Metabolic effects of poisoning

Alan Jones

Abstract

Biochemical abnormalities due to disturbed metabolic processes are common in severely poisoned patients. These may be of diagnostic value, but most importantly their recognition and treatment are important in the management of these patients. Acid–base abnormalites, particularly respiratory and metabolic acidoses, are common. Respiratory acidoses due to central nervous system depression or pulmomary toxicity, and metabolic acidoses due to lactic acidaemia or derangements of intermediary metabolism are particular features of poisoning. Plasma electrolyte abnormalities, particularly hyper- or hypokalaemia are found commonly in poisoned patients, most often due to redistribution of potassium across cell membranes. Hypoglycaemia is most frequently due to drug overdose.

Keywords acid–base disturbances; anion gap; hyperkalaemia; hypoglycaemia; hypokalaemia; metabolic acidosis; osmolal gap; respiratory acidosis; rhabdomyolysis

What's new?

- The traditional approach to acid–base abnormalities relies heavily upon the use of the carbonic acid/bicarbonate buffer system using the Henderson–Hasselbalch equation, together with anion gaps to explain and interpret disorders. This approach may have shortcomings in describing the complexities which arise in critically ill patients in an intensive care setting
- The physiochemical approach originally described by Stewart has some benefits in such patients and is increasingly used in the intensive care literature

Metabolic abnormalities are common in critically ill patients. In poisoned patients metabolism may be disturbed by either:

- a primary effect of the poison on a biochemical pathway
- a secondary effect of the dysfunction of one or more organs which have been damaged by the poison.

Biochemical disturbances may be of diagnostic or prognostic value, and their recognition and management is an essential part of the care of severely poisoned patients.

Acid–base disturbances

Acid–base disturbances are common and may develop/or change rapidly. Major abnormalities are likely to impair cell and organ function. Ready access to a blood gas analyser and an ability to interpret these analytical data are essential.

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Metabolic acidosis

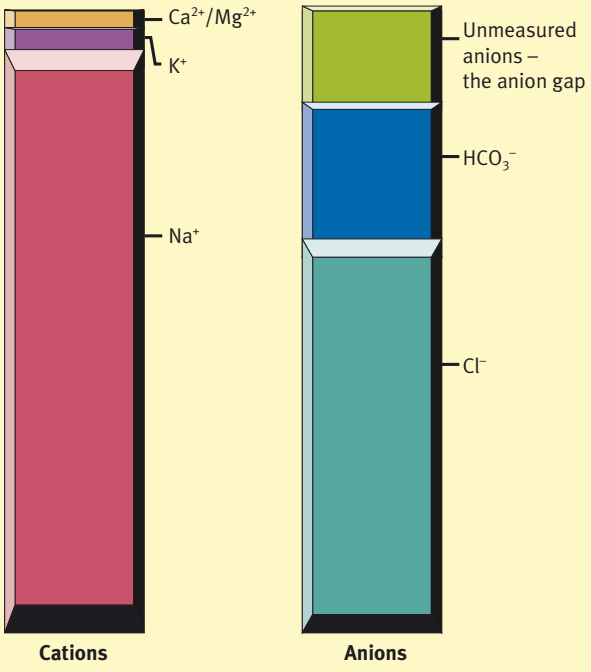
Acidaemia (pH <7.35 or H^+ >45 nmol/L with low standard bicarbonate (<21 mmol/L) or a base deficit (<–2.3 mmol/L) indicates metabolic acidosis. pCO_2 is also usually low (<4.6 kPa, 35 mm Hg) as a result of compensatory hyperventilation (Kussmaul's breathing). Metabolic acidosis arises either through the accumulation of non-volatile acids or, less commonly, loss of bicarbonate. These may be differentiated by the measurement of the plasma anion gap by the laboratory.[1,2] The electrostatic charge of the plasma cations must balance that of the anions, but conventional laboratory profiles do not measure all of the anions. Hence, there is an apparent deficiency of anions (the gap) that represents these unmeasured plasma anions (Figure 1).

- The anion gap is increased when metabolic acidosis is caused by accumulation of acids (the conjugate anions of which contribute to the gap).
- The anion gap is normal when metabolic acidosis is caused by loss of bicarbonate. Bicarbonate loss is balanced by retention of chloride to maintain the electroneutrality of the plasma. Such acidoses are also described as 'hyperchloraemic'.

High anion gap metabolic acidoses are more common than those with a normal gap in all critically ill patients. The differential diagnosis of high anion gap metabolic acidosis is shown in Table 1. Simple biochemical measurements of urea/creatinine, glucose and blood pO_2/oxygen saturation (which lead to lactic acidosis) should be performed and if these are excluded the cause of the acidosis is likely to be due to poisoning with aspirin, or alcohols/glycols.

