Newsletter



Update on Malaria Part 3

Treatment Guidelines

Compiled by Dr Trisha Moodley

UNCOMPLICATED



DEFINED AS: Parasite count < 4%

CLINICAL FEATURES:

Mild symptoms, ambulant, normal mental function, no repeated vomiting, no jaundice, no other features of severe malaria

Cause:

Plasmodium ovale or P. vivax OR

Mixed infections of Plasmodium falciparum PLUS P. ovale or P. vivax

TREATMENT: Coartem® followed by Primaquine for 14 days to cure P. ovale & P. vivax (*Appendix 4)



Treatment



Cause:

- * Plasmodium falciparum
- * Plasmodium malariae
- * Plasmodium knowlesi

USE: Coartem® (Artemether 20 mg lumefantrine 120 mg) (* APPENDIX 1)

Oral Quinine PLUS either Doxycycline or Clindamycin (*APPENDIX 3)

Coartem® can be used to treat uncomplicated malaria in pregnant women in 2nd & 3rd trimester, & also considered as an alternative to Quinine plus Clindamycin in the 1st trimester of pregnancy





CLINICAL RESPONSE to treatment in 24 - 48 hours. Repeat blood smear performed at 72 hours of treatment. Treatment failure defined as: Positive blood smear after 72 hours due to:

- Poor patient compliance
- Parasite resistance to anti-malarials
- **Underdosing** of anti-malarials
- Vomiting of oral medication
- Failure to take fatty food with artemether-lumefantrine
- Relapse due to P. ovale or P. vivax because of failure to take Primaguine for radical cure of hypnozoites



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DEFINED AS: Hyperparasitaemia > 4%

CLINICAL FEATURES:

- Impaired consciousness
- Prostration
- Multiple convulsions: > 2 episodes in

24 hours

- Acidotic breathing & respiratory distress
- Acute pulmonary oedema & acute respiratory distress syndrome
- Circulatory collapse or shock
- Anuria
- Jaundice
- Abnormal bleeding



LABORATORY FEATURES:

- Hypoglycaemia (< 2.2 mmol/L or < 40 mg/dL)
- Metabolic acidosis (plasma bicarbonate < 15 mmol/L)
- Severe normocytic anaemia (< 7 g/dL)
- Haemoglobinuria
- Hyper-lactataemia (lactate > 5 mmol/L)
- Renal impairment (serum creatinine > 265 µmol/L)
- Pulmonary oedema (radiological)

SEVERE/COMPLICATED Malaria in Adults



Treatment



Cause: Usually P.falciparum:

TREATMENT: Artesunate IVI OR if not available Quinine IVI (*APPENDIX 5)

Once able to tolerate ORAL treatment, follow with: Coartem® (Artemether 20 mg - lumefantrine 120 mg) (* APPENDIX 1) OR Oral Quinine PLUS either Doxycycline or Clindamycin (*APPENDIX 3)

PRE-TRANSFER MANAGEMENT:

Drug treatment

- IM artesunate 2.4 mg/kg stat
- IM quinine 20 mg salt/kg stat divided into 10 mg/kg diluted to a concentration of 60 100 mg/mL given into each anterior thigh).

GENERAL MANAGEMENT:

- · Check blood glucose correct the hypoglycaemia
- Hypotensive/shock IV fluid resuscitation with normal saline
- Respiratory distress oxygen per mask
- Fever > 39 C administer paracetamol
- Convulsions IV or rectal diazepam

SUPPORTIVE MANAGEMENT

- · Admission to ICU
- Intravenous fluid management + urine
- output monitoring
- · Regular glucose monitoring
- Temperature regulation + management
- Monitor BP, Pulse rate, Respiratory rate
- · and Level of consciousness
- · Administer IVI antibiotics
- Stress ulcer prophylaxis



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Malaria in PREGNANCY

Travel history to malaria area
History of fever
Malaria rapid antigen test
should be performed
Patient should be admitted
to hospital for management

Management of UNCOMPLICATED malaria

1 trimester use Quinine PLUS Clindamycin (*APPENDIX 3)

2nd & 3rd trimester use Artemether-lumefantrine (*APPENDIX 1)

CONTRAINDICATED THROUGHOUT PREGNANCY:

Doxycycline & Primaguine

High index of suspicion is needed for the diagnosis Differentiate from the complications of pregnancy:

• Intrauterine sepsis, eclampsia, pyelonephritis **Patients at RISK** in the 2nd and 3rd trimesters of pregnancy.

Frequently complicated by:

 Cerebral malaria, hypoglycaemia, pulmonary oedema/ARDS

Increased risk of:

 Spontaneous abortion, stillbirth, premature delivery, low birth weight, rarely congenital malaria
 Severe malaria extends into the postpartum period, therefore it is important to follow-up mother and infant more closely.

