# 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	Recruitment status	Prospectively registered		
27/07/2004	No longer recruiting	☐ Protocol		
Registration date	Overall study status	Statistical analysis plan		
28/07/2004	Completed	[X] Results		
Last Edited	Condition category	Individual participant data		
25/08/2011	Nervous System Diseases			

## Plain English summary of protocol

Not provided at time of registration

## Contact information

# Type(s)

Scientific

#### Contact name

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#### Contact details

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# Additional identifiers

Protocol serial number 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

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

<sup>\*</sup>Bacteriologic failure will be reappearance of bacteria in CSF between 6-40 days

#### Primary study design

Interventional

#### Study type(s)

Treatment

#### 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(s)

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

## Key secondary outcome(s))

- 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

#### 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

#### Healthy volunteers allowed

No

#### Age group

Child

#### Lower age limit

2 months

#### Upper age limit

71 months

#### Sex

All

#### 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 cvanotic 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

# 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)

#### **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**

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