A Study of Clinical Features, Management and Outcome of Organophosphate and Carbamate Poisoning in Children

Koirala DP[1], Rao KS[2], Malla KK[3], Malla T[4]

[1]Dr. Deepak Prasad Koirala, MBBS, MD, Lecturer, [2]Dr. K.S Rao, MBBS, DCH, MD, Professor and HOD, [3]Dr. Kalpana K Malla, MBBS, MD, Associate Professor, [4]Dr. Tejesh Malla, MBBS, MD, Associate Professor. All from the Department of Paediatrics, Manipal College of Medical Sciences, Pokhara, Nepal.

Abstract

Introduction: Organophosphates (OP) are commonly used pesticides in rural agricultural regions of Nepal and carbamates are popular household insecticides. Because of poor legislation these poisons are easily accessible and are the most popular suicidal poisons. **Materials and Methods:** This was a retrospective study done in poisoning cases admitted in PICU of Manipal Teaching Hospital (MTH) over a seven year period. **Results:** Out of 187 cases of poisoning, 30 (16.04%) were OPs and 4 (2.13%) were Carbamates. The male to female ratio was 56:44 and these poisonings were more common in rural areas (56%). Accidental poisoning (82.4%) was more common but suicidal attempts (17.6%) were also observed. Atropine and pralidoxime were used in 82.4% of the cases. The total atropinizing dose was 0.77±0.6 mg/kg and patients required 56.6±23.7 hours of atropinization. In our study 94.1% of the patients survived and none of them developed any sequel. Children developed muscarinic, nicotinic and CNS symptoms similar to adults. Complications were seen in 41.1% of the children and most common being seizure (85.7%). The most common OP observed in childhood poisoning was Metacid (methyl parathion) seen in 26.4% of the cases. **Conclusion:** OP and Carbamate poisonings are common in children. Possibility of self-harm poisoning in adolescent females cannot be ignored. Atropine is the mainstay of therapy after initial resuscitation and complications are common in children. With prompt treatment the outcome is good even with complications. The case fatality rate is much less as compared to adults.

Key words: Acetylcholinesterase, Atropine, Carbamates, Organophosphates, Poisoning, Pralidoxime

Introduction

Organophosphate (OP) poisoning is a global health problem and most of the deaths due to these poisonings occur in developing countries[1,2]. In countries like Nepal, these pesticides are easily available because of economy based on rural agriculture and poor legislation. Carbamates are commonly used in households as insecticides. OPs are the most commonly used pesticides and in children are mostly unintentional exposures[3]. It is a most popular suicidal poison and children are the usual victims of accidental exposure because of their inquisitiveness. Adolescents consume with suicidal intention in the periods of stress as these are easily available[4]. It kills an estimated 200,000 people worldwide every year with a case fatality rate of more than 15%[5] .

This is a first study of its kind in Nepal in the pediatric age group (0-18 yrs) in which the clinical features, management and outcome of organophosphate and carbamate poisoning has been focused.

Materials and Methods

This was a retrospective observational study done in Pediatric Intensive Care Unit (PICU) of Manipal Teaching Hospital, a tertiary referral centre in the Western region of Nepal. All the case records of poisoning cases admitted to the PICU from 2006 January to 2012 December (7 year period) in the pediatric age group (<18yrs) were studied. As the clinical features and management of OP and carbamate poisonings are almost the same with few differences, both were studied together.

The demographic features, clinical presentation, management and drugs used, complications associated

Address for correspondence
Dr. Deepak P Koirala
Department of Paediatrics
Manipal College of Medical Sciences
Pokhara, Nepal.
E-mail: dpkoirala19@hotmail.com

How to cite this article ?
Koirala DP, Rao KS, Malla KK, Malla T. A Study of Clinical Features, Management and Outcome of Organophosphate and Carbamate Poisoning in Children. J Nepal Paediatr Soc 2013;33(2):85-90.

and outcome of the cases were studied and relevant data were collected. The data was collected in a standard performa and analyzed using Microsoft excel.

OP and carbamate poisoning was diagnosed by presence of any two of – (a) History of exposure to OP/ Carbamate compounds, (b) Characteristic muscarinic and nicotinic manifestations and (c) Reversal of signs and symptoms after administration of atropine[1,2,4]. As RBC cholinesterase and plasma pseudo cholinesterase level estimation is not available in our setup, these tests were not done in our study and also these tests are of limited value in acute OP and carbamate poisoning[1]. Cases not consistent with OP and carbamate poisoning were excluded from the study.

