Intensive Care Management of Organophosphate Poisoned Patient: A Test of Critical Care Services in Nigeria

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Abstract

The management of organophosphate poisoning is challenging, more so in the setting of poor critical care facilities. The management requires the administration of atropine, an antidote (oxime) and supportive care often provided in the ICU.

We report a 35year old male who presented with a history of ingestion of an organophosphate insecticide and features of cholinergic and central nervous system affectation. The patient was managed with intravenous atropine, pralidoxime, ventilator support and other supportive care.

This paper highlights those challenges associated with the management of organophosphate poisoning in our environment.

Keywords: Poisoning; organophosphate; ICU; Developing countries.

Introduction

Pesticide poisonings remain a serious public health problem worldwide. According to the World Health Organization's estimate, 3 million cases of pesticide poisoning occur every year, resulting in more than 250,000 deaths (1). It is known that the pesticides that cause most deaths in rural Asia, and in the world, are WHO Class I and II organophosphorus (OP) pesticides - causing an estimated 200,000 deaths (2). They include nerve agents (Sarin, Toman, Soman), dimethyl compounds (Dichlorvos, Fenthion, Malathion) and diethyl compounds (Chlorpyrifos, Diazinon, Parathion-ethyl). They are cholinesterase inhibitors, and act by phosphorylating acetylcholinesterase (AChE) at nerve endings, this leads to accumulation of acetylcholine(Ach) at nerve endings and overstimulation of effector organs, causing effects due to overstimulation of muscarinic receptors (muscarinic effects) and nicotinic receptors (nicotinic effects).

The oximes are used as antidotes for organophosphate poisoning, they reactivate AChE by attaching to the phosphorus atom, forming an oxime-phosphonate which then splits away from the AChE molecule, examples include Pralidoxime, Obidoxime. Atropine is an anticholinergic drug which acts as a competitive antagonist of the muscarinic effects of organophosphates.

We use the following case of a 35-year old man with organophosphate poisoning to illustrate the challenges associated with the management of organophosphate poisoning in the intensive care unit (ICU) of a hospital in a developing country.

Case report

A 35year old male paint factory worker was admitted in the A&E with altered level of consciousness for a day. He had been found unconscious, with excessive mouth secretions, sweating and with generalized tonic-clonic seizures in his room. A bottle of insecticide labeled Chlorpyrifos was found at his side, no suicide note was found at the scene. He had three episodes of passage of watery stool. He had a pre- morbid history suggestive of depression but no previous history of deliberate self harm.

Patient was immediately taken to a peripheral hospital with secondary health care facility where a gastric lavage was done and he also received intravenous atropine (dose not known) and intravenous fluids (volume not known). After about six hours in the peripheral hospital, he was referred to our centre- a tertiary hospital. On examination at the accident and emergency unit, he was acutely ill looking, febrile, dyspnoeic, on intranasal oxygen, unconscious with a Glasgow coma scale (GCS) of 7/15 and dehydrated, with a

nasogastric tube in situ draining brownish fluid. His pupils were pin point and sluggishly reactive to light, muscle tone was decreased globally. His pulse rate was 82 per minute, blood pressure was 170/100mmHg, respiratory rate was 36 per minute and except for transmitted breadth sounds, the chest was otherwise clear.

Laboratory results showed packed cell volume of 41%, random blood glucose of 115mg/dl, blood film showed one plus of trophozoites of malaria parasite. Results of serum electrolytes, urea and creatinine were within normal limits, except for potassium of 3.1mmol/l.

He was decontaminated by removal of contaminated clothing; skin was cleaned with water and soap and gastric lavage was repeated. Correction of serum potassium then started, in addition to intermittent atropine therapy based on a suspicion of organophosphate poisoning.

The medical team reviewed the patient and commenced him on Amlodipine in view of the elevated blood pressure. He was subsequently admitted into the Intensive Care Unit (ICU) where he had endotracheal intubation and was commenced on mechanical ventilation because of respiratory insufficiency. After administering 2mg of atropine as a bolus dose, an infusion of 0.6mg per hour via a syringe pump continued. In view of the non-availability of facilities for assessing the arterial blood gases, measurements of arterial oxygen saturation and end-tidal carbon dioxide guided ventilator therapy.

Patient was reviewed by the clinical pharmacologist who recommended administration of pralidoxime, atropinisation and monitoring of the renal function. The antidote to organophosphate, which is pralidoxime was not available in the country and frantic effort were made to source it from abroad. A toxicology screen could not be done as facilities for it were unavailable. Meanwhile, intravenous administration of atropine continued at 0.6mg per hour and titrated to effect.

On the 2nd day of admission, he still had copious secretions from the mouth, hourly urine output was adequate, the patient's Glasgow Coma Scale remained 7/15, pulse rate was 78/min, and blood pressure was 147/96mmHg. Fluid input and output were 3350 and 830 ml respectively and feeding via nasogastric tube was commenced. On the 3rd day of admission, the vital signs were stable and urine output was adequate. On the 4th day he had one episode of focal seizure involving the face, lasting 30 seconds, and

seizure was aborted with 2mg intravenous diazepam. On the 5th day of admission, the GCS dropped to 4/15, following seven episodes of focal seizures, each lasting 2 minutes and aborted each time with intravenous diazepam. Fundoscopy did not reveal any evidence of raised intracranial pressure. In addition to other on-going treatment, anti-convulsant (Phenytoin) was commenced.

On the 6th day of admission, GCS was remained 4/15, pupils were 3.5mm bilaterally and sluggishly reactive, there was hypotonia and hyporeflexia in all limbs. On the 7th day of admission, i.e. 8 days after ingestion of the poison, two vials of pralidoxime (each containing 1g) were made available at about 11a.m. One gram of the drug was administered slowly for about 30minutes. Patient's condition improved transiently over the next 24hours with GCS improving from 4/15 to 10/15(tracheal tube in-situ). The second dose of pralidoxime was administered 24 hours later. On the 8th day, patient could communicate by blinking the eyelids, had been seizure free for 24 hours. Urinalysis showed triple phosphate crystals, serum electrolytes and urea results were essentially normal except for low serum potassium of 2.6mmol/l and packed cell volume was 43%. Plan was put in place to correct the serum potassium correction over 48 hours. On the 9th day, patient was still seizure free, however examination of the chest revealed bilateral coarse crepitations. He had a chest X-ray which did not show remarkable findings, however, he was started on broad spectrum antibiotics, chest and limb physiotherapy.

By the 12th day, the endotracheal got dislodged and because of inadequate oxygen saturation and tachypnoea, the endotracheal tube was replaced and patient continued on ventilator support. He was subsequently scheduled to have an elective tracheostomy, unfortunately, his condition deteriorated the same day and he suffered a cardiac arrest for which all resuscitative efforts failed. The average daily dose of Atropine was 14mg and a total of 2gm of pralidoxime was administered.

Discussion

The features observed in our patient were highly suggestive of a severe exposure to the poison, evident by coma, seizures and respiratory depression necessitating respiratory support. This necessitated admission into the ICU where acute care and support were offered. It has been shown that mortality following severe OP poisoning can be reduced with effective critical care support. (3)

The presence of an organophosphate substance at the scene of the incident, signs and symptoms of organophosphate poisoning and improvement in the clinical condition of the patient following atropination and commencement of the antidote-pralidoxime, strongly supported our diagnosis of organophosphate poisoning. However, toxicity screening and cholinesterase activity test could have helped to confirm the diagnosis.

The presence of signs and symptoms of severe OP poisoning should alert the attending physician of the need to institute a proactive management plan. These should include, but not limited to prompt decontamination, definitive airway management to ensure protection of the lungs- in view of associated seizures and early mechanical ventilation. These will assist with prevention of aspiration pneumonitis and chest infection, both of which can lead to the development of respiratory failure. Systolic blood pressure of less than 100 mmHg and the necessity of a FiO2 > 40% to maintain adequate oxygenation were predicted to be responsible for poor outcome in OP poisoned patients mechanically ventilated in the ICU in a study by Munidasa et al. (4) Also, early commencement of anticonvulsant therapy can help to prevent or increase threshold for the development of seizure, which increase the morbidity in this group of patients.

The mainstay of medical therapy in organophosphate (OP) poisoning includes the use of atropine and pralidoxime (2-PAM). Chest x-ray is very useful as patients are prone to aspiration pneumonia. Electrocardiography (ECG) may show QT prolongation and arrhythmias.

Atropine acts as physiological antidote as it antagonizes muscarinic receptor-mediated actions. To achieve adequate atropinisation, large amounts of atropine may be required for patients with organophosphate poisoning, limited hospital stock and/or inadequate funds to procure large quantities may hamper adequate care, a problem encountered during the management of our patient. Atropine is usually given as the initial loading dose of 2 to 5 mg and repeated every 5 to 10 minutes until signs of atropinisation appear. Subsequently, as infusion at the rate of 0.02 to 0.08 mg/kg/min and the dose is titrated as per the clinical response. (5, 6) In view of the limited doses of atropine available, we employed 0.6mg per hour of atropine instead of the calculated 1.4mg/hour of atropine; this had implication on the attainment of adequate atropinisation.

In settings where parenteral atropine supply is limited, reconstitution of powdered atropine has been suggested as a viable option; especially in mass-casualty settings (7) unfortunately this is not be readily available in our centre. Rajpal et al (8) demonstrated the clinical safety and efficacy of sublingual atropine to healthy volunteers, this may offer another route of administration for the OP poisoned patient, especially in a mass-casualty scenario.

