Dapsone

Dapsone is a bacteriostatic antimicrobial that may cause oxidative stress to haemoglobin, leading to methaemoglobinaemia and / or haemolysis

Toxicity / Risk Assessment

Dapsone can cause methaemoglobinaemia (MetHb) in both therapeutic dosing and acute overdose

Dapsone metabolism leads to free radical induced RBC damage + reticuloendothelial destruction via haemolysis

Dapsone's metabolites act as oxidizing agents to convert haemoglobin to methaemoglobin

MetHb and haemolysis can occur separately or together

MetHb and haemolysis both impede O_2 delivery

(Haemolysis generally occurs at doses > 200 mg per day)

- Clinically significant MetHb can occur up to 3 days post exposure and may be persistent, lasting for many days
- ½-life in OD up to 77 hours (30 hours in therapeutic)
- Children: 1 dapsone tablet may cause significant MetHb
- G6PD deficiency patients are more susceptible to MetHb

Maculopathy and renal failure can occur as a secondary result of RBC fragmentation and microvascular occlusion

Venous blood gas analysis is a reliable method of measuring MetHb fraction

Clinical Features

Dependent on the MetHb fraction and the compensatory response to reduced O_2-carrying capacity

Pulse oximetry in the presence of MetHb is inaccurate & will usually read 85-90% despite supplemental O_2

Severity of clinical effects increases with MetHb fraction: - Cyanosis, tachycardia, tachypnoea, anxiety, confusion, seizures, acidosis, arrhythmias, CNS depression

Heinz bodies on blood film is an early sign of haemolysis, which may lead to jaundice, hypoxaemia & shock

Management

Discontinuation of dapsone and monitoring of MetHb fraction % will be sufficient Rx in many cases

Provide oxygen if symptomatic

AC 50 g (1 g/kg in children) within 2 hours of acute ingestion

Enhanced elimination: Multi-dose activated charcoal is indicated if MetHb is present in cases of acute OD

Indications for antidotal Rx with methylene blue (see separate methylene blue guideline)

- MetHb fraction > 20%
- MetHb fraction > 10% AND symptomatic OR co-existing anaemia / chronic lung disease / cardiac failure
- Initial dose: 1-2 mg/kg (0.1-0.2 mL/kg of 1% solution) IV over 5 minutes, followed by a 20 mL saline flush
  - Measure MetHb fraction % every 30 minutes to assess response
  - A methylene blue infusion may be required for hours – days (long dapsone ½ life)
    (commence methylene blue infusion at 0.25 mg/kg/hour and discuss with a toxicologist)

Other interventions in cases of severe toxicity (please discuss with clinical toxicologist)

Failure to respond to methylene blue Rx is an indication for exchange RBC transfusion

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