Results

In a seven year study period, 187 cases of poisoning including animal poisonings (wasp bite, bee stings and snake bites) were admitted and treated, out of which 30 cases (16.04%) were of OP and 4 cases (2.13%) were of Carbamates poisonings. The demographic distribution of subjects is shown in Table 1. Poisoning was more seen in males than the females (56% Vs 44%) and more so in rural than urban areas (56% Vs 44%). Maximum number of children we treated was in 1-5 year age group (47%). The mean age was 5.74 years (SD=4.75) and the youngest child we treated in our unit was an infant of 45 days weighing 5 Kg.

Year 2012 had maximum admissions of 11(32.3%) and there were few admissions in the year 2006 and 2007 (Fig 1). OP and carbamate poisonings were seen throughout the year with peak during January, May, July, August and December (Fig 2).

The names of 10 (29.4%) poisons were not known whereas Metacid (Methyl Parathion) was the most common OP poison (26.4%) in children and Malathion the least common (2.9%) as shown in Fig 3.

Table 2 provides information on poisoning. Home was the source of poison in 50% of the cases and in 35.3% cases the child consumed poison from neighbor's home while playing. As MTH is a tertiary referral centre, most of the cases we treated were referred (70.6%) and only 29.4% of cases came directly to MTH for treatment. Most patients were decontaminated in the emergency department (55.9%) and rest in PICU (38.3%). Accidental poisoning (82.4%) was more common but self-harm was also observed in 6 (17.6%) children, out of which 4 (66.66%) were females and 2 (33.34%) were males. Self-harm cases were in the age range of 12-14 years. Sixty-seven percent of the parents had full knowledge and 8.9% of the patients no knowledge at all about the poisonous nature of the substance ingested. Most of the patients were treated with atropine and pralidoxime (82.4%), only atropine was used in Carbamate poisoning and two cases (5.88%) of Baygon (Propoxur) poisoning were treated without any antidote.

Table 3 shows the clinical features that were observed in the admitted cases. All of the children developed muscarinic, nicotinic and CNS symptoms with percentages as shown but none of the patients developed mydriasis as a symptom.

Table 4 focuses on treatment parameters. The time since ingestion on arrival to the hospital was 7.3±6.4 hrs. The total atropinizing dose (mg/kg) was 0.77±0.6 with 2.0±0.8 doses of PAM given to each patient with 56.6±23.7hrs of atropinization. Patients were hospitalized for 8.0±4.1 days and 94.1% of the patients survived with none developing any sequel. Out of two mortality cases, one was 6 year old male child of Metacid (Methyl parathion) poisoning who expired at 3 days of admission and another was 1 ½ year old male child of Baygon (propoxur) poisoning who expired at 5 hrs of admission.

Fourteen of the patients (41.1%) developed complications (Fig 4). Some patients developed more than one complication. The complications observed were seizures (85.7%), aspiration pneumonia (35.7%), respiratory failure (28.5%), coma (21.4%) and metabolic acidosis (21.4%).

Table 1: Demographic characteristics of subjects.

	Parameters	Number (%)
Total subjects (34)	Male	19(56%)
	Female	15(44%)
Locality	Rural	19(56%)
	Urban	15(44%)
Age group (Years)	0-1	4(11.7%)
	1-5	16(47%)
	5-10	6(17.64%)
	>10	8(23.52%)

Table 2: Information on poisoning (n=34)

Parameters		Number (%)
Source of poison	Home	17(50%)
	Neighborhood	12(35.3%)
	Bought from shop	5(14.7%)
Types of cases	MTH	10 (29.4 %)
	Referred	24 (70.6 %)
Decontamination Place	Emergency-	19 (55.9 %)
	PICU-	13 (38.3 %)
	Referred place-	2 (5.8 %)

Table 2 cont...

