TERUMO PENPOL REVIEW
ON BLOOD MANAGEMENT SYSTEMS

JUL-SEP 16 NUMBER 87

Ahila Ayyavoo et al. J Clinic Toxicol 2011, S:1

Published in every quarter by TERUMO PENPOL Private Limited

TERUMO PENPOL®

Plasmapheresis in Organophosphorus Poisoning – Intensive Management and its Successful Use

Ahila Ayyavoo DNB[1*], Nagarajan Muthialu[2] and P Ramachandran[3]

[1]Department of Paediatrics, G Kuppuswamy Naidu Memorial Hospital, P N Palayam, Coimbatore, India

[2]Department of Paediatric Cardiothoracic Surgery, G Kuppuswamy Naidu Memorial Hospital, P N Palayam, Coimbatore, India

[3]Department of Nephrology, G Kuppuswamy Naidu Memorial Hospital, P N Palayam, Coimbatore, India

Abstract

Management of Organophosphorus poisoning can be difficult at times, especially when there is no history of poisoning or where the compound is not known to begin with & which is compounded by the absence of odour. Plasmapheresis has been tried effectively in toxicology in the treatment of various toxic substances ingestion, and can replace circulating cholinesterase in these patients with organophosphate poisoning. We report a case of young boy who initially presented with unknown compound poisoning, but subsequently had clinical features of organophosphorus

poisoning alongwith reduced levels of acetyl cholinesterase, managed by plasmapheresis.

Keywords :

Plasmapheresis; Organophosphorus; Poisoning

Introduction

Organophosphorus poisoning can be very challenging to treat, especially when the character of the compound is not fully known. We report a case of a young boy with poisoning, and managed successfully with parenteral atropine and pralidoxime and various intensive managements including plasmapheresis for intermediate syndrome and hypernatremia; repeated bronchoscopic removal of mucous plug on either side following obstruction due to atropinization.

Case Report

A 12 year old boy was seen in the outpatient clinic with the history of six episodes of non bilious vomiting and four episodes of loose stools in one hour. There was no history of fever. He had taken a cool drink an hour prior to the onset of symptoms. Clinically, the boy was anxious. His general and systemic examinations were normal. He was initially admitted for observation with a provisional diagnosis of acute gastroenteritis. His vital parameters were within normal limits.

Within thirty minutes, his mentation altered with no other change in his clinical condition. Parents vehemently denied any possibility of poisoning and there was no abnormal smell in his breath. A differential diagnosis between unknown poisoning and early encephalitis was considered. Management was commenced with intravenous fluids and oxygen and gastric lavage. The gastric aspirate was negative for any specific smell and contents.

Shortly thereafter, his clinical condition deteriorated with papillary constriction amounting to pinpoint nature. There were generalized tonic-clonic seizures along with brainstem type of breathing and soon the boy went into cardiorespiratory arrest. He was resuscitated and ventilated. There were copious secretions from endotracheal tube. So an empirical treatment with atropine was started with

organophosphorus poisoning in mind. It was given at a dose of 0.04mg/kg every 10 minutes for three doses. Then it was repeated every 1 hour for 4 hours and then every 2 hours for hours and every 3 hours for the next 24 hours. Atropine was given 6th hourly for the next 24 hours. Midazolam 0.2 mg/ kg bolus was followed by 2 micg/ kg/min intravenous infusion for the next 48 hours and the dosage was titrated based on the neurological status.

As part of work-up, a contrast enhanced computerized scan of brain (CT scan) was done after stabilising him, which was normal. His initial haematological and biochemical parameters were within normal limits.

As there was no definite history of poisoning, serum cholinesterase was done by Butyrylthiocholine iodide hydrolysis /colorimetric method and it showed an extremely low level of cholinesterase 177.9 U/L (Normal range: 2180 – 9180 U/L). This suggested a very high possibility of organophosphorus poisoning in the absence of clinical evidence and convincing history. Based on this, Pralidoxime was added in addition to the atropine at a dose of 25mg/kg intravenously for 48 hours. This was started eight hours after admission (after receiving the results of cholinesterase estimation). But his toxicology report continued to be negative for all opiates.

With treatment, the general condition initially improved. But by second day after commencing the management, there was acute clinical deterioration with development of desaturation, with associated mediastinal shift. Needle aspiration ruled out tension pneumothorax and chest x-ray showed a collapse of the right lung. A fibreoptic bronchoscopy was done to remove an obstructing mucus plug from the right main bronchus. Bronchoscopy had to be repeated again in 24 hours for further clearance of respiratory tract and then the boy was weaned from the ventilator and connected to non invasive ventilation.

90 hours after admission, he was unresponsive for more than an hour while he was still on non-invasive ventilation. There were no clinical clues except for the mild constriction of pupils. He had respiratory arrest

fairly soon after the clinical deterioration from which he was revived and ventilated again. A repeat CT brain and chest xray were normal. The serum cholinesterase showed a value of 1896.5U/L, which was low. A diagnosis of intermediate syndrome was made as he relapsed with miosis, low cholinesterase levels and respiratory arrest 90 hours after admission with no other contributing factor. His serum sodium had increased to181 mmol/L. Another course of atopinisation was tried with no improvement. As the boy was atropinised adequately and with high sodium, he was considered for a possible plasmapheresis aiming to increase the cholinesterase levels further while optimally reducing the serum sodium. Plasmapheresis was performed via a double-lumen subclavian catheter and one sitting involving 20 ml/Kg of plasma volume exchange (involving fresh frozen plasma) was performed. The cholinesterase increased from 1896.5 to 2437.5 U/L after this and the serum sodium became 177mmol/L. With conservative management the serum sodium continued to be high and the child underwent haemodialysis which helped the sodium to drop to 166mmol/L within 24 hours of the episode of relapse. Subsequently, the sodium levels returned to normal in the next 24 hours with conservative management. The child improved gradually over the next few days and he was weaned off the ventilator. Psychiatric counselling was arranged for the child and the parents and the child was discharged home in a stable condition after a period of two weeks from the time of admission.

Discussion

Most organophosphate poisonings in children are due to accidental exposure. Suicidal attempts using organophosphates are more common in communities involved in agriculture. The major clinical manifestations in children are neurological, rather than nicotinic or muscarinic symptoms in contrast to adults [1]. Organophosphates inhibit acetylcholinesterase (AChE) activity by phosphorylating the serine hydroxyl group located at the active site of AChE. The phosphorylation occurs by loss of an organophosphate leaving group and establishment of a

covalent bond with AChE. Once AChE has been inhibited, acetylcholine (Ach) accumulates throughout the nervous system, resulting in overstimulation of muscarinic and nicotinic receptors.

The phosphorylated enzyme will either be spontaneously reactivated or will undergo the "aging process". Aging is the reaction that, after phosphorylation of serine at the active site of AChE or BuChE (butryl cholinesterase), dealkylation of the phosphyl moiety can occur. This results in the loss of an alkyl group [2]. This negatively charged monophosphylate ester of serine is resistant to spontaneous or oxime-mediated reactivation [3].

Clinical effects are manifested via activation of the autonomic and central nervous systems and at nicotinic receptors on skeletal muscle. Lung collapse, as part of manifestations due to thickening of secretions after the use of atropine, is often reported and quite often needs bronchoscopy for respiratory clearance [4].

Acute neurotoxic effects during the cholinergic phase of organophosphorus insecticide poisoning and delayed neurotoxic effects appearing two to three weeks later are well recognized. Patients who appear to improve after the initial cholinergic crises relapse 24-96 hours later. They have a classical presentation of proximal limb muscle weakness which progresses onto state of muscle paralysis which includes the respiratory muscles. This was described by Wadia et al as [5] Type II paralysis and renamed as Intermediate Syndrome by Senanaayake. He reported 10 patients who had paralysis of proximal limb muscles, neck flexors, motor cranial nerves, and respiratory muscles 24 to 96 hours after poisoning, after a well-defined cholinergic phase [6]. The intermediate syndrome is due to the overstimulation of the nicotinic acetyl choline receptors in the muscles [7]. This is called intermediate as it occurs after the muscarinic effects and before the onset of peripheral neuropathy. Atropine is not effective in intermediate syndrome as it is specific for the muscarinic effects [5].

The fundamental management principle in organophosphate (OPC)

poisoning revolves around atropine and pralidoxime (2-PAM). Atropine is a muscarinic antagonist and forms a mainstay treatment for this.

Oximes reactivate acetyl cholinesterase by removing the phosphoryl group inserted by the organophosphates at the active site of AChE. Oximes are generally supportive, and can be sometimes harmful as mentioned in various reports [8]. Pralidoxime increase the red cell cholinesterase reactivation, but has not shown an improvement in survival or decrease in the need for intubation [9].

