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Vitamin E as a novel therapy in the treatment of acute aluminum phosphide poisoning

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Background/aim: Aluminum phosphide (AlP) is commonly used as a fumigant in developing countries. Induction of oxidative stress is one of the most important mechanisms of its toxicity. In this regard, and considering that there is no specific antidote for its treatment, the aim of this study was to evaluate the effect of vitamin E in the treatment of acute AlP poisoning.

Materials and methods: This was a clinical trial on acute AlP poisoned patients. All patients received supportive treatment. In addition, the treatment group received vitamin E (400 mg/BD/IM). Level of malondialdehyde (MDA) and total antioxidant capacity of plasma were measured.

Results: There was no significant difference between the treatment and control groups with regard to demographic, clinical, or paraclinical data or Simplified Acute Physiology Score II ($SAPS_{II}$) on admission. Systolic blood pressure significantly increased during the first 24 h in the treatment group ($P < 0.05$). The plasma MDA level significantly decreased in the treatment group ($P < 0.05$). Vitamin E administration decreased the necessity (30% vs. 62%, $P < 0.05$) and duration of intubation and mechanical ventilation ($P < 0.05$). It significantly reduced the mortality rate in the treatment group compared to the control group (15% vs. 50%, respectively, $P < 0.05$).

Conclusion: Vitamin E along with supportive treatment could have a therapeutic effect in acute AlP poisoning.

Key words: Aluminum phosphide, oxidative stress, poisoning, vitamin E

1. Introduction

Aluminum phosphide (AlP) is used widely throughout the world as a pesticide and fumigant because of its efficacy and low cost (1). AlP is one of the most frequently reported causes of acute chemical poisoning in Asia (2–4). In Iran, it is available in 3-g tablets containing 1 g of AlP and known as "rice tablet"; it causes acute poisoning with a high mortality rate (5–7).

AlP toxicity is due to liberating phosphine (PH_3) gas after its reaction with moisture, water, or hydrochloric acid in the stomach (8,9). The major of mortality occurs during the first 12–24 h after exposure and is mostly due to cardiovascular and respiratory involvement (8,9).

The exact mechanism of phosphine toxicity is not clear and some mechanisms are reported (8,9). Previous studies suggested that the induction of oxidative stress has the main role in AlP toxicity (10,11), which is emphasized by recent studies (12–15).

As there is no specific antidote for acute AlP poisoning, its treatment is mainly supportive and symptomatic (1,8,9). By considering the induction of oxidative stress as the main mechanism of AlP toxicity and with regard to the role of vitamin E in the enzymatic antioxidants defense and function as a free radical scavenger (16–18), its use may have a therapeutic effect in the treatment of AlP-poisoned patients.

The aim of the present study was to investigate the therapeutic effects of vitamin E in acute human AlP poisoning.

2. Materials and methods

2.1. Patients

This was a prospective, randomized, control open label trial on acute AlP intoxicated patients that were treated in the intensive care unit (ICU) over a 1-year period.

Acute AlP-intoxicated patients above the age of 12 years who were admitted during the first 6 h after exposure

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with no advanced medical management for AlP poisoning in any medical center before admission were included in this study. The exclusion criteria were history of diabetes mellitus, cardiovascular, respiratory, renal, and hepatic failure, substance abuse, and co-ingestion.

The diagnosis was confirmed based on history of exposure, clinical manifestations, laboratory findings, and other circumstantial evidence such as availability of a poison bottle or a label. In fatal cases, toxicological analysis and a histopathological examination were performed. A positive silver nitrate test for PH_3 gas on stomach contents and tissues along with the liver postmortem histopathological findings confirmed the AlP poisoning.

According to the mentioned criteria, 36 patients were included in the study consecutively. Each patient with an even file number was included in the vitamin E treatment group (n = 20) and the patients with odd file numbers were included in the control group (n = 16).

