Acid-Base Tutorial

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Overview

- Physiology
- Buffering systems
- Control mechanisms
- Laboratory assessment of acid-base
- Disorders of H^+ ion homeostasis
  - Respiratory acidosis
  - Metabolic acidosis
  - Respiratory alkalosis
  - Metabolic alkalosis

Physiology (1)

- Normal metabolism
  - 40-80 mmol H^+ generated per day (mainly oxidation of S-containing amino acids)
  - Excreted via kidney
  - 20,000 mmol of CO_2 produced per 24h (through energy yielding metabolism)
  - Excreted via lungs

Physiology (2)

- $[H^+]$ maintained within tight limits 35 – 43 nmol/L (pH 7.35 – 7.45)
- CO_2 and H^+ excretion precisely balance the rate of formation – homeostatic mechanisms very efficient
- Acid-base disturbance indicates severe metabolic disease
  - Affects trans-membrane gradients, biochemical reactions, protein conformations etc

Physiology (3)

- H^+ ion homeostasis depends on:
  - Buffering in tissues and blood
  - Acid (H^+) excretion by kidneys
  - CO_2 excretion through lungs

Buffering systems (1)

- Bicarbonate / carbonic acid
  - Most important buffering system in plasma

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

RENAL RESPIRATION

  - As H^+ generated, buffered by HCO_3^-, this limits increase in $[H^+]$
  - Capacity of buffer system enhanced by fact H_2CO_3 readily formed or disposed of via CO_2

Buffering systems (2)

- Haemoglobin
  - Most important system within red cells

$$H^+ + Hb \leftrightarrow HHb$$

- Other
  - Plasma – albumin
  - Intracellular – phosphate in bone

Control mechanisms (1)

- Respiratory control (pCO_2)
  - CO_2 diffuses out of cells into plasma then into RBC's down a concentration gradient
  - Carbonic acid (H_2CO_3) is formed (catalysed by carbonic anhydrase), which then dissociates into H^+ and HCO_3^-
  - H^+ produced is buffered by Hb, while HCO_3^- diffuses out into plasma
  - In the lungs, process is reversed and CO_2 is lost in expired air

Control mechanisms (2)

- Renal control (H^+ and HCO_3^-)
  - Bulk of HCO_3^- reabsorbed in the proximal convoluted tubule (no H^+ excreted at this stage)
  - In the distal convoluted tubule, H^+ is secreted in exchange for Na^+, which allows HCO_3^- to be regenerated.

Control mechanisms (3)

- Urinary buffers
  - allow increased amounts of H^+ to be excreted (max urine pH 4.6)
  - phosphate (most important)

    $HPO_4^{2-} + H^+ \leftrightarrow H_2PO^{4-}$
  - ammonia

    $H^+ + NH_3 \leftrightarrow NH_4^+$

Laboratory assessment of acid-base status (1)

- Sample requirements for blood gases
  - Syringe of arterial heparinised blood
  - Air must be excluded from syringe and analysis performed within 15 min.
  - May get venous samples (low pO_2)
- POC blood gas analysers

Laboratory assessment of acid-base status (2)

- pH / $[H^+]$
  - pH electrode (ion selective electrode, measures $[H^+]$)
- pO_2, pCO_2 – specific electrodes
- Total bicarbonate
  - Chemical methods for bicarbonate (i.e., automation) measure total CO_2 in plasma (HCO_3^- and H_2CO_3 and dissolved CO_2).

    (Typical CO_2 of 26 mmol/L will represent 24 mmol/L true bicarbonate and 2 mmol/L of carbonic acid and dissolved CO_2).

Laboratory assessment of acid-base status (3)

- Actual bicarbonate
  - Blood gas analyzer calculates bicarbonate from pH and pCO_2 using Henderson Hasselbalch equation:

$pH = constant + \log_{10} ([HCO_3^-] / a.pCO_2)$

(a = constant)

or $[H^+] = K (pCO_2 / [HCO_3^-])$

Laboratory assessment of acid-base status (4)

- Standard bicarbonate
  - Derived parameter, calculated from pH and an assumed pCO_2 of 5.3 KPa.
  - Corrects for any respiratory component to the acid-base disturbance so only reflects the metabolic component
- Base excess
  - Derived parameter – gives indication of extent of metabolic disturbance (i.e., how much acid or alkali required to correct the metabolic alkalosis or acidosis respectively)

Reference ranges

- pH 7.35 – 7.45
- [H+] 35 – 45 nmol/L
- pCO2 4.5 – 6.0 kPa
- pO2 11 – 15 kPa (arterial blood)

Disorders of H^+ ion homeostasis (1)

- Four basic processes in pathophysiology of acid-base disorders:
  - generation
  - buffering
  - compensation
  - correction

Disorders of H^+ ion homeostasis (2)

- Two types of disorder:
  - respiratory (mainly reflected in pCO_2)
  - metabolic (mainly reflected in HCO_3^-)