Type of poisoning	Accidental		28 (82.4 %)
	Self-harm	Total	6 (17.6 %)
		Male	2
		Female	4
Antidote	None		2 (5.8 %)
	Atropine only		4 (11.8 %)
	Atropine+Pralidoxime		28 (82.4 %)
Parent's knowledge about poison	No idea		3 (8.9%)
	Some idea		8 (23.5%)
	Full idea		23 (67.6%)

Table 3: Clinical features (n=34)

Muscarinic	No. (%)
1) Miosis	26 (76)
2) Salivation	25 (73)
3) Emesis	25 (73)
4) Lacrimation	23 (67)
5) Diarrhea	21 (61)
6) Bronchorrhea, bronchospasm	21 (61)
7) Urination	14 (41)
8) Defecation	18 (52)
9) GI cramping	10 (29)
10) Diaphoresis	9 (26)
11) Bradycardia	7 (20)

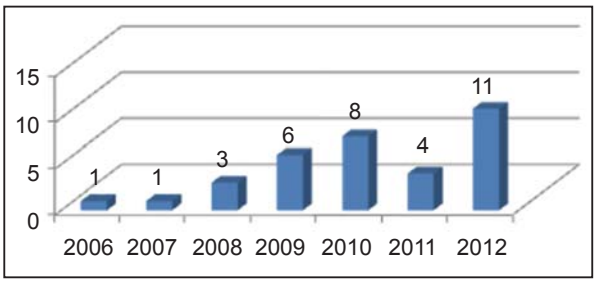

Fig 1: Year wise distribution of poisoning cases (n=34)

Nicotinic	No. (%)
1) Tachycardia	22 (64)
2) Dyspnea	18 (52)
3) Tachypnea	16 (47)
4) Twitching	16 (47)
5) Weakness/Paralysis	12 (35)
6) Muscle cramping	9 (26)
7) Cyanosis	8 (23)
8) HTN	1 (3)
9) Mydriasis	0 (0)

CNS	No. (%)
1) Anxiety/restlessness	27 (79)
2) Lethargy	18 (52)
3) Slurred speech	15 (44)
4) Seizures	12 (35)
5) Headache	7 (20)
6) Coma	3 (8)
7) Hypotension	3 (8)
8) Ataxia	1 (3)

Table 4: Treatment parameters

Parameters	Mean ± SD	
Time since ingestion on arrival in hospital(hrs)	7.3 ± 6.4	
Total atropinizing dose(mg/kg)	0.77 ± 0.6	
Number of doses of Pralidoxime(PAM)	2.0 ± 0.8	
Duration of atropinization(hrs)	56.6 ± 23.7	
Duration of hospitalization(days)	8.0 ± 4.1	
Outcome	**Improved**	**32(94.1%),**
	Expired	**2(5.9%)**

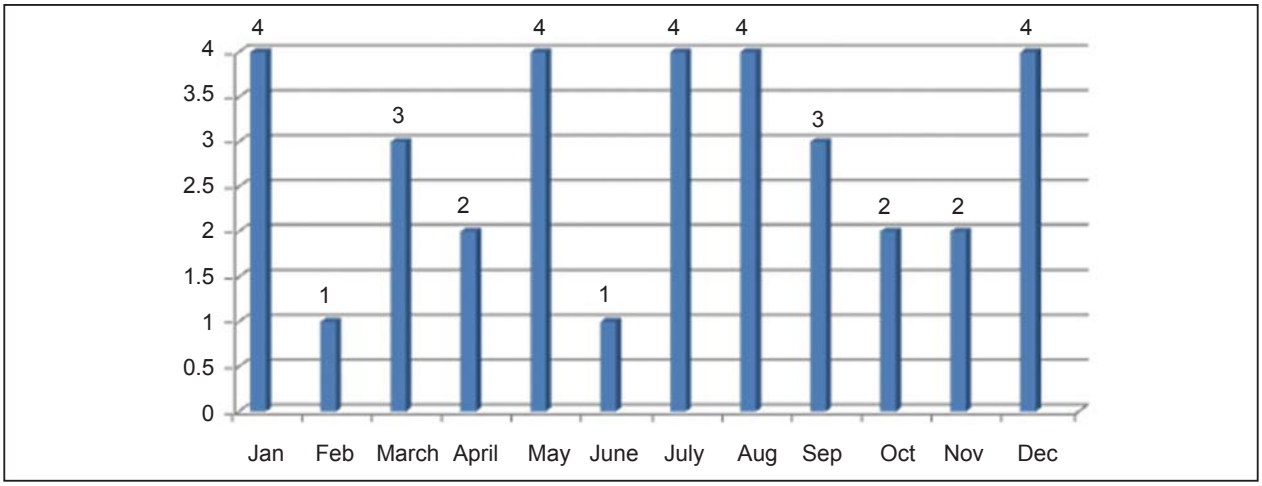

Fig 2: Month wise distribution of poisoning cases over 7 years (n=34)

