

MALARIA TREATMENT PROTOCOL (As per National Drug Policy 2008)

1. All clinically suspected cases should preferably be investigated for malaria by microscopy and/ or Rapid Diagnostic Kit (RDK).

Diagnosis by RDK is must in

- (a) Clinically suspected malaria patient with altered sensorium attending OPD/ IPD/ emergency department of hospital/ BPHC/ PHC
- (b) Patient, residing in/ from malaria high risk area, but microscopy results is not available within 24 hours.
- (c) Outbreak of fever, where malaria is clinically suspected

In addition, simultaneous **blood smears collection for malaria microscopy** is mandatory for (a), (b) and (c).

2. For uncomplicated malaria

- (a) Microscopically positive **PV cases** should be treated with Tab. Chloroquine in full therapeutic dose of 25 mg/ kg body weight (bw) divided over three days as detailed below:
 - Day 0: (First day of treatment) 10 mg/ kg of bw single dose
 - Day 1: 10 mg/ kg of bw single dose
 - Day 2: 5 mg/ kg of bw single dose

This practice is to be followed at all levels including FTDs/ ASHA.

Primaquin should be given in single dose of 0.25 mg/ kg body weight daily for 14 days preferably under medical supervision to prevent relapse except in contraindicated patients which include patients of G6PD deficiency, infants and pregnant women.

- (b) **Plasmodium Falciparum cases** should be treated with
 - (i) **Chloroquin sensitive areas:** Tab. Chloroquin in full therapeutic dose of 25 mg/ kg bw divided over three days.
This practice is to be followed at all levels including FTDs/ ASHA
 - (ii) **Chloroquin resistant areas**, cluster of Blocks and identified districts on the basis of epidemiological situation: The ACT (Artesunate plus Sulphadoxine Pyrimethamin) combination orally is recommended for treatment of Pf cases. The dose is 4 mg/ kg bw of Artesunate daily for 3 days plus 25 mg/ kg bw of sulphadoxine + 1.25 mg/ kg bw of Pyrimethamin on the first day. ACT should be given only to confirmed Pf cases found positive by microscopy or Rapid Diagnostic Kits. Compliance and full intake is to be ensured. **ACT tablet are not to be used in pregnant women.**
 - (iii) In case of resistance to Chloroquin and SP-ACT, oral Quinine 10 mg/ kg bw daily for 3 days with Tab Doxycycline (100 mg) can be prescribed.
 - (iv) Tab. Mefloquin (25 mg/ kg bw, but total dose does not exceed 1000 mg) should only be given to Chloroquin/ multi resistant uncomplicated Pf cases as prescribed by WHO against the prescription of medical practitioners supported by laboratory report showing asexual stages of Pf parasite and not gametocyte alone and other species.
 - (v) **Tab. Primaquin in single dose of 0.75 mg/ kg bw, may be given for gametocyte clearance in Pf and will facilitate effective interruption with transmission irrespective of Chloroquin resistance status of the area.**
- (c) **Chemoprophylaxis** should be administered only in selective Pf endemic areas.
 - i) For short term (less than six weeks) Doxycycline daily in the dose of 100 mg in adults and 1.5 mg/ kg for children (if not contraindicated). The drug should be started 2 days before travel and continued for 4 weeks after leaving the malarious area (not recommended in pregnant women and children less than 8 years of age).
 - (ii) For longer stay (six weeks or more) Mefloquin 250 mg weekly and should be administered two weeks before, during and four weeks after exposure (contraindicated in cases with history of convulsion, neuro-psychiatric and cardiac problem)

3. For severe and complicated malaria

Severe malaria is an emergency and treatment should be given as per severity and associated complications which can be best decided by the treating physicians.