  (mixed disorders common)
- Two resulting states:
  - Acidosis (tendency to low pH, increased $[H^+]$)
  - Alkalosis (tendency to high pH, decreased $[H^+]$)

  N.B. Acidosis more common than alkalosis

Disorders of H^+ ion homeostasis (3)

- Compensation
  - Homeostatic mechanisms oppose disturbance
  - Metabolic disturbance, respiratory compensation (fast response)
  - Respiratory disturbance, metabolic compensation (slow response)
  - Disturbance never completely corrected

Respiratory acidosis (1)

- **Causes**: decreased CO_2 elimination
  - e.g., airway obstruction – COPD, asthma
  - depressed respiratory centre – anaesthetics, cerebral tumours
  - Increased pCO_2 (and therefore carbonic acid), decreased pO_2

Respiratory acidosis (2)

- **Compensation:** Increased renal H^+ excretion and regeneration of bicarb
  - pH returns towards normal if chronic (takes days)

Acute (flail chest)		*Chronic (COPD)*	
pH	7.24	pH	7.24
pCO_2	8.0 KPa	pCO_2	8.3 KPa
pO_2	8.0 KPa	pO_2	7.5 KPa
HCO_3	25 mmol/L	HCO_3	35 mmol/L

Respiratory acidosis (3)

- **Correction**
  - Restore pCO2 to normal by correcting primary cause – improve alveolar ventilation

Metabolic acidosis (1)

- **Causes**: Increased production / decreased excretion of H^+
  - e.g., *increased production* – DKA, lactic acidosis, poisoning (salicylates, methanol, ethylene glycol), inherited metabolic diseases
  - *decreased excretion* – renal failure, renal tubular acidosis type I
  - *loss of bicarbonate* – severe diarrhoea, fistulae, renal tubular acidosis type II
- Decreased HCO_3^- due to buffering of H^+ ions

Metabolic acidosis (2)

- **Anion gap**
  - Concentrations of plasma cations and anions are roughly balanced to maintain electroneutrality.

    $([Na^+] + [K^+]) – ([Cl^-] + [HCO_3^-])$ = 12 – 18 mmol/L
- Used to establish cause of acidosis
  - High anion gap (normochloraemic) due to unmeasured anions – e.g., ketoacids in DKA, lactic acid in lactic acidosis, formic acid in methanol poisoning
  - Normal anion gap (hyperchloraemic) due to bicarb loss, e.g., fistulae (gut), renal tubular acidosis (kidney)

Metabolic acidosis (3)

- **Compensation**
  - Lowering of pCO_2 (hyperventilation)
  - Fast response (minutes to hours)
- *DKA*

pH	7.09
pCO_2	3.0 KPa
pO_2	13.1 KPa
HCO_3	6 mmol/L

- **Correction**
  - Where non-renal cause – H^+ excreted by kidneys and bicarb regenerated.
  - Treat underlying cause, give bicarbonate in severe cases

Respiratory alkalosis (1)

- **Causes**: Increased elimination of CO_2 from lungs
  - e.g., hysteria
  - hypoxia
  - respiratory stimulation – salicylates, hyperammonaemia
- Decreased pCO_2 (and therefore carbonic acid)

Respiratory alkalosis (2)

- **Compensation:** Renal bicarbonate loss (days)
- *Acute (panic)*

pH	7.52
pCO_2	3.5 KPa
HCO_3	22 mmol/L

Chronic (overventilation)

pH	7.44
pCO_2	3.6 KPa
HCO_3	19 mmol/L

- **Correction**
  - Remove cause

Metabolic alkalosis (1)

- **Causes**: Increase in plasma HCO_3^- (usually with contracted ECF volume)
  - e.g., *loss of H^+ ions* – vomiting (pyloric stenosis), potassium depletion, diuretic therapy, excess mineralocorticoids
  - *administration of alkali*
- **Compensation**
  - Increase pCO_2 (hypoventilation)
  - Less effective mechanism than hyperventilation to compensate for metabolic acidosis.

Metabolic alkalosis (2)

- *Vomiting*

pH 7.56		Na	146 mmol/L
pCO_2	7.2 KPa	K	2.8 mmol/L
HCO_3	45 mmol/L	urea	34.2 mmol/L

  - Hypokalaemia and dehydration
- **Correction**
  - Correct volume depletion, allow renal excretion of bicarbonate

Mixed acid-base disorders

- Mixed acid-base disorders (respiratory and metabolic) commonly exist and may be difficult to interpret
  - Salicylate poisoning (8h after aspirin o/d)

pH	7.53
pCO_2	2.0 KPa

  - Alkalosis – low pCO_2 indicates respiratory cause
  - pH not as high as would expect from low pCO_2
  - Co-existent respiratory alkalosis (respiratory stimulation) and metabolic acidosis (metabolic effects of salicylate).
  - Expect raised anion gap

Conclusions

- Acid-base disturbances represent severe metabolic disease
- Bicarbonate – carbonic acid buffering system is the most important in plasma and is controlled at the kidneys and lungs
- Anion gap is useful in determining the cause of a metabolic acidosis