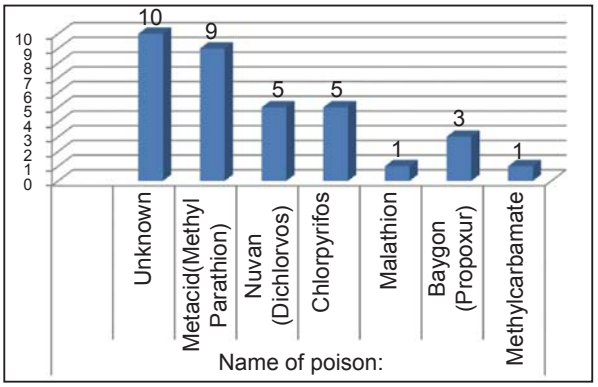

Fig 3: Types of Organophosphates and Carbamates (n=34)

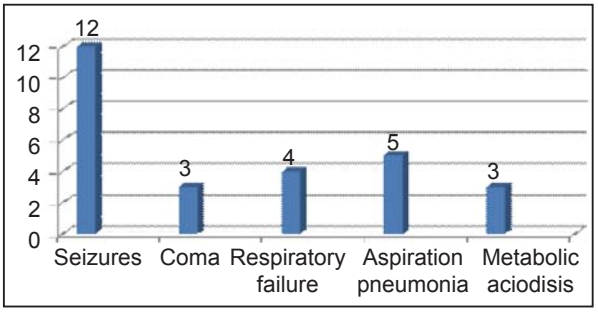

Fig 4: Complications (n=14)

Discussion

In our study, OP and Carbamates comprised of 18.18% of the total poisoning cases and is the commonest form of poisoning in children excluding the Snake bite. It was more common in males than females (M:F=56:44=1.27:1). Similar finding was shown in a study from South Africa[2]. Male children are inquisitive and adventurous, they are in a hurry to explore their surroundings and at this stage they are accidentally exposed to pesticides. The percentage of OP poisoning was similar in a study done in adults by Khadka SB et al[6]. A study done in adults showed female dominance in the incidence of poisoning (F:M=1.35:1)[7]. In adults, poisoning is more common in females because of increase incidence of self-harm because of increased stress from day to day activities. OP poisoning is more frequent in the rural areas than urban areas (56% Vs 44%) and similar findings were found in other studies as well[8]. Our country being agriculture dependent pesticides are readily available at home and children are prone to accidental poisonings.

The poisoning was more common in 1-5 year age group (47%) and the mean age was 5.74 yrs (SD= 4.75), which is a very vulnerable age group for poisoning. The finding is consistent with age group of children shown in other studies because of increased activity at younger age group to explore their surroundings[6,8]. A study by Zwiener RJ et al[9] showed further younger mean age group, as this study focused mainly in accidental poisoning in infants and younger children. The youngest child we have treated in our hospital was a 45 day old female infant of accidental Nuvan (Dichlorvos) poisoning who was referred to us from another hospital as a case of bronchopneumonia. The mother of this child was a divorced lady with psychiatric illness under medication. The mother alleges that she gave the pesticide to her child thinking it as a medication. The child required one day of mechanical ventilation and was treated with atropine and pralidoxime. The child was discharged after 12 days of hospitalization.

Metacid (methyl parathion) was the most common OP poisoning observed in our study and similar was the scenario in a study done in adults[8]. In 50% of the cases, home was the source of poison and in 14.7% of the cases the child bought it from the market. Nepal being an agricultural country, these pesticides are readily available at home and because of poor legislation adolescents have easy access to these pesticides. Accidental poisoning was the most common form of exposure (82.4%) to these pesticides but it was not uncommon to find 17.6% of the children with self-harm in age range of 12-14 years. Out of these, 66.66% were females and 33.34% were males. Similar findings were shown in a study by Mishra A et al[8]. Children are active and have the habit of exploring the substances orally and put anything in mouth, so accidental poisoning is common in small children. Adolescents especially females are emotionally labile and are disturbed by minor incidents in their life and that may be reason behind suicidal tendencies in our study group. Most parents (67.6%) were fully aware of the poisonous nature of the substances ingested by their children. They had the knowledge about the nature of the substance ingested, storage, usage, precautions to be taken and availability of treatment.