2.2. Study design and treatments

All the patients received gastric decontamination with sodium bicarbonate (44 mEq), permanganate potassium (1:10,000), and activated charcoal (1 g/kg) in the first 6 h after exposure. All the patients were admitted to the ICU, as they needed intubation, mechanical ventilation, and intensive monitoring. They were treated with the same protocol (magnesium sulfate 4–6 g by IV infusion daily, calcium gluconate 4 g by IV infusion daily, adequate hydration, and norepinephrine 10 µg/min as vasopressor) under the supervision of the same physicians and nurses. The described treatments were based on the clinical toxicology department protocols. In the vitamin E treatment group, vitamin E (as DL-alpha tocopheryl acetate, 100 IU/mL, OSVAH Pharmaceutical Co. Tehran, Iran; 400 mg/IM, every 12 h) was administered up to 72 h. We followed the patients up to discharge from the hospital or death.

The protocol of the study was approved by the ethical committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran.

2.3. Sampling and bioanalysis

Blood sampling was performed at the admission on hospital and repeated each 24 h up to 72 h of hospitalization in the ICU. Venous blood samples (5 mL) were collected in different heparinized tubes and then plasma samples were separated via centrifugation at 3500 rpm for 10 min and frozen at –80 °C. On average, the time interval between sampling and analysis was 1 week. Lipid peroxidation in the plasma in two groups was evaluated by the thiobarbituric acid reactive substances (TBARS) method (19). First 250 µL of 20% trichloroacetic acid (TCA) in 10 mL of sodium sulfate (2 M) was added to 0.5 mL of plasma. After precipitation of the protein with TCA, washing with 300 µL of sulfuric acid (0.05 M) was performed. Then 300 µL of thiobarbituric acid (TBA) (0.67% w/v) solution was added to the mixture. The mixture was incubated in a boiling water bath for 30 min. After cooling, the samples were extracted with n-butanol and centrifuged at 3500 rpm. The absorbance was read at 530 nm by ELISA microplate reader (Synergy, BioTech Instruments Inc, Germany). 1,1,3,3-Tetramethoxy propane was used for drawing the calibration curve. Malondialdehyde (MDA) was expressed as micromoles of MDA per liter of plasma.

The total antioxidant capacity (TAC) of plasma was evaluated using the ferric reducing ability of plasma (FRAP) assay (20). Ferric tripyridyltirazine (Fe^{3+}-TPTZ) complex is reduced to the blue color marker ferrous (Fe^{2+}) form at acidic pH. To 50 µL of plasma was added 1500 µL of freshly prepared FRAP reagent [25 mL of acetate buffer (pH = 3.6, 300 mmol/L), 2.5 mL of $FeCl_3$, $6H_2O$ (20 mmol/L), 2.5 mL of TPTZ (10 mmol/L TPTZ in 40 mmol/L HCl)]. After 15 min incubation at 37 °C in a water bath, absorbance was determined by ELISA microplate reader (Synergy, BioTech Instruments Inc, Germany) at 593 nm. Then samples were placed at 37 °C in the water bath and absorption was measured after 4 min. FRAP values were measured by calculation of the absorbance change in plasma sample compared with that of trolox standard (20).

2.4. Data collection and statistical analysis

We collected patients' information regarding sex, age, cause of poisoning, number of ingested AlP tablets, time interval between exposure and beginning of treatment, route of exposure, clinical and laboratory findings at admission and during the first 24 h of hospitalization, duration of hospitalization, and outcome and prepared qualifying case records. All data were kept confidential during the study.

The Glasgow Coma Scale (GCS) and Simplified Acute Physiology Score II ($SAPS_{II}$) were calculated at admission (21,22). All data were analyzed with SPSS version 12. Data were expressed as mean ± SD for quantitative variables and as frequency and percentage for qualitative variables. The chi-square test was used for statistical comparison of qualitative variables. The normal distribution of quantitative variables was tested by Kolmogorov–Smirnov test. The Mann–Whitney U-test was used for nonparametric variables and the independent Student's t-test was used for parametric variables. P values of 0.05 or less were considered statistically significant.

3. Results

In the present study, 36 patients (13 men, 23 women) with acute AlP poisoning were included, of whom 20 (5 men, 15 women) were in the treatment group and 16 (8 men, 8 women) were controls. The route of exposure was deliberate ingestion in all patients. The main clinical manifestation was vomiting, observed in the most of the patients in the treatment and control groups (90% vs. 87.5%, respectively). Table 1 summarizes the demographic, clinical, and

Table 1. Distribution of the AlP intoxicated patients according to demographic, clinical, and paraclinical characteristics at admission.

