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A randomised, open, comparison of penicillin and metronidazole for the treatment of tetanus

Submission date	Recruitment status	[_] Prospectively registered
13/09/2005	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
14/10/2005	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
25/10/2022	Infections and Infestations	

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
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
077166

Study information

Scientific Title
A randomised, open, comparison of penicillin and metronidazole for the treatment of tetanus

Acronym
TS Study

Study objectives
Penicillin given parenterally has been the standard antibiotic treatment for tetanus for more than 50 years. However there are several theoretical disadvantages to its use. Because many patients with tetanus cannot take medicines orally, penicillin must be administered by injection, either IntraMuscular (IM) or IntraVenous (IV). Any noxious stimulus, such as an injection, has the potential to induce potentially lethal spasms.

Penicillin is known to block post-synaptic Gamma-AminoButyric Acid (GABA) and thus is pro-convulsant. It could lower the threshold for convulsions, which may be seen in severe tetanus. Since GABA transmission occurs in skeletal muscles as well as the central nervous system, penicillin could in theory worsen spasms as well. Metronidazole may be given rectally by suppository, thus obviating the need for painful injections. Bioavailability by this route is reasonably high. Metronidazole is known to be effective against Clostridia species. In a small study from Indonesia metronidazole was at least as effective as penicillin in patients with tetanus of moderate severity, although many patient details were not given in the published report. This study aimed to compare IV penicillin and metronidazole suppositories for the treatment of tetanus.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

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
Tetanus

Interventions
Patients entered into the study were randomised to receive:
1. Benzylpenicillin 2 million units (child 25,000 units/kg) IV six-hourly for seven days
2. Metronidazole 1 g (child):
a. 125 mg age four weeks to less than 12 months
b. 250 mg age one to four years
c. 500 mg age five to 12 years
Rectally (PR) eight-hourly for three days then 12-hourly for four days.

Once the patient could reliably tolerate oral medicines the appropriate dose of penicillin G or metronidazole was given by mouth instead of IV or PR, respectively. Patients who were known to be allergic to penicillin received erythromycin instead.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Penicillin and metronidazole

Primary outcome measure
The primary endpoint was mortality.

Secondary outcome measures
The secondary endpoints were recovery times and complication rates.

Overall study start date
01/04/1993

Completion date
01/01/1997

Eligibility

Key inclusion criteria
1. Clinical diagnosis of tetanus
2. Aged more than one month
3. Informed consent from patient or attendant relative (if comatose or aged less than 16 years)

Participant type(s)
Patient

Age group

Not Specified

Sex
Both

Target number of participants
To be added

Key exclusion criteria
Lack of informed consent or age less than one month

Date of first enrolment
01/04/1993

Date of final enrolment
01/01/1997

Locations

Countries of recruitment
Bangladesh

Thailand

Study participating centre
c/o Dr Nick Day
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Sponsor information

Organisation
University of Oxford (UK)

Sponsor details
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Sponsor type
University/education

Website
http://www.jr2.ox.ac.uk/ndm/Tropical_Medicine

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Charity

Funder Name
The Wellcome Trust (UK) (grant ref: 077166)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results	conference abstract	01/03/2002	23/10/2019	No	No