All of the children developed muscarinic, nicotinic and CNS symptoms. The common muscarinic symptoms were- miosis (76%), salivation (73%), emesis (73%) and lacrimation (67%); bradycardia (20%) was the least common manifestation. The common nicotinic symptoms were- tachycardia (64%), dyspnea (52%), tachypnea (47%) and twitching of muscles (47%); none of the patients developed mydriasis. The common CNS symptoms were- anxiety and restlessness (79%), lethargy (52%), slurred speech (44%) and seizures (35%); ataxia (3%) was the least common manifestation. Studies done in infants and children show similar results and the clinical features in children were similar to that of adults[2,8,9].

After initial resuscitation with management of airway, breathing and circulation; the patients were

decontaminated and activated charcoal given. Then IV atropine 0.05 mg/kg bolus every 3-5 mins was given. The patient was given atropine till the signs of atropinization appeared which was characterized by dry mucosa and bronchial secretions with dilatation of pupils. The total atropinizing dose was calculated and atropine infusion maintained at 20-30% of total atropinizing dose per hour via infusion pump. This infusion dose was continued for 48-72 hrs depending upon the severity of poisoning and tapering of atropine was done daily by lowering the infusion rate by 25-30% of the previous day dose. Pralidoxime (PAM) was used in doses of 30-50 mg/kg given by slow IV infusion and repeated every 12 hourly as required. Pralidoxime was used within 24 hrs of OP poisoning and was not used in Carbamate poisoning. Cases of mild poisoning were admitted for observation and no antidotes were given[1, 3-5,10, 11].

We treated 28 (82.4%) patients of OP poisoning with atropine and pralidoxime. Two cases (5.8%) of OP poisoning, 1 case of Baygon and 1 case of methyl carbamate were treated with atropine alone. Two cases (5.8%) of Baygon (Propoxur) were mild poisoning and managed by just giving supportive care and no antidotes were given.

OP pesticides inhibit the enzyme acetylcholinesterase (AChE) in the synapses and on red-cell membranes resulting in accumulation of acetylcholine at neuromuscular junctions, autonomic nervous system and central nervous system (CNS) leading to a variety of nicotinic, muscarinic and CNS symptoms. When OP compounds bind to AChE enzyme the covalent bond thus formed is initially reversible and within this period hydrolysis of the enzyme is possible. But after 24-72 hrs they become irreversibly bound which is known as “aging.” The period of aging depends upon the type of OP compound. After aging there is no possibility of hydrolysis. Carbamates inactivate the enzyme in a similar manner with same clinical features as OP poisoning but there is no aging and spontaneous hydrolysis of the enzyme occurs within 24 hrs[1,3-5,12] .

Atropine is a muscarinic antagonist and cornerstone of therapy in both the OP and Carbamate poisonings. It only reverses the muscarinic effects and not the nicotinic effects of OPs and carbamates. Pralidoxime (PAM) is a drug which reactivates the AChE enzyme and also has some antimuscarinic effect. It has to be given only with atropine before aging has occurred and should not be used in Carbamate poisonings as there is spontaneous hydrolysis. We used PAM in all but two cases of OP poisonings who presented after 24 hrs. The PAM doses were repeated depending upon the clinical improvement of the child. We used PAM as per the standard textbooks and teachings[3,4] although there are adult studies including Cochrane review that showed PAM use does not improve survival in OP poisonings[13-15].

The mean total atropinizing dose (mg/kg) required by the patients was 0.77 (SD=0.6, range= 0.12-2.9) with mean duration of atropinization (hrs) of 56.6 (SD=23.7, Range =24-96). Patients were hospitalized for mean duration of 8 days (SD=4.1, Range=2-17) with case fatality rate of 5.9%. The findings were consistent with studies done in children.[2,9] A study done in adults showed the mortality as high as 18.17%.[8] The higher mortality in adults is probably due to self-harm ingestion and thus higher doses of OP compounds.[2,8] The 6 year old male child who expired was a case of Metacid (methyl parathion) poisoning. He was referred from a district hospital of a remote area and presented to MTH at 12 hrs of poisoning. He had aspiration pneumonia at admission, later went into respiratory failure and died in course of treatment at 72 hrs of admission. Another mortality was a 1 ½ year old male child of Baygon (propoxur) poisoning. He also was from rural area and presented to MTH at 38 hrs of poisoning. He had respiratory failure and associated metabolic acidosis and died at 5 hrs of admission and treatment. Both the cases were referred to us without initial resuscitation, decontamination and stabilization. Both were late in reaching to our hospital partly because of geographical location and partly they were ignorant in realizing the seriousness of the situation.