Plasma can be an effective source of cholinesterase. Use of fresh frozen plasma in a setting of OPC poisoning is not new, and is very advantageous as it replaces deficient cholinesterases but will involve replacement with large volumes and associated transfusion-related complications [10].

Plasmapheresis is not new in toxicology and its role is clearly established in various clinical conditions. This can be an effective alternative by increasing cholinesterase levels in these difficult circumstances. Guven et al reported a successful use of plasmapheresis in a septic setting associated with organophosphorus poisoning [11].

They demonstrated an increase in the level of AChE in this patient when plasmapheresis was done for sepsis. This had been suggested as a possible mode of therapy in resistant cases, though it had not been tried before for organophosphate poisoning. With deteriorating clinical scenario as seen in our setting, one would choose plasmapheresis for the benefit of using less transfusion volume while maintaining circulatory equilibrium and also to bring down the sodium level optimally in a more controlled manner.

References

1. Bryant S, Singer J (2003) Management of toxic exposure in children. Emergency medicine clinics of North America 21: 240.
2. Worek F, Diepold C, Eyer P (1999) Dimethylphosphoryl-inhibited human cholinesterases: inhibition, reactivation, and aging kinetics. Archives of toxicology 73: 7-14.
3. Amitai G, Ashani Y, Gafni A, Silman I (1982) Novel pyrene-containing organophosphates as fluorescent probes for studying aging-induced conformational changes in organophosphate-inhibited acetylcholinesterase. Biochemistry 21: 2060-2069.

4. Ashok AC (2002) Organophosphorus poisoning - Still a challenging proposition. Indian Journal of Anaesthesia 46: 40-43.

5. Wadia RS, Sadagopan C, Amin RB, Sardesai HV (1974) Neurological manifestations of organophosphorous insecticide poisoning. Journal of Neurology, Neurosurgery & Psychiatry 37: 841.

6. Senanayake N, Karalliedde L (1987) Neurotoxic effects of organophosphorus insecticides. The New England journal of medicine 316: 761.

7. DeBleecker JL (1995) The intermediate syndrome in organophosphate poisoning: an overview of experimental and clinical observations. Clinical Toxicology 33: 683-686.

8. Samuel J, Thomas K, Jeyaseelan L, Peter JV, Cherian AM (1995) Incidence of intermediate syndrome in organophosphorous poisoning. The Journal of the Association of Physicians of India 43: 321.

9. Eddleston M, Eyer P, Worek F, Juszczak E, Senarathna L et al (2009) Pralidoxime in acute organophosphorus insecticide poisoning—a randomised controlled trial. PLoS medicine 6: e1000104.

10. Guven M, Sungur M, Eser B, Sari I, Altuntas F (2004) The Effects of Fresh Frozen Plasma on Cholinesterase Levels and Outcomes in Patients with Organophosphate Poisoning. Clinical Toxicology 42: 617-623.

11. Guven M, Sungur M, Eser B (2004) The effect of plasmapheresis on plasma cholinesterase levels in a patient with organophosphate poisoning. Human & experimental toxicology 23: 365.

REGISTERED OFFICE

Terumo Penpol Private Limited
P.B.No. 6105, I-2 , Jawahar Nagar,
Thiruvananthapuram - 695003, Kerala, India.
Ph.No : 0471-3015500 / 501
Fax : 0471-2721519
CIN : U33112KL1985PTC004531

www.terumopenpol.com
www.terumobct.com

Toll Free No. 1800 3000 7070

CENTRAL SALES OFFICE

New No.71, Gandhi Court,
4th Main Road, Gandhi Nagar,
Adayar, Chennai - 600020
Tel: 044-42054538, 044-30957200 /01 / 02 / 03 / 04 / 05
tplmarketing@terumopenpol.com

MARKETING OFFICE

YGRA-12, TC 4/1399(3),
Kuravankonam,
Kowdiar Post,
Thiruvananthapuram-695003
pmt@terumopenpol.com

ZONAL OFFICE

DELHI

3E/9, Second Floor,
Jhandewalan Etn, Delhi
Tel : 011-46921062

KOLKATA

839/1, Lake Town, Block A
Kolkatta -700089
West Bengal
Tel : 033-25344609

MUMBAI

Divya Jyot CHS Ltd.,
B-7, Ground floor,
R. K. Singh Marg, Old Nagardas Road,
Andheri (East), Mumbai – 400 069
Tel : 022-2824 0304 / 09320231762

TERUMO PENPOL®