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N-acetylcysteine as an Adjuvant in The Treatment of Acute Aluminum Phosphide Poisoning: A Randomized Clinical Trial

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Abstract

Aluminum phosphide (ALP) is a common pesticide used for agricultural and non-agricultural purposes. Being cheap, widely available and highly toxic, it is responsible for many cases of poisoning. Aluminum phosphide poisoning has no specific antidote, therefore, based on role of oxidative stress in ALP poisoning, N-acetylcysteine (NAC) was suggested as adjuvant therapy in acute ALP poisoning.This study is a randomized clinical trial. It was conducted in Poison Control Center (Emergency Hospital, Tanta University). Thirty acute ALP intoxicated patients were randomly allocated into two equal groups A and B using the sequentially numbered, opaque sealed envelopes method. Group Areceived NAC 140 mg/Kg IV infusion as a loading dose followed by 70 mg/KgIV infusion every 4 hours up to 17 doses in addition to the routine treatment. Group B received only the routine treatment. Complete physical examination, routine laboratory investigations and oxidative stress markers; Malondialdehyde (MDA) and total antioxidant capacity (TAC) were performed for each patient.Results of the current study revealed no statistical significant difference between group A and group B patients regarding sociodemographic, toxicologicaland clinical data as well as routine laboratory investigation. On admission, MDA and TAC serum levels showed no statistical significant difference between group A and B. After treatment a statistical significant difference was observed in serum MDA and TAC levels between group A and B. Also, significant differenceswere noticed between group A and group B patients concerning mortality, dose of dopamine and hospitalization time.The study concluded that NAC might be a promising adjuvant therapy in treatment of acute ALP toxicity.

Keywords Aluminum phosphide; poisoning; N-acetylcysteine; oxidative stress; malondialdehyde; total antioxidant capacity.

Introduction

Aluminum phosphide (ALP) is a common pesticide used for agricultural andnon-agricultural purposes(Singh et al., 2014). It has been registered in USA and many other countries for indoor fumigation of agricultural compounds, processed foods and animal feeds. Furthermore, it has been used for structural as well as outdoor pest control (Mehrpour and Singh, 2010).Being cheap, widely available and highly toxic, it is responsible for many cases of poisoning (Taramsari et al., 2011).

Aluminum phosphide is available as tablets or pellets; the specified fatal dose is 0.15-0.5gm(Taramsari et al., 2011). Time interval between poison intake and death ranges between 1-48 hours with average of three hours. The commonest cause of death is arrhythmia within 24 hours in addition to shock, acidosis and ARDS after 24 hours(Wahab et al., 2008).

Following contact with water, moisture in air, or hydrochloric acid in stomach, ALPliberates toxic phosphine gas, which is rapidly absorbed by inhalation, dermally, orgastrointestinally(Taramsari et al., 2013).

Although,the exact mechanism of action of phosphine is still unknown, however, non-competitive cytochrome oxidase binding of phosphinehas been suggested by initial survey on different animals (Mostafazadeh, 2012).

Phosphine induced inhibition of mitochondrial cytochrome c oxidase leads to generation of reactive oxygen species and cellular peroxides (Chaudhry and Rai, 2014). Imbalance between free radicals production and elimination exhibits an oxidative stress that results inlipid peroxidation and oxidant mechanisms with subsequentbiological macromolecular damage specially cell membrane ultimately leading to cell death (Mirakbari, 2015; Yousef et al., 2015).

Aluminum phosphide poisoning has no specific antidote,therefore different modalities have been suggested for its treatment (Hassanian-Moghaddam and Zamani, 2016). Based on the role of oxidative stress in ALP poisoning, N-acetylcysteine (NAC) was the most promising antioxidant that has been tried in experimental studies(Azad et al., 2001; Chaudhry and Rai, 2014). It serves as a precursor for glutathione thus it can replenish intracellular glutathione stores. Moreover, NAC can act as a direct scavenging agent of oxygen free radicals (Nurulain et al., 2013).Therefore, NACwas evaluated for safety and effectiveness as an adjuvant therapy in treatment of patients with acute ALP poisoning.

