ISRCTN55264358 https://doi.org/10.1186/ISRCTN55264358

Acute organophosphate pesticide poisoning in Sri Lanka: management, complications and pharmacogenetics

Submission date	Recruitment status
29/07/2002	No longer recruiting
Registration date	**Overall study status**
29/07/2002	Completed
Last Edited	**Condition category**
17/02/2015	Injury, Occupational Diseases, Poisoning

[X] 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

GR063560

Study information

Scientific Title
Acute organophosphate pesticide poisoning in Sri Lanka: management, complications and pharmacogenetics

Study objectives
We propose to carry out a double-blind randomised controlled trial (RCT) of pralidoxime in adult patients presenting with a history and symptoms of organophosphate (OP) poisoning. Primary outcome will be in-hospital mortality; secondary outcomes will include the occurrence of serious complications (respiratory arrest, intermediate syndrome) and time requiring assisted ventilation. Analysis will be on an intention-to-treat basis; the effects of reported time to treatment after poisoning and status on admission will also be assessed.

This RCT will be nested into a study of activated charcoal in unselected cases of poisoning (ISRCTN02920054). All investigations and outcome assessments for ISRCTN02920054 will suffice for this RCT. Extra blood samples will not be taken from patients in this RCT.

The main hypothesis is that the pralidoxime will reduce the case fatality rate from 25% to 19%, hence the primary comparison will be pralidoxime versus placebo. The dimethyl versus diethyl state of the OPs is thought to be fundamental for the effectiveness of oximes in OP poisoning. Dimethylated acetylcholinesterase ages quickly such that oximes do not work in vitro more than 12 hours post-ingestion; in contrast, diethylated acetylcholinesterase age slower so that oximes in vitro work for three to four days post-ingestion. Therefore, once the dimethyl/diethyl status has been retrospectively determined, the analysis will be repeated separating the two groups of OP agents.

It is possible that the oxime, if effective in reducing case fatality rates, will be more effective the earlier it is started. Therefore we will assess the trends in clinical effectiveness according to time post-ingestion to start of therapy. This will be repeated once dimethyl compounds have been distinguished from diethyl compounds. We also want to determine whether treatment should be started irrespective of severity. We will therefore assess trends in case fatality rates across a gradient of severity.

We hypothesise that pralidoxime treatment will prevent the occurrence of the intermediate syndrome; this will therefore be an important secondary outcome. This analysis will be repeated once retrospective toxicological analysis has separated dimethyl compounds from diethyl compounds.

Subgroup analyses are planned to look at the consistency of treatment effect across different types of pesticide, i.e. dimethylated versus diethylated OP pesticides, and for locally common pesticides. A further subgroup analysis will be performed according to the presence of reactivatable acetylcholinesterase before treatment, following retrospective assays of ex-vivo reactivatability.

On 14/12/2007 the overall trial end date was changed from 31/05/2007 to 01/07/2007.

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)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Acute organophosphate self-poisoning

Interventions
Atropine and pralidoxime chloride (2 g stat followed by 500 mg/h for up to seven days) versus atropine and saline placebo.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Atropine, pralidoxime chloride

Primary outcome measure
All-cause mortality at hospital discharge

Secondary outcome measures
1. Percentage of patients requiring intubation
2. Time requiring ventilation
3. Percentage of patients developing the intermediate syndrome (cranial nerve palsies and/or proximal weakness, without distal weakness, after resolution of the cholinergic crisis)

Overall study start date
01/05/2004

Completion date
01/07/2007

Eligibility

Key inclusion criteria
All patients (aged 14 years of above, either sex) presenting with history and signs of acute organophosphate self-poisoning in selected Sri Lankan hospitals, requiring atropine.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
1500

Key exclusion criteria
We hope to recruit all patients admitted to the medical wards with a history of acute poisoning and symptoms and signs of organophosphate poisoning, except for those:
1. Under the age of 14 years
2. Known to be pregnant
3. Have previously received Pralidoxime
4. Patients under the age of 16 or unconscious, who are present without relatives

Date of first enrolment
01/05/2004

Date of final enrolment
01/05/2007

Locations

Countries of recruitment
Scotland

Sri Lanka

United Kingdom

Study participating centre
Scottish Poisons Information Bureau
Edinburgh
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Sponsor information

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Sponsor type
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Funder(s)

Funder type
Charity

Funder Name
Wellcome Trust

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

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	30/06/2009		Yes	No