranging

Other Anions which are not measured – = $Na^+ - (Cl^- + HCO_3^-)$
Other Cations which are not measured

So

$$\textbf{Anion Gap} = Na^+ - (Cl^- + HCO_3^-)$$

Now this value (Sum of Unmeasured Anions – Sum of Unmeasured Cations) is called as Anion Gap which is equal to the difference between measured cations and measured anions

So
Anion Gap is

- **Difference between Measured Cations and Measured Anions**

or

- **Difference between Unmeasured Anions and Unmeasured Cations**

Why is this Anion Gap so important Clinically.
Say you are treating a case of Diabetic Ketoacidosis. You want to know the level of acids in the blood. For that the easiest way is to measure the concerned acid. But that facility is not available in all centres. So you measure Serum Sodium, Potassium and Bicarbonate. When you find that there is a lot of unmeasured anions, you assume that that is because of the ketoacids. All evaluations of acid-base disorders should include a simple calculation of the anion gap (AG);

- It represents those unmeasured anions in plasma (normally 10 to 12 mmol/L)
- It is calculated as follows: AG = $Na^+ - (Cl^- + HCO3^-)$.
- The unmeasured anions include anionic proteins, phosphate, sulfate, and organic anions.

Before proceeding further, please note that few books include Potassium in the calculation of Anion Gap and few books take that as an unmeasured cation.

Now Anion Gap will Increase when (Such conditions, when, associated with Metabolic Acidosis, are called as **High Anion Gap Metabolic Acidosis or HAGMA**)

- Unmeasured Anions are increased
    1. Lactic acidosis
        - Anaerobic Metabolism Predominating - Shock / Cardio Pulmonary Arrest
        - Severe Anaemia,
        - Poisoning with CO or Cyanide,
    2. Ketoacidosis,
        - Diabetes
        - Alcoholics
        - Starvation
    3. Ingested toxins
        - Ethylene Glycol
        - Salicylates
        - Methanol

4. Acute and chronic renal failure.
5. In addition, the AG may increase with an increase in anionic albumin, either because of increased albumin concentration or alkalosis, which alters albumin charge.

- Unmeasured Cations are decreased
  1. Hypokalemia (when Potassium is not included in the calculation of Anion Gap)
  2. Hypocalcemia
  3. Hypomagnesemia

Now Anion Gap will Decrease when (Such conditions, when, associated with Metabolic Acidosis, are called as **Low Anion Gap Metabolic Acidosis or LAGMA**)

- Unmeasured Cations are increased
  1. Multiple Myeloma (remember that Globulin is positively charged)
  2. Hypercalcemia
  3. Lithium Toxicity
- Unmeasured Anions are decreased
  1. Low Albumin - A reduction in the major plasma anion albumin concentration (nephrotic syndrome)
  2. A decrease in the effective anionic charge on albumin by acidosis; or
  3. Hyperviscosity and severe hyperlipidemia, which can lead to an underestimation of sodium and chloride concentrations.

There will be no Change in Anion Gap when (Such conditions, when, associated with Metabolic Acidosis, are called as **Normal Anion Gap Metabolic Acidosis or NAGMA** eg Diarrhoea, Fistula, Ureterosigmoidostomy, Renal Tubular Acidosis, Ingestion of Ammoniumj Chloride, Mineralocorticoid deficiency)

- Measured Anions are increased
- Measured Anions are decreased
- Measured Cations are increased
- Measured Cations are decreased

How to find Solve MCQs regarding this topic – Ask the following questions

1. What ion increases or decreases in this condition
2. It is an measured ion (Sodium, Chloride or Bicarbonate) or an unmeasured ion

Then follow the following Flow Chart

- Increase or Decrease of a Measured Ion → Normal Anion Gap Metabolic Acidosis (NAGMA)
- Increase of an Unmeasured Anion (for example lactate) → That is High Anion Gap Metabolic Acidosis
- Increase of an Unmeasured Cation (or example lithium) → That is Low Anion Gap Metabolic Acidosis
- Decrease of an Unmeasured Anion (for example albumin) → That is Low Anion Gap Metabolic Acidosis
- Decrease of an Unmeasured Cation (or example Calclium) → That is High Anion Gap Metabolic Acidosis

The osmole gap

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The osmole gap may be helpful in diagnosing a suspected ingestion of a toxic substance. An elevated osmole gap (>20 mOsm/L) with a metabolic acidosis can suggest the presence of osmotically active agents such as methanol, ethylene glycol, or ethanol.

Osmole Gap = Measured Serum Osmolality – Estimated Serum Osmolality

Estimated Serum Osmolality = 2(Na+) + [Glucose /18] + [BUN /2.8]
Normal serum osmolality is 280-295 mOsm/L

Question

109. A 50 Kg. man with severe metabolic acidosis has the following parameters:pH 7.05. pCO2 12mm Hg., pO2 108mm Hg. HCO3 5 meq/L. base excess-30 mEq/L. The approximate quantity of sodium bicarbonate that he should receive in half hour is: (AIPG 2003)

1. 250mEq.
2. 350mEq.
3. 500mEq.
4. 750mEq.

