Organophosphate Poisoning and Cholinesterase Level: Case Report

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Abstract

Female patient forty four years old presented in the emergency department due to suicidal attempt with organophosphorous poisoning. The patient admitted to ICU and treated with atropine and obidoxim for two weeks. The patient improved clinically and discharged in a very good general condition but the ACH level does remain low. In this report I try to discuss this case.

Keywords: organophosphorous, acetylcholine(ACH), obidoxim, poisoning, atropine

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Introduction

Organophosphates(OPP) are compounds capable of inhibiting the action of acetylcholinesterase enzyme(ACHE) in the nerve ends resulting in accumulation of acetylcholine (ACH). The symptoms of accumulation of ACH depend on the concentration of substance and the receptors affected, generally present muscarinic, nicotinic and central effects [1-3]. These compounds mostly used in agriculture as pesticides and insecticides, but it is also used in medicine post operative for surgery to overcome high doses of muscle relaxants and myasthenia graves [4,5]. Toxicity most commonly occurs suicidal and accidentally due to exposure to agriculture pesticides. Worldwide, an estimated 3,000,000 people are exposed to organophosphate or carbamate agents each year, with up to 300,000 fatalities [6,7]. In the United States, there were more than 8000 reported exposures to these agents in 2008, resulting in fewer than 15 deaths [8]. The signs and symptoms resulted from accumulation of ACH in the nerve ends due to nicotinic effect as hypertension, and hypoglycemia. Overstimulation of nicotinic acetylcholine receptors in the central nervous system, due to accumulation of ACh, results in anxiety, headache, convulsions, ataxia, depression of respiration and circulation, tremor, general weakness, and potentially coma [9,10]. The effects of organophosphate poisoning on muscarinic receptors are salivation, lacrimation, urination, defecation, gastrointestinalmotility, emesis, miosis, urination, diarrhea, diaphoresis, lacrimation, excitation, and salivation [11,12]. Management of orgnophosphorous poisoning include remove the patient from the place, washing patient, gastric lavage, fluid replacement, oxygen, supporative therapy administration of atropine to overcome the muscrinic effects and the specific antidote Oxime which include pyridoxime, obidoxime or trimedoxime. Oximes are contraindicated in carbamate poisoning since it worsen the case because it compete the oxime to its binding site [1,5,13-15]. In some instances aging process occur in which the ACH level remain low for long period may reach one year despite antidote administration and improvement in clinical condition of the patient, this is mostly occur due to delay treatment. Oximes should be administer as early as possible but also it can be administer after one week [1]. Recent advances done for management of poisoning these include administration of intravenous infusion of sodium bicarbonate to produce mild to moderate alkalinization. Gacyclidine; an antiglutamatergic compound, was also proved to be beneficial in conjunction with atropine, pralidoxime, and diazepam in nerve agent poisoning, fresh frozen plasma and haemoperfusion. Intravenous magnesium sulfate decreased

hospitalization duration and improved outcomes in patients with organophosphorous poisoning [16-18]. The use of "-oximes" has been found to be of no benefit, or possibly harmful, in at least two meta-analyses [19,20]. Several studies try to estimate the role of ACH level and the prognosis of OPP but the results was controversial but these studies confirm that low ACHE associated with longer duration of hospital stay [21-24].

Case

Female patient 44 years old weight nearly 100 kg presented in the emergency department on 2- 5 -2015 due to consumption of large quantity of ethyl 3-methyl 4-(methylthio)phenyl-(1-methylethyl) phosphoramidate 10% (Nemacor 10%)R. The patient was conscious oriented and underwent gastric lavage. The patient admitted to the internal department for follow up. The physician wrote order to measure acetylcholinesterase (ACHE) blood level very four hours and administration of atropine. The first ACHE level was 3572 IU (normal value 4000-8000IU), after four hours the level decreased to 3069 IU but the patient still stable. Arterial blood gazes(ABG) was done and chemistry, the results were within normal range as seen below. On the second day 3/5 the patient clinically good, chemistry, CBC, electrolytes, KFT and RBG are normal. The total and direct bilirubin were normal (total 0,7 mg/dl and direct 0,3 mg/dl). Blood pressure 110/70 and body temp 37 c. The exception is low ACHE level 404 IU. The third day 5/5 patient general condition deteriorated and the patient suffers from acute atrial fibrillation and become semiconscious and disoriented, patent admitted to intensive care unit (ICU). In ICU the patent continuo treatment with atropine and treated for Atrial fibrillation. All investigations were normal except ACHE level was low 333 IU. On 6/5 patent general condition deteriorated and become comatose despite that all investigations were normal except ACHE. Organophosphorous anti dote Obidoxim started with loading dose 750mg administered over 5 minutes followed by 750 mg as continuous infusion administered over 24 hours with rate of 30 mg/hour. After administration of Obidoxim the general condition of the patient started to improve and the patient become fully conscious oriented, CBC, ABG and chemistry were normal except ACHE still low. On 9/5 the patient is normal clinically well conscious oriented all investigations and KFT and liver function test are normal but ACHE become lower than previous 116 IU. The physician decided to stop Obidoxim on the next day and maintain the patient on atropine only and under observation. Routine investigations were normal except ACHE level. On 11/5 the patient suffers from

bradycardia but pupils are dilated and normal. Obidoxim re-administered again, patent investigations are normal except ACHE level was low. The patient improved on 12/5 and again Obidoxim weaned and the patient only maintained on atropine the investigations were normal except ACHE level. On 13/5 atropin administration become intermittent, on 14/5 was stopped completely. The patient was under observation without any medications. On 15/5 full investigations were done all investigations were normal except ACHE. On 16/5 the patient discharged with good general conditions, all investigations were blood pressure 138/80 and body temperature 37 C normal except ACHE level. See table below for the investigations done during treatment.

