ISRCTN96218197 https://doi.org/10.1186/ISRCTN96218197

Clinical care Bundles for Adult Meningitis in Malawi

Submission date
11/11/2011

Recruitment status
No longer recruiting

Registration date
17/11/2011

Overall study status
Completed

Last Edited
30/10/2017

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
Bacterial meningitis is a very serious infection of the membranes around the brain. In the UK and Europe approximately 20% of adults die of this infection, but in Africa up to 50-60% of adults will die. The survivors are often left with deafness, epilepsy or inability to work. We do not understand why the death rate in Africa is so much higher than in Europe. Two drugs which have been shown to reduce the death rate in Europe (dexamethasone and glycerol) do not work in Africa. We suspect that lack of access to emergency medicine and rapid antibiotics may be part of the reason for the high death rates in Africa. Researchers in America and Europe have dropped the death rate from serious bacterial blood stream infections (sepsis) by initiating rapid treatment including antibiotics and fluid treatments as soon as the sick person comes to hospital. This study is taking this concept, called Early goal directed therapy or known as clinical care bundles and testing if this idea of rapid antibiotics and early treatment of complications like seizures is possible in Africa, and if it can reduce the death rate and complications for patients with meningitis.

Our aims are:
1. To test if the care bundle is feasible by assessing if various clinical targets can be met such as giving antibiotics within one hour of arrival in hospital
2. To see if we can demonstrate that giving the care bundle results in lower numbers of deaths from meningitis and lower rates of complications in survivors.

Who can participate?
We will be asking everyone over the age of 12 who comes to the emergency department of our hospital in Malawi who may have meningitis. To be included you have to have a fever and either a headache, fits, confusion or coma (reduced level of consciousness). We will include both men and women including pregnant women.

What does the study involve?
The study is going to be done in two phases. This is because the emergency department is new in the hospital and we do not know if the care given there will alter the current death rate from meningitis. The first phase will last 1 year and we will monitor the care given in the emergency department, but we will not give any additional treatments to any patient beyond what is

prescribed by the doctor who sees you.
In the next year, phase 2, we will give the following treatments to everyone who presents with meningitis:

- Antibiotics in a drip within 1 hour of arrival in hospital
- Fluids in a drip in the arm if the blood pressure is low
- Oxygen treatment if the blood oxygen levels are low
- Medicine (diazepam and phenobarbitone) in a drip if you have a seizure
- We will elevate your head to 30 degrees from horizontal if you are drowsy
- Glucose in a drip if the blood sugar is low

We will monitor your care for 6 hours in the emergency department and give you any of the above treatments that you may need. Once the 6 hours is completed you will be moved to the medical ward and your care will be taken over by the doctors on that ward. We will come and see you every day on the ward to see how you are doing.
We will then compare the death rates between the first year and second year and see if there is a difference or not.
All of the participants in the second year will be given the same basic treatment and then any additional treatments from the list that you will may need, such as diazepam if you have a fit. All of the participants in the first year Phase 1 will be given the treatments prescribed by the emergency doctor.

What are the possible benefits and risks of participating?
In the first phase of the study you will gain close monitoring by the study nurses, but no additional treatments will be given. There is no additional harm predicted from enrolling in phase 1.
In the second phase when we will give you the care bundle, the main benefit is that your medical care should be given quickly and tailored to your needs. The main risk of this phase is that some of the treatments we are giving such as fluids or anti seizure medication into a drip may worsen the brain swelling from meningitis. We will be closely monitoring this and will be stopping any treatments at the first sign of any problem. The main symptoms of this are worsening sleepiness or coma or fits. Other signs of excessive fluid or other treatments are breathlessness and swelling. We will do our best to minimise any harm that may occur with the treatments that are given.

Where is the study run from?
This study is run from Queen Elizabeth Central Hospital in Blantyre, Malawi in Africa. This is a single site study, and no other sites will be involved. QECH has a long history of meningitis research and has been the site for other major meningitis studies.

When is the study starting and how long is it expected to run for?
We are starting in January 2012 and we expect to recruit for 2 years.