Answer

1. 250mEq.

Reference

Harrison 15th Edition Chapter

Discussion

Estimated replacement dose of sodium bicarbonate = (Base deficit in mEq/L) x (Body weight in kg) x 0.25 (some books give the formula as Base Deficit x Body Weight x 0.3)

This is Used in metabolic acidosis with severe sodium bicarbonate deficit. In cardiac arrest give 1/2 the deficit immediately, otherwise replace with 1/2 the deficit over 8-12 hrs.

Calculating the amount of bicarbonate replacement necessary must take into account the effect of nonbicarbonate buffers on exogenously administered bicarbonate. Multiply the desired increase in plasma bicarbonate concentration by the apparent volume of distribution and weight. The bicarbonate deficit can be calculated as follows:

Bicarbonate Replacement

- Not usually recommended unless pH < 7.2 or HCO3- deficit is greater than 5 meq/L.
- 8.4% NaHCO3 = 1 meq/ml
- 1 gm of baking soda = 12 mEq of NaHCO3
- Formula for Bicarbonate Replacement
  - 0.3 × (BW in Kg) × (HCO3- deficit) = mEq of NaHCO3 needed
  - 0.3 assumes 30% of BW is extracellular fluid.
  - If the figure of 0.3 is used, bicarbonate replacement can be given fairly rapidly (30 minutes to 1 hour). If figure of .5 is used bicarbonate replacement should be given over 12-24 hour period and half of it should b given in the first half hour

- If you have a mixed respiratory/metabolic acidosis, important to address the respiratory acidosis first, before treating the metabolic acidosis

Explanation

In our case Replacement = 0.5 x Body Weight x (Desired HCO3 – Measured HCO3)
Replacement in ½ hour = 0.25 x Body Weight x (Desired HCO3 – Measured HCO3)
= 0.25 x 50 x (25-5) = 250 mEq

Comments

- The base excess is defined as the Base that must be added to Restore a normal pH The base excess is defined as the amount of H+ ions that would be required to return the pH of the blood to 7.35 if the pCO2 were adjusted to normal.
- It is a calculated figure which provides an estimate of the metabolic component of the acid-base balance.
- Base Excess = (Actual_pH - Predicted_pH) * 67 and the predicted pH is calculated based on PaCO2 (see Blood Gas)
- Normal Range: -2 to +2 meq/L
-
- Because the base excess is a calculated (not a measured) value, it may be inaccurate and misleading. Despite these problems it is important to understand the concept.
- When interpreting blood gas results the following heuristic is useful:
  - a base excess > +3 = metabolic alkalosis
  - a base excess < -3 = metabolic acidosis
- Simple Logic Interpretation
  - Positive (Base Excess) Metabolic Alkalosis
  - Negative (Base Deficit) Metabolic Acidosis
- Application in Neonatology : In Severe Acidosis (Base Excess < -10) (When Base Excess is negative, it is base deficit) Calculate Total Body Bicarbonate deficit Deficit = (Base Deficit) x (Weight in kg) x 0.3 and Administer 25% of bicarbonate deficit (~1 meq/kg)
- Note that in our case the Base Excess is –30 and this confirms metabolic Acidosis

Question

110. Causes of metabolic alkalosis include all the following except. (AIPG 2003)
1. Mineralocorticoid deficiency.
2. Bartter's syndrome.
3. Thiazide diuretic therapy.
4. Recurrent vomiting.

Answer

1. Mineralocorticoid deficiency.

Reference

Harrison 15th Edition Chapter 50, Table 50.4 and Page 288

Discussion

Metabolic alkalosis occurs as a result of net gain of Bicarbonate [$HCO3^-$] or loss of nonvolatile acid (usually HCl by vomiting) from the extracellular fluid. Since it is unusual for alkali to be added to the body, the disorder involves a generative stage, in which the loss of acid usually causes alkalosis, and a maintenance stage, in which the kidneys fail to compensate by excreting $HCO3^-$ because of volume contraction, a low GFR, or depletion of Cl^- or K^+.

Under normal circumstances, the kidneys have an impressive capacity to excrete $HCO3^-$. Continuation of metabolic alkalosis represents a failure of the kidneys to eliminate $HCO3^-$ in the usual manner. For $HCO3^-$ to be added to the extracellular fluid, it must be administered exogenously or synthesized endogenously, in part or entirely by the kidneys. The kidneys will retain, rather than excrete, the excess alkali and maintain the alkalosis if volume deficiency, chloride deficiency, and K^+ deficiency exist in combination with a reduced GFR, which augments distal tubule H^+ secretion; or hypokalemia exists because of autonomous hyperaldosteronism. In the first example, alkalosis is corrected by administration of NaCl and KCl, while in the latter it is necessary to repair the alkalosis by pharmacologic or surgical intervention, not with saline administration