Management of COMPLICATED malaria



1st, 2nd & 3rd trimester use IVI Artesunate (*APPENDIX 5)

Once oral medication is tolerated, change to Artemetherlumefantrine (6 doses) (*APPENDIX 1) OR Oral Quinine PLUS Clindamycin for 7 days (*APPENDIX 3)

If parenteral artesunate is unavailable START parenteral Quinine immediately until parenteral artesunate is available Monitor Glucose levels and Electrocardiogram (ECG) tracing while infusing Quinine

Cerebral malaria vs eclampsia

- Both conditions present with fever, headaches, convulsions, confusion & depressed level of consciousness.
- Treat for both malaria and eclampsia.

Respiratory failure due to Acute Respiratory

Distress Syndrome (ARDS)

- Monitor fluid balance carefully.
- Hypervolaemia may potentiate ARDS.

Hypovolaemia may lead to renal failure, metabolic acidosis & circulatory collapse.

Postpartum bacterial infection is a common complication and should be managed swiftly and appropriately.

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Malaria in the Paediatric Population

Management of UNCOMPLICATED malaria

Infants weighing > 5 kg

Infants weighing < 5 kg

Artemetherlumefantrine (*APPENDIX 1)



Quinine plus clindamycin (*APPENDIX 3) OR Artemether-lumefantrine (off label use) (*APPENDIX 1)

GENERAL MANAGEMENT

- Check airway, breathing, circulation (ABC).
- Hypoglycaemia, cerebral malaria, anaemia, and metabolic acidosis are important complications.
- Agitation and respiratory distress (due to metabolic acidosis) are ominous signs.
- Fluid boluses are **NOT** recommended. Crystalloids
- should be administered slowly over three to four hours.
- Secondary bacterial infections, including septicaemia, are common and broad-spectrum antibiotics (e.g. third-generation cephalosporins) should be given to children with severe malaria.
- Meningitis is important in the differential diagnosis of malaria as they both may present clinically with a depressed level of consciousness or convulsions.
- Convulsions in children with malaria may be subtle and may be due to hypoglycaemia, cerebral malaria or pyrexia.
- Renal failure and acute respiratory distress syndrome are rare in young children.

Signs & symptoms

- Poor feeding
- Lethargy
- Irritability
- Coughing
- Convulsions

Management of COMPLICATED/SEVERE malaria

Children < 20 kg

Children > 20 kg

Intravenous artesunate (3 mg/kg), doses given

at 0, 12 & 24 hours, then

daily until oral

treatment is tolerated

R

Intravenous artesunate (2.4 mg/kg), doses given at 0, 12 & 24 hours, then daily until oral treatment is tolerated

Alternative treatment = Quinine IVI
Correct the dose according
to the body weight
(*APPENDIX 5)

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Malaria in HIV & AIDS



Treatment

Co-infected patients with HIV/AIDS & malaria

- Admit to hospital for close monitoring.
- Treatment as for uncomplicated OR complicated malaria algorithms as on pages 1 & 2.
- Assess HIV status

 As immune suppression worsens, the risk of severe malaria increases.
- Assess renal function
 o Renal failure is a complication
 in HIV/AIDS patients.
- Monitor electrolyte disturbances and correct as needed.
- Empiric antibiotic therapy (3rd generation cephalosporin) is recommended to prevent secondary bacterial infections.

KEY FACTS TO NOTE WITH TREATMENT OF MALARIA IN PATIENTS WITH HIV/AIDS: (*APPENDIX 2)

- Co-treatment with artemether-lumefantrine & efavirenz-based ARV's reduces lumefantrine concentrations - HIGH RISK of treatment failure.
- Recommendation: extend artemetherlumefantrine treatment duration to 5 days.
- HIV-infected children on zidovudine, receiving artesunate + amodiaquine = are at an increased risk of neutropaenia.
- Hepatoxicity develops in patients taking artesunate + amodiaquine + efavirenz (Amodiaquine is not available in South Africa).
- Sulfadoxine pyrimethamine is not recommended for the treatment of malaria in South Africa, AND should not be given to patients taking cotrimoxazole.







* Appendices adapted from: South African Guidelines for the Prevention of Malaria - updated January 2019.

