

# N-AcetylCysteine as anti-oxidative treatment in severe malaria

**Submission date**  
12/09/2005

**Recruitment status**  
No longer recruiting

☐ Prospectively registered

☐ Protocol

**Registration date**  
14/10/2005

**Overall study status**  
Completed

☐ Statistical analysis plan

☒ Results

**Last Edited**  
21/03/2013

**Condition category**  
Infections and Infestations

☐ Individual participant data

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Dr Arjen Dondorp

**Contact details**  
Wellcome Unit  
Faculty of Tropical Medicine  
420/6 Rajvithi Road  
Bangkok  
Thailand  
10400  
+66 (0)2 3549172  
arjen@tropmedres.ac

## Additional identifiers

**Protocol serial number**  
077166

## Study information

**Scientific Title**  
A randomised, double-blind, placebo-controlled trial of N-AcetylCysteine as adjunctive therapy in the treatment of severe falciparum malaria

**Acronym**

NAC Study

**Study objectives**

A previous pilot study in Thailand in patients with severe malaria suggested that N-acetylcysteine (NAC) shortened the time to normalisation of plasma lactate and Glasgow Coma Score, both well established markers of disease severity and prognosis. NAC is an antioxidant drug widely used in the treatment of paracetamol poisoning and is being investigated for beneficial effects in a diverse range of diseases. It is very safe. We propose to extend the malaria pilot study to a larger randomised, double-blind, placebo-controlled trial of N-acetylcysteine as adjunctive therapy in the treatment of severe falciparum malaria.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Not provided at time of registration

**Study design**

Randomised controlled trial

**Primary study design**

Interventional

**Study type(s)**

Treatment

**Health condition(s) or problem(s) studied**

Falciparum malaria

**Interventions**

This will be a randomised, double-blind, placebo-controlled trial of the efficacy and safety of N-acetylcysteine in the adjunctive treatment of severe falciparum malaria, enrolling 100 patients.

Antimalarial and supportive treatment will be in accordance with international (World Health Organisation [WHO] 2000) and local hospital guidelines. Antimalarial drug treatment will be with intravenous artesunate (2.4 mg/kg body weight stat followed by 2.4 mg/kg at 12 hours and 24 hours and then every 24 hours) and, when able to take oral medication, artesunate (50 mg) tablets to give a total artesunate dose of 12 mg/kg over a total of seven days. NAC will be given in the standard regime used in the treatment of paracetamol toxicity:

1. 150 mg/kg in 200 ml 5% dextrose water (5% DW)/15 min
2. Then 50 mg/kg in 500 ml 5% DW/4 hours
3. Then 100 mg/kg in 1000 ml 5% DW/16 hours

The anticipated end date of this trial has been extended to the end of 2007. The previous end date was 1st October 2006.

**Intervention Type**

Drug

**Phase**

Not Applicable

**Drug/device/biological/vaccine name(s)**

N-acetylcysteine

**Primary outcome(s)**

1. Serial plasma lactate, glucose, serum creatinine, bilirubin and acid-base status
2. Serial Glasgow Coma Score (GCS) and vital signs
3. Parasite clearance time
4. Adverse events

**Key secondary outcome(s)**

1. Serial red cell deformability
2. Serial observation of the microcirculation on the mucosal surface using a non-invasive method, Orthogonal Polarising Spectrometry (Groner et al, 1999)
3. Serial plasma cytokine (Interleukin [IL]-6, 8, 10 and Tumour Necrotising Factor [TNF]) concentrations and measures of oxidative stress (F2-isoprostanes)
4. Mortality

**Completion date**

31/12/2007

## Eligibility

**Key inclusion criteria**

Adults patients (more than or equal to 16 years old, either sex) with a diagnosis of severe malaria: asexual Plasmodium falciparum parasitaemia with one or more of the following criteria:

1. Glasgow coma scale less than 11
2. Haematocrit less than 20% with parasite count more than 100,000/mm<sup>3</sup>
3. Jaundice with bilirubin more than 2.5 mg/dl with parasite count more than 100,000/mm<sup>3</sup>
4. Serum creatinine more than 3 mg/dl with urine less than 400 ml/24 hours
5. Hypoglycaemia with venous glucose more than 40 mg/dl
6. Systolic blood pressure less than 80 mmHg with cool extremities
7. Peripheral asexual stage parasitaemia more than 10%
8. Peripheral venous lactate more than 4 mmol/l
9. Peripheral venous bicarbonate less than 15 mmol/l

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Sex**

All

**Key exclusion criteria**

1. Inability or unwillingness to give informed consent by patient or attendant relatives
2. Pregnancy or breast feeding. A pregnancy test will be performed on indication
3. Known hypersensitivity to NAC
4. History of asthma or wheeze detected on auscultation on admission
5. Previous treatment with lactate containing intravenous fluid (e.g. Ringers Lactate Solution)

**Date of first enrolment**

01/06/2004

**Date of final enrolment**

31/12/2007

## Locations

**Countries of recruitment**

Thailand

**Study participating centre**

Wellcome Unit

Bangkok

Thailand

10400

## Sponsor information

**Organisation**

University of Oxford (UK)

**ROR**

<https://ror.org/052gg0110>

## Funder(s)

**Funder type**

Charity

**Funder Name**

The Wellcome Trust (UK) (grant ref: 077166)

## Results and Publications

## Individual participant data (IPD) sharing plan

### IPD sharing plan summary

Not provided at time of registration

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/02/2009		Yes	No