Explanation

1. In patients with Decreased Mineralocorticoid Production or Action, disorders of aldosterone biosynthesis or action are associated with high renin levels, salt wasting, and hyperkalemia. The aldosterone levels may be low or elevated. In patients with a deficiency in aldosterone biosynthesis, the transformation of corticosterone into aldosterone is impaired, owing to a mutation in the aldosterone synthase (CYP11B2) gene. These patients have low to absent aldosterone secretion, elevated plasma renin levels, and elevated levels of the intermediates of aldosterone biosynthesis (corticosterone and 18-hydroxycorticosterone). Pseudohypoaldosteronism type I (PHA-I) is an autosomal recessive disorder that is seen in the neonatal period and is characterized by salt wasting, hypotension, hyperkalemia, and high renin and aldosterone levels. In contrast to the gain-of-function mutations in the epithelial sodium channel (ENaC) in Liddle's syndrome, mutations in PHA-I result in loss of ENaC function
2. Hypokalemia, metabolic alkalosis, and normal to low blood pressure are the clinical findings characteristic of Bartter's syndrome. In antenatal and classic Bartter's syndrome, impaired Cl^- reabsorption in the thick ascending limb of the loop of Henle is the underlying defect. Inadequate Cl^- reabsorption causes volume depletion and activates the renin-angiotensin system. Distal delivery of NaCl and water are high in the presence of high aldosterone, promoting secretion of K^+ and H^+ ions. Prostaglandin overproduction is mediated by volume depletion, hypokalemia, and high angiotensin II and kallikrein levels. Increased prostaglandin production contributes to the severity of disease by inducing resistance to the pressor effects of angiotensin II and reducing reabsorption in the thick ascending limb of the loop of Henle. Mutations in the bumetanide-sensitive Na:K:2Cl channel, the apical ATP-regulated K^+ channel, and the basolateral Cl^- channel have been described in classic and antenatal Bartter's.
3. Thiazide diuretics increase urinary excretion of sodium and water by inhibiting sodium reabsorption in the early distal tubules. They increase the rate of delivery of tubular fluid and electrolytes to the distal sites of hydrogen and potassium ion secretion, while plasma volume contraction increases aldosterone production. The increased delivery and increase in aldosterone levels promote sodium reabsorption at the distal tubules, thus increasing the loss of potassium and hydrogen ions. And this leads to Alkalosis
4. Recurrent vomiting leads to loss of Acid and that leads to Alkalosis.

Comments

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Metabolic acidosis leads to hyperkalemia as a result of cellular shifts in which H^+ is exchanged for K^+ or Na^+. For each decrease in blood pH of 0.10, the plasma K^+ should rise by 0.6 mmol/L. This relationship is not invariable. Diabetic ketoacidosis, lactic acidosis, diarrhea, and renal tubular acidosis (RTA) are often associated with potassium depletion because of urinary K^+ wasting

Question.

111. All of the following statements are correct about potassium balance, except: (AIPG 2003)
1. Most of potassium is intracellular.
2. Three quarter of the total body potassium is found in skeletal muscle.
3. Intracellular potassium is released into extra-cellular space in response to severe injury.
4. Acidosis leads to movement of potassium from extracellular to intracellular fluid compartment.

Answer

4. Acidosis leads to movement of potassium from extracellular to intracellular fluid compartment.

Reference

Ganong 20th Edition Page 30
Harrison 15th Edition Page 278

Discussion

- Potassium is a major intracellular cation and is one of the determinants of Resting membrane potential as well as the process of Depolarisation and Repolarisation
- Total body stores account to 150 gms and the skeletal muscle stores is 110 gms
- 98 % intracellular and 2 % extracellular
- Intracellular concentration maintained by Na+K+ATPase Pump
- In acidosis, the "pump" mechanism is altered and the intracellular Potassium "wanders out of its home into the ECF"
- During Tissue injury, due to the loss of cell membrane integrity, hyperkalemia occurs
- Hypokalemia (Increased Potassium INSIDE cells)
    - Insulin
    - Aldosterone
    - Alkalosis
    - Beta adrenergic drugs (Salbutamal)
- Hyperkalemia (Decreased Potassium OUTSIDE cells)
    - Diabetes
    - Addisons
    - Acidosis
    - Beta Blockers – Propanolol
    - Cell Injury
    - Exercises

Explanation

1. Most of potassium is intracellular.
2. Three quarter of the total body potassium is found in skeletal muscle.

3. Intracellular potassium is released into extra-cellular space in response to severe injury. Remember that Rhabdomyolysis leads to Hyperkalemia

4. Acidosis leads to movement of potassium from intracellular to extracellular fluid compartment. During a metabolic acidosis, excess hydrogen ions move toward the intracellular compartment and potassium moves out of the cell into the extracellular space (serum). For every decrease in the serum pH by 0.1, a concomitant increase in the serum potassium level by 0.5 mEq occurs. As a result, hyperkalemic arrhythmias (peaked T waves and QRS widening) and ventricular fibrillation may occur. Other acute metabolic effects of acidemia include insulin resistance, increased protein degradation, and reduced adenosine triphosphate (ATP) synthesis. During acidemia, the oxyhemoglobin dissociation curve shifts to the right; oxygen has a lower affinity for hemoglobin, but hemoglobin releases oxygen more readily. Also, nonspecific gastrointestinal complaints, such as abdominal pain, nausea, or vomiting, may be present.