Table 1. Represent the value of investigations done for the patient during hospital stay

Analysis	**Date**														
	2/5	3/5	4/5	5/5	6/5	7/5	8/5	9/5	10/5	11/5	12/5	13/5	14/5	15/5	16/5
Ph	7,44	N	N	7.45	N	N	N	N	N	N	N	N	N	7,41	7,43
PCO2	37	N	N	38	N	N	N	N	N	N	N	N	N	41	43
PO2	64	N	N	79	N	N	N	N	N	N	N	N	N	47	46
Bicarb	24	N	N	26	N	N	N	N	N	N	N	N	N	26	28
sO2	93%	N	N	96	N	N	N	N	N	N	N	N	N	99	97
ACHE	3572	404	400	333	334	450	480	116	330	273	335	300	312	280	234
HGb	12,9	N	N	N	N	N	N	N	N	N	N	N	N	9,6	9,6
RBC	4,3	N	N	N	N	N	N	N	N	N	N	N	N	3,83	4,2
WBC	11,8	N	N	N	N	N	N	N	N	N	N	N	N	7,5	7,6
PLT	337	N	N	N	N	N	N	N	N	N	N	N	N	251	254
Na		134	137	N	N	N	N	N	N	N	140	N	N	139	134
K		3,6	3,7	N	N	N	N	N	N	N	4,5	N	N	4,2	42
Cl		109	109	N	N	N	N	N	N	N	109	N	N	108	107
Tca		9,16	9,38	N	N	N	N	N	N	N	9,34	N	N	9,06	9,08
CPK			149	N	N	N	N	N	N	N	217	N	N	N	145
LDH			320	N	N	N	N	N	N	N	329	N	N	N	295
Cr		0,7	0,7	N	N	N	N	N	N	N	0,6	N	N	0,8	1
R.B.S		142	105	N	N	N	N	N	N	N	123	N	N	115	113
INR		0,8	N	N	N	N	N	N	N	N	1	N	N	1,2	1,1
Pt		13	N	N	N	N	N	N	N	N	11,8	N	N	16	14
aPTT		25	N	N	N	N	N	N	N	N	26,8	N	N	33,5	33

Abbreviations: (HGB: haemoglobulin, WBC: white blood cells, RBC: red blood cells, ACHE: acetyl cholinesterase, PLT : platelets, Na: sodium, K: potassium, Cl: chlorine ion, TCa: total calcium, R.B.S:random blood sugar, Cr: createnin, INR: international normalized ratio, Pt, partial thrombin time, aPTT: activated partial thrombim time, LDH: lactate dehydrogenase, CPK:createnin phosphor kinase, sO2: oxygen saturation, bicarb: bicarbonate, PO2 partial pressure of oxygen, PCO2 :partial pressure of carbon dioxide, N: the value is within normal range and this symbol is used to simplify the table)

Discussion

Organophosphorous poisoning is a major health problem with dangerous outcome. As mentioned above nearly 3000000 patients suffer from poisoning. It is fatal if not treated early. Treatment has different strategies ranging from gastric lavage to administration of antidote. In our country and most countries normal ACHE level is considered the most important marker of improvement in addition to clinical status. In our case the patient improved clinically but the level of ACHE remains very low. The interpretation of low ACHE level is that this patient underwent aging of organonophosphorous toxicity. The patient arrived at the hospital at least 2-4 hours after ingestion of high quantity of OPP according to data received from the patient. Since the patient is overweight and OPP are high lipid soluble the toxin will absorb easy and store in the fat tissue and brain in addition to the peripheral effect. Administration of atropine is to counter the muscarinic effect while oxime is antidote for the drug. When the concentration of drug in blood becomes low some of the stored in fat released into the blood and re-distributed again to other parts of the body which explain why there was remission relapse in the condition. Delay treatment and consumption of large quantity of OPP explain the mechanism of aging and why ACHE remains low in our patient. If a patient underwent aging he needs up to one year to improve ACHE level. Also the measurements of ACHE in the blood does not reflect the actual value of the neuromuscular junction, so it is not necessary to make clinical decision based on the blood measured level of ACHE. Other investigations remain normal because OPP only affects ACHE level and do not affect CBC or ABG or other investigations.

Conclusion

OPP poisoning is an important health problem worldwide; it needs education how to work with these substances and how to deal with its toxicity in place before hospital arrival. The

most useful marker for improvement is ACHE level but it is not essential for judgment, because its value does not reflect the neuromuscular concentration. It reflects blood ACHE concentration; low concentration is associate with long hospital stay. Clinical condition is the most important marker for decision on improvement or worsens of the patient.

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