

ORIGINAL PAPER

# Evaluation of Management of Organophosphorus Toxicity in Tripoli City Hospitals (Libya) and that in Minia University Hospital (Egypt)

**Khaled M. Gdarah<sup>1</sup>, Basheer A. Belkhair<sup>2</sup>, Osama A. Hassan<sup>3</sup>  
Mahmoud S. Annajar<sup>4</sup>, Nouri M. Elmiladi<sup>5</sup>**

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## ABSTRACT

*Anticholinesterase insecticides are used worldwide causing serious poisoning. This study was done to evaluate the management of organophosphorus poisoning in Tripoli, and in Minia. 49 cases were studied in Tripoli city hospitals. The study of Minia research was chosen to evaluate the effect and outcome of used fresh frozen plasma (FFP) and magnesium sulphate (MgSO<sub>4</sub>) in addition to the routine managements of poisoning by organophosphorus compounds (OP) which manifested in the form of gastric lavage, atropine and oximes and the routine methods of treatments of OP toxicity in Tripoli and 64 in Minia university hospital, divided into 4 groups 16 patients/group of both sexes. Group I: (control group); and other groups treated with atropine and oximes plus MgSO<sub>4</sub> (Group II), FFP (Group III), FFP and MgSO<sub>4</sub> (Group IV). Groups III and IV received two plasma bags (300-400 ml/bag)/day. FFP doses were repeated according to BuChE levels (e" 2100 IU/L). There was significant decrease in total plasma bags dose needed in-group IV. There was significant decrease in hospital stay in groups II, III and IV. 2 patients developed intermediate syndrome in-group I, and one in-group II. Use of MgSO<sub>4</sub> and FFP gave best result by reducing dose of atropine and oximes, mortality rate and days of hospitalization. 40.8% of Tripoli cases were treated by atropine in addition to the supportive treatment. This study concluded that use of atropine sulphate as antidote for treatment of OP in Tripoli hospitals is not enough, the use of oximes and FFP should be introduced if possible to decrease the fatality rate and the toxicity complications.*

**Keywords:** organophosphorus insecticides, anticholinesterase, plasma, magnesium sulphate, oximes, atropine

## INTRODUCTION

Organophosphate compounds (OP) are commonly used as agricultural insecticides. Thus, acute OP pesticides poisoning is widespread in the world.

It has been estimated that around 3 million severe cases of acute pesticide poisonings occur yearly with about 220000 deaths. It is estimated that 95% of fatal pesticide poisonings occur in developing countries.<sup>1</sup>

OP irreversibly bind to the enzyme AChE, inhibiting its activity and inducing accumulation and prolonged effects of acetylcholine at a variety of neurotransmitter receptors including sympathetic and parasympathetic ganglionic nicotinic sites, postganglionic cholinergic sympathetic and parasympathetic muscarinic sites, skeletal muscle nicotinic sites, and central nervous system sites.<sup>2</sup>

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### Address for correspondence and reprint:

<sup>1</sup>Prof. of Toxicology (**Corresponding Author**)

Forensic Medicine and Toxicology

**Email:** kgdara@yahoo.co.uk

**Mobile:** +218925001830

<sup>2</sup>Forensic Medicine and Toxicology

Faculty of Medicine, University of Tripoli, Libya

<sup>3</sup>Forensic Medicine and Clinical Toxicol. Department,  
Faculty of Medicine, Minia University, Egypt

<sup>4</sup>Biochemistry Department, Faculty of Medicine, University  
of Tripoli, Libya,

General Courses Department, Faculty of Medicine,  
University of Tripoli, Libya

Atropine and oximes (pralidoxime or obidoxime) are traditionally used in the management of such poisonings but their efficacy remains an issue of debate.<sup>3</sup> **MgSO<sub>4</sub>** and **FFP** have been reported to reduce the toxicity of **OP** compounds in animal experiments.<sup>4</sup>

In this study we planned to evaluate the management of organophosphorus poisoning in Tripoli and in Minia cities, and to enhance the treatment of Tripoli patients.

