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What is the safe dose of diazepam that can be used as an effective adjunct treatment in organophosphate poisoning?

Submission date	Recruitment status	[ ] Prospectively registered
23/01/2009	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
28/01/2009	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
28/01/2009	Injury, Occupational Diseases, Poisoning	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Study information

Scientific Title
A dose-finding phase II study of diazepam in adult patients presenting with signs or symptoms of acute organophosphate poisoning

Study objectives
What is the safe and effective diazepam regimen in organophosphate (OP) poisoning that could:
1. Reduce mortality and/or the need for ventilation
2. Provide moderate sedation
3. Not cause symptomatic adverse effects on blood pressure

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Sri Lanka Medical Association Ethical Committee gave approval on the 13th January 2006 (ref: 05-023)
2. University of Peradeniya, Faculty of Medicine, Ethical Review Committee gave approval on the 16th November 2007 (ref: 2006/EC/40)
3. Australian Nation University Ethics Committee gave approval on 15th February 2006 (ref: 2005 /354)

Primary study design
Interventional

Study design
Dose escalation phase II randomised controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Organophosphate poisoning

Interventions
The dose escalation relates to a course of diazepam. The first three doses are single doses of 2.5 mg, 5 mg, and 10 mg. The fourth group will receive a dose of 10 mg - and then two subsequent doses of 5 mg at 6 hour intervals. The first cohort of patients (2 controls and 6 diazepam) would receive a loading dose of 2.5 mg. If this is tolerated the next cohort would receive the next highest loading dose (i.e. 5 mg) and so on. If any patients do not tolerate a dose then the trial will be terminated at that dose level. Diazepam would be administered by a slow infusion with the total dose being given over 30 minutes. The study will be nested into observational trials being conducted in the same hospitals.

This standard treatment is determined by the attending physician who maintains clinical responsibility for all patients. While there may be some minor variation between hospitals current care consists of patient resuscitation, gastrointestinal decontamination when indicated, atropinisation and the use of pralidoxime (typically one gram every six hours). All treatment is recorded by the research team. This intervention represents an added treatment to the existing standard of care.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
Number of patients that exhibit possible adverse effects such as:
1. A decrease in level of consciousness (measured using the Glasgow Coma Scale)
2. Respiratory depression (measured by a respiratory rate less than 10, and a tidal volume of less than 180 ml/breath using a Wright's spirometer)
3. Hypotension (blood pressure [BP] less than 90/60 mmHg, or a drop of greater than 20 mmHg systolic in a normotensive patient, i.e. systolic BP less than 140 mmHg)

Monitored every 15 minutes for the first 2 hours of administration of diazepam or placebo and then monitored hourly for the next 3 hours, and thereafter 4-hourly if the patient is clinically well, or more frequently if there are any clinical concerns.

Key secondary outcome(s)
1. Number of patients that required ventilation
2. Changes in electroencephalogram (EEG), arterial blood gas (ABG), tidal volume and capnography
3. Patients who had seizures or died
Monitored at baseline, 1 hour, 12 hours, 24 hours and daily. Continuous capnographic recording shall also be performed.

Completion date
09/06/2009

Eligibility

Key inclusion criteria
Patients (aged 16 to 60 years, either sex) with symptomatic acute OP poisoning

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Patients who do not consent
2. Aged less than 16 years or greater than 60 years
3. Pregnant women and lactating mothers
4. Unavailability of ventilator
5. Patients in whom endotracheal (ET) intubation is likely to be difficult
6. Have a Glasgow Coma Score (GCS) less than 12 at the time of recruitment

7. Ingested benzodiazepines in addition to OP
8. Have established renal or hepatic failure
9. Have indications for therapeutic diazepam
10. Patients who have respiratory failure requiring ventilatory support
11. Patients who have systolic blood pressure of less than 90 mmHg within 2 hours of administration of diazepam

Date of first enrolment
01/11/2008

Date of final enrolment
09/06/2009

Locations

Countries of recruitment
Sri Lanka

Study participating centre
Program Director, Visiting Professor of Medicine
Peradeniya
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Sponsor information

Organisation
South Asian Clinical Toxicology Research Collaboration (SACTRC) (Sri Lanka)

ROR
https://ror.org/04z435g27

Funder(s)

Funder type
Charity

Funder Name
International Collaborative Research Grant:

Funder Name
The Wellcome Trust (UK) (grant ref: 071669)

Funder Name
National Health and Medical Research Council (NHMRC) (Australia)

Alternative Name(s)
National Health and Medical Research Council, Australian Government, NHMRC National Health and Medical Research Council, NHMRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Australia

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary