Therapeutics Bulletin

Chloroquine toxicity

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Chloroquine (CQ) is an aminoquinoline which is rapidly and completely absorbed. It has a large volume of distribution and undergoes hepatic metabolism. About 50-70% of the drug is renally excreted as unchanged drug.[1]

In South Africa, it has been used in low doses in the management of autoimmune diseases and parasitic infections. Current doses used in rheumatic conditions are well tolerated. CQ will potentially be used more widely in the near future in higher doses, as it is being investigated in the management of COVID-19. Toxic doses of CQ are close to the therapeutic dosing range. Toxic effects can be seen from doses equal to 10 mg/kg per dose.[2,3]
In children, doses as little as 300 mg may be fatal.[1]

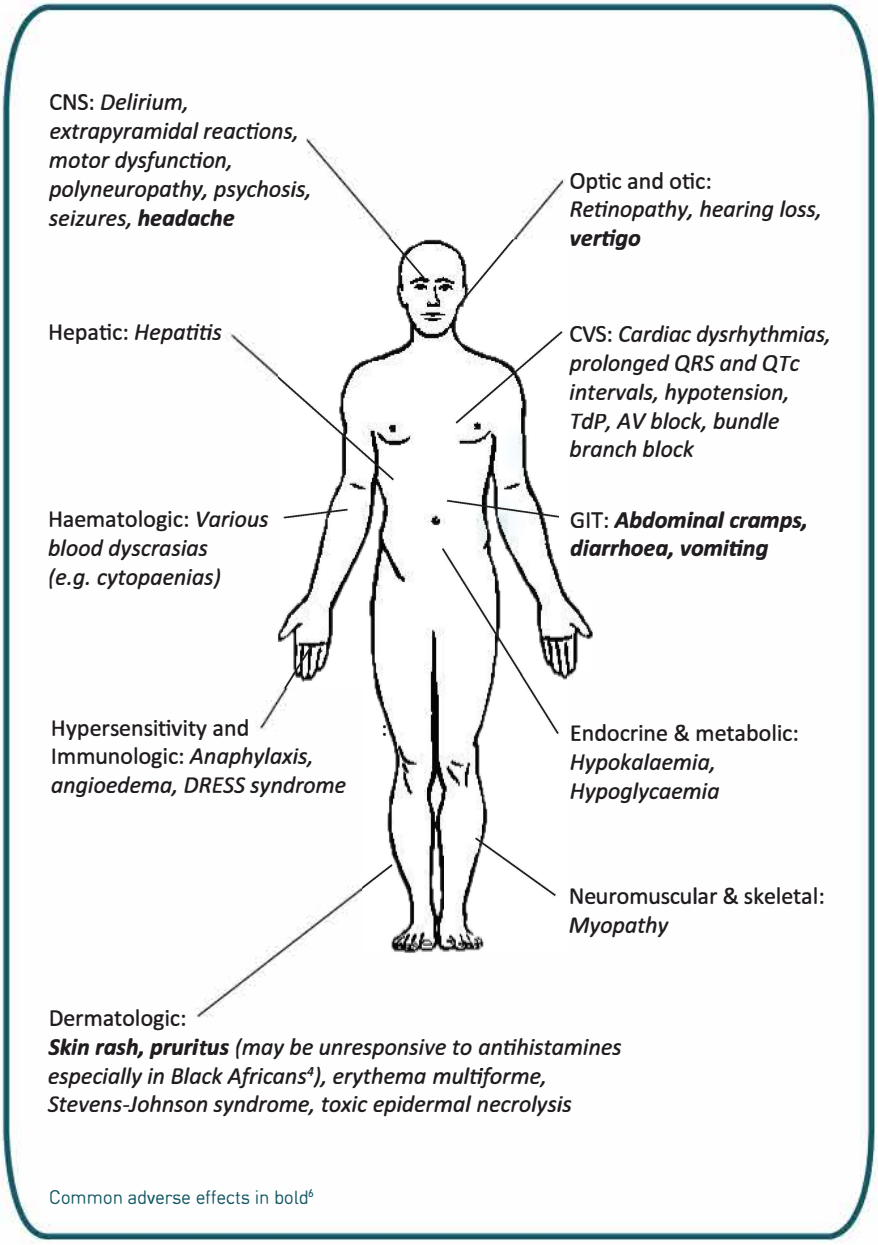
Drug interactions:

- Any drug with QT-prolongation risk[1]
  - May potentiate QT prolongation and increase risk of torsades de pointes (TdP)
- Any drug with significant liver enzyme inhibition[1]
  - Potential CQ toxicity by increased CQ concentrations and decreased elimination, e.g. lopinavir/ritonavir, cimetidine, ketoconazole/itraconazole

Signs of severe toxicity

- Severe toxicity classically presents as a triad of:
  - Hypotension
  - Hypokalaemia
  - QRS prolongation
- After a large ingestion, life-threatening symptoms may develop within 1 to 2 hours.[3]

Adverse effects that may be seen with chloroquine use[5]



Common adverse effects in bold[6]

Management of chloroquine toxicity:

	Management recommendation
Decontamination	• Not recommended due to lack of evidence of efficacy • Activated charcoal can be considered if a patient presents shortly after a significant oral overdose and is not yet manifesting symptoms of toxicity
Supportive therapy	• Early intubation and mechanical ventilation should be considered in patients with cardiovascular collapse or who cannot maintain their airway • **IV fluids** for hypotension • Adrenaline infusion for hypotension not responding to IV fluids
Directed therapy	• If hypotension, dysrhythmias, QRS widening, or circulatory collapse is present: **- Adrenaline infusion** Dose: Initiate at 0.25 mcg/kg/min, and titrate to effect **- High-dose diazepam*** (reportedly competes for chloroquine binding sites) Dose: 2 mg/kg loading dose over 30 minutes If cardiotoxicity persists, follow with 1 – 2 mg/kg/day Also indicated for chloroquine-induced seizures • If significant QRS widening or ventricular tachycardia present, consider: **- Sodium bicarbonate** Dose: 1 – 2 mEq/kg bolus, repeated as needed Endpoints include resolution of dysrhythmias, narrowing of QRS complex, and a blood pH 7.45 – 7.55 • If cardiotoxicity persists despite adrenaline and sodium bicarbonate, consider: **- Lignocaine IV** Dose: 1 – 1.5 mg/kg stat Repeat 0.5 – 0.75 mg/kg at 5 – 10 minute intervals if refractory VF/VT (max. total dose 3 mg/kg) • *If torsades de pointes* (TdP) develops - Follow relevant ACLS protocols • **Hypokalaemia** - Initial hypokalaemia should be corrected cautiously with potassium supplementation - Note that intensive administration of potassium may lead to a sudden hyperkalaemia
Enhanced elimination	• Enhanced elimination - Haemodialysis is not effective

*Dose obtained from observational studies

Monitoring:

- Continuous ECG monitoring
- Vital signs and mental status
- Basic bloods, especially urea, creatinine, electrolyes and glucose

References:

1. Micromedex Drug Interaction Checker
2. Micromedex monograph: Chloroquine toxicology
3. AfriTox monograph: Chloroquine
4. Ajayi AA, Akinleye AO, Udoh SJ, et al. The effects of prednisolone and niacin on chloroquine-induced pruritus in malaria. Eur J Clin Pharmacol. 1991;41:383-385.
5. Anatomical position figure copyrighted to Clipart Panda
6. South African Medicines Formulary (SAMF), 13 edition