Who is funding the study?
The study is funded by the Wellcome Trust as part of the Wellcome Trust Clinical PhD Fellowships scheme run through Liverpool University www.liverpoolwttc.org.uk

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
P.09/10/980

Study information

Scientific Title
Early goal directed therapy for adult meningitis in Malawi

Acronym
BAM

Study objectives
Early goal directed resuscitation provided through a bundle of standard interventions will have an impact on the outcome in acute adult bacterial meningitis (ABM) in Malawi.

Updated 16/01/2014: this clinical trial has completed recruitment and follow-up; analysis of the results is ongoing.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Liverpool School of Tropical Medicine Research Ethics Committee, UK, 03/11/2010, ref: 10.70
2. College of Medicine Research and Ethics Committe, Malawi, 31/01/2011, ref: P.09/10/980

Study design
Observational non-randomised before/after trial in two phases

Primary study design
Observational

Secondary study design
Non randomised controlled trial

Study setting(s)
Other

Study type(s)
Prevention

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
Bacterial meningitis

Interventions
Participants will be recruited from the triage assessment area if they meet the inclusion criteria by a study nurse.

The duration of the intervention will be 6 hours from initial screening to the point at which attempts to meet all targets have been achieved. Each subject will receive hourly observations including GCS scoring, blood pressure and pulse measurements. A lumbar puncture for the diagnosis of ABM will be performed at the earliest opportunity.

Study nurses and a clinical officer will deliver the bundle following training, using defined targets (table 2) within the AETC. At the end of the 6 hour study period, the bundle will stop, and the subject will be transferred to the medical ward for ongoing routine care.

Clinical care bundle consisting of:
1. Antibiotics (ceftriaxone 2g IV) within 1 hour of arrival
2. Oxygen if SpO2 <92%
2. Intravenous (IV) fluid bolus if mean arterial pressure (MAP) < 70 or systolic blood pressure (BP) <90 plus maintance fluids
3. Seizure treatment with IV diazepam
4. Head elevation 30 degrees if Glasgow Coma Score (GCS) <11
5. Bolus of 50% dextrose if blood glucose <3.5mmol/L

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure

Percentage of targets achieved by the care bundle measured 6 hours from the care bundle initiation

Secondary outcome measures
1. Mortality
2. Seizure frequency
3. Neurological disability at follow up
Measured at day 10 of discharge from hospital and day 40 follow-up in the community for survivors.

Overall study start date
02/01/2012

Completion date
23/12/2013

Eligibility

Key inclusion criteria
1. Screening inclusion criteria
1. 1. All adults > 12 years presenting to the adult emergency trauma centre with fever plus one of headache/convulsions/confusion/neck stiffness (Note: In Malawi the cut off for paediatric medicine is <12 years and all admissions over this age are referred to the adult service)
2. Final inclusion criteria
2.1. Cerebrospinal fluid (CSF) white cell count of >50 cells/mm2, irrespective of human immunodeficiency virus (HIV) status, or visible bacteria in the counting chamber

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
200, 100 in each phase

Key exclusion criteria
1. Screening exclusion criteria
1.1. Known terminal disease
1.2. Head injury
1.3. Proven cerebral malaria
2. Final exclusion criteria
2.1. CSF culture, antigen test or stain for fungal or mycobacterial organisms, or CSF <100 cells /mm3 HIV negative or CSF <5 cells/mm3 HIV positive, or a CSF WCC <50% neutrophils

Date of first enrolment
02/01/2012

Date of final enrolment
23/12/2013

Locations

Countries of recruitment
Malawi

Study participating centre
Malawi-Liverpool-Wellcome Trust clinical research programme
Blantyre
Malawi
Blantyre 3

Sponsor information

Organisation
Liverpool School of Tropical Medicine (UK)

Sponsor details
Pembroke Place
Liverpool
England
United Kingdom
L5 3QA

Sponsor type
University/education

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

ROR
https://ror.org/03svjbs84

Funder(s)

Funder type
Charity

Funder Name
Wellcome Trust (UK) - Clinical PhD scheme through Liverpool University (089671/B/09/Z)

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	27/10/2017		Yes	No