L-Carnitine as an Adjuvant Treatment in Acute Organophosphorus Pesticides Poisoning: A Randomized Clinical Trial

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ABSTRACT

Organophosphorus compounds are widely used pesticides. They are associated with a significant risk of acute intoxication. Oxidative stress is a contributing factor of acute organophosphorus poisoning morbidity and mortality. L-carnitine was found to have free-radical scavenging and antioxidant properties. Therefore, we aimed to evaluate the efficacy and safety of L-carnitine as an adjuvant in treatment of patients with acute organophosphorus poisoning. A randomized clinical trial was conducted on 30 patients suffering from acute organophosphorus poisoning admitted to Poison Control Center, Tanta University Emergency Hospital, Egypt, from April 2017 till January 2018. Patients were randomly divided into two equal groups. Group I received the standard treatment only and group II received the standard treatment plus L-carnitine in a dose of 1gm/8 hours IV.At time of admission, malondialdehyde, reduced glutathione, serum total antioxidant capacity and psudocholinesterase enzyme activity registered no significant difference between the two studied groups. After treatment, malondialdehyde, reduced glutathione and serum total antioxidant capacity showed significant improvement in group II. The mean value of atropine dose in group II (5.6mg) was significantly lower than group I(10.9mg). We concluded that the use of L-carnitine improved the antioxidant status and reduced total atropine dose required for treatment of patients with acute organophosphorus poisoning.

Introduction

Organophosphorus (OP) compounds are widely used pesticides because of their relatively low cost and rapid degradation (Coskun et al., 2015; Gündüz et al., 2015). However, they are associated with a significant risk of acute intoxication especially in developing countries owing to unrestricted sale, lack of protective equipment and poorly educated farmers (Kır et al., 2012; Saad et al., 2017).

In Egypt, acute OP poisoning is a toxicological problem of considerable concern. According to Ibrahim et al. (2011), insecticide intoxication represented 49% of the total number of chemical poisoning and OP insecticides accounted for 55% of insecticide poisoned cases. El-Maddah (2012) found that OP poisoning was the second most common incidence (30.4%) of acute poisoning.

Manifestations of acute OP poisoning are mediated mainly through irreversible inhibition of cholinesterase enzyme with subsequent

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accumulation of acetylcholine and over-stimulation of muscarinic and nicotinic receptors (Shah and Mundhra, 2016). Moreover, different studies showed that metabolism of OP compounds by cytochrome P450s is associated with production of reactive oxygen species making oxidative stress another factor contributing to acute OP poisoning morbidity and mortality (Ranjbar et al., 2005; Kumar et al., 2010; Hundekari et al., 2013; Mirakbari, 2015).

Oxidative stress markers can be used for evaluation and monitoring of OP poisoned patients (Lukaszewicz-Hussain, 2010). As lipid peroxidation is considered one of the molecular mechanisms of acute OP poisoning, so malondialdehyde (MDA) is a suitable marker to assess oxidative status in acute OP poisoning (Hundekari et al., 2011). Reduced glutathione (GSH) is a major antioxidant that protects cells against reactive oxygen species (Mercer et al., 2016). Measurement of total antioxidant capacity (TAC) is one of the common strategies to assess free radical/antioxidant equilibrium (Fraga et al., 2014).

Stabilization of the patients followed by administration of atropine and oximes and decontamination are considered the corner stone of acute OP poisoning treatment (Bajracharya et al., 2016). Beside standard treatment, antioxidant medications may have a promising role through counteracting increased reactive oxygen species and enhancement of antioxidant system (Žunec et al., 2014).

L-carnitine (LC); a non-protein amino acid; is synthesized in mammalian liver, kidney and brain (Cao et al., 2011). It was found to have free-radical scavenging and antioxidant properties. It is considered a safe antioxidant where mild nausea and vomiting are major side effects (Singh and Aslam, 1998). In addition, it is used in different pathological conditions associated with increased oxidative stress and can ameliorate oxidative damage in animal models (Calo et al., 2005). Therefore, this study aimed to evaluate efficacy and safety of LC as an adjuvant in treatment of acute OP intoxicated patients.

