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Multicentre randomised clinical study to compare the efficacy of chloramphenicol with that of ampicillin plus gentamicin in children aged 2 to 59 months with very severe pneumonia: multicentre study conducted in Bangladesh, India, Mexico, Pakistan, Yemen, Vietnam, and Zambia

Submission date
27/07/2004

Registration date
28/07/2004

Last Edited
25/08/2011

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Respiratory

[_] 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 98022

Study information

Scientific Title

Study objectives
Primary objective:
To evaluate whether injectable ampicillin plus gentamicin reduces treatment failure in children, aged 2 - 59 months, with very severe pneumonia by 30% or more compared to chloramphenicol after completing 5 days of therapy. The specific null hypothesis to be tested is that treatment failure will be equal in children aged 2 - 59 months with very severe pneumonia whether treated with injectable chloramphenicol or injectable ampicillin plus gentamicin.

Secondary objectives:
1. To determine the proportion of treatment failures by 48 hours after randomisation
2. To determine the proportion of children with treatment failure at 11 days after randomisation
3. To determine the proportion of children with treatment failure at 21 - 30 days after randomisation
4. To report the proportion of children who died up to Day 30 after randomisation
5. To determine bacterial pathogens in the etiology of very severe pneumonia
6. To determine the antimicrobial susceptibility of bacterial pathogens causing very severe pneumonia
7. To determine predictors of treatment failure in children with very severe pneumonia

Please note that the following changes have been made to this record: the site at Zambia only enrolled patients form April 2001 to November 2001 and then the enrolment was stopped there. The DSMB ended accrual at the Zambia site after 23 enrolments (2.4% of total) in November 2001 because of a high mortality rate - likely due to Human Immunodeficiency Virus (HIV)/Acquired Immune Deficiency Syndrome (AIDS). A new site at in Ecuador was added in March 2003 that started enrolling patients in April 2003.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval was received from the following Institutional Review Boards (IRBs):
1. Dhaka Shishu Hospital, Institute of Child Health, Dhaka, Bangladesh
2. Dr. Francisco de Icaza Bustamente Children's Hospital, Guayaquil, Ecuador
3. Post Graduate Institute of Medical Research and Education, Chandigarh, India
4. National Institute of Pediatrics, Mexico City, Mexico
5. Rawalpindi General Hospital, Rawalpindi, Pakistan
6. Nishter Medical College Hospital, Multan, Pakistan
7. Al-Sabeen Hospital, Sana'a University, Sana'a, Yemen
8. Children Hospital No 1, Ho Chi Minh City, Vietnam

9. University Teaching Hospital, Lusaka, Zambia
10. Boston University
11. 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
Severe pneumonia

Interventions
For the primary end-point, a total of two looks at the data would require 1,182 patients (591 in each group) to be studied. This sample size assumes a study power of 80% to look for differences between the groups, and maintains an overall two-sided alpha level of 0.05 and includes adjustment for 2% loss to follow-up.

Patients will be radomised to:
Group 1: 5 days of injectable chloramphenicol in hospital followed by 5 days of oral chloramphenicol at home
Group 2: 5 days of injectable ampicillin and gentamicin in hospital followed by 5 days of oral ampicillin and gentamicin at home

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Chloramphenicol, ampicillin, gentamicin

Primary outcome measure
The primary outcome variable is "treatment failure at day 6" defined as follows:
1. If at any time after randomisation the following occur:
1.1. Death
1.2. Development of bacterial meningitis, empyema, septic shock or renal failure
1.3. Serious adverse events leading to change of therapy or any modification of antibiotic

therapy before day 6 (modification of the dosage of the antibiotic will not be considered as a "treatment failure")
1.4. Left Against Medical Advice (LAMA), or withdrawal of consent (reason of including this in treatment failure is because parents may LAMA or withdraw the consent thinking their child is not improving on the study treatment), or loss to follow-up

OR

2. Development of any of the two signs at 48 hours after randomisation:
2.1. Worsening of tachypnoea (defined as 20 breaths above baseline), or
2.2. Development/persistence of abnormal sleepiness or difficulty in awakening, or
2.3. Development/persistence of inability to drink

OR

3. Development of two or more of the following at Day 6 after randomisation:
3.1. Worsening of tachypnoea (defined as 20 breaths above baseline, or
3.2. Development/persistence of abnormal sleepiness or difficulty in awakening, or
3.3. Development/persistence of inability to drink

Secondary outcome measures
1. Treatment failures, as defined above, 48 hours after randomisation
2. Treatment failures, as defined above, 11 days after randomisation
3. Treatment failures, as defined above, 21 - 30 days after randomisation (if a patient develops signs given for treatment failure within two weeks after stopping treatment it will be considered a relapse)
4. Deaths by 21 30 days after randomisation
5. Bacterial pathogens isolated in blood cultures from children with very severe pneumonia
6. Antimicrobial susceptibility in blood culture isolates from children with very severe pneumonia

Overall study start date
01/10/2000

Completion date
01/06/2002

Eligibility

Key inclusion criteria
1. Age 5 - 59 months
2. History of cough or difficult breathing
3. Central cyanosis or inability to drink
4. Caretaker is willing to sign informed consent form

Participant type(s)
Patient

Age group
Child

Lower age limit

5 Months

Upper age limit
59 Months

Sex
Both

Target number of participants
1,182 patients (591 in each group)

Key exclusion criteria
1. Current illness greater than 10 days old
2. Past history of more than two wheezing episodes or diagnosed asthma
3. Known cardiac patient
4. Known Human Immunodeficiency Virus (HIV) infected
5. Known family member to be HIV infected
6. More than 24 hours hospitalisation within the last 7 days
7. History of severe adverse reaction to study drugs
8. Prior enrolment in the study
9. Injection of antibiotic more than 24 hours prior to enrolment
10. Stridor
11. Known renal failure or not passed urine in last 24 hours
12. Cerebral malaria
13. Bacterial meningitis
14. Clinical jaundice
15. Oral thrush
16. Hepatosplenomegaly
17. Follow-up to home not possible

Date of first enrolment
01/10/2000

Date of final enrolment
01/06/2002

Locations

Countries of recruitment
Bangladesh

Ecuador

India

Mexico

Pakistan

Switzerland

Viet Nam

Yemen

Zambia

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
20, Avenue Appia
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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	12/01/2008		Yes	No