Parameter (normal range, unit)		All patients (n = 36) (%) Mean ± SD (range)	Treatment group (n = 20) (%) Mean ± SD (range)	Control group (n = 16) (%) Mean ± SD (range)	P-value
Sex	Male	13 (26)	5 (25)	8 (50)	0.17▲
	Female	23 (64)	15 (75)	8 (50)	
Age (years)		25.56 ± 8.37 (14–50)	24.95 ± 8.11 (15–44)	26.31 ± 8.90 (14–50)	0.46♦
Number of AlP tablets		1.40 ± 0.86 (0.25–4)	1.28 ± 0.75 (0.25–3)	1.57 ± 1 (0.5–4)	0.48♦
TBOPAH[$] (min)		87.50 ± 64.36 (15–300)	98.25 ± 76.66 (15–300)	74.06 ± 43.29 (15–180)	0.52♦
Level of consciousness	consciousness	20 (56)	11 (55)	9 (56)	1▲
	unconsciousness	16 (44)	9 (45)	7 (44)	
Systolic blood pressure (≤120 mmHg)		89.46 ± 15.76 (56–130)	89.16 ± 17.95 (56–130)	89.81 ± 13.29 (60–110)	0.90•
Diastolic blood pressure (≤80 mmHg)		57.79 ± 11.06 (37–80)	55.76 ± 11.03 (37–80)	60.67 ± 10.91 (40–70)	0.25•
Pulse rate (60–100 beats/min)		92.46 ± 15.94 (65–130)	90.50 ± 16.68 (65–130)	95.07 ± 15.04 (70–122)	0.41•
Respiratory rate (16–24 breaths/min)		19.25 ± 4.08 (12–30)	19.95 ± 4.16 (14–30)	18.38 ± 3.93 (12–26)	0.32♦
Electrocardiogram	Normal	20 (56)	13 (65)	7 (44)	0.31▲
	Abnormal	16 (44)	7 (35)	9 (56)	
pH (7.35–7.45)		7.39 ± 0.08 (7.22–7.49)	7.40 ± 0.07 (7.24 ± 7.48)	7.38 ± 0.09 (7.22–7.49)	0.50•
PCO_2 (35–45 mmHg)		30.03 ± 7.35 (16.90–43.10)	31.81 ± 7.06 (16.90–42.20)	27.81 ± 7.30 (18.10–43.10)	0.11•
Serum HCO_3 (22–26 mEq/L)		18.64 ± 5.15 (9–29.1)	20.06 ± 5.47 (9.90–29.10)	16.88 ± 4.24 (9–24.5)	0.06•
Blood glucose (70–110 mg/dL)		148.75 ± 55.73 (74–282)	125.25 ± 48 (74–242)	178.13 ± 51.70 (101–282)	0.003**•
Blood urea nitrogen (7–18 mg/dL)		27.25 ± 11.61 (12–60)	29.45 ± 12.85 (12–60)	24.50 ± 9.51 (12–40)	0.20•
Creatinine (0.6–1.2 mg/dL)		0.94 ± 0.21 (0.60–1.40)	0.91 ± 0.21 (0.70–1.40)	1 ± 0.21 (0.60–1.30)	0.20♦
Sodium (135–145 mEq/L)		143.94 ± 5.07 (135–156)	143.40 ± 4.89 (137–155)	144.67 ± 5.38 (135–156)	0.48♦
Potassium (3.5–5 mEq/L)		3.94 ± 0.46 (3–5.10)	3.86 ± 0.41 (3–4.60)	4.05 ± 0.53 (3.20–5.10)	0.52♦
Calcium (8.4–10.2 mg/dL)		8.82 ± 0.79 (7.50–10.50)	8.74 ± 0.86 (7.50–10.40)	8.91 ± 0.72 (8–10.50)	0.55♦
Magnesium (1.9–2.5 mg/dL)		2.18 ± 0.58 (1.40–4)	2.08 ± 0.58 (1.40–4)	2.41 ± 0.56 (1.90–3.50)	0.07♦
White blood cell count (7–10 × 1000/μL)		15.55 ± 22.61 (3.20–141)	17.47 ± 29.42 (3.20–141)	12.81 ± 4.35 (5.80–20.60)	0.44♦
Hematocrit (35–45%)		38.53 ± 5.58 (27.50–48.10)	37.04 ± 6.05 (27.50–48.10)	40.65 ± 4.16 (32–46.60)	0.06•
Platelet (150–450 × 1000/μL)		268.76 ± 110.01 (95–609)	289.85 ± 122.86 (95–609)	238.64 ± 83.68 (101–374)	0.19•
Serum total protein (6.6–8.8 g/dL)		6.35 ± 0.78 (5.10–8.20)	6.54 ± 0.80 (5.10–8.20)	5.92 ± 0.58 (5.10–7.00)	0.08•
Albumin (3.5–5.3 g/dL)		4.00 ± 0.64 (3.10–5.10)	4.16 ± 0.63 (3.20–5.10)	3.71 ± 0.60 (3.10–4.60)	0.15•
Aspartate transaminase (up to 37 U/L)		26.48 ± 14.96 (10–64)	28 ± 15.53 (10–64)	24.38 ± 14.47 (11–62)	0.44♦
Alanine transaminase (up to 41 U/L)		49.96 ± 75.35 (5–298)	46.11 ± 61.91 (12–242)	55.30 ± 93.34 (5–298)	0.31♦
Alkaline phosphatase (80–306 U/L)		157.54 ± 37.53 (95–233)	143.38 ± 32.08 (95–187)	178 ± 36.83 (113–233)	0.03*•
Total bilirubin (0.1–1.2 mg/dL)		1.2 ± 0.52 (0.50–2.70)	1.17 ± 0.61 (0.50–2.70)	1.23 ± 0.37 (0.60–1.90)	0.29♦
Lactate dehydrogenase (up to 513 U/L)		457.32 ± 135.85 (279–752)	445.45 ± 131.81 (298–740)	474.28 ± 144.66 (279–752)	0.55•
Creatine phosphokinase (24–195 U/L)		170.18 ± 64.69 (53–305)	190.15 ± 59.74 (56–305)	139.46 ± 61.84 (53–295)	0.03*•

[$] Time between onset of poisoning and admission to hospital, SD = Standard deviation

* The difference between the two groups is significant at $P < 0.05$

** The difference between the two groups is significant at $P < 0.005$

▲ Chi-square test was used for statistical analysis

♦ Mann–Whitney U-test was used for statistical analysis

• t-test was used for statistical analysis

laboratory results. $SAPS_{II}$ was determined in the treatment (4.7 ± 2) and control groups (5.05 ± 3.13). The results showed no significant difference (P = 0.68).

Systolic blood pressure (SBP) significantly increased during the first 24 h in the treatment group (89.16 ± 17.95 mmHg at admission vs. 98.95 ± 15.45 mmHg 24 h after onset of poisoning, P < 0.05). The results also showed that there was no significant difference between the two groups due to SBP 24 h after the onset of poisoning (98.95 ± 15.45 mmHg in the treatment group vs. 89.21 ± 20.25 mmHg in the control group, P = 0.13).

We observed significant increases in diastolic blood pressure (DBP) in the treatment group (55.76 ± 11.03 mmHg at admission vs. 60.63 ± 13.58 mmHg 24 h after the onset of poisoning, P < 0.05) and significant decreases in DBP in the control group (60.67 ± 10.91 mmHg at admission vs. 50.43 ± 12 mmHg 24 h after the onset of poisoning, P < 0.05). The data showed a significant difference between the two groups with regard to DBP 24 h after the onset of poisoning (P < 0.05).

The results showed a significant difference in blood pH between the treatment and control groups (7.43 ± 0.04 vs. 7.33 ± 0.1, P < 0.001) 24 h after onset of poisoning. In addition, there was no significant difference between the two groups due to PCO_2 (36.24 ± 7.57 mmHg in the treatment group vs. 34.19 ± 6.91 mmHg in the control group, P = 0.4). We observed a significant difference in serum bicarbonate between the two groups 24 h after the onset of poisoning (24.22 ± 6.55 mEq/L in the treatment group vs. 18.91 ± 5.62 mEq/L in the control group, P < 0.05).