Patients and Methods

Study Design and Population:

An open-label, phase II trial was conducted on 30 patients suffering from acute OP poisoning admitted to Poison Control Center, Tanta University Emergency Hospital, Tanta, Egypt, from April 2017 till January 2018.

Diagnosis is based on history of exposure, availability of poison bottle or label, characteristic odor of gastric contents, typical clinical toxidrome of cholinergic and nicotinic manifestations following exposure to OP and reduced serum pseudocholinesterase (PChE) activity below reference range.

Poisoning severity was graded according to Minton and Murray (1988) and Bey et al.(2001) into mild (fatigue, headache, blurred vision, dizziness, nausea, vomiting, excessive sweating, salivation, abdominal pain and chest tightness), moderate (symptoms of mild poisoning plus muscular fasciculation, weakness, inability to walk, chest crepitations and miosis) and severe (symptoms of moderate poisoning plus unconsciousness, flaccid paralysis, respiratory distress, cyanosis and marked miosis with loss of pupil reflexes).

*Inclusion criteria:*All symptomatic patients aged 18 years or more with acute OP poisoning were included.

Exclusion criteria: Patients aged less than 18 years, pregnant and lactating females, patients with mixed intoxication and debilitated or cachectic patients were excluded. Patients with medical conditions that may induce

oxidative stress as cardiovascular diseases, renal, hepatic failure or neurodegenerative disorders and those presented more than 12 hours after exposure to OP compounds or received medical treatment for OP poisoning before admission were also excluded.

Methods

Thirty patients were randomly divided into two equal groups (15 patients each) by using the sequentially numbered, opaque, sealed, envelopes method (Doig and Simpson, 2005). Group I (standard treatment group) received standard treatment only and group II (L-carnitine group) received standard treatment plus LC.

Patients of both groups received standard treatment as guided by attending physician according to Tanta Poison Control Center Protocol.This standard treatment included patient resuscitation (if indicated), dermal or gastric decontamination with administration of single dose activated charcoal (1gm/kg) and antidotal therapy (atropine and oxime). Atropine was given as a bolus dose of 1 to 3 mg IV, repeated every 10 to 15 minutes till full atropanization, then maintained by continuous infusion of 10–20% of the loading dose every hour (Eddleston et al., 2008). Toxogonin® (1 ampoule contains 250 mg of obidoxime chloride in 1 ml, produced by Merck, Darmstadt, Germany) was given when nicotinic manifestations appeared as a loading dose of 250 mg bolus IV, followed by 750 mg every 24 hours until at least 12 hours after stopping of atropine (Roberts and Aaron, 2007). Patients of group II received LC in a dose of 1gm/8 hours IV (Elabbassia et al., 2014). It was given till stopping of standard treatment. Patients were closely monitored to detect any adverse effects of LC. If any occurred, LC was immediately stopped and the patient was registed as having side effect of the drug.

For all patients, sociodemographic and toxicological data were collected, physical examination including measurement of vital signs was done and blood samples were obtained at time of admission and before administration of any treatment. In adults, the normal ranges of blood pressure, pulse, respiratory rate and temperature are 90-130/60-90 mmHg, 60-100 beats/min., 16-24 cycles/min. and 36.5-37.5°C respectively (Flomenbaum et al., 2006 and Middleton, 2008).

An arterial blood sample (one ml) was obtained from each patient for blood gas analysis according to Kokholm (1990). A venous blood sample (five ml) of each patient was kept into a clean dry centrifuge tube and left to stand for few hours before centrifugation to avoid hemolysis, then serum was separated. Routine investigations including liver enzymes according to Reitman and Frankel (1957), blood urea according to Fawcett and Scott (1960) and Chaney and Marbach (1962), serum creatinine according to Houot (1985) and serum electrolytes according to Woo (1999) were measured.

Serum PChE activity was measured using butyrylthiocholine substrate according to Blawen et al. (1983). Serum level of MDA, GSH and TAC were assayed according to Satoh (1978), Tietez (1969) and Koracevic et al. (2001) respectively. Each of PChE activity, MDA, GSH and TAC were measured twice; at admission and when standard treatment was stopped.

Outcome measures:

The primary outcome was mortality, whereas secondary outcomes included hospital stay, total doses of atropine and oxime

received, occurance of atropine complications and the need of ICU admission and/or mechanical ventilation.

Ethical consideration:

The study was carried out after approval of the research ethics committee of Tanta Faculty of Medicine (Approval Number: 31451/03/17). A written informed consent was taken from each patient or his/her guardians (if the patient was unfit for giving consent) after receiving detailed information about the study. To conserve confidentiality, code number was given for each patient and data were analyzed anonymously. The disposal of blood collection syringes, tubes and body fluids (blood samples) was safely done to avoid any risk of environmental pollution.

Statistical Analysis

The collected data were organized and statistically analyzed using SPSS statistical software version 22 for windows. For quantitative data, the Shapiro-Wilk test for normality was performed. For data that were not normally distributed median and interquartile range (expressed as 25th-75th percentiles) were calculated and Mann-Whitney was used for comparison between groups. For normally distributed data, values were expressed as mean ± standard deviation and independent samples T test was used for comparison between two groups while paired t test was used to compare two related samples. For qualitative data, Pearson's Chi square, Fisher's exact, or Fisher-Freeman-Halton exact tests were used to examine association between two variables. Significance was adopted at $p < 0.05$ for interpretation of results of tests (Dawson and Trapp, 2001).

Results

The present study was carried out on 30 patients with acute OP poisoning admitted to Tanta Poison Control Center. Patients were divided into two groups randomly. Sociodemographic and toxicological data of the studied patients were demonstrated in table (1). Age of participants showed mean values 32.8 and 33.3 years in group I and II respectively. Male patients represented 60% of group I and 66.7% of group II. There was no significant difference between the two groups regarding sociodemographic and toxicological data at time of admission.

Table (1): Evaluation of sociodemographic and toxicological data of the studied acute organophosphrus poisoned patients (n=30).

Variables		Groups			Tests of significance	
		Total (n = 30)	**Group I (n = 15)**	**Group II (n = 15)**	**Test statistic**	**P**
Age (years)	Mean ±SD	33.1±11.8	32.8±11.6	33.3±12.3	t= -0.122	0.904
		n (%)	**n (%)**	**n (%)**		
Age groups (years)	18 – 30	14 (46.7%)	7 (46.7%)	7 (46.7%)	X^2_{FFH} =0.710	1.000
	30 - <40	4 (13.3%)	2 (13.3%)	2 (13.3%)		
	40 - <50	9 (30%)	5 (33.3%)	4 (26.7%)		
	≥ 50	3 (10%)	1 (6.7%)	2 (13.3%)		
Sex	Male	19 (63.3%)	9 (60%)	10 (66.7%)	X^2_{ChS}= 0.144	0.705
	Female	11 (36.7%)	6 (40%)	5 (33.3%)		
Occupation	Farmers	18 (60%)	9 (60%)	9 (60%)	X^2_{FFH} = 2.880	0.208
	Housewives	7 (23.3%)	2 (13.3%)	5 (33.3%)		
	Students	5 (16.7%)	4 (26.7%)	1 (6.7%)		
Residence	Rural	24 (80%)	11 (73.3%)	13 (86.7%)	FE	0.651
	Urban	6 (20%)	4 (26.7%)	2 (13.3%)		
Marital state	Married	21 (70%)	10 (66.7%)	11 (73.3%)	FE	1.000
	Single	9 (30%)	5 (33.3%)	4 (26.7%)		
Route of exposure	Oral	14 (46.7%)	6 (40%)	8 (53.3%)	X^2_{ChS}= 0.536	0.464
	Combined	16 (53.3%)	9 (60%)	7 (46.7%)		
Mode of exposure	Suicidal	13 (43.3%)	6 (40%)	7 (46.7%)	X^2_{ChS}= 0.136	0.713
	Accidental	17 (56.7%)	9 (60%)	8 (53.3%)		
Delay time (hrs)	Mean ±SD	4.5±2.5	4.7±2.4	4.3±2.6	t=0.401	0.691

n: number; SD: standard deviation; X^2_{ChS}: Pearson's Chi square test; X^2_{FFH}: Fisher-Freeman-Halton Exact tests; FE: Fisher's exact test; t: Independent samples t test, Group I: standard treatment group, Group II: L-carnitine group.

Regarding table (2), majority of the studied cases were evaluated as moderately intoxicated (73.3% and 60%), while cases of mild intoxication constituted (26.7% and 33.3%) of group I and II respectively. Only one case was severely intoxicated in group II. No significant difference was observed between the studied groups regarding poisoning severity grading, vital signs and oxygen saturation on admission.

Table (2): Assessment of vital signs, oxygen saturation and poisoning severity grading of the studied acute organophosphrus poisoned patients on admission (n=30).

Variables		Groups			Tests of significance	
		Total (n = 30) n (%)	Group I (n = 15) n (%)	Group II (n = 15) n (%)	Test statistic	P
Blood pressure	Normal	16 (53.3%)	8 (53.3%)	8 (53.3%)	X^2_{FFH} = 0.188	1.000
	Hypotension	10 (33.3%)	5 (33.3%)	5 (33.3%)		
	Hypertension	4 (13.3%)	2 (13.3%)	2 (13.3%)		
Pulse	Normal	14 (46.7%)	6 (40%)	8 (53.3%)	X^2_{FFH} = 1.819	0.466
	Bradycardia	15 (50%)	9 (60%)	6 (40%)		
	Tachycardia	1 (3.3%)	0 (0%)	1 (6.7%)		
Temperature	Normal	15 (50%)	9 (60%)	6 (40%)	X^2_{FFH} = 1.343	0.573
	Decreased	12 (40%)	5 (33.3%)	7 (46.7%)		
	Increased	3 (10%)	1 (6.7%)	2 (13.3%)		
Respiration	Normal	14 (46.7%)	7 (46.7%)	7 (46.7%)	X^2_{FFH} = 0.144	1.000
	Bradypnea	8 (26.7%)	4 (26.7%)	4 (26.7%)		
	Tachypnea	8 (26.7%)	4 (26.7%)	4 (26.7%)		
Oxygen saturation (%)	Minimum-maximum	88-98	88-99	88-98	t=1.346	0.189
	Mean ± SD	94±3.3	94.8±2.88	93.2±3.59		
Poisoning severity grading	Mild	9 (30%)	4 (26.7%)	5 (33.3%)	X^2_{FFH} =1.289	0.700
	Moderate	20 (66.7%)	11 (73.3%)	9 (60%)		
	Severe	1 (3.3%)	0 (0%)	1 (6.7%)		

n: number; X^2_{FFH}: Fisher-Freeman-Halton Exact tests; t: Independent samples t test, Group I: standard treatment group, Group II: L-carnitine group.

Table (3) showed that there was no statistical significant difference between group I and II concerning routine laboratory investigations on admission.

Table (3): Routine laboratory investigations of the studied acute organophosphrus poisoned patients on admission (n=30).

Variables	Groups						Independent samples t test	
	Total (n = 30)		Group I (n = 15)		Group II (n = 15)		t	P
	Range	Mean±SD	Range	Mean±SD	Range	Mean±SD		
ALT(U/L)	14-42	22.2±6.8	14-40	21.9±6.5	16-42	22.5±7.4	-0.237	0.815
AST(U/L)	17-47	29.4±9.7	18-47	28.8±10.3	17-46	22.9±9.5	-0.313	0.756
Urea (mg/dl)	15-45	27.6±7.5	16-39	26.9±6.6	15-45	28.3±8.6	-0.502	0.619
Creatinine (mg/dl)	0.6-1.2	0.9±0.2	0.7-1.2	0.9±0.2	0.6-1.2	0.9±.2	0.096	0.925
pH	7.36-7.503	7.414±.051	7.36-7.503	7.417±.052	7.34-7.502	7.411±.053	0.294	0.771
$PaCO_2$ (mmHg)	26.1-52.1	41.3±7.2	26.1-50.2	39.2±7.0	29.9-52.1	43.3±7.0	-1.611	0.118
HCO_3(mmol/l)	20.4-33.2	28±4	21.7-33.2	28±4	20.4-32.9	27±3	0.712	0.482
PaO_2 (mmHg)	34.9-98.6	77.3±15.6	39.9-92.3	76.0±15.4	34.9-98.6	78.6±16.1	-0.446	0.659
Na(mEq/L)	132.1-150.6	140.9±5.5	133.9-150.6	141.4±6.0	132.1-149.9	140.5±5.2	0.431	0.670
K(mEq/L)	2.8-5.3	3.9±.6	2.8-4.9	3.8±0.6	2.8-5.3	4.0±.7	-0.858	0.398

SD: standard deviation; n: number; t : Independent samples t test; ALT: Alanine aminotransferase, AST, Aspartate aminotransferase. Group I: standard treatment group, Group II: L-carnitine group.

According to table (4), MDA, GSH, TAC and PChE activity registered no significant difference between the two studied groups on admission. After treatment, there was statistically significant difference between the two groups in MDA, GSH and TAC (P = 0.020, <0.001, <0.001) respectively. Whereas PChE activity did not show significant difference after treatment between the two groups (p=0.275).

Table (4): Analysis of malondialdehyde, reduced glutathione, total antioxidant capacity and pseudocholineaterase enzyme activity in the studied acute organophosphorus poisoning patients on admission and after treatment (n=30).

Variables	Time of analysis	Groups			Independent samples t test between two groups	
		Total (n= 30) Mean ± SD	Group I (n = 15) Mean ± SD	Group II (n = 15) Mean ± SD	t	P
MDA (nmol/ml)	On admission	6.99±1.04	6.97±1.01	7.01±1.1	-0.107	0.915
	After treatment	4.83±1.13	5.3±0.86	4.36±1.2	2.477	0.020*
GSH (mg/dl)	On admission	1.02±0.38	0.97±0.35	1.07±0.42	-0.754	0.462
	After treatment	1.75±0.69	1.25±0.38	2.24±0.57	-5.602	<0.001*
TAC(mmol/l)	On admission	0.80±0.24	0.87±0.27	0.74±0.21	0.607	0.165
	After treatment	1.67±0.73	1.08±0.32	2.25±0.5	-7.630	<0.001*
PChE activity (U/L)	On admission	2781.8 ±1353.2	3134.3 ±943.6	2429.3 ±1623.7	1.454	0.157
	After treatment	6112.5 ±2329.1	6584.3 ±2091.6	5640.8 ±2526.9	1.114	0.275

* significant; n: number; SD: standard deviation; t: Independent samples t test, Group I: standard treatment group, Group II: L-carnitine group.

The mean value of atropine dose in group II (5.6 mg) was significantly lower than in group I (10.9 mg). While, atropine complications appeared only in group I (13.3%) with no significant difference between the two groups. The medians of toxogonin dose were 5 and 4 ampoules in group I and II respectively with no significant difference between the two studied groups. Mean values of hospital stay were 52.6 and 46.9 hours in group I and II respectively with no significant difference. Neither mortality nor the need for ICU admission and/or mechanical ventilation was recorded in both groups (Table 5).

Table (5): Assessment of the outcome measures of the studied acute organophosphrus poisoned patients (n=30).

Variables		Groups			Tests of significance	
		Total (n = 30)	Group I (n= 15)	Group II (n = 15)	Test statistic	P
Atropine dose (mg)	Mean ± SD	8.2±3.8	10.9±3.4	5.6±1.6	t=5.379	<0.001*
Toxogonin intake	No (n, %)	12 (40%)	6 (40%)	6 (40%)	X^2_{ChS}= 0.000	1.000
	Yes (n, %)	18 (60%)	9 (60%)	9 (60%)		
Toxogonin dose in ampoules (Ampoule=250mg)	Median (IQR)	5 (4– 5)	5 (4– 5)	4 (3– 5)	Z_{MW}=- 1.303	0.193
	Mean ranks		11.1	7.9		
Atropine complications	Present (n, %)	2 (6.7%)	2 (13.3%)	0 (0%)	FE	0.483
	Absent (n, %)	28 (93.3%)	13 (86.7%)	15 (100%)		
Hospital stay (hrs)	Mean ± SD	49.8±11.4	52.6±11.7	46.9±10.9	t=1.377	0.180

* : significant; n: number; SD: standard deviation; IQR: interquartile range; Z_{MW}: Mann Whitney test; X^2_{ChS}: Pearson's Chi square test; FE: Fisher's exact test; t: Independent samples t test, Group I: standard treatment group, Group II: L-carnitine Group.

Discussion

Acute OP poisoning is a major global clinical problem associated with high morbidity and mortality, especially in rural areas of developing countries (Eddleston et al., 2008; Dündar et al., 2015). Organophosphrus compounds irreversibly inhibit cholinesterase enzyme, causing excessive accumulation of acetylcholine with paralysis of cholinergic transmission in the central nervous system, autonomic ganglia, parasympathetic nerve endings, some sympathetic nerve endings and neuromuscular junction (Goel and Aggarwal, 2007).

This study was designed to evaluate the role of the antioxidant L-carnitine (LC) as an adjuvant therapy in acute OP poisoning. Findings of the current research regarding sociodemographic and toxicological characteristics and clinical data were more or less in accordance with previous studies performed in many Egyptian and international poisoning centers (Rehiman et al., 2008; Abd El AL et al., 2016; Kumar and Sahna, 2017).

Proper randomization using the sequentially numbered, opaque, sealed, envelopes method justifies lack of significant difference between the two groups regarding sociodemographic characteristics, toxicological and clinical data, vital signs, routine laboratory investigations, PChE activity and oxidative stress markers at the time of admission.

Herein, it was observed that MDA was significantly lower and each of GSH and TAC were significantly higher in group II versus group I after treatment. These findings were in accordance with previous experimental and

clinical studies that showed that, use of antioxidants had a protective effect in acute OP poisoning (Shadnia et al., 2007; Balali-Mood and Saber, 2012; El-Ebiary et al., 2016).

Organophosphorus compounds were found to generate excessive free radicals during their biotransformation, detoxification or even through mitochondrial impairment. This mitochondrial impairment can increase reactive oxygen species production with subsequent further mitochondrial damage generating a vicious circle (Abdel-Salam et al., 2016). Therefore, oxidative stress occurs as a result of imbalance between pro-oxidants and the antioxidant capacity with redox circuit disruption (Antonijevic et al., 2018).

In light of this data, it is expected to find improvement of oxidative stress parameters in group II patients who received LC which is a free radical scavenger. L-carnitine regulates enzymes activity involved in defense against oxidative damage and protects antioxidant enzymes; glutathione peroxidase, catalase and superoxide dismutase from oxidative damage (Uchenduet al., 2012; Mohammadi et al., 2018).

L-carnitine can facilitate β-oxidation of long-chain fatty acids, participate in branched chain amino acids metabolism and stabilize cellular membranes. Moreover, it can increase antioxidant enzymes activities in human (Lee et al., 2014). Furthermore, LC could improve antioxidant status and free radicals detoxification and provide strong antigenotoxic effect in OP intoxicated rats (Shokrzadeh et al., 2013; Shadboorestan et al., 2015). Additionally, LC administration to healthy volunteers significantly increased the antioxidant enzymes activities (Cao et al., 2011).

Data obtained from the current study revealed lack of significant difference between the two groups regarding PChE activity after treatment. Oximes can restore cholinesterase activity by removing phosphate group of the inhibited enzymes (Goel et al., 2012). In the current study, all cases were treated within 12 hours after exposure that allowed early oxime administration before aging of the inhibited enzyme. This could explain lack of significant difference between the two groups regarding PChE activity after treatment.

In this study, the dose of atropine in group II was significantly lower than in group I. This finding is in match with Shadnia et al. (2011) and El-Ebiary et al. (2016) who found that the use of the antioxidant N-acetylcysteine significantly lowered the required atropine dose in comparison with patients who did not receive it.

L-carnitine has compensated consumption of antioxidant agents which could not be replaced in a short time. This might be utilized to overcome damage produced by free radicals and depletion of TAC resulted from OP poisoning (Eddleston et al., 2008). This could explain LC ability to ameliorate oxidative stress effect with subsequent reduction of atropine dose.

This study showed non-significant difference between the two groups regarding atropine complications. However, 13.3% of group I had atropine complications. This can be explained by the ability of the LC to reduce the required atropine dose with subsequent low incidence of atropine complications.

There was no significant difference between the two groups regarding toxogonin dose. This could be explained according to the current study by absence of significant difference between the two groups regarding PChE activity after treatment. Similar data were obtained by Shadnia et al. (2011) who found that, antioxidants use in acute OP poisoned patients had no effect on toxogonin dose.

Despite there was no significant difference between the two groups regarding duration of hospital stay, it was slightly shorter in group II in comparison with group I. Shadnia et al.(2011) and Motawei and Elbiomy (2017) found that, N-acetylcysteine significantly lowered hospital stay in acute OP poisoned patients. Generally, the presence of other diseases or development of complications and even medical facilities in each country could affect the duration of hospital stay after poisoning (El-Naggar et al., 2009; Baydin et al., 2014).

Conclusion

The results of the current study declared that, LC improved antioxidant capacity and lowered atropine dose with subsequent lower incidence of atropine complications without any serious side effects. Additionally, LC is available in IV form so it can be easily administered to comatose patients. Hence, it is concluded that, LC could be considered a promising adjuvant antioxidant therapy in acute OP intoxication.

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Study Limitations

The major limitation of this study was the small sample size. Subsequently, severe cases were limited. Therefore, further studies with larger sample size in different poisoning centers are suggested to confirm the results of the current study. However, to the author's best knowledge; this is the first clinical trial to assess LC as adjuvant therapy in treatment of acute OP toxicity in Egypt.

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ل- كارنيتين كعلاج مساعد في حالات التسمم الحاد بمبيدات الآفات العضوية الفوسفورية: تجربة سريرية عشوائية

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تعد مركبات الفوسفات العضوية واحدة من مبيدات الآفات المستخدمة على نطاق واسع. إلا أنها ترتبط بشكل كبير بحالات التسمم الحاد. ويعتبر الإجهاد التأكسدي أحد العوامل التي تساهم في الحالات المرضية والوفيات الناجمة عن التسمم الحاد بهذه المركبات. ونظرا لخواص عقار ل- كارنيتين الكاسحة للشوارد الحرة والمضادة للأكسدة فإن هدفنا من هذه الدراسة هو تقييم فعالية وسلامة ل- كارنيتين كعلاج مساعد في حالات التسمم الحاد بمركبات الفوسفات العضوية.وقد تم إجراء تجربة سريرية عشوائية على ثلاثين مريض يعانون من التسمم الحاد بمركبات الفوسفات العضوية و الذين تم إدخالهم إلى مركز مكافحة التسمم ، مستشفى الطوارئ بجامعة طنطا ، مصر ، من إبريل ٢٠١٧ حتى يناير ٢٠١٨ . تم تقسيم المرضى عشوائياً إلى مجموعتين متساويتين. تلقت المجموعة الأولى العلاج الأساسى فقط وتلقت المجموعة الثانية العلاج الأساسى بالإضافة إلى ل- كارنيتين بجرعة ١ جم / ٨ ساعات وريديا. وقد أظهرت النتائج عدم وجود فرق ذى دلالة إحصائية بالنسبة لقياسات المالوندهيد ، الجلوتاثيون المختزل ، القدرة التأكسدية الكلية وانزيم سودو كولين استيريز بين المجموعتين عند الدخول. بينما أظهرت الدراسة وجود تحسن واضح بين المجموعتين بالنسبة لقياسات المالوندهيد، الجلوتاثيون المختزل والقدرة التأكسدية الكلية بعد العلاج. وكذلك كانت القيمة المتوسطة لجرعة الأتروبين في المجموعة الثانية (٥,٦ مجم) أقل بدلالة إحصائية من المجموعة الأولى (١٠,٩ مجم). وقد خلصنا إلى أن استخدام ل- كارنيتين يحسن حالة مضادات الأكسدة و يقلل من جرعة الأتروبين الكلية المطلوبة لعلاج المرضى الذين يعانون من التسمم الحاد بمركبات الفوسفات العضوية.