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Timing of enteral feeding in cerebral malaria in the tropical setting: a randomised trial

Submission date	Recruitment status	[X] Prospectively registered
21/05/2008	Stopped	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
30/05/2008	Stopped	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
29/07/2010	Infections and Infestations	[_] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr Arjen Dondorp

Contact details
Mahidol-Oxford Research Unit
Faculty of Tropical Medicine, Mahidol University
3rd Floor, 60th Anniversary Chalermprakiat Building
420/6 Rajvithi Road
Khet Ratchathevi
Bangkok
Thailand
10400

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
BKMAL0802; 077166

Study information

Scientific Title

Study objectives
Although the treatment with artesunate compared to quinine considerably reduces mortality in severe and cerebral malaria, the case fatality rate remains high at between 20% and 30%. Improved supportive care can importantly further reduce mortality; a series from a well equipped intensive care unit in Paris showed a mortality of 11% in patients with severe malaria. Supportive treatments include highly technical aids like renal replacement therapy and mechanical ventilation, but also easier to achieve treatments like enteral feeding.

In the well equipped intensive care setting early start of enteral feeding in a wide variety of patients, including those with sepsis, is now common practice. Nutrition supplies vital cell substrates, antioxidants, vitamins, and minerals, essential for normal cell function. Studies have shown that early enteral feeding preserves the barrier function of the gut, has positive effects on immune functions, is associated with a decrease in hypermetabolism and organ failure, and reduces the chance of bacteraemia. In severe malaria, patients are often poorly nourished and hypoglycaemia is a common complication, especially in patients receiving quinine. Also, bacteraemia with Salmonella species is more common in severe malaria, associated with increased bacterial translocation in the gut. Enteral feeding might have a beneficial effect here.

The downside of starting enteral feeding in the dependent comatose patient is the risk of aspiration pneumonia; this risk is also present in the mechanically ventilated patient, although the risk is lower with the use of post-pyloric enteral feeding tubes. A supine position of the patient is a risk factor. Routine endotracheal intubation to protect the airway in comatose malaria patients is not a feasible option in most of the tropical countries where malaria is endemic. The use of enteral feeding through a naso-gastric (NG) tube might thus induce a much higher risk of aspiration pneumonia, outweighing the theoretical benefits.

At Chittagong Medical College Hospital (CMCH), the current practice is to start early enteral feeding through a NG-tube, with a volume of 2 - 4 ml/kg per feed every two hours, avoiding two late night feeds, resulting in a total of 10 feeds per day (for adults); in case of children daily fluid supplementation are as such from aged 2 - 4 years 100 - 120 ml/kg, 4 - 8 years 90 - 100 ml/kg, 8 - 12 years 70 - 90 ml/kg and greater than or equal to 12 years 60 - 70 ml/kg. Enteral feeding consists of a mix of blended local food. The energy content will be approximately 1 kcal/ml. Although not formally assessed, aspiration pneumonia is a rather common complication of NG feeding in CMCH. Factors that can contribute include the supine position of the patient and no check for gastric retention before the next feeding. We therefore propose a randomised trial to compare the start of early versus late nasogastric tube feeding, with aspiration pneumonia, incidence of hypoglycaemia and coma recovery times as primary outcome measures.

Please note that as of 29/07/2010 this record has been updated with the following status change: "Based on the recommendation of our Data and Safety Monitoring Committee, the trial was stopped because of high incidence of aspiration pneumonia on 02/09/2009". The initial anticipated end date of this trial was 21/12/2010. The intial target number of participants was 200.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval pending as of 21/05/2008 from:
1. The Oxford Tropical Research Ethics Committee
2. The Chittagong Medical College Ethics Committee

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Cerebral Plasmodium falciparum malaria

Interventions
1. Enteral feeding upon admission through the NG tube
2. No feeding until able to take oral food or maximum until 60 hours after admission, followed by enteral feeding

Duration of treatment for both arms: until patient is able to take oral food. Follow up is made up to the point of discharge from the hospital.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
1. Incidence of aspiration pneumonia
2. Incidence of hypoglycaemia (less than 2.2 mmol/L)
3. Coma recovery time. The coma recovery time is defined as the time until a Glasgow Coma Score of 15/15 (BCS 5/5 in preverbal kids).

Secondary outcome measures
1. Incidence of sepsis. Sepsis is defined as the presence of infection (other than malaria) in combination with systemic inflammatory response syndrome (SIRS) as indicated by greater than

or equal to three of the following criteria:
1.1. Prolonged fever, i.e. axillary temperature greater than or equal to 38°C or core temperature of 36°C or lower
1.2. A heart rate of greater than or equal to 90 beats/min
1.3. A respiratory rate of greater than or equal to 20 breaths/min (up to 5 years greater than or equal to 40 breaths/min) or the use of mechanical ventilation for an acute respiratory process
1.4. A white-cell count of greater than or equal to 12 x 10^9/l or less than or equal to 4 x 10^9/l, or a differential count showing greater than 10% immature neutrophils
2. Time to sit independently, which will be assessed daily
3. Time to stand independently, which will be assessed daily
4. Time to eat independently, which will be assessed daily
5. Total duration (days) of admission in the hospital
6. Survival. In hospital mortality will be recorded.

Overall study start date
01/06/2008

Completion date
02/09/2009

Reason abandoned (if study stopped)
Objectives no longer viable

Eligibility

Key inclusion criteria
1. Male and female patients with cerebral falciparum malaria defined as a Glasgow Coma Score (GCS) less than 11 or Blantyre Coma Scale (BCS) less than 3 (for pre-verbal children), and the presence of asexual forms of Plasmodium falciparum in the peripheral blood smear
2. The patient or attending relative able and willing to give informed consent
3. Greater than or equal to 2 years of age

Participant type(s)
Patient

Age group
Other

Sex
Both

Target number of participants
56

Key exclusion criteria
1. Patient or relatives unable or unwilling to give informed consent
2. Patients who already have the features of aspiration pneumonia
3. Contraindications to enteral feeding:
3.1. Circulatory shock
3.2. Mechanical bowel obstruction/ileus/ischaemic colitis

3.3. Severe diarrhoea, severe vomiting
3.4. Pancreatitis
4. Known allergies to artesunate or quinine
5. Pregnancy
6. Severely malnourished child (according to World Health Organization [WHO] criteria)

Date of first enrolment
01/06/2008

Date of final enrolment
02/09/2009

Locations

Countries of recruitment
Bangladesh

Thailand

Study participating centre
Mahidol-Oxford Research Unit
Bangkok
Thailand
10400

Sponsor information

Organisation
University of Oxford (UK)

Sponsor details
Manor House
John Radcliffe Hospital
Headington
Oxford
England
United Kingdom
OX3 9DU

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