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

Recruitment status	Prospectively registered
No longer recruiting	☐ Protocol
Overall study status	Statistical analysis plan
Completed	Results
Condition category	Individual participant data
	Record updated in last year
	No longer recruiting Overall study status

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 N/A

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)

Study design

Dose escalation phase II randomised controlled trial

Primary study design

Interventional

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 Sri Lanka 20400

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

Study outputs

Output typeDetailsDate createdDate addedPeer reviewed?Patient-facing?Participant information sheetParticipant information sheet11/11/202511/11/2025NoYes