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Sulfadoxine-pyrimethamine combinations study

Submission date 06/04/2005	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 22/07/2005	**Overall study status** Completed	
Last Edited 19/10/2016	**Condition category** Infections and Infestations	

Plain English summary of protocol

Background and study aims
Malaria is a serious tropical disease caused by a parasite that is spread by mosquitoes. Antimalarial medication is used to prevent and treat malaria. However, resistance to antimalarial drugs can develop when genetic mutations allow the parasite to survive in the presence of the drug. The development of resistance is of huge public health concern. In Malawi, sulphadoxine-pyrimethamine (SDX-PYM) replaced chloroquine (CQ) in 1993 as the first-line treatment for uncomplicated malaria because of high levels of CQ resistance. However, SDX-PYM resistance is increasing. Combination treatment with two or more drugs working by different mechanisms is proposed as a means to delay the development of resistance. Combination treatments containing artemisinin (ART) are proposed as ideal for this purpose because they kill malaria parasites very rapidly and no resistance had been reported at the time of this study. There is also evidence supporting the possible use of a non-ART combination treatment as a possible alternative. Since CQ was withdrawn in 1993 there has been evidence suggesting a possible return of CQ sensitivity. Amodiaquine (AQ) in combination with SDX-PYM has been shown to be effective and well tolerated in Uganda in an area of high-level CQ resistance. This issue is of huge public health importance as combinations of CQ or AQ plus SDX-PYM would be considerably more affordable compared to ART combination treatment. The aims of this study are:
1. To compare the effectiveness of different antimalarial combination treatments
2. To compare the development of resistance when using these different treatments
3. To investigate what happens to the drugs after they are taken – their absorption and how fast they are eliminated from the body

Who can participate?
Children aged between 1 and 5 with uncomplicated malaria

What does the study involve?
Participants are randomly allocated to receive one of four treatment combinations:
1. SDX-PYM (single oral dose) and placebo (dummy drug)
2. SDX-PYM (single oral dose) + CQ (once daily for 3 days)
3. SDX-PYM (single oral dose) + Artesunate (once daily for 3 days)
4. SDX-PYM (single oral dose) + AQ (once daily for 3 days)
Participants are followed up for 42 days to assess their response to treatment and the development of resistance or side effects.

What are the possible benefits and risks of participating?
The treatments offered all contain SDX-PYM, the standard treatment for malaria in Malawi, plus an additional medicine – placebo, CQ, AQ or ART. Apart from the placebo, all of these treatments are expected to improve the cure rates for the children. Participation in the study involves additional blood tests for all the children and additional visits to the clinic. These may be an inconvenience for the children and mothers, but do provide a higher level of care than is otherwise available.

Where is the study run from?
Chileka Health Centre (Malawi)

When is the study starting and how long is it expected to run for?
September 2003 to March 2006

Who is funding the study?
Wellcome Trust (UK)

Who is the main contact?
Dr David Bell
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Contact information

Type(s)
Scientific

Contact name
Dr David Bell

Contact details
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
066681

Study information

Scientific Title
Evaluating strategies to delay the emergence of resistance to antimalarial drugs

Acronym
SP Combinations Study

Study objectives
Compared to sulfadoxine-pyrimethamine monotherapy, the addition of chloroquine or amodiaquine or artesunate results in:
1. Improved clinical and parasitological outcomes at 14, 28 and 42 days
2. Decreased selection of resistance mutations
3. Clinical failures that cannot be explained by the parasite genotype have a pharmacokinetic basis

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Liverpool School of Tropical Medicine, Research Ethics Commitee, 02/03/2002, ref: 01.72
2. University of Malawi, College of Medicine Research Ethics Committee, 05/08/2002, ref: P.01/02/140

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 contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Uncomplicated malaria

Interventions
Four armed, blinded, randomised trial comparing:
1. SP (single oral dose) and placebo
2. SP (single oral dose) and chloroquine (once daily for 3 days)

3. SP (single oral dose) and amodiaquine (once daily for 3 days)
4. SP (single oral dose) and artesunate (once daily for 3 days)

Total duration of follow up in study was 42 days for all participants.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Sulfadoxine-pyrimethamine, chloroquine, amodiaquine, artesunate

Primary outcome measure
1. World Health Organization (WHO) treatment response endpoints on days 14, 28 and 42
2. Selection of Dihydrofolate Reductase (DHFR) and Dihydropteroate Synthetase (DHPS) resistance associated genotypes
3. Fever clearance time
4. Parasite clearance time
5. Change in haemoglobin between day zero to 14
6. Gametocyte prevalence on day seven or 14
7. Adverse events clinical and laboratory

Secondary outcome measures
No secondary outcome measures

Overall study start date
01/09/2003

Completion date
15/03/2006

Eligibility

Key inclusion criteria
1. Age more than or equal to 12 and less than 60 months, either sex
2. Weight more than or equal to 6 kg
3. Pure (on microscopic grounds) P. falciparum parasitaemia of 2000 to 200,000 ul
4. Written consent has been obtained from the parent or legal guardian

Participant type(s)
Patient

Age group
Child

Lower age limit
12 Months

Upper age limit
60 Months

Sex
Both

Target number of participants
450

Key exclusion criteria
1. Severe malaria
2. Antimalarials in previous week
3. Other comcomitant infection at time of presentation
4. Allergy to sulphonamides
5. Involvement in the study in the previous 12 months

Date of first enrolment
01/09/2003

Date of final enrolment
01/02/2006

Locations

Countries of recruitment
England

Malawi

United Kingdom

Study participating centre
Wellcome Trust Tropical Centre
Liverpool
United Kingdom
L69 3GF

Sponsor information

Organisation
University of Liverpool (UK)

Sponsor details
Research Support
Senate House

Abercromby Square
Liverpool
England
United Kingdom
L69 3BX

Sponsor type
University/education

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

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Charity

Funder Name
Wellcome Trust

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

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	13/02/2008		Yes	No