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N-AcetylCysteine as anti-oxidative treatment in severe malaria

Submission date	Recruitment status	[_] Prospectively registered
12/09/2005	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
14/10/2005	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
21/03/2013	Infections and Infestations	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet

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 measure
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

Secondary outcome measures
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

Overall study start date
01/06/2004

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^3
3. Jaundice with bilirubin more than 2.5 mg/dl with parasite count more than 100,000/mm^3
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 extremeties
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

Age group
Adult

Sex
Both

Target number of participants
100 - recuitment ends 1st October 2006

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)

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Sponsor type
University/education

Website
http://www.ox.ac.uk/

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Charity

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

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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?
Results article	results	01/02/2009		Yes	No