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

Submission date	<b>Recruitment status</b> No longer recruiting	[X] Prospectively registered		
29/07/2002		[_] Protocol		
Registration date	Overall study status	Statistical analysis plan		
29/07/2002	Completed	[X] Results		
Last Edited 17/02/2015	<b>Condition category</b> Injury, Occupational Diseases, Poisoning	Individual participant data		

### Plain English summary of protocol

Not provided at time of registration

### **Contact information**

**Type(s)** Scientific

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#### **Contact details**

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# Additional identifiers

EudraCT/CTIS number

**IRAS number** 

ClinicalTrials.gov number

Secondary identifying numbers

### 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 United Kingdom EH16 4SA

### Sponsor information

**Organisation** University of Oxford (UK)

#### Sponsor details

University Offices Wellington Square Oxford England United Kingdom OX1 2JD +44 (0)1865 270000 Research.services@admin.ox.ac.uk

**Sponsor type** University/education

Website http://www.ox.ac.uk/

ROR https://ror.org/052gg0110

### 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?
<u>Results article</u>	results	30/06/2009		Yes	No