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Packed RBCs versus sodium bicarbonate in the treatment of aluminum phosphide-induced cardiotoxicity and metabolic acidosis in rats

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Abstract

Background: Human toxicity with aluminum phosphide (ALP) is usually associated with intense metabolic acidosis and cardiac ischemia which are the main cause of death. **Aim of the study** is to assess and compare the effectiveness of fresh packed RBCs and sodium bicarbonate in treatment of ALP toxicity. **Methodology**: This experimental study was conducted during the period from 1st to 8th March 2022 on 50 rats divided randomly into five groups: group I received Almond oil (control group), while the others were exposed to aluminum phosphide (12 mg/kg). Group III was given $NaHCO_3$ (3 mmol/kg), group IV received packed RBCs (1.5 ml) and group V was treated by both packed RBCs and $NaHCO_3$. Electrocardiogram, arterial blood gases, serum levels of cardiac troponin I, and histopathological examination of the heart were done for all rats. **Results**: ALP resulted in significant bradycardia ($p=0.002$), prolongation of QT interval ($p<0.001$), widening of QRS complex ($p<0.001$), elevation of ST segment ($p<0.001$), resistant metabolic acidosis ($p<0.001$) and increased troponin level ($p<0.001$). Histopathological examination revealed severe cardiac ischemic changes due to ALP exposure. Packed RBCs + $NaHCO_3$ significantly improved bradycardia ($p=0.025$). Packed RBCs alone and packed RBCs plus $NaHCO_3$ significantly improved chemical and histopathological changes. However, the combination therapy demonstrated greater benefits compared to packed RBCs alone. **Conclusion**: These findings suggest using packed RBCs alone or with NaHCO3 to boost survival rates in ALP poisoning

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Key words ALP, packed RBCs, ECG, $NaHCO_3$, ABG

Introduction

Aluminum phosphide (AlP) is a commonly used pesticide in several countries to safeguard stored cereals and commonly known as wheat pill or rice pill (Yadav et al., 2021). Unfortunately, human exposure to AlP, whether accidental or intentional, has been associated with alarmingly high mortality rates (Anand et al., 2011).

When AlP comes in contact with gastric hydrochloric acid, it breaks down into phosphine gas (PH3), which is an extremely toxic chemical. The toxic effects of phosphine gