

RCoA Research, Education & Travel Grants 2012
Award: The Stanley Rowbotham Fund

Applicant: Surg Lt Cdr Elspeth Hulse

Project Title: Pulmonary complications from organophosphate poisoning in a Gottingen minipig aspiration model

Project Description

Introduction

Organophosphate (OP) pesticide poisoning is a global problem resulting from both accidental and deliberate exposure. Self-poisoning with ingested shop-bought agricultural pesticide is common and has resulted in 175,000 annual deaths in China, with tens of thousands more in the rural Asia-Pacific region. In Western countries the main threat is the weaponization of organophosphorus compounds. Organophosphates exert their lethal effect predominantly through respiratory failure, followed by cardiovascular collapse which can be complicated by aspiration pneumonitis and the development of Acute Lung Injury (ALI) in the unconscious patient.

One causative factor for the observed increase in mortality and respiratory complications from OP pesticide poisoning may be the solvents contained in formulated pesticides. Treatments for OP poisoning (atropine and oximes) have not changed since the 1950s and so further understanding of the pathophysiological process with an application of potential novel therapies is long overdue.

Methodology

This proposed PhD project will develop a Gottingen minipig model of aspiration pneumonitis and ALI under terminal anaesthesia. This model will be used to answer the research question; What is the relative importance of OP, solvent, and gastric contents as causes of acute lung injury when aspirated?

Once the model is established, we will test drugs that can potentially reduce the severity of ALI in OP pesticide poisoning. If the results are promising they will be used to guide the design of phase II clinical trials.

The minipig model will involve anaesthesia and invasive monitoring including: ECG, LiDCO, BIS, arterial and central lines, with observation of pulmonary mechanics. Protective ventilation strategies will use ARDSnet protocol and SERVO 300A ventilators. After instillation of either OP/solvent/gastric juice in the right distal lobe of the lung via bronchoscope, subsequent BALs, 16 slice CTs and plasma inflammatory markers will be measured for a period of 48-72 hours. During my first PhD year I hope to undertake 2 studies using the new Gottingen minipig model to assess the pulmonary and systemic toxicity of the aspirated OPs dimethoate and methyl parathion.

The technical grade Active Ingredients (AI) [n=5 minipigs], commercial Emulsifiable Concentrate (EC)[n=5] and their solvents [n=5] will be tested alongside gastric juice [n=5] alone. Ideally a control group using saline would be advantageous but is currently not financially viable.

Justification

The results of this research could have profound effects for world health if the common solvent used in shop bought OP pesticide is found to act synergistically with the OP to create a worse ALI. We

would then be able to lobby the commercial companies to try and change the solvent used in the OP manufacture and packaging and therefore decrease needless deaths from OP poisoning. The funding will be used to present these findings at the end of the year.