Patients and Methods

This randomized clinical trial was conducted on 30 patients suffering from acute ALP poisoning admitted to the Poison Control Center (Emergency Hospital, Tanta University) from January to October 2016. The study was approved from the Research Ethics Committee of Faculty of Medicine, Tanta University. An informed written consent was obtained from each patient or his/her guardian (if the patient was unable to participate in consent process) after receiving detailed information about the study.Confidentiality of the data was maintained by making code number for each patient.

Inclusion criteria

Patients (male or female, aged 18 years or older) with symptomatic acute ALP poisoning (deliberate or accidental), were included in this study.The diagnosis was based ontypical clinical manifestations due to and following shortly after a single exposure to ALP, together with reliable identification of the compound (the container brought by patient attendants).Subsequent confirmation by silver nitrate test for phosphine detection in stomach contents was carried out for oral route exposure.

Exclusion criteria

Patients less than 18 years of age,pregnant and lactating women, patients with ingestion or exposure to other substances in addition to phosphide, patients with other major medical conditions (e.g. cardiovascular disease, renal or hepatic failure), patients presenting more than 6 hours of having consumed the phosphide compound and patients treated for acute phosphide poisoning in any medical center before admission were excluded from the study.

Interventions

The study subjects (30 patients) were randomly allocated into two equal groups A and Busing the sequentially numbered, opaque, sealed, envelopes method (Doig and Simpson, 2005).Group A patients received NAC 140 mg/Kg IV infusion (as a loading dose), then 70 mg/KgIV infusion every 4 hours up to 17 doses (Tehranietal., 2013). In addition, the routine treatment wasgiven, and it consists of patient resuscitation, gastric decontamination (with sodium bicarbonate and activated charcoal [1 g/Kg, orally] in the first 6 hours after the onset of poisoning), adequate hydration and supportive measures. Patients in group B only received the previously described routine treatment.

All patients were subjected to full history takingwith emphasis on age, gender, occupation, residence, mode of poisoning, amount and route of exposure, time elapsed before hospital admission and history of medical diseases that induce oxidative stress such as liver, renal, cardiac and/or active infections.Complete physical examination includedassessment of consciousness level by Glasgow coma score (GCS), general clinicalexamination and monitoring of vital signs and oxygen saturation. All patients were followed up until discharge or death.

Blood samples were collected under complete aseptic conditions forroutine laboratory work as well as oxidative stress markersonadmission before administration of any medication.Another blood sample was collected from each patient after treatment for oxidative stress markers.Routine laboratory work included;arterial blood gases, liver function tests, renal function tests, Sodium, Potassium and complete blood count.Oxidative stress markersincludedmalondialdehyde (MDA) and total antioxidant capacity (TAC)using commercial kits supplied by Biodiagnostic, Egypt.

Outcome measures

The primary outcome was mortality, but secondary outcomes included need for mechanical ventilation, the dopamine dose,duration of hospital stay and incidence of adverse events. These parameters represent the study outcomes to be monitored. Significant differences between the two study groups regarding any of these parameters is of great significance regarding the evaluation of safety and effectiveness of NAC as an adjuvant in treatment of patients with acute ALP poisoning.

Statistical methods

The collected data were organized and statistically analyzed using SPSS software statistical computer package for windows version 22. For quantitative data, the Shapiro-Wilk test for normality was performed. For normally distributed data, values were expressed as mean and standard deviation and independent sample t-test was used for comparison between groups. For data that were not normally distributed median and interquartile range (expressed as 25^{th}-75^{th} percentiles) were calculated and Mann-Whitney test was used for comparison between groups For qualitative data, Pearson's Chi-square for association or Fisher's exact test were used as appropriate. Significance was adopted at $p<0.05$ for interpretation of results of tests.

Results

The current study was conducted over 10 months from the start of January till the end of October 2016.A total of 30 patients with acute ALP poisoning were included in the study. They were randomly divided into group A and group B,the majority of them (13 patients from group A and 12 patients from group B) were in the age group 18-28.Males represented 7 (46.7%) and 6 (40.0%) of patients in group A and B respectively, females represented 8 (53.3%) and 9 (60.0%) of patients in group A and B respectively. Eight (53.3%) and ten (66.7%) patients were recorded from rural areas in group A and B respectively. Group A registered one (6.7%) unemployed patient, 8 (53.3%) students, 4 (26.7%)housewife and 2 (13.3%) workers while in group B there were one (6.7%) unemployed patient,4 (26.7%) students, 6 (40.0%) housewife and 4 (26.7%) workers.Sociodemographiccharacteristics of the participant patients were illustrated in table 1. There was no statistical significant difference between group A and group B patients considering age, gender, residence and occupation.