## MATERIALS AND METHODS

**A. Minia:** 64 adult patients of both sexes with acute **OP** insecticide poisoning were available for study; patients were divided into 4 groups 16/group:

**Group 1: (control group):** The patients treated with routine management in the form of gastric lavage, administration of 1 g/kg activated charcoal, appropriate bolus and maintenance doses of atropine. Atropine was given either as a continuous infusion (0.02-0.08 mg/kg) /hour or intermittent dosing 0.5-2 mg atropine every 15 min until secretions were controlled. The starting dose of obidoxime was 250-500 mg *i.v.* Additional doses were given in a bolus of 250-500 mg *i.v.* over 30-60 min every 6-12 hours according to severity of poisoning. The other groups treated in same manner plus:

**MgSO<sub>4</sub>** (4 g/day) *i.v.* (Group II), **FFP** (Group III), **FFP** and **MgSO<sub>4</sub>** (Group IV).

**Group III:** Plasma therapy was started after admission in 14 patients and after developing intermediate syndrome in 2 patients. The last 2 patients were in the atropine and pralidoxime group, but human plasma was given to these patients in order to observe any neuromuscular effects of BuChE after they developed intermediate syndrome. Two bags of plasma (300-400 ml/bag) were given daily until the patients no longer needed atropine. **FFP** doses were repeated according to BuChE levels until a normal level was achieved ( $\geq 2100$  UI/l).

### The following parameters were investigated:

1. Serum pseudo Cholinesterase level was measured on admission, a day after a day till patient discharge.
2. Aspartate transeaminase (AST) and Alaninetranseaminase (ALT): Normal value: **AST:** 20-30 u/l, **ALT:** 15-35 u/l.<sup>5</sup>
3. Blood Urea Nitrogen (BUN). Normal value 15-45mg/dl.<sup>6</sup>

4. Serum Creatinine Level: Normal value: 0.5-1.5mg/dl.<sup>7</sup>
5. Serum Electrolytes: (Model 288 Ciba Corning Co.) Standard samples were injected in blood gas analyzer and they were 140 meq/l for sodium, 5.0 meq/l for potassium and 1.4 meq/L for magnesium. Normal value **Na:** 130-145 mEq/l, **K:** 3.5-5.5 mEq/l, **Mg:** 1.5-2.6 mEq/l.
6. Blood Glucose Level Determination: Blood glucose level was determined by enzymatic colorimetric method.<sup>8</sup>
7. Treatment Parameters: Atropine, oximes, **MgSO<sub>4</sub>**, Total doses of **FFP** if given, was measured.

**B. Tripoli:** The study included 49 cases of organophosphorus toxicity. 41% were children.

The estimated average time between exposure and ICU admission to hospital was about 2 hours (ranged from 1 to 3 hours). The investigations: blood glucose, urea, sodium and potassium electrolyte, complete blood picture, pH, and electrocardiography. Treatment was as follow: supportive and symptomatic treatment, Gastric lavage was made to the majority of cases (91.8%), only 4 cases exempted while atropine administrated in 40.8% (20 cases).

**Statistical Analysis:** Basic analysis of variance allows quick comparison of several groups at once is used in Minia study group.

### Data are expressed as means $\pm$ SD

One Way ANOVA test for quantitative data between the groups

$P > 0.05$  Insignificant correlation

$P < 0.05$  Significant correlation

\* (**P value < 0.05**)

## RESULTS

**Minia:** Ages were 18 to 60 years. The estimated average time between exposure and ICU admission to MUH was 2.6 hours (range, 1–17 hours). The muscarinic features of anticholinesterase poisoning were predominant clinical manifestations (87.5%). Central nervous system (CNS) disturbances (57.81%) and manifested nicotinic symptoms (48.43%).

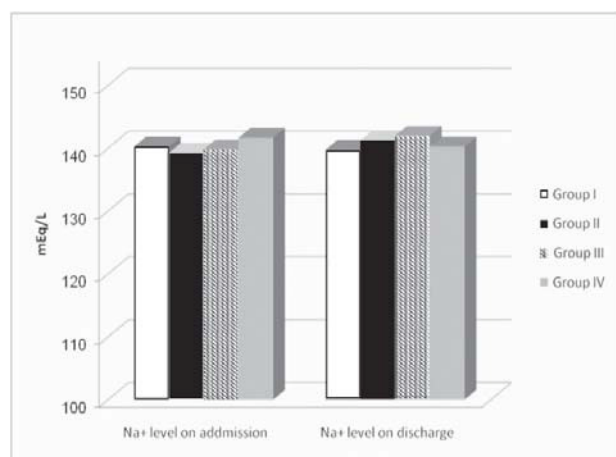
**Biochemical Parameters in Minia:**

**Table 1** Pseudocholesterase (BuChE) level in different groups on admission and discharge

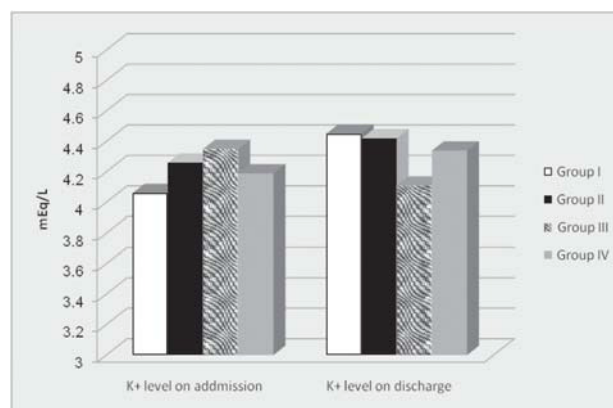
BuChE (U/l)	BuChE on admission (U/L)	BuChE on discharge(U/L)
Group I	448.44 ± 139.45	954.06 ± 275.65
Group II	436.88 ± 125.20	1036.65 ± 258.65
Group III	444.50 ± 75.75	2450.94 ± 412.19
Group IV	450.31 ± 131.59	2568.75 ± 425.21
P value	0.990	<0.001*
Group I vs. II	0.787	0.509
Group I vs. III	0.927	<0.001*
Group I vs. IV	0.965	<0.001*
Group II vs. III	0.859	<0.001*
Group II vs. IV	0.754	<0.001*
Group III vs. IV	0.892	0.347

**Table 2** Na<sup>+</sup> and K<sup>+</sup> level on admission and on discharge

Groups Na <sup>+</sup> & K <sup>+</sup> level on	Group I	Group II	Group III	Group IV	P value
Na <sup>+</sup> admission	140.25 ± 4.78	139.31 ± 5.92	139.81 ± 4.49	141.69 ± 5.71	0.615
Na <sup>+</sup> discharge	139.75 ± 10.54	141.25 ± 4.37	142 ± 5.56	140.29 ± 3.86	0.775
K <sup>+</sup> admission	4.16 ± 0.6	4.26 ± 0.73	4.05 ± 0.56	4.19 ± 0.48	0.596
K <sup>+</sup> discharge	3.95 ± 0.43	3.92 ± 0.46	3.89 ± 0.47	3.92 ± 0.69	0.254



**Figure 1** Na<sup>+</sup> level on admission and on discharge in each group



**Figure 2** K<sup>+</sup> level on admission and on discharge in each group

Glucose level was more than normal values in all groups on admission. Serum ureanitrogen, and creatinine levels showed insignificant changes on admission & discharge.

**TREATMENT PARAMETERS**

The total dose of atropine & Obidoxime was significantly reduced in groups II, III and IV.

**Table 3** Atropine & Obidoximes dose

Total dose of Atropine & Obidoxime Groups	Total atropine dose (mg)	Total obidoximes (gm)
Group I	203.5 ± 77.89	4.73 ± 1.99
Group II	200 ± 70.29	4.9 ± 1.86
Group III	133.88 ± 66.84	3.2 ± 1.18
Group IV	130 ± 58.52	3.12 ± 1.12
P value	0.002*	0.001*
Group I vs. II	0.886	0.756
Group I vs. III	0.006*	0.009*
Group I vs. IV	0.004*	0.006*
Group II vs. III	0.009*	0.004*
Group II vs. IV	0.006*	0.002*
Group III vs. IV	0.874	0.881

**Table 4** Hospital stay of the patients for each group (in days)

Groups	Hospital stay (days)
Group I	11.5 ± 2.58
Group II	7.94 ± 1.73
Group III	7.81 ± 1.38
Group IV	5.75 ± 1.34
P value	<0.001*
Group I vs. Group II	<0.001*
Group I vs. Group III	<0.001*
Group I vs. Group IV	<0.001*
Group II vs. Group III	0.847
Group II vs. Group IV	0.001*
Group III vs. Group IV	0.002*

## DISCUSSION

Better prognosis and outcome was noted with patients who arrived earlier to the hospital, *Colli*<sup>9</sup> postulated that the more the time delay the more is the prolonged gastrointestinal absorption, hepatic conversion of OPC to more toxic agents, irreversible inhibition of acetylcholinesterase (AChE) Aging, delayed respiratory management and subsequent tissue damage. The muscarinic features of anticholinesterase poisoning were 87.75%. CNS disturbances were 61.22% (Minia) and 48.43% (Tripoli), nicotinic symptoms were 44.89% (Minia) and 48.43% (Tripoli).

*Ozturk*<sup>10</sup> reported that loss of consciousness and respiratory tract symptoms were the most common features on admission.

The predominance of muscarinic manifestations in adult cases was similar to that reported in previous studies.<sup>11</sup> Agarwal and Wali<sup>12</sup> who revealed that muscarinic effects are usually the first to appear followed by nicotinic effects. CNS manifestations are less common than other features.

In contrast, Haddad LM *et al.*<sup>13</sup> reported that 47.3% of cases presented with ocular manifestations; 61.1% of cases presented with neuromuscular manifestations. Significant increase of pseudoacetylcholinesterase level was found in groups that received FFP.

After exposure to a toxic dose of anticholinesterase pesticide, plasma cholinesterase activity is rapidly reduced. Untreated patients may see a gradual return to normal activity in 4-6 weeks. Most of the patients showed marked reactivation in plasma ChE within several hours and recovered completely within 24 h. Plasma ChE reactivation

were observed, over the lower limit (1,900 U/l), for 50% of the patients after 12 h of admission. Abd El-Rahman<sup>14</sup> reported same results.

Pseudoacetylcholinesterase levels elevation can be used as a prognostic value for effect of treatment of Organophosphorus poisoning.<sup>15</sup> Unfortunately these investigations carried out in Tripoli hospitals.

*Amr et al.*<sup>16</sup> noted that there is no significant elevation of blood urea nitrogen and serum creatinine in persons exposed to OP, as the results that we have.

There was significant increase in magnesium blood level in Group II & Group IV. Also, *Pajoumand et al.*<sup>4</sup> reported that the serum Mg<sup>+2</sup> level increased in Mg<sup>+2</sup> treated subjects after treatment with MgSO<sub>4</sub> and the difference between Mg-treated and Mg<sup>+2</sup> non treated in Mg<sup>+2</sup> levels was significant (1.869/0.06 mEq/L in Mg-treated versus 1.619/0.03 mEq/L in Mg<sup>+2</sup> non treated, (P= 0.01).

There was insignificant change in serum sodium level in patients of Minia and Tripoli but there was significant decrease in serum potassium level in Minia only, this no change depend on time of hospital arrive or the ingested dose in Tripoli case.

Blood glucose levels significantly increase in Minia and Tripoli. Osmundson<sup>17</sup> stated that hypokalemia and hyperglycemia are well-documented findings in anticholinesterase intoxication.

The treatment with atropine (as an anticholinergic agent) and oximes (as cholinesterase reactivators) has failed to prevent morbidity or mortality in some cases.<sup>18</sup>

*De Silva et al.*<sup>19</sup> reported that pralidoxime & atropine does not have any benefit over atropine alone. Moreover, hepatotoxicity and cholinesterase inhibition may be seen due to oximes.

E. Gunay<sup>20</sup> reported that single dose of MgSO<sub>4</sub> therapy may be not sufficient in poisoning with OP compounds. Although there was a reduction in the mortality with MgSO<sub>4</sub> treatment, this decrease in incidence did not reached statistical significance.

There was significant decrease in total plasma bags doses needed in Group IV to which we added MgSO<sub>4</sub> plus frozen plasma.

*Guyen et al.*<sup>21</sup> used FFP in the treatment of OP poisoning in addition to traditional therapy, and its effects on outcomes and BuChE levels were excellent.



**Zhong et al.**<sup>22</sup> suggested that the transfusion of fresh blood may prove useful in the treatment of OP poisoning.

There was significant reduction in hospital stay in groups receiving magnesium sulphate and **FFP**. **Eddleston**<sup>23</sup> demonstrated that the mortality rate and hospitalization days of patients who received MgSO<sub>4</sub> treatment were significantly lower than those who had not received MgSO<sub>4</sub>.

Finally, further studies are needed to follow up patients exposed to anticholinesterase poisoning for early detection and treatment to avoid complications and mortality.

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