The outline of management is:

1. General Management

- (a) Maintain airway, breathing and circulation (ABC of critical care)
- (b) Monitor temperature, pulse, respiration and other vital signs every 4-6 hours
- (c) Insert a urethral catheter in those with reduced urine output using a sterile technique and attached to a closed urinary drainage system or as otherwise indicated
- (d) Insert a naso-gastric tube to prevent aspiration pneumonia, to look for gastro-intestinal (GI) tract bleeding and for administration of medicines and nutrients
- (e) Change intravenous sites every 72 hours to prevent infection and thrombophlebitis
- (f) Cover eyes with pad to prevent corneal ulcers
- (g) Mouth care should be done to prevent parotid gland infections
- (h) Back care is needed to prevent bedsores
- (i) Fluid intake and output chart should be maintained and reviewed regularly

2. Specific treatment with anti malarials

Parenteral artemisinin derivatives (contraindication - pregnancy) or quinine should be used irrespective of Chloroquin resistance status of the area. However, the guidelines for specific antimalarial therapy as per WHO recommendation are given below:

- (a) **Quinine** salt 20 mg/ kg bw on admission (IV infusion or divided IM injection) followed by maintenance dose of 10 mg/ kg bw 8 hourly; infusion rate should not exceed 5 mg/ kg bw per hour. The parenteral treatment should be given for minimum of 48 hours and once the patient tolerates oral therapy, Quinine 10 mg/ kg bw three times a day with Doxycycline 100 mg once a day or Clindamycin in pregnant women and children under 8 years of age, should be given to complete 7 days of treatment in patient treated with parenteral Quinine. **Quinine is not contraindicated in pregnancy.** Intravenous quinine should be administered at recommended dosage for the first 48 hours even if acute renal failure (ARF) or severe jaundice is present. If there is no clinical improvement after 48 hours of parenteral therapy, the maintenance dose of parenteral quinine should be reduced by one third to a half (i.e., 5-7 mg/kg bw of quinine). The total daily dose of quinine in patients requiring parenteral therapy beyond 48 hours is as follows:

Adults: Day 0: (First day of treatment) 30-40 mg salt/kg of bw

Day 1: 30 mg salt/kg of bw

Day 2 and subsequent days: 15-21 mg salt/kg of bw

Children: Day 0: (first day of treatment) 30-40 mg salt/kg of bw

Day 1: 20 mg salt/kg of bw

Day 2 and subsequent days: 10-14 mg salt/kg of bw

OR

- (b) Artesunate: 2.4 mg/ kg body weight IV or IM given on admission, then at 12 hours and 24 hours, then once a day for 7 days;

OR

- (c) Artemether: 3.2 mg/ kg body weight IM given on admission then 1.6 mg/ kg body weight per day for 7 days;

OR

- (d) Arteether: 150 mg daily IM for 3 days in adults only (not recommended for children);

Followed by full course of ACT to patients completed treatment with artemisinin derivatives (b, c and d).

Use of Mefloquin alone or in combination with Artesunate should be avoided in cerebral malaria due to neuro-psychiatric complications associated with it.

3. Treatment of complications

Detail is summarized in table below:

Clinical Manifestation	Recognition	Laboratory finding	Management
Cerebral Malaria	Unrousable coma in Pf malaria. Every patient of malaria with altered sensorium (abnormal behaviour in a conscious patient in milder form to deep coma in most severe form) should be treated as cerebral malaria, until proved otherwise.	Pf malaria in microscopy and/ or RDK. High parasitaemia, growing stage of parasites (trophozoites and schizonts) and pigment-laden neutrophils indicate poor prognosis. CSF is clear with fewer than 10 WBC per μ l; the protein is often slightly raised	Principals are (1) Care of the unconscious patient (2) Symptomatic management (3) specific antimalarials and (4) management of associated complication
Severe Anaemia	Conjunctiva; tongue, lips and palms are pale	Hb < 5 g/dl; Haematocrit < 15%	Transfusion of whole blood, preferably packed cells or settled cell. Selected indication of blood transfusion (1) rate of fall of Hb 20% or more per day (2) Hb concentration < 5 g/ dl (3) DIC
Oliguria or anuria/ Acute renal failure	Urine output < 400 ml/ 24 hrs in adults and < 0.5 ml/ kg/ hour in children	Serum creatinine > 3 mg/ dl in adults and > 1.5 mg/ dl in Children	Principals are (1) fluid replacement (2) Loop diuretics (furosemide IV 40 – 250 mg) (3) Treatment of associated hypervolaemia, shock, hyperkalamia, acidosis and anaemia.
Hypoglycaemia	Anxiety, sweating, palpitation, dilatation of pupils, breathlessness, convulsion	Blood sugar < 40 mg/ dl or 2.2 mmol/ L. Monitor sugar level to regulate dextrose infusion	50% glucose injection 50 ml (1 ml/ kg in children) followed by 5% or 10% dextrose infusion.
Metabolic acidosis	Laboured hyperventilation with increased inspiratory effort and clear chest on auscultation	Arterial pH < 7.35 or plasma bicarbonate < 15 mmol/ L	Rehydration of patient; care to avoid over hydration. Sodium bicarbonate may be given once only in severe acidosis (Arterial pH < 7.35). Treatment of severe anaemia with blood transfusion
Ac. Pulmonary Oedema	Tachypnoea, dyspnoea and bilateral basal rales	Bilateral infiltration of lungs on chest X-ray	Keep the patient semi-upright at 45 ⁰ ; O ₂ ; IV furosemide (if vol. overload)
Spontaneous bleeding	Gums, nose, vene puncture sites, G I tract	Blood test suggestive of DIC	Fresh blood, blood clotting factors or platelet may be transfused
Haemoglobinuria	Dark red or black coloured urine	Urine is positive for haemoglobin	Continue antimalarial and donot withdraw Quine doses if patient receiving it. Transfuse fresh blood if needed. In case of renal failure dialysis is required
Circulatory collapse	Cold, clammy and cyanotic skin and extremities(core skin temperature difference is > 10 ⁰ C), weak peripheral pulse and hypotension (systolic BP < 80 mg Hg)	Blood culture for gram identification of negative septicemia	5% Dextrose saline for correction of hypovolemia. If patient does not response adequately administer inotropic drugs dopamine 5-20 μ g/ kg/ min Third generation Cephalosporines for gram negative septicemia

Common error in management

(A) Failure to diagnose malaria infection

- a) Index of suspicion of Pf malaria at the earliest is the hallmark of better prognosis
- b) Malaria may not be diagnosed because of similar clinical presentation of several diseases like viral encephalitis, meningitis, hepatitis, enteric fever, leptospirosis, dengue, influenza and other viral diseases.
- c) Wrongly diagnosed if history of recent travel to endemic area is not properly elicited.

(B) Failure to diagnose associated or complicating condition

- a) Hypoglycaemia
- b) Gram-negative septicaemia

(C) Error in fluid and electrolyte replacement

(D) Errors in anti malarial chemotherapy

- a) Delay in starting treatment: Mortality is higher in severe malaria patients who have not received any antimalarials before hospitalization than those who have received the same.
- b) Unjustified withholding/ inadequate dosage: **Quinine dosage should not be altered in the first 48 hours even in case of renal failure or jaundice.**
- c) Dangerous route of administration: Quinine if given **rapidly** through the IV route (IV push) may cause serious cardiovascular complications and even lead to death. Intramuscular Quinine may cause severe local reaction and chloroquine may lead to fatal hypotension because of erratic absorption in severe malaria. Therefore these drugs can be administered through the intramuscular route only when the intravenous access is not available. Failure to control the rate of intravenous infusion: Volume of infusion fluid for administration of quinine can be reduced to half (Quinine dihydrochloride 10 mg salt/kg bw diluted into 5 ml, or 1 mg of quinine salt /0.5 ml of fluid) if volume overload is suspected. However, the duration of infusion should be the same.
- d) Early ambulation of patients under Quinine therapy: Patient should be kept in bed while on parenteral quinine to avoid severe postural hypotension

Important Monitoring parameters

- i. **Pulse and blood pressure should be monitored ideally every hour and at least once in six hours while the patient is on quinine, particularly for those with underlying heart diseases or taking anti-arrhythmic drugs**
- ii. **Intake and Output chart**
- iii. **Haemoglobin percentage**
- iv. **Blood sugar estimation (6 hourly) specially in pregnant women/ patient treated with quinine**
- v. **Serum Creatinine (in case of oliguria or anuria/ renal failure)**
- vi. **Follow up blood smear for level of parasitaemia**

Referral of patient with severe malaria to tertiary care hospital

- (a) Patient requiring dialysis
- (b) Patient requiring artificial ventilation
- (c) Severe anaemia require blood component transfusion
- (d) Multi-organ failure