Treatment of uncomplicated malaria

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The treatment of uncomplicated malaria
P.falciparum and P.vivax

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Some important points

- The correct approach:
  - Early: within 48 hours of fever onset.
  - Diagnosis: confirmed biological diagnosis.
  - Treatment with an Artemisinin based Combination Therapy (ACT).

- Aim is to obtain a complete parasitological cure.

- Prevent resistance by:
  - Using drugs in combination.
  - Using quality drugs.
  - Promoting good adherence to treatment and optimum dosing.
  - Using drugs only in patients who need them.
  - Interrupting transmission.
WHO treatment guidelines 2010

- Guidelines are evidence based and revised regularly
- ACTs first line (3 days)
- Use Fixed Combinations
- High parasitological cure (95%)
- Change policy if < 90% cure rate


Pharmacokinetics and Pharmacodynamics

- The dispositions of the drugs are essential determinants of their efficacy.
  - Absorption, elimination
- The pharmacodynamic parameter of interest is the parasite killing rate.
  - PRR_{48}: parasite reduction ratio at 48h (1 cycle)

Adapted from: N. White 1998

Total parasites

- Detection limit
- Drug concentration
- weeks
**Rational of ACTs**

![Graph showing the rational of ACTs](image)

**Available treatments**

- **ACTs**
  - Artemether-lumefantrine
  - Artesunate-mefloquine
  - Artesunate-SP (Fansidar)
  - Artesunate-Amodiaquine
  - Di-hydroartemisinin-Piperaquine
  - Artesunate-Pyronaridine

- **Non-ACTs**
  - Quinine (7 days)
  - Atovaquone-proguanil
  - Suphadoxine-pyrimethamine
  - Halofantrine
  - Tetracyclines
  - Clindamycin

**Drugs in the pipeline**

- Ferroquine
- Artemisinin + naphtoquine
- Artemisone
- Trioxolane (OZ439)
- KAE609 (spiroidolones) and KAF156 (imidazolpiperazines)
ACTs: Three day treatments

- Mefloquine (25 mg/kg) + artesunate (12 mg/kg): 1 dose a day
- Artemether (10 mg/kg) + lumefantrine (60 mg/kg): 2 doses /d with food
- DHA (6.4 mg/kg) + piperaquine (51 mg/kg): 1 dose per day
- Dosing will need to be adapted to particular patients such as young children and pregnant women.

Primaquine, 0.25 mg/kg single dose to further reduce transmission
Recommendations for uncomplicated P. falciparum malaria

1. Use an ACT (3 day) as first line treatment.
2. Prefer quality (GMP) fixed combinations.
4. Encourage adherence to treatment.
5. For recrudescence infections use:
   - A different ACT
   - Quinine + antibiotic (7 days)
   - Artesunate + antibiotic (7 days)
6. Primaquine: 0.25 mg base/kg single dose

http://www.who.int/malaria/diagnosis_treatment/treatment/who_ps_policy_recommendation/en/

Treatment options for P. vivax

- Chloroquine (25 mg base/kg)
- Amodiaquine (30 mg base/kg)
- ACTs
- Primaquine
  - (0.25 to 0.5 mg base/kg for 14 days)
- Tafenoquine (single dose)
- Requires G6PD testing.
Special groups of patients

- **Infants:**
  - More likely to develop severe infections.
  - Often under-dosed.

- **Pregnant women:**
  - More susceptible to malaria.
  - More likely to develop complications.
  - Detrimental effects on the fetus.

- **Travellers:**
  - Non-immune, at risk of complications because of delayed diagnosis.

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