Complications were seen in 41.1% of the patients. Seizure (85.7%) was the most common and, coma and metabolic acidosis (21.4%) were the least common complication. This finding was comparable to other studies[2,9]. Two (5.8%) patients required intubation and ventilator management. Seizure and coma probably is due to hypoxia and also because of direct depressant action of OPs on CNS. Seizure was managed by giving diazepam in doses of 0.1-0.2 mg/kg[4,5,10].

Conclusion

Accidental poisoning is common in children but the possibility of suicidal attempts in adolescent females cannot be ignored. Atropine is the mainstay of therapy after initial resuscitation and duration of atropinization depends upon the severity of poisoning. Symptoms of OP and carbamate poisoning in children are similar to that in adults. PAM is useful in the management of OP poisoning in children although there are controversies regarding its use in adults. Timely referral after initial resuscitation, stabilization and decontamination will probably save lives. Complications are common in children which when managed properly significantly reduces morbidity and mortality. The case fatality rate is much less as compared to adults.

Acknowledgement: I would like to thank Associate Prof. Dr Amar Nagila, PhD (Biochemistry and molecular biology) for helping me in the analysis of my data.

Funding: None

Conflict of interest: None

Permission from IRB: Yes

References

1. Paudyal BP. Organophosphorus Poisoning. *J Nepal Med Assoc* 2008;47(172):251-8.
2. Verhulst L, Waggie Z, Hatherill M et al. Presentation and outcome of severe anticholinesterase insecticide poisoning. *Arch Dis Child* 2002; 86: 352-355.
3. O'Donnell K A, Ewald M B. Poisonings. In: Kliegman, Stanton, St. Geme, Schor, Behrman, editors. Nelson Textbook of Pediatrics. 19th Edition. Philadelphia: Elsevier Saunders; 2011.p. 250-267.
4. Singh U K, Layland F C, Prasad R, Singh S. Poisoning in Children. 3rd Edition. New Delhi: Jaypee Brothers; 2006.
5. Eddelston M, Buckley NA, Eyer P, Dawson AH. Management of acute organophosphorus pesticide poisoning. *Lancet* 2008;371(9612): 597–607.
6. Khadka SB, Ale SB. A study of poisoning cases in emergency Kathmandu Medical College Teaching Hospital. Kathmandu Univ Med J 2005;3(4):388-391.
7. Marahatta SB, Singh J, Shrestha R, Koju R. Poisoning cases attending emergency department in Dhulikhel Hospital- Kathmandu University Teaching Hospital. Kathmandu Univ Med J 2009;7(2):152-56.
8. Amarnath M, Shukla SK, Yadav MK et al. Epidemiological Study of Medicolegal Organophosphorus Poisoning in Central Region of Nepal. *J Forensic Res* [Internet]. 2012 Sept 29[cited 2013 Jan 30]; 3(9):[5 pages]. Available from: http://dx.doi.org/10.4172/2157-7145.1000167.
9. Zwiener RJ, Ginsburg CM. Organophosphate and Carbamate Poisoning in Infants and Children. *Pediatrics* 1988;81:121-26.
10. Bhattarai MD, Singh DL, Chalise BS, Koirala P. A case report and overview of organophosphate (OP) poisoning. Kathmandu Univ Med J 2006;4(1):100-104.
11. Roberts DM, Aaron CK. Managing acute organophosphorus pesticide poisoning. *BMJ* 2007; 334:629-34.
12. Kang J, Seok J, Lee H et al. Factors for Determining Survival in Acute Organophosphate Poisoning. *Korean J Intern Med* 2009;24:362-367.
13. Eddleston M, Eyer P, Worek F et al. Pralidoxime in Acute Organophosphorus Insecticide Poisoning—A Randomised Controlled Trial. PLoS Med [Internet]. 2009 June 30; [cited 2013 March 1]; 6(6): [12 pages]. Available from: http://dx.doi.org/10.1371/journal.pmed.1000104.
14. Rahimi R, Nikfar S, Abdollahi M. Increased morbidity and mortality in acute human organophosphate-poisoned patients treated by oximes: a meta-analysis of clinical trials. *Hum Exp Toxicol* 2006;25(3):157-62.
15. Buckley NA, Eddleston M, Li Y et al. Oximes for acute organophosphate pesticide poisoning (review). Cochrane Database of Systematic Reviews c2011- [cited 2013 March 11]. Available from- http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005085.pub2/pdf.