The administration of the specific antidote (oximes) can be employed, though the role and dose of oximes are controversial. The major pharmacological action of oximes such as pralidoxime is to reactivate acetyl cholinesterase by removal of the phosphate group bound to the esteratic site. (9) Oximes should be given as soon as possible before aging takes place, and was initially reported to be beneficial when administered within 24 hours after exposure, (10) however Howland and Aaron (11) opined that oximes can be effective when given after 24 hours especially following ingestion of lipophilic agents like chlorpyrifos. It is possible that pralidoxime may still be useful up to a week after ingestion of OP, because of the clinical improvement we observed in our patient following its use.

Oximes are believed to be effective and to be especially useful in treating moderate or severe OP poisoning and may also reverse the central nervous system effects of OP. (12) However, the major challenge is the unavailability of oximes in most developing countries, partly as a result of the cost and/or its low priority on the ICU list of drug requirements. Inadequate provision of basic drugs and facilities for an ICU as a result of poor health care financing remains a challenge in developing countries like Nigeria. Procurement of consumables and equipment are restricted to those required for common ICU conditions in that particular locality.

Therefore, in patients with uncommon ICU conditions, substantial part of the cost for drugs, laboratory tests, and ICU procedures will be borne by patients and/or their relatives, and this puts enormous financial burden on them often leading to suboptimal care.

An important part of the management of OP poisoned patient in the ICU is the monitoring of arterial blood gases; to guide ventilator therapy and monitor respiratory failure and metabolic acidosis. In view of the unavailability of facility for blood gases monitoring at the time this patient presented, we resorted to the use of capnograph and serial serum electrolytes to guide ventilator therapy and monitor metabolic acidosis respectively. This challenge limited

our ability to effectively manage the respiratory failure that complicated this condition.

A meta-analysis and review of the literature performed by Peter et al emphasized that optimal supportive care along with discriminate use of oxime, especially early in the course of treatment of moderately to severely OP poisoned patients, are the hallmarks of successful treatment. (13)

Conclusion

Management of OP poisoned patients in the ICU is a challenge in a developing country like ours. There is no doubt that our patient had a fatal exposure to the OP, however, prompt provision of required drugs and efficient ICU support could have made a difference.

There is a need for the provision of facilities that provides for adequate support during diagnosis and management of patients with poisoning. This includes, but not limited to provision of common reversal drugs and equipment for toxicology screening and blood gases estimations. In view of these daunting challenges for health care professionals with regard to the ICU care of patients with OP in a developing country like ours, we may be able to achieve some success if we are proactive in our approach and at least provide symptomatic relief of cholinergic side effects in addition to providing the basic supportive care available.

SUMMARY OF CLINICAL EVENTS/MANAGEMENT IN THE ICU

Day on admission	Presentation	Plan instituted
1	Unconscious, tachypnoeic. Copious oral secretion with peripheral oxygen saturation less than 90%	Endotracheal intubation with mechanical ventilation (SIMV). Multiparameter monitoring including pulse oximetry and capnography. Intravenous bolus of Atropine 2mg followed by an infusion of 0.6mg/hour. Prophylactic antibiotics
2	Still unconscious, oral secretion reduced. Stable haemodynamics.	Above plan continued
3	Same as above	Above plan continued
4	An episode of tonic-clonic seizure that lasted for about 30 seconds. GCS remained 7/15.	Seizure aborted with diazepam. Phenytoin Sodium commenced. Mechanical ventilation and Atropine infusion continued.
5	More episodes of tonic-clonic seizure. GCS subsequently dropped to 4/15.	Seizure aborted each time with diazepam. Fundoscopy did not reveal features suggestive of high intracranial pressure. The dose and frequency of Phenytoin was increased.
6	GCS– 4/15.Global hypotonia and hyporeflexia. No seizure	No major change in line of management.
7	Conditions remain same.	IV Pralidoxime 1gm over 3minutes in addition to the on-going treatment.
8	GCS improved to 10/15. No seizure.	Weaning from mechanical ventilation commenced. Ventilatory mode now CPAP with assist. Second dose of Pralidoxime 1gm given.
9	No seizure. Clinical features suggestive of chest infection.	Chest X-ray, Microbiological testing of blood, Urine and tracheal aspirate. Antibiotics changed to a broader spectrum one.
10-11	GCS - 10/15.	Weaning still unsuccessful. Atropine infusion still on at 0.6mg per hour.
12	Dislodged endotracheal tube. Respiratory distress and poor oxygen saturation.	Endotracheal tube replaced. Plan was put in place for Tracheostomy
	Patient suffered a cardiac after about 6- 8 hours of re-intubation.	Unsuccessful CPR.

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