Toxicological data of the participant patients are demonstrated in table 1. It revealed that, 13 (86.7%) and 15 (100.0%) of patients were suicidal attempts in group A and B respectively. Similarly, oral route exposure was registered in 13 (86.7%) and 15 (100.0%)of cases in group A and B respectively. Pre hospital period range was1.5-6 and 1-4.5 hours with a median value of 3and 2.8 hours in groups A and B respectively. The ingested amount ranged between 0.5-1.0 and 1.0-1.0 tablet in group A and B respectively. No statistical significant difference was detected between groups A and B regarding manner of poisoning, route of poisoning, amount of poison ingestedor pre-hospitalization period.

Table 2 indicated clinical data of the study participants on admission.Glasgow coma score registered aninterquartile range of 15. Group A showed that, tachycardia and normalpulse were recorded in 5 (33.3%) and 10 (66.7%) of patients respectively. Meanwhile,in group B, undetected pulse, bradycardia, tachycardia and normal pulse were registered in 2 (13.3%), 1 (6.7%), 7 (46.7%) and 5 (33.3%) of patients respectively. Systolic blood pressure showed hypotension in 11 (73.3%) and 14 (93.3%) of patients in group A and B respectively and was normal in 3 (20.0%) and 1 (6.7%) of patients in group A and B respectively. Respiratory rate, temperature and O_2 saturation recorded mean values of 24.6, 37.1 and 89.3 respectively in group A patients and mean values of 26.6, 36.8 and 84.5 respectively in group B patients. There was no statistical significant difference between group A and group B patients on admission regarding GCS, heart rate, systolic blood pressure, respiratory rate, temperatureand O_2 saturation.

On admission, the mean values of blood pH, Pa Co2 and Pa O2 were 7.4, 27.2 and 67.8 respectively in group A and were 7.3, 23.8 and 51.8 respectively in group B. Alanine aminotransferase, aspartate aminotransferase and bilirubin levels registered mean values of 22.3, 24.0 and 0.87 respectively in group A and mean values of 33.7, 31.1 and 0.96 respectively in group B. The mean values of blood urea and serum creatinine were 30.0 and 1.04 respectively in group A and were 31.5 and 1.21 respectively in group B. Sodium and Potassium levels showed mean values of 141.1 and 3.2 respectively in group A and mean values of 143.2 and 3.0respectively in group B.Hemoglobin level, hematocrite value, white blood cells and platelets recorded mean values of 11.6, 38.1, ٩٣٨٠.0 and 178,580 respectively in group A and mean values of 11.5, 36.1, 10300.0 and 210,067 respectively in group B. Random blood sugar revealed a mean value of 125.1 and 161.7 in group A and B respectively. Table 3 showed nostatistical significant difference between group A and group B patients regarding the results of routine laboratory investigation.

On admission, the mean values of MDA serum levels were17.48 ± 7.48 and 16.23 ± 7.91 nmol/ml in groups A and B respectively.No statistically significant difference could be noticed between the two groups. After treatment the mean serum MDA levelswere 2.79 ± 1.82and17.26 ± 6.39 nmol/ml in groups A and B respectively with astatistical significant difference observed between the two groups ($p<0.001$) (table 4).

On admission, TAC levels revealed mean values of 1.99 ± 0.77 and 3.23 ± 2.16 mmol/l in groups A and B respectively with no significant difference between the two groups. However, after treatment serum TAC levels were 0.66 ± 0.26 mmol/l and 2.15 ± 1.44 mmol/l in groups A and B respectively, showed a statistical significant difference between the two groups ($p=0.001$) (table 4).

At the time of discharge, 13(43.3%)patients were improved, 17(56.7%) patients died. During their hospital stay,19(63.3%) patients required intubation and mechanical ventilation assistance. Dopaminerequirementsin patient treatment registered mean values of 12.86±4.88 µg/minuteand 18.57±3.78

µg/minutein groups A and B respectively. Hospitalization time showed a median of 48 hours in group A and of 12 hours in group B. No adverse effects for NAC administration were recorded in any of group A patients. Statistical significant differences could be noticed between group A and group B patients concerning mortality, dose of dopamine or epinephrine and hospitalization time. On the contrary, need for intubation and mechanical ventilation registered no statistical significant difference between group A and group B patients(table 5).