Lactic acidosis most commonly arises through impaired oxidative metabolism of pyruvate as a result of tissue hypoxia (type A lactic acidosis).[3] Pyruvate is normally oxidized aerobically within mitochondria. In hypoxia pyruvate is reduced to lactate, which re-generates nicotinamide adenine dinucleotide (NAD) and allows energy production by anaerobic glycolysis to proceed. Lactate is released from the cell and in excess causes a lactic acidosis (Figure 2). A low blood pO_2 or oxygen saturation is good presumptive evidence that metabolic acidosis is caused by accumulation of lactic acid, but the plasma lactate measurement confirms the diagnosis and is now often measured by modern blood gas analysers. Lactic acidosis (lactate conventionally >5 mmol/L) is associated with a poor prognosis.

Measurement of the anion gap



Anion gap = Σ Measured cations – Σ Measured anions
= $([Na^+] + [K^+] + [Ca^{2+}] + [Mg^{2+}]) - ([HCO_3^-] + [Cl^-])$
Mean = 12 mmol/L
Range = 8–16 mmol/L

Figure 1

In poisoned patients, type A lactic acidoses may occur as a result of:

- cardiorespiratory depression (e.g. in β-blocker or calcium channel-blocker poisoning)
- repeated convulsions (e.g. in theophylline or tricyclic antidepressant poisoning)
- impaired oxygen-carrying capacity of the blood; for example, in patients who have inhaled carbon monoxide (carboxyhaemoglobinaemia) or ingested oxidizing agents that oxidize haemoglobin (methaemoglobinaemia).

Causes of high anion gap metabolic acidosis

- Uraemia
- Ketoacidosis
- Lactic acidosis
  - Type A – hypoxic
  - Type B – non-hypoxic
- Poisoning
  - Salicylate
  - Methanol
  - Ethylene glycol

Table 1

Formation of lactic acidosis

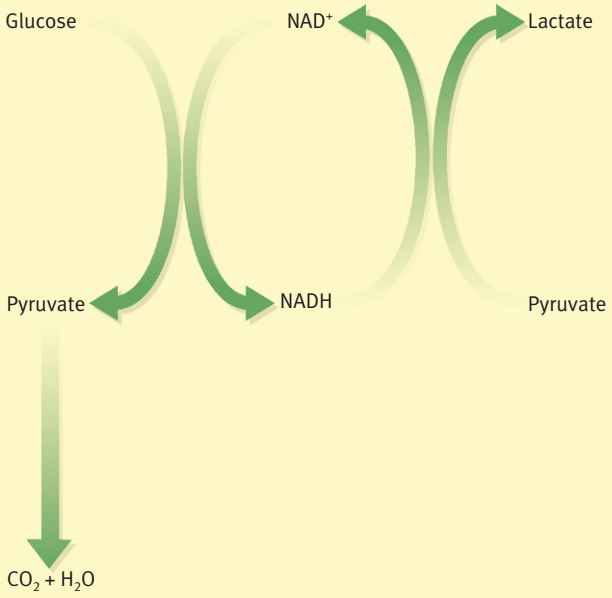


Figure 2

Type B lactic acidosis occurs despite normal tissue oxygenation. Poisons that directly inhibit the mitochondrial respiratory chain (e.g. cyanide, hydrogen sulphide) prevent normal oxidative metabolism of pyruvate. The liver normally takes up lactate from plasma, which after conversion to pyruvate, is either used to synthesize glucose by gluconeogenesis or oxidized within the mitochondria. Clinically significant hepatic dysfunction impairs these processes, and leads to a lactic acidosis and hypoglycaemia. Thus type B lactic acidosis may arise in severe paracetamol poisoning as a result of hepatic dysfunction. Acidaemia in paracetamol overdose has important prognostic significance; about 90% of such patients die.[4]

Poisonings – in the absence of uraemia, ketoacidosis and lactic acidosis, high anion gap metabolic acidosis should prompt consideration of certain poisonings (Table 1). Such acidoses may be caused by ingestion of acids, or of neutral compounds that are subsequently metabolized to strong acids. In poisoning with methanol or ethylene glycol, formation of formic or glycolic acid respectively follows sequential oxidation of the parent compound to the respective aldehyde and then acid by hepatic alcohol and aldehyde dehydrogenases. The clinical course is dominated by progressive development of severe metabolic acidosis.

Normal anion gap metabolic acidosis usually reflects inappropriate renal loss of bicarbonate or, occasionally, loss of bicarbonate from the bowel, and is uncommon in poisoned patients. Certain nephrotoxic drugs (e.g. amphotericin) and carbonic anhydrase inhibitors (e.g. acetazolamide) cause renal tubular acidosis with loss of bicarbonate in the urine, but acidosis usually occurs only on prolonged use, and overdose of these drugs is uncommon. Abuse of volatile solvents (particularly toluene) can cause renal damage with loss of bicarbonate and potassium, and acute presentations with hypokalaemic paralysis and acidosis have been described.[5]