Lactic Acidosis

Description

Lactic acidosis is a form of metabolic acidosis due to the inadequate clearance of lactic acid from the blood. Lactate is a byproduct of anaerobic respiration and is normally cleared from the blood by the liver, kidney and skeletal muscle. Lactic acidosis occurs when the body's buffering systems are overloaded and tends to cause a pH of ≤7.25 with plasma lactate ≥5 mmol/L. It is usually caused by a state of tissue hypoperafusion and/or hypoxia. This causes pyruvic acid to be preferentially converted to lactate during anaerobic respiration. Hyperlactataemia is defined as plasma lactate >2 mmol/L.

Classification

Cohen and Woods devised the following system in 1976 and it is still widely used:[1]

- Type A: lactic acidosis occurs with clinical evidence of tissue hypoperfusion or hypoxia.
- Type B: lactic acidosis occurs without clinical evidence of tissue hypoperfusion or hypoxia. It is further subdivided into:
  - Type B1: due to underlying disease.
  - Type B2: due to effects of drugs or toxins.
  - Type B3: due to inborn or acquired errors of metabolism.

Epidemiology

- The prevalence is very difficult to estimate, as it occurs in critically ill patients, who are not often suitable subjects for research. It is certainly a common occurrence in patients in high-dependency areas of hospitals.[2]
- The incidence of symptomatic hyperlactataemia appears to be rising as a consequence of the use of antiretroviral therapy to treat HIV infection. It appears to increase in those taking stavudine (d4T) regimens.[3]

Causes of lactic acidosis

The list of causes is virtually endless, but the major causes are covered below. Lactic acidosis may occur in conjunction with a wide variety of underlying disease, in extremis, and indeed is a marker for severe progression and deterioration of the primary illness. Lactic acidosis is commonly found in cardiopulmonary failure, other causes of tissue ischaemia, or due to the effects of drugs/toxins/severe illness. A variety of acquired and congenital diseases may cause it, or contribute to its presence in ill patients. Lactic acidosis may occur as a consequence of vigorous or prolonged exercise but is usually of no consequence and self-correcting, unless other pathology such as hyperthermia is present.

Type A - tissue hypoxia

- Hypoperfusion: left ventricular failure, impaired cardiac output, myocardial suppression due to toxicity, abnormal vascular tone or hyperpermeability.
- Hypoxaemia: asphyxiation, respiratory failure, acute anaemia, haemorrhage, carbon monoxide poisoning, methaemoglobinaemia.

Type B - tissue hypoxia absent

- Type B1 - underlying disease: for example, sepsis, chronic kidney disease, hepatic failure, diabetes, cancer or consequences of its treatment, diabetes mellitus, acute severe viral illness, malaria, cholera.
Type B2 - drug- or toxin-mediated: for example, biguanides*, paracetamol, anticonvulsants, alcohol, aspirin, antituberculous therapy, ethylene glycol, cyanide, sorbitol, sodium nitroprusside, overzealous total parenteral nutrition (TPN) regimen, lactulose, theophylline, adrenaline (epinephrine), noradrenaline (norepinephrine), cocaine, amphetamines, papaverine, paraldehyde.

Type B3 - inborn errors of metabolism (or (rarely) acquired metabolic errors): for example, organic acidaemias, primary lactic acidoses (eg, pyruvate dehydrogenase deficiency, pyruvate carboxylase deficiency, cytochrome oxidase deficiency), severe vitamin deficiency (particularly thiamine), aminoacidopathies, glycogen storage disorders, mitochondrial disease (eg, mitochondrial encephalomyelopathy with lactic acidosis and stroke (MELAS)), D-lactic acidosis in short gut syndrome, overexertion, prolonged generalised seizures.

*The reputation of the biguanide metformin for causing lactic acidosis may be overstated, and largely based on experience with its more toxic predecessor phenformin. It can cause lactic acidosis in overdose or if continued in those with diabetes who are severely ill and become dehydrated, but seems to be well tolerated on the whole, with many of the current cautions for conditions such as heart failure probably being overzealous and denying a safe and useful therapy to many patients. A Cochrane systematic review found no evidence of an association with lactic acidosis or hyperlactataemia in study-based use.

Presentation

History
Lactic acidosis occurring in the face of concomitant illness is an ominous sign and a relatively grave prognostic indicator. It signifies a critical, acute illness and the history should be directed at finding the underlying cause of shock. It is important to enquire (from the patient if possible; if not from friends/family) about antecedent symptoms of:

- Infection.
- Cardiorespiratory disease.
- Abdominal complaints.
- Trauma.
- Recent prescribed or non-prescribed drug ingestion (particularly antiretroviral therapy).
- Exposure to toxins at work or in the home.
- Episodes of overdose or self poisoning.
- Family history of similar problems.

Physical examination
There are no specific signs indicating lactic acidosis but its aetiology may be determined through careful examination.

