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To compare the response of children with sickle cell disease (SCD) and malaria to artemisinin combination therapy (ACT) antimalarials and the response of children without SCD treated with ACT for malaria

Submission date
25/09/2013

Recruitment status
No longer recruiting

Registration date
02/10/2013

Overall study status
Completed

Last Edited
23/09/2014

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Although there has been a general improvement in the availability of treatment for malaria, information on how currently recommended drugs work on patients with sickle cell disease (SCD) is unavailable. This study will provide some evidence and tell us whether current doses for treating malaria in SCD patients (which are the same for patients without SCD) may be appropriate.

Who can participate?
Children with SCD aged 6 months to 12 years, and children without SCD, with uncomplicated malaria can participate in the study.

What does the study involve?
All children will have a blood test for malaria and any other test that would be deemed necessary for treatment by the doctor. Children with a confirmed diagnosis of malaria will be randomly allocated to one of two treatments: artesunate-amodiaquine or artemether-lumefantrine. Recruited children will attend follow-up visits so that doctors will check if they are recovering and how quickly, whether the malarial parasites are being cleared from their blood, and whether any initially cleared parasites will recur. The follow-up visits are also for the purpose of checking for possible side effects of the treatment. There will be at least eight follow-up visits. Children who do not recover as expected will be given alternative medications. On days 1 and 2, only a finger prick blood test will be done to check for the presence of parasites. On days 3, 7, 14, 28, 35 and 42, a small amount of blood (about a teaspoonful) will be taken to find out the state of certain components of the blood in addition to a parasite check.

What are the possible benefits and risks of participation?
There will be no direct financial benefits. Participation will allow investigators to find out if

children with SCD show a similar response to treatment as children without SCD. However, the child will be watched closely for a period of six weeks during which any illness could be promptly diagnosed and treated without any additional costs. No direct incentives will be provided, although all treatment and laboratory costs during the period will be borne by the study, and all transport costs for the follow-up visits will be reimbursed. The volume of blood collected is small and similar to what is normally collected during similar illness, and is unlikely to affect the health of the participant. As with any drug, there is a small risk that participants may experience certain side effects associated with the use of these medicines. However, these drugs have been shown to be safe in children without SCD and the purpose of the follow-up visits is to find out if this is so in SCD patients. In addition, the investigators will be monitoring for these potential effects during the follow-up visits and would act appropriately should these occur.

Where is the study run from?
The study is run from Paediatric Sickle Cell Clinic and Emergency Department of the Department of Child Health, Korle Bu Teaching Hospital (Ghana) and Outpatients Department of the Polyclinic, Korle Bu Teaching Hospital (Ghana).

When is the study starting?
The study started in January 2011 and ended in December 2012.

Who is funding the study?
The study is funded by the Consultative Council for Development Research of Denmark, through the DANIDA Fellowship Centre, Denmark.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title
Artesunate-amodiaquine versus artemether-lumefantrine for uncomplicated malaria treatment in children with or without sickle cell disease: a randomized efficacy and safety trial

Study objectives
1. The response to malaria treatment with artemisinin combination therapies in children with sickle cell disease is different from children without sickle cell disease.
2. The haematological profile of children with sickle cell disease treated with artesunate-amodiaquine is different from that of children treated with artemether-lumefantrine.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics and Protocol Review Committee, University of Ghana Medical School; Ref: MS-Et/M.1-P.5.4

Study design
Open label randomized clinical trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Sickle cell disease/malaria

Interventions
1. Artesunate-amodiaquine (Coarsucam®, Sanofi Aventis, France) - 25/50/100mg artesunate and 67.5/135/270mg amodiaquine, single daily dose, administered for three days according to body weight: 4.5-9kg (25mg/67.5mg), 1 tablet/dose; 9-18kg (50mg/135mg), 1 tablet/dose; 18-36kg (100mg/270mg), 1 tablet/dose; 36kg and over (100mg/270mg), 2 tablets/dose

2. Artemether-lumefantrine (Coartem®, Novartis Pharma AG, Basel, Switzerland) - 20mg artemether and 120mg lumefantrine administered at 0 and 8 hours on the first day, and then twice daily for two subsequent days according to body weight: 5-14kg, one tablet/dose; 15-24kg, 2 tablets/dose; 25-34kg, 3 tablets/dose; 35kg and over, 4 tablets/dose

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Artesunate-amodiaquine, artemether-lumefantrine

Primary outcome(s)
1. Parasite clearance rates in the initial 48 hours of treatment: survival analysis
2. Parasite reduction ratio on days 1, 2, and 3: the ratio of the parasite count before treatment to the parasite count on days 1, 2, and 3

Key secondary outcome(s))
1. Cure rates as determined by PCR-corrected adequate clinical and parasitological response (ACPR): the proportion of patients with ACPR on days 28 and 42
2. Parasitological response on days 28 and 42: any recurrence of parasitaemia after initial clearance till day 28 or 42
3. Changes in haematological profiles during the follow-up period: changes from baseline (day 0) in the following parameters: haemoglobin (Hb), total white blood cell count (WBC), absolute neutrophil count (ANC) and platelet counts (PLT) on days 3, 7, 28, and 42
4. Incidence of adverse events: incidence of new or treatment-emergent adverse events on days 3, 7, 28 and 42

Completion date
31/12/2012

Eligibility

Key inclusion criteria
1. Children with SCD
2. Aged 6 months to 12 years
3. With acute P. falciparum malaria of parasite density < 200,000/µl
4. Consent obtained and willingness by parent or guardian to comply with the follow-up schedule

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
6 months

Upper age limit
12 years

Sex
All

Key exclusion criteria
1. Symptoms or signs of severe malaria requiring parenteral treatment
2. Weight less than 5 kg
3. Presence of danger signs of malaria
4. Known intolerance or allergy to study medications

5. Reported treatment with any of the study drugs one month preceding enrolment
6. Blood transfusion preceding 3 months before enrolment

Date of first enrolment
04/01/2011

Date of final enrolment
31/12/2012

Locations

Countries of recruitment
Ghana

Study participating centre
Centre for Tropical Clinical Pharmacology & Therapeutics
Accra
Ghana
KB

Sponsor information

Organisation
Danida Fellowship Centre (Denmark)

ROR
https://ror.org/05qvpbw57

Funder(s)

Funder type
Research organisation

Funder Name
Consultative Research Committee for Development Research (Denmark) (FFU)/Danida Fellowship Centre, (DFC project no. 09-080RH)

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?
Results article	results	19/09/2014		Yes	No