metabolic acidosis [created by Paul Young 12/12/07]

definition

- A metabolic acidosis is an abnormal primary process or condition leading to an increase in fixed acids in the blood. This causes the arterial plasma bicarbonate to fall to a level lower than expected.

causes

Pathophysiological mechanism
- A decrease in plasma bicarbonate can be caused by two mechanisms:
(i) A gain of strong acid
(ii) A loss of base
- All causes of a metabolic acidosis must work by these mechanisms. The gain of strong acid may be endogenous (eg ketoacids from lipid metabolism) or exogenous (NH_4Cl infusion). Bicarbonate loss may occur via the bowel (diarrhoea, small bowel fistulas) or via the kidneys (carbonic anhydrase inhibitors, renal tubular acidosis).

metabolic acidosis with increased anion gap:
Methanol, metformin
Uraemia
DKA
Phenformin, paraldehyde, propylene glycol, pyroglutamic acidosis
Iron, isoniazid
Lactic acidosis
Ethanol ketoacidosis, ethylene glycol
Salicylates, starvation ketoacidosis, solvent

classified by anion gap
metabolic acidosis with normal anion gap:
Ureteroenterostomy (K+ decreased)
Small bowel fistula (K+ decreased)
Extra chloride (K+ increased)
Diarrhoea (K+ decreased)
Carbonic anhydrase (K+ decreased)
Renal tubular acidosis (K+ decreased - type 1)
Addison's disease (K+ increased)
Pancreatic fistula (K+ decreased)

maintenance

- The disorder is maintained as long as the primary cause persists.
- Additionally, in many cases the acid-base disturbance tends to increase in severity while the problem causing it persists though this is not absolute.

effects

Respiratory Effects
(i) Hyperventilation (Kussmaul respirations) - this is the compensatory response
(ii) Shift of oxyhaemoglobin dissociation curve (ODC) to the right
(iii) Decreased 2,3 DPG levels in red cells (shifting the ODC back to the left)
- The shift of the oxygen dissociation curve to the right due to the acidosis occurs rapidly. After 6 hours of acidosis, the red cell levels of 2,3 DPG have declined enough to shift the oxygen dissociation curve (ODC) back to normal.

Cardiovascular Effects
(i) Depression of myocardial contractility
(ii) Sympathetic overactivity (incl tachycardia, vasoconstriction,decreased arrhythmia threshold)
(iii) Resistance to the effects of catecholamines
(iv) Peripheral arteriolar vasodilatation
(v) Venoconstriction of peripheral veins
(vi) Vasoconstriction of pulmonary arteries
(vii) Effects of hyperkalaemia on heart
- The cardiac stimulatory effects of sympathetic activity and release of catecholamines usually counteract the direct myocardial depression while plasma pH remains above 7.2.
- At systemic pH values less than this, the direct depression of contractility usually predominates.
- The direct vasodilatation is offset by the indirect sympathetically mediated vasoconstriction and cardiac stimulation during a mild acidosis. The venoconstriction shifts blood centrally and this causes pulmonary congestion. Pulmonary artery pressure usually rises during acidosis.

Other Effects
(i) Increased bone resorption (chronic acidosis only)
(ii) Shift of K+ out of cells causing hyperkalaemia

compensation

- Compensation for a metabolic acidosis is hyperventilation to decrease the arterial pCO_2.
- The metabolic acidosis is detected by both the peripheral and central chemoreceptors and the respiratory center is stimulated. The initial stimulation of the central chemoreceptors is due to small increases in brain ISF $[H^+]$. The subsequent increase in ventilation causes a fall in arterial pCO_2 which inhibits the ventilatory response.
  - Maximal compensation takes 12 to 24 hours
  - The chemoreceptor inhibition acts to limit and delay the full ventilatory response until bicarbonate shifts have stabilised across the blood brain barrier. The increase in ventilation usually starts within minutes and is usually well advanced at 2 hours of onset but maximal compensation may take 12 to 24 hours to develop.
- The arterial pCO_2 at maximal compensation has been measured in many patients with a metabolic acidosis. A consistent relationship between bicarbonate level and pCO_2 has been found. It can be estimated from the following equation:
Expected pCO_2 = 1.5 (Actual $[HCO_3^-]$) + 8 mmHg
(Units: mmols/l for $[HCO_3^-]$, and mmHg for pCO_2).
- The limiting value of compensation is the lowest level to which the pCO_2 can fall - this is typically 8 to 10mmHg, though lower values are occasionally seen.
- If a patient with a severe metabolic acidosis requires intubation and controlled ventilation in hospital, the acidosis can markedly worsen unless the hyperventilation is maintained. The ventilation should be set to mimic the compensatory hyperventilation to keep the pCO_2 low.
- Carbon dioxide crosses cell membranes readily so intracellular pH falls rapidly also, resulting in depression of myocardial contractility, arrhythmias and a rise in intracranial pressure.

correction

General principles are as follows:
1. Accurate diagnosis of the cause of the metabolic acidosis is essential because this allows correct treatment of the underlying disorder
2. Treat the underlying disorder as the primary therapeutic goal
3. Provide supportive treatment (eg fluids, oxygen, treatment for hyperkalaemia) including all appropriate emergency management
4. In most cases, IV sodium bicarbonate is NOT necessary, NOT helpful, & may even be harmful in the treatment of metabolic acidosis.

Kidney: Renal generation of new bicarbonate
- This usually occurs as a consequence of an increase in ammonium excretion.

Liver: Hepatic metabolism of acid anions to produce bicarbonate
- The normal liver has a large capacity to metabolise many organic acid anions (eg lactate, ketoanions) with the result that bicarbonate is regenerated in the liver. In severe ketoacidosis there is often a large loss of ketoanions due to the hyperglycaemia induced osmotic diuresis. This leaves a shortfall of ketoanions to be used to regenerate bicarbonate as a consequence of their metabolism in the kidney.

Exogenous Administration of sodium bicarbonate
- This is the time honoured method to 'speed up' the return of bicarbonate levels to normal. Indeed, this may be useful in mineral acidosis (hyperchloraemic metabolic acidosis) where there are no endogenous acid anions which can be metabolised by the liver. However, in most other cases of metabolic acidosis this administration is either not helpful or may be disadvantageous.

assessment

- A metabolic acidosis is often strongly suspected because of the clinical presentation of the patient (eg diabetes, renal failure, severe diarrhoea). Three clues from a typical hospital automated biochemical profile are:
(i) Low 'bicarbonate' (or low 'total CO_2')
(ii) High chloride
(iii) High anion gap
  - In addition to arterial blood gases, some other investigations useful for indicating a metabolic acidosis and for differentiating between the various major causes are:
  (i) Urine tests for glucose and ketones
  (ii) Electrolytes (incl chloride, anion gap, 'bicarbonate')
  (iii) Plasma glucose
  (iv)Urea and creatinine
  (v) Lactate
    - useful additional indices in assessment of metabolic acidosis include:
    (i) Anion gap
    (ii) Delta ratio
    (iii) Urinary anion gap
    (iv) Osmolar gap