There was no significant difference in the TAC of plasma in the treatment and control groups at admission (Table 2). Twenty-four hours after the onset of poisoning, the TAC of plasma in the control group was significantly higher than that in the treatment group (Table 2).

At admission, the plasma MDA level was not significantly different between the treatment and control groups. The plasma MDA level significantly decreased in the treatment group and it significantly increased in the control group. The plasma MDA level in the treatment group was significantly lower than that in the control group 24 h after the onset of poisoning (Table 2).

The percentage of patients who required intubation and mechanical ventilation was significantly lower in the treatment group than in the control group (30% vs. 62%, P < 0.05). In addition, the duration of intubation and mechanical ventilation in the treatment group was significantly lower compared to the control group. The total dose of norepinephrine was not significantly different between the two groups (Table 3).

Although the duration of hospitalization was not significantly different between the two groups (Table 3), the results showed that most of the fatality occurred during the first 12 h after admission in the control group, and in the treatment group most of the fatality was observed 20 h after admission (Figure). In addition, the data showed that the mortality rate was significantly lower in the treatment group than in the control group (15% vs. 50%, P = 0.02).

4. Discussion

AlP poisoning is a major health problem with a high mortality rate in Iran and other countries (2–4,6). Unfortunately, to date, there is not a specific antidote for treatment of this type of fatal poisoning and the only therapeutic measures are supportive and symptomatic (9). In this regard, performing studies that evaluate other therapeutic protocols is necessary.

There are many suggested mechanisms for AlP poisoning. One of the most important mechanisms is involvement of oxidative stress (10–14). From this viewpoint, the antioxidants may have a therapeutic role in the treatment of AlP poisoning (10,12).

Table 2. Comparison of plasma TAC and MDA levels at admission and 24 h after the onset of poisoning in the treatment and control groups.

Parameters	Group	At admission Mean ± SD	24 h after onset of poisoning Mean ± SD	P-value
MDA (μmol/L)	Treatment	130.91 ± 14.11▪	124.88 ± 8.23▲	0.02*
	Control	142.45 ± 29.28	151.51 ± 37.34	0.04*
TAC (mmol/L)	Treatment	11.57 ± 6.05▪	10.45 ± 3.48▲	0.23
	Control	12.79 ± 3.63	13.26 ± 4.02	0.57

* The difference between two groups is significant at P < 0.05

▪ There is no significant difference between the treatment and control groups at admission

▲ There is a significant difference between the treatment and control groups 24 h after the onset of poisoning at P < 0.05

Mann–Whitney U-test was used for all the statistical analysis

Table 3. Comparison of treatment and control groups according to duration of intubation, ventilation, hospitalization, and dose of vasopressor

Parameters	Treatment group (n = 20) Mean ± SD (range)	Control group (n = 16) Mean ± SD (range)	P-value
Duration of intubation and ventilation (h)	4.15 ± 9 (0–32)	18.36 ± 28.37 (0–85.5)	0.04*
Total dose of norepinephrine (mg)	10.34 ± 14.35 (0–50.40)	10.15 ± 12.79 (0–43.20)	0.42
Duration of hospitalization (h)	69.09 ± 35.19 (21–159)	62.53 ± 68.87 (3.25–229)	0.16

*The difference between the two groups is significant at $P < 0.05$
t-test was used for all the statistical analysis

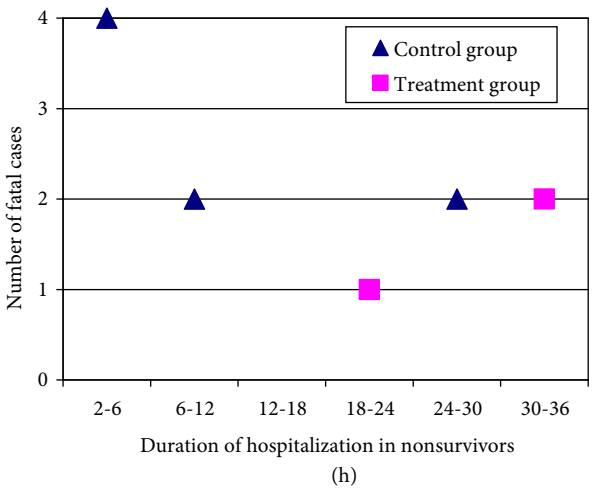

Figure. Comparison of the duration of hospitalization between nonsurvivors in the treatment and control groups.

