

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

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

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

Contact name

Prof Andrew Dawson

Contact details

Program Director, Visiting Professor of Medicine
South Asian Clinical Toxicology Research Collaboration (SACTRC)
University of Peradeniya
Peradeniya
Sri Lanka
20400
+94 (0)81 447 9822
adawson@sactrc.org

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

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

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

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 measure

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.

Secondary outcome measures

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.

Overall study start date

01/11/2008

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

Age group

Adult

Sex

Both

Target number of participants

32

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)

Sponsor details

c/o Professor Andrew Hamilton Dawson
Program Director, Visiting Professor of Medicine
University of Peradeniya
Peradeniya
Sri Lanka
20400
+94 (0)81 447 9822
adawson@sactrc.org

Sponsor type

Research organisation

Website

<http://www.sactrc.org>

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)

NHMRC

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

Australia

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