ISRCTN38717320 https://doi.org/10.1186/ISRCTN38717320

Comparison of 5 versus 10 days of ceftriaxone therapy for bacterial meningitis in children: multicentre study in Bangladesh, Malawi, Pakistan, South Africa, Vietnam and Egypt

Submission date
27/07/2004

Recruitment status
No longer recruiting

Registration date
28/07/2004

Overall study status
Completed

Last Edited
25/08/2011

Condition category
Nervous System Diseases

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

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
WHO/CAH ID 98011

Study information

Scientific Title

Study objectives

Primary objective:
To determine if the bacteriologic failure* between 6 - 40 days is equivalent (after randomising the day 5 survivors) between 10 days versus 5 days of ceftriaxone therapy for treatment of acute bacterial meningitis in children aged 2 months up to 12 years.

Secondary objectives:
1. In children who receive 5 versus 10 days of ceftriaxone therapy for acute bacterial meningitis following rates will be compared by day 40 (after admission):
1.1. Mortality rates by day 40
1.2. Hearing loss on day 40
1.3. Blindness on day 40
1.4. Neurologic, motor deficits by day 40
1.5. Treatment failure
1.6. Bacterial pathogens
2. In children who receive 5 versus 10 days of ceftriaxone therapy for acute bacterial meningitis we will compare the rates of the following at 190 + 30 days after admission:
2.1. Mortality rates
2.2. Hearing loss
2.3. Blindness
2.4. Neurologic, motor and developmental deficits

*Bacteriologic failure will be reappearance of bacteria in CSF between 6-40 days

Please note that after discussions with the Data Safety Monitoring Board (DSMB), the following was decided:
1. In the DSMB meeting in 2002, in order to improve enrolment, the age of enrolment was increased to 144 months. Therefore, the upper limit of weight was also increased from 18.5 kg (see changes made to inclusion criteria)
2. In the DSMB meeting in 2006, due to the challenge in enrolling 1500 children (the original target number of participants, the DSMB decided to stop enrolment after reviewing the interim analysis data. They felt that continuing the trial to achieve the sample size to that originally planned is unlikely to alter in an important way the findings, or the recommendations based on those findings.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Ethics approval received from the Institutional Review Board (IRB) of:
1. Dhaka Shishu Hospital, Institute of Child Health, Dhaka, Bangladesh
2. Abbasiyya Fever Hospital, Cairo, Egypt
3. College of Medicine, Blantyre, Malawi
4. Pakistan Institute of Medical Sciences, Islamabad, Pakistan
5. Aga Khan University, Karachi, Pakistan

6. Children Hospital No 1, Ho Chi Minh City, Vietnam
7. University of Natal, Durban
8. World Health Organization (WHO) Ethical Review Committee

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Bacterial meningitis

Interventions
All children to receive ceftriaxone once daily for 1 - 5 days.
From 6 - 10 days children will be randomised to receive the same dose of ceftriaxone or placebo.

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome measure
Rate of bacteriologic failure defined as:
1. Cerebrospinal Fluid (CSF) or blood culture positive* on day 6 to 40 for original organism, or
2. CSF or blood culture positive on days 6 to 40 in a patient who had culture negative bacterial meningitis

Note: Repeat lumber puncture will be done between 48-72 hours of admission. A repeat blood cultures will only be done if condition of the patient requires it.

*for H. influenzae, S. pneumoniae, N. meningitidis

Secondary outcome measures
1. Perceived treatment failure
2. Hearing loss: Day 40 screen Otoacoustic Emissions (OAE), Auditory Brainstem Response (ABR)

greater than 40 db
3. Blindness diagnosed at day 40
4. Motor deficit at day 40 including:
4.1. Two or more abnormalities of tone or strength in any of the limbs or neck, or
4.2. Any palsy of VI or VII cranial nerves
5. Developmental score: abnormal developmental screening on day 190 + 30 days as evaluated by Denver Screening method
6. Seizures: any seizure without fever presenting on days 10 to 40 or 41 to 190 + 30 days
7. Hydrocephalus: defined as any patient with ventriculo-peritoneal shunting or clinical signs and head circumference measurements consistent with hydrocephalous and the perceived need of ventricular derivation
8. Death of an enrolled patient by any cause between days 6 - 40
9. Death of an enrolled patient by any cause between 41 - 190 days
10. Bacterial pathogen

Overall study start date
01/09/2002

Completion date
14/06/2006

Eligibility

Key inclusion criteria
1. Aged 2 - 71 months (as of 11/10/07 the upper age limit was increased to 144 months)
2. Weight 3.0 kg - 18.5 kg (as of 11/10/07 the upper weight limit was increased)
3. Children of acute bacterial meningitis with positive Cerebrospinal Fluid (CSF) culture or latex for H. influenzae, St. pneumoniae, N. meningitidis
4. If CSF culture negative, then CSF White Blood Cell count (WBC) greater than 10/ml and blood culture positive by day 3
5. Treatment with injectable ceftriaxone since admission
6. Informed consent from parent/guardian

Participant type(s)
Patient

Age group
Child

Lower age limit
2 Months

Upper age limit
71 Months

Sex
Both

Target number of participants
1500 (787 recruited as of end of trial)

Key exclusion criteria
1. Neurological conditions
2. Known cerebral palsy, immunodeficiency or chronic afebrile seizure disorder
3. Progressive brain degenerative disorder
4. Cranial fracture with or without CSF leak
5. Known cyanotic heart disorder
6. Known deafness prior to admission
7. Evidence of measles, mumps or chicken pox present
8. Child randomised to the study before
9. Illness more than 7 days
10. Allergic to cephalosporins
11. Lives outside follow-up area of study

Date of first enrolment
01/09/2002

Date of final enrolment
14/06/2006

Locations

Countries of recruitment
Bangladesh

Egypt

Malawi

Pakistan

South Africa

Switzerland

Viet Nam

Study participating centre
20, Avenue Appia
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Sponsor information

Organisation

The Department of Child and Adolescent Health (CAH)/World Health Organization (WHO) (Switzerland)

Sponsor details
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Sponsor type
Research organisation

Website
http://www.who.int

ROR
https://ror.org/01f80g185

Funder(s)

Funder type
Research organisation

Funder Name
The Department of Child and Adolescent Health (CAH)/World Health Organization (WHO) (Switzerland)

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	28/05/2011		Yes	No