Previous studies showed that vitamin E had a protective role in the in vivo or in vitro toxicity of some poisons through its antioxidant activity and lowering cell death by decreased the levels of MDA, reactive oxygen species production, and lipid peroxidation (18,23–25).

In the present study, we aimed to evaluate the efficacy of intramuscular administration of vitamin E as an antioxidant agent in patients with acute AlP poisoning.

The results showed significant rises in SBP and DBP in the treatment group 24 h after the onset of poisoning, which could be due to the role of vitamin E in reduction of myocardial and vessels injury through the decrease in lipid peroxidation (26,27).

The results in the control group showed progressive metabolic acidosis during the first 24 h after the onset of poisoning, which could be due to tissue hypoperfusion.

In the present study, the TAC and MDA levels at admission showed no significant difference between the two groups. In addition, the results showed that the serum levels of MDA were significantly decreased after 24 h in the treatment group, while in the control group they were significantly increased. These results are in concordance of our previous study, in which the administration of N-acetyl cysteine as an antioxidant resulted in similar findings (12).

Vitamin E administration decreased the necessity for intubation and mechanical ventilation and was associated with a decrease in duration of intubation and mechanical ventilation. This result was similar to that of our previous study (12). Although in the previous studies mortality rates of 60%–80% were reported in the AlP poisoning cases with conventional supportive and symptomatic treatment (7,28,29), in the present study administration of vitamin E significantly reduced the mortality rate in the treatment group compared to the control group (15% vs. 50%, respectively).

In conclusion, the present study showed that the administration of vitamin E along with supportive treatment decreased the mortality rate and so it could be considered in the treatment of acute AlP poisoning in combination with other therapeutic protocols.

The limitations of this study were small sample size and lack of blinding in the study design.