- Look for signs of hypovolaemic, cardiogenic, septic or toxic shock.
- To classify the lactic acidosis look for signs of tissue hypoperfusion such as hypotension, tachypnoea, confusion, peripheral shutdown (check capillary refill) and oliguria.
- Look for evidence of a septic focus and hyperthermia, or even hypothermia in advanced sepsis.
- Kussmaul's breathing (rhythmic, deep, gasping breaths at normal or reduced frequency) indicates severe acidosis with attempted respiratory compensation.

Investigations
Arterial blood gases will reveal a metabolic acidosis (pH < 7.35 with low or normal pCO₂) and electrolytes reveal a low plasma bicarbonate (< 22 mmol/L). Lactic acidosis is suggested by the presence of metabolic acidosis without an obvious cause, such as ketosis or the presence of other acidic toxins. The anion gap should be calculated as below:

Anion gap
- The anion gap is the difference between the sum of the cations (sodium plus potassium) and the anions (chloride plus bicarbonate), ie (\[Na mmol/L\] + [K mmol/L]) - ([Cl mmol/L] + [HCO₃ mmol/L]).
- The normal reference range for the anion gap varies between different laboratories but is 8-16 mmol/L when not including potassium in the equation and 10-20 mmol/L when including potassium.
Hypoalbuminaemia lowers the normal anion gap by approximately 2.5 mmol/L for every 10 g/L reduction in serum albumin. The anion gap will be elevated in lactic acidosis. It is also elevated in chronic kidney disease and other organic acidoses, ketoacidosis, and some poisoning/drug-induced acidoses. Plasma lactate should be measured to confirm that this is the likely anion causing the acidosis, to help distinguish from these other causes. Values in the range 2-5 mmol/L are significant. Clinically significant hyperlactataemia can occur in the absence of a raised anion gap. Samples for lactate estimation should be taken from arterial or mixed central venous sites. Peripheral values may reflect local rather than systemic concentrations. The sample should be transported to the laboratory on ice and may utilise a special reagent that inhibits glycolysis, giving a true spot reading. In shocked patients, particularly those with cardiogenic shock, lactate concentrations >2.5 mmol/L are associated with a poor prognosis and the lactate level can be measured as a semi-quantitative marker of deterioration or improvement.

Further investigations aimed at detecting the underlying cause should be requested as thought necessary. Blood, urine and other cultures are useful for detecting occult septic causes.

Differential diagnosis

Any other cause of metabolic acidosis, particularly those due to diabetic ketoacidosis, other organic acidosis, chronic kidney disease, alcoholic ketoacidosis, hyperosmolar hyperglycaemic non-ketotic coma (HONK), poisoning or drug toxicity.

Management

The principles of management of lactic acidosis are:

- Diagnose and correct any underlying cause if possible.
- Restore adequate oxygen delivery to the tissues, especially adequate tissue perfusion.

Emergency management

- Check airway, breathing and circulation. Immediate resuscitation as indicated.
- Put the patient on an SaO_2 monitor.
- Give 100% oxygen.
- Consider intubation and ventilatory support for patients with deteriorating SaO_2 (take senior A&E/medical/anaesthetic advice).
- Obtain intravenous access and give a fluid bolus of crystalloid or colloid if tachycardia, hypotension or signs of hypoperfusion such as poor capillary refill exist.
- If cardiac failure is the suspected aetiology, be cautious about fluid infusion.
- Put the patient on a cardiac monitor as there is a predisposition to arrhythmia.
- Refer urgently to the acute medical team.
- Arrange transfer to a high-dependency area as soon as feasible.
- Treat any obvious underlying causes - eg, intravenous antibiotics for infection, intravenous thiamine if there is suspected deficiency.

Further management[1]

- Sodium bicarbonate is used by some to correct the acidosis but its use should not be routine and remains controversial. It generates CO_2 that may worsen acidosis if there is insufficient respiratory balance. There are no good, reliable trials that support its efficacy in routine use.
- Dichloroacetate may be used to stimulate pyruvate dehydrogenase, the alternative aerobic respiratory pathway. It also has positive inotropic effects. It has been shown to improve acid-base status but this did not translate into improved outcome or survival.
- Carbicarb (equimolar mixture of sodium bicarbonate and sodium carbonate) is a promising buffering agent that appears effectively to reduce lactate levels without CO_2 generation, but no randomised controlled trials have yet reported.
- Dialysis is an effective treatment in expert critical care/nephrology hands. Haemoperfusion or haemodialysis may be indicated in association with ethylene glycol and methanol poisoning. Dialysis may also be useful when severe lactic acidosis exists with chronic kidney disease or congestive heart failure, or with metformin intoxication.[7]
Complications

- The major problem is the increasing myocardial suppression that occurs with decreasing blood pH. A vicious cycle of lactic acidosis, further hypoperfusion and multiorgan failure may lead to death.
- There is an increased risk of a variety of cardiac arrhythmias.

Prognosis

- Very poor overall, especially in severe cases.
- Using blood lactate monitoring for risk assessment in the critically ill patient remains controversial.\[8\]
- However, a high blood lactate level at admission to hospital appears to be independently associated with, and predictive of, in-hospital mortality in the general population of critically ill children.\[9\]

Further reading & references

4. Inborn Errors of Metabolism; Intensive Care Nursery House Staff Manual, UCSF Children's Hospital

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