Table 1.Fisher's exact test, Pearson's Chi square test and Mann Whitney analyses of sociodemographic and toxicological data of acute aluminum phosphide poisoning patients(15 patients in each group).

Variable		Group A (n=15) n (%)	Group B(n=15) n (%)	Test statistics	*p*
Age (years)	18-28	13 (86.7%)	12 (80.0%)	X^2_{FE}= 2.081	0.598
	28-38	2 (13.3%)	1 (6.7%)		
	38-48	0 (0.0%)	2 (13.3%)		
Sex	Males	7 (46.7%)	6 (40.0%)	X^2_{ChS}= 0.136	0.713
	Females	8 (53.3%)	9 (60.0%)		
Residence	Urban	7 (46.7%)	5 (33.3%)	X^2_{ChS}= 0.556	0.456
	Rural	8 (53.3%)	10 (66.7%)		
Occupation	Unemployed	1 (6.7%)	1 (6.7%)	X^2_{FE}= 2.588	0.555
	Student	8 (53.3%)	4 (26.7%)		
	Housewife	4 (26.7%)	6 (40.0%)		
	Worker	2 (13.3%)	4 (26.7%)		
Manner of poisoning	Suicidal	13 (86.7%)	15 (100.0%)	X^2_{ChS}= 0.536	0.464
	Accidental	2 (13.3%)	0 (0.0%)		
Route of poisoning	Oral	13 (86.7%)	15 (100.0%)	X^2_{ChS}= 0.536	0.464
	Inhalational	2 (13.3%)	0 (0.0%)		
Amount (tablet)	Median (IQR)	1.0 (0.5-1.0)	1.0 (1.0-1.0)	Z_{MW}= 1.001	0.317
Pre-hospitalization period (hour)	Median (IQR)	3 (1.5-6.0)	2.8 (1-4.5)	Z_{MW}= -0.838	0.402

P ≤ 0.05 = significant, P >0.05 = non-significant, X^2_{FE}: Fisher's Exact test, X^2_{ChS}: Pearson's Chi square test Z_{MW}: Mann -Whitney test, IQR: Interquartile range.*

Table 2.Mann Whitney test, Fisher's Exacttest and Independent samples *t*-test analyses of clinical data of acute aluminum phosphide poisoning patients on admission (15 patients in each group)

Variable		Group A (n=15) n (%)	Group B (n=15) n (%)	Test statistics	*p*
GCS	Minimum- Maximum	13- 15	3-15	Z_{MW}=-2.375	0.067
	Median (IQR)	15 (15-15)	15 (14-15)		
Heart rate	Undetected	0 (0.0%)	2 (13.3%)	X^2_{FE}=4.516	0.119
	Bradycardia	0 (0.0%)	1 (6.7%)		
	Tachycardia	5 (33.3%)	7 (46.7%)		
	Normal	10 (66.7%)	5 (33.3%)		
Systolic blood pressure	Hypotension	11 (73.3%)	١٤ (93.3%)	X^2_{FE}=2.220	0.330
	Hypertension	1 (6.7%)	0 (0.0%)		
	Normal	3 (20.0%)	1 (6.7%)		
Respiratory rate	Minimum- Maximum	17.0-37.0	18.0-39.0	*t*=-0.866	0.394
	Mean±SD	24.6±5.6	26.6±7.0		
Temperature	Minimum- Maximum	36.0-38.0	36.0-38.0	*t*=1.130	0.270
	Mean±SD	37.1±0.5	36.8±0.8		
O_2saturation (%)	Minimum- Maximum	60.0-99.0	70.0-98.0	*t*=1.300	0.204
	Mean±SD	89.3±11.4	84.5±8.9		

P ≤ 0.05 = significant, P >0.05 = non-significant, GCS: Glasgow coma score, t: Independent samples t-test Z_{MW}: Mann -Whitney test, IQR: Interquartile range.*

Table 3.Independent samples *t*-test analysis of laboratory data of acute aluminum phosphide poisoning patients on admission (15 patients in each group)

Variable	Group A (n=15)		Group B (n=15)		*t*-test	*p*
	Range	Mean±SD	Range	Mean±SD		
pH	7.2-7.5	7.4±0.1	7.1-7.5	7.3±0.1	0.520	0.608
PCO_2	17.0-47.0	27.2±8.1	15.0-34.0	23.8±5.6	-0.122	0.904
PO_2	12.0-154.0	67.8±37.1	11.0-100.0	51.8±36.9	-1.079	0.290
ALT	5.0-50.0	22.3±11.7	10.0-85.0	33.7±23.8	0.190	0.851
AST	10.0-56.0	24.0±12.0	6.0-78.0	31.1±21.1	0.343	0.734
Bilirubin	0.4-1.5	0.87±0.38	0.50-1.50	0.96±0.32	1.771	0.088
Urea	21.0-38.0	30.0±5.3	19.0-45.0	31.5±7.9	1.187	0.246
Creatinine	0.6-1.4	1.04±0.20	0.72-2.40	1.21±0.39	1.070	0.294
Sodium	135.0-149.0	141.1±4.1	136.0-155.0	143.2±5.0	1.719	0.097
Potassium	2.2-5.0	3.2±0.7	2.2-3.9	3.0±0.4	-1.671	0.231
HB	9.3-14.9	11.6±1.8	9.0-15.8	11.5±1.8	0.405	0.689
Ht	26.3-46.0	38.1±5.2	26.0-47.0	36.1±5.3	-0.290	0.774
WBCs	3400.0-16000.0	٩٣٨٠.0±4025.1	5000.0-18700.0	10300.0±4408.3	-0.597	0.555
Platelets	25,700-344,000	178,580±80,878	650,00-324,000	210,067±786,97	-0.941	0.355
RBS	80.0-180.0	125.1±32.9	52.0-288.0	161.7±72.6	-0.594	0.557

P ≤ 0.05 = significant, P >0.05 = non-significant, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase HB: Hemoglobin, Ht: Hematocrite WBCs: White blood cells RBS: Random blood sugar*

Table 4.Independent samples *t*-test analysis ofplasma MDA and TAC levels in acute aluminum phosphide poisoning patients (15 patients in each group).

Variable	Samples collected	Group A (n=15) Mean ± SD	Group B (n=15) Mean ± SD	*t*-test	*p*
MDA (nmol/ml)	On admission	17.48 ± 7.48	16.23 ± 7.91	0.445	0.660
	After treatment	2.79 ± 1.82	17.26 ± 6.39	-8.428	<0.001*
TAC (mmol/l)	On admission	1.99 ± 0.77	3.23 ± 2.16	-2.087	0.052
	After treatment	0.66 ± 0.26	2.15 ± 1.44	-3.939	0.001*

P* ≤ 0.05 = significant, P >0.05 = non-significant, MDA: Malondialdehyde, TAC: Total antioxidant capacity

Table 5.Pearson's Chi square test, Independent samples *t*-test and Mann Whitney analyses of outcome measures in acute aluminum phosphide poisoning patients (15 patients in each group).

Outcome			Group A (n=15)	Group B (n=15)	Test statistics	*p*
Mortality	Died	n (%)	5 (33.3)	12 (80.0)	X^2_{ChS}=6.652	0.010*
	Survived	n (%)	10 (66.7)	3 (20.0)		
Dopamine doseμg/minute	Mean±SD		12.86±4.88	18.57±3.78	*t*=-2.449	0.031*
Need for ventilation	No	n (%)	8 (53.3)	3 (20.0)	X^2_{ChS}=3.589	0.058
	Yes	n (%)	7 (46.7)	12 (80.0)		
Hospitalization time (hours)	Median (IQR)		48 (13-48)	12 (8-13)	Z_{MW}=-2.471	0.013*

P* ≤ 0.05 = significant, P >0.05 = non-significant. IQR: Interquartile range, X^2_{ChS}: Pearson's Chi square test, *t*: Independent samples *t*-test, Z_{MW}: Mann-Whitney test

Discussion

Aluminum phosphide is a potent pesticide. It is used for crops protection during storage and transportation (Bumbrah et al., 2012). During the past four decades, ALP has shown an increased misuse to commit suicide (Singh et al., 2014). Aluminum phosphide is known to have no specific antidote (Hassanian-Moghaddam and Zamani, 2016);therefore, the current study was designed to evaluate efficacy and safety ofNAC as an adjuvant therapy in treatment of patients with acute ALP poisoning.

The results of sociodemographic characteristics, toxicological data and clinical findings obtained in this study were comparable to results gathered from different poison control centers in Egypt and across the developing world (Wahab et al., 2008; El Naggar& El Mahdy, 2011; Hosseinian et al., 2011; Vijayanath et al., 2011; Soltaninejad et al., 2012).

The current study revealed that, no significant difference could be detected between group A and group B patients regarding sociodemographic characteristics,

toxicological data, clinical findings, routine laboratory investigation or oxidative stress markers; MDA and TAC on admission. Such findingsindicate optimum randomization and could be attributed to the faultless randomization performed in this study using the sequentially numbered, opaque sealed envelopes method (Doig and Simpson, 2005).

Reaction of oxygen with unsaturated lipids produces a wide variety of oxidation products. Among aldehydes that can be formed secondary to lipid peroxidation is MDA, which has been widely used for many years as a convenient biomarker for lipid peroxidation (Ayala et al., 2014). Determination of TAC is based on reaction of endogenous antioxidants with a defined amount of exogenously provided hydrogen peroxide (H_2O_2). The endogenous antioxidants eliminate certain amount of the provided H_2O_2 and residual H_2O_2 is determined. Therefore, TAC increases by consumption of endogenous antioxidants i.e. by oxidative stress (Koracevic et al., 2001). Based on these facts, elevated serum levels of MDA and TAC in ALP intoxicated patients, compared to the reference values, was seen as indicator for ALP-induced oxidative stress.

Aluminum phosphide-induced oxidative stress been established in insects, mammalian cell lines, rats andnematodes (Chaudhry and Price, 1992; Hsu et al., 1998; Hsu et al., 2000; Valmas et al., 2008). It has been demonstrated that phosphine can rapidly perturb mitochondrial conformation, block electron transport chain and oxidative phosphorylation resulting in severe decrease in mitochondrial membrane potential with subsequent failure of cellular respiration and non-competitive inhibition of cytochrome-c oxidase. Furthermore, it inhibits catalase, induces superoxide dismutase and reduces glutathione concentration; thus enhances formation of highly reactive hydroxyl radicals by lipid peroxidation. Subsequently, protein denaturation of cell membrane and hypoxic cell damage are suggested (Duaand Gill, 2004; Singh et al., 2006;Mehrpour et al., 2008;Kariman et al., 2012).

Changes in different indicators of oxidative stress such ascatalase, superoxide dismutase, glutathione,total antioxidant capacity and malondialdehydewere evident within 48 hours of acute ALP exposure (Chugh et al., 1996; Chugh et al., 1997a; Chugh et al., 1997b;Kariman et al., 2012). Most previous reports were confined to animal studies and experimental models (Nath et al., 2011).

In the current study, treatment with NAC significantly decreased MDA and TAC in group A compared to group B that received only the routine treatment. Such reduction in oxidative stress parameters could be explained by direct scavenging effect of NAC on oxygen free radicals. In addition, it can serve as a precursor for glutathione thus it can replenish intracellular glutathione stores (Nurulain et al., 2013). Reduction in MDA level after NAC treatment in the current study is in accordance with previous research works assessing different antioxidant modalities (Azad et al., 2001; Chugh et al., 1997b; Hsu et al., 2000; Hsu et al., 2002a; Hsu et al., 2002b;Moghadamnia et al., 2000).

Results from previous studies signified a protective role for endogenous glutathione, melatonin and magnesium in ALP-induced oxidative stress. These studies were experimentalexcept for one human model byChugh and his colleagues (1997b). They assessedthe antioxidant effect of intravenous magnesium in management of acute ALP poisoning.

Tehrani and his colleagues (2013) were the first to evaluate antioxidant effect of NAC in acute ALP toxicity in humans. They registered significant reduction in malondialdehyde level in patients treated by NAC infusion. However, their study was limited by small sample size, lack of blinding and difference in total antioxidant capacity of the two groups on admission time, hence poor randomization. Moreover, it is understandable that data from one study in one particular population cannot be used to judge another population. This makes the current study rational, as well as other studies.

Results of the present study pointed to a statistically significant reduction in both mortality and dopamine dose in group A compared to group B. This could be explained according to Oghabian and Mehrpour (2016) through the antioxidant effect of NAC that has been shown by previous experimental studies to have significant benefits in treatment of ALP poisoning. Where Shakeri and Mehrpour (2014) have proved that NAC could prevent cardiovascular complications by protecting myocardial cells from phosphine induced oxidative stress in animal models. Furthermore, Chugh and his colleagues (1996)proposed a direct relation between oxidative stress markers including MDA in post-mortems and mortality. This was supported by normalization of these markers in survivors due to oxidative stress restriction.

Based on the previous observation, it is expected to find a statistically significant increase in hospitalization time in group A compared to group B. This might be because group A patients have survived, subsequently, have stayed in the hospital to complete their treatment. Meanwhile, group B patients have not survived and, subsequently, have not stayed in the hospital.No side effects for NAC administration were recorded in any of group A patients, that could be attributed to the small sample size and safety of the drug.

From the results of the current study it could be concluded that, NAC might be a promising adjuvant therapy in treatment of acute ALP toxicity. The major limitation of this study was the small sample size.However, to the author's best recent knowledge; this

is the first clinical trial to assess NAC as adjuvant therapy in treatment of acute ALP toxicity in Egypt. Nevertheless, several clinical trials on larger scale with bigger sample sizes and further mechanistic investigationsare required to confirm the results of this study.

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الملخص العربى

ن-أستيل سيستايين كعلاج مساعد في علاج التسمم الحاد بفوسفيد الألومنيوم:تجربة سريرية عشوائية

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يعتبرفوسفيد الألومنيوم مبيد للآفات شائع الأستخدام للأغراض الزراعية غيرالزراعية،وهومسؤول عن العديد من حالات التسمم كونه رخيص ومتاح على نطاق واسع كما أنه شديدالسمية،ولايوجد ترياق محدد لعلاج التسمم بفوسفيد الألومنيوم،ولذلك انطلاقا من الدورالذي يلعبه الإجهاد التأكسدي في التسمم بفوسفيد الألومنيوم تم اقتراح ن-أستيل سيستايين كعلاج مساعد في حالات التسمم الحاد بفوسفيد الألومنيوم. إن هذه الدراسة هي تجربة سريريةعشوائية،وقدأجريت في مركزعلاج التسمم (مستشفى الطواريء،جامعة طنطا)،حيث تم تقسيم ثلاثين مريضا مصابا بالتسمم الحاد بفوسفيد الألومنيوم عشوائيا إلى مجموعتين متساويتين أ وب باستخدام طريقة المظاريف المختومة المبهمة والمرقمة بالتسلسل،تلقت المجموعة الأولى ن-أستيل سيستايين بجرعة قدرها١٤٠ مجم/كجم بالتسريب في الوريد كجرعة تحميل و ٧٠ مجم/كجم بالتسريب في الوريد كل ٤ ساعات حتى ١٧ جرعة بالإضافة إلى العلاج الروتيني،أما المجموعةالثانية فلم تتلق سوى العلاج الروتيني،وقدأجري الفحص البدني الكامل والاختبارات المعملية الروتينية وعلامات الإجهادالتأكسدي(المالوندايألدهيد وكامل الطاقة المضادة للأكسدة) لكل مريض.كشفت نتائج الدراسةالحالية عدم وجود فروق ذات دلالة إحصائية بين مرضى المجموعة أ والمجموعة ب بشأن الخصائص الاجتماعية والديموغرافية وبيانات السمية والفحص السريري والفحص المعملي الروتيني،ولم تسجل مستويات المالوندايألدهيد وكامل الطاقة المضادة للأكسدة أي فروق ذات دلالة إحصائية بين المجموعتين أ وب عند الدخول،وفي الوقت نفسه أمكن ملاحظة فروق ذات دلالة إحصائية في مستويات المالوندايألدهيد وكامل الطاقة المضادة للأكسدة بين المجموعتين أ وب بعدالعلاج،كما أمكن ملاحظة فروق ذات دلالة إحصائية بين مرضى المجموعتين أ وب بشأن عددالوفيات وجرعةالدوبامين ووقت الإقامة في المستشفى.من هذه الدراسة يمكن استنتاج أن ن-أستيل سيستايين قد يكون علاجا مساعدا واعدا في حالات التسمم الحاد بفوسفيدالألومنيوم

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