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References

1. Moghadamnia AA. An update on toxicology of aluminum phosphide. DARU 2012; 20: 25. doi:10.1186/2008-2231-20-25.
2. Sharma AD, Gupta V, Kaushik JS, Mittal K. Aluminum phosphide (Celphos) poisoning in children: a 5-year experience in a tertiary care hospital from northern India. Indian J Crit Care Med 2014; 18: 33-36.
3. Anand R, Binukumar BK, Gill KD. Aluminum phosphide poisoning: an unsolved riddle. J Appl Toxicol 2011; 31: 499-505.
4. Shadnia S, Sasanian G, Allami P, Hosseini A, Ranjbar A, Amini-shirazi N, Abdollahi M. A retrospective 7-years study of aluminum phosphide poisoning in Tehran: opportunities for prevention. Hum Exp Toxicol 2009; 28: 209-213.
5. Mehrpour O, Singh S. Rice tablet poisoning: a major concern in Iranian population. Hum Exp Toxicol 2010; 29: 701-702.
6. Soltaninejad K, Nelson LS, Bahreini SA, Shadnia S. Fatal aluminum phosphide poisoning in Tehran-Iran from 2007 to 2010. Indian J Med Sci 2012; 66: 66-70.
7. Shadnia S, Mehrpour O, Soltaninejad K. A simplified acute physiology score in the prediction of acute aluminum phosphide poisoning outcome. Indian J Med Sci 2010; 64: 532-539.
8. Bumbrah GS, Krishan K, Kanchan T, Sharma M, Sodhi GS. Phosphide poisoning: a review of literature. Forensic Sci Int 2012; 214: 1-6. doi:10.1016/j.forsciint. 2011.06.018.
9. Proudfoot AT. Aluminium and zinc phosphide poisoning. Clin Toxicol (Phila) 2009; 47: 89-100.
10. Hsu CH, Chi BC, Casida JE. Melatonin reduces phosphine-induced lipid and DNA oxidation in vitro and in vivo in rat brain. J Pineal Res 2002; 32: 53-58.
11. Hsu CH, Chi BC, Liu MY, Li JH, Chen CJ, Chen RY. Phosphine-induced oxidative damage in rats: role of glutathione. Toxicology 2002; 179: 1-8.
12. Tehrani H, Halvaie Z, Shadnia S, Soltaninejad K, Abdollahi M. Protective effects of N-acetylcysteine on aluminum phosphide-induced oxidative stress in acute human poisoning. Clin Toxicol (Phila) 2013; 51: 23-28.
13. Kariman H, Heydari K, Fakhri M, Shahrami A, Arhami Dolatabadi A, Mohammadi HA, Gharibi M. Aluminium phosphide poisoning and oxidative stress: serum biomarker assessment. J Med Toxicol 2012; 8: 281-284.
14. Anand R, Sharma DR, Verma D, Bhalla A, Gill KD, Singh S. Mitochondrial electron transport chain complexes, catalase and markers of oxidative stress in platelets of patients with severe aluminum phosphide poisoning. Hum Exp Toxicol 2013; 32: 807-816.
15. Anand R, Kumari P, Kaushal A, Bal A, Wani WY, Sunkaria A, Dua R, Singh S, Bhalla A, Gill KD. Effect of acute aluminum phosphide exposure on rats - a biochemical and histological correlation. Toxicol Lett 2012; 215: 62-69.
16. Singh M, Sandhir R, Kiran R. Effects on antioxidant status of liver following atrazine exposure and its attenuation by vitamin E. Exp Toxicol Pathol 2011; 63: 269-276.
17. Singh M, Sandhir R, Kiran R. Oxidative stress induced by atrazine in rat erythrocytes: mitigating effect of vitamin E. Toxicol Mech Methods 2010; 20: 119-126.
18. Shadnia S, Dasgar M, Taghikhani S, Mohammadirad A, Khorasani R, Abdollahi M. Protective effects of α-tocopherol and N-acetyl-cysteine on diazinon-induced oxidative stress and acetylcholinesterase inhibition in rats. Toxicol Mech Methods 2007; 17: 109-115.
19. Satih K. Serum lipid peroxide in cerebrovascular disorders determined by a new calorimetric method. Clin Chim Acta 1978; 90: 37-43.
20. Benzie IE, Strain JJ. The ferric reducing ability of plasma (FRAP) as a measure of "antioxidant power": the FRAP assay. Anal Biochem 1996; 239: 70-76.
21. Teasdale G, Jennett B. Assessment of coma and impaired consciousness: a practical scale. Lancet 1974; 2: 81-84.
22. Le Gall JR, Lemeshow S, Saulnier F. A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. JAMA 1993; 270: 2957-2963.
23. Wiser J, Alexis NE, Jiang Q, Wu W, Robinette C, Roubey R, Peden DB. In vivo gamma-tocopherol supplementation decreases systemic oxidative stress and cytokine responses of human monocytes in normal and asthmatic subjects. Free Radic Biol Med 2008; 45: 40-49.
24. Soltaninejad K, Abdollahi M. Current opinion on the science of organophosphate pesticides and toxic stress: a systematic review. Med Sci Monit 2009; 15: RA75-90.
25. Ozden S, Catalgol B, Gezginci-Oktayoglu S, Arda-Pirincci P, Bolkent S, Alpertunga B. Methiocarb-induced oxidative damage following subacute exposure and the protective effects of vitamin E and taurine in rats. Food Chem Toxicol 2009; 47: 1676-1684.
26. Pryor W. Vitamin E and heart disease: basic science to clinical intervention trials. Free Radic Biol Med 2000; 28: 141-164.
27. Iannitti T, Palmieri B. Antioxidant therapy effectiveness: an up to date. Eur Rev Med Pharmacol Sci 2009; 13: 245-278.
28. Mehrpour O, Alfred S, Shadnia S, Keyler DE, Soltaninejad K, Chalaki N, Sedaghat M. Hyperglycemia in acute aluminum phosphide poisoning as a potential prognostic factor. Hum Exp Toxicol 2008; 27: 591-595.
29. Hajouji Idrissi M, Oualili L, Abidi K, Abouqal R, Kerkeb O, Zeggwagh AA. Severity factors of aluminum phosphide poisoning (Phostoxin). Ann Fr Anesth Reanim 2006; 25: 382-385.