*APPENDIX 1

Artemether-lumefantrine (Oral) Coartem® (fixed dose artemisinin-based combination therapy, ACT; Novartis South Africa (Pty) Ltd) One tablet contains artemether 20 mg PLUS, lumefantrine 120 mg	5 to < 15 kg	One tablet stat, followed by one tablet after 8 hours. Then one tablet twice daily for the following 2 days (total course = 6 tablets).
 ADVANTAGES FOR USE: Rapid clinical & parasitological response Improved cure rates Decreased malaria transmission Delayed antimalarial drug resistance Short treatment course (6 doses over 3 days) Good tolerability ONLY indicated for treatment of uncomplicated malaria 	15 to < 25 kg 25 to < 35 kg 35 to < 65 kg	Two tablets stat, followed by two tablets after 8 hours. Then two tablets twice daily for the following 2 days (total course = 12 tablets). Three tablets stat, followed by three tablets after eight hours. Then three tablets twice a day for the following 2 days (total course = 18 tablets). Four tablets stat, followed by four tablets after eight hours. Then four tablets twice daily for the following 2 days (total course = 24 tablets).
SIDE EFFECTS: sleep disturbances, headaches, dizziness, palpitation, abdominal pain, anorexia, cough, arthralgia, asthma, fatigue.	> 65 kg	Dosage as for > 35 kg. Close monitoring required.
 SPECIAL PRECAUTIONS: Do not administer in patients with prolonged QT interval OR in patients with a family history of congenital prolonged QT syndrome. Don't administer in patients with risk factors for cardiotoxicity. i.e. hypokalaemia or hypomagnesaemia. 	> 85 kg	Extend the treatment course to FIVE days, administering FOUR tablets per dose, twice daily for a total of 10 doses. (off-label recommendation)

NOTE: administer with food/milk containing at least 1.2 g fat to ensure adequate absorption







*APPENDIX 2

	Increased concentrations	Decreased concentrations
Artemether	Ketoconazole	Lopinavir/ritonavir
	i	Nevirapine
		Efavirenz
		Etravirine
		Rifampicin
Lumefantrine	Lopinavir/ritonavir	Rifampicin
	Darunavir/ritonavir	Efavirenz
	Ketoconazole	Mefloquine
	Nevirapine	Etravirine

*APPENDIX 3

Quinine (Oral)

(Aspen quinine® oral)
One tablet contains 300 mg quinine sulphate

10 mg salt/kg body weight every 8 hours Duration: 7 days

Doxycycline (Oral)

One capsule/tablet contains 50 mg or 100 mg doxycycline

Clindamycin (Oral)

One tablet contains 150 mg clindamycin

Use in combination with quinine: 100 mg (OR 2.2 mg/kg in children) twice daily for at least 7 days. NOTE: avoid in pregnancy and children under eight years of age.

Use in combination with quinine in pregnancy and children under eight years of age: 10 mg/kg twice daily for seven days.

*APPENDIX 4

Chloroquine (Oral)

Use for CONFIRMED non-falciparum malaria only. One tablet contains 150 mg chloroquine base.

ADULTS

1.5 g over 3 days. Initially 600 mg, Followed by 300 mg 6 - 8 hours later, and, 300 mg once daily on 2nd & 3rd days. **CHILDREN**

Initial dose: 10 mg base/kg then 5 mg base/kg 6 – 8 hours later, AND 5 mg base/kg once daily on nd 3rd 2 and days.

Primaquine (Oral)*

One tablet contains 26.3 mg primaquine phosphate = 15 mg primaquine base.

*Not registered in South Africa; provision for Section 21 use. **ADULTS**

15 mg base daily for 14 days following standard treatment, OR 0.25 - 0.5 mg base/kg daily for 14 days.

(a 14-day course is needed for radical cure of P. ovale & P. vivax) In mild G6PD deficiency - 45 mg base once a week for eight weeks. CONTRAINDICATED in pregnancy & women who are breastfeeding a child under 6 months of age.

CHILDREN

0.25 - 0.3 mg base/kg daily for 14 days.

In mild G6PD deficiency: 0.5 - 0.8 mg base/kg weekly for 8 weeks. CONTRAINDICATED in children under 6 months of age, G6PD deficiency.



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*APPENDIX 5

Artesunate (intravenous) Garsun® injectable Equity Pharmaceuticals (Pty) Ltd Patients weighing > 20 kg: 2.4 mg/kg at 0, 12 and 24 hours then daily until patient can tolerate oral treatment.

Children weighing < 20 kg: 3 mg/kg at 0, 12 and 24 hours then daily until patient can tolerate oral treatment.

Quinine Adco-quinine® injectable (Adcock Ingram)

ADULTS

Loading dose: 20 mg/kg body weight of quinine dihydrochloride salt, diluted in 5 - 10 mL/kg body weight of 5% Dextrose water, given by intravenous infusion over 4 hours.

Maintenance dose: eight hours after loading dose, 10 mg/kg body weight of quinine dihydrochloride salt, diluted in 5 - 10 mL/kg of a Dextrose containing solution, given intravenously over 4 hours.

Administered every 8 hours until the patient can tolerate oral medication

(usually by 48 hours).

CHILDREN

Loading dose: 20 mg/kg body weight of quinine dihydrochloride salt, diluted in 5 - 10 mL/kg body weight of 5% Dextrose water, given by intravenous infusion over 4 hours.

Maintenance dose: 10 mg/kg body weight of quinine dihydrochloride salt, diluted in 5 - 10 mL/kg of a Dextrose containing solution, given intravenously over 4 hours.

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