

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	<input type="checkbox"/> Prospectively registered
Registration date 28/07/2004	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 25/08/2011	Condition category Nervous System Diseases	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

Contact name

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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 lumbar 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

Geneva -27

Switzerland

CH 1211

Sponsor information**Organisation**

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

Sponsor details

20, Avenue Appia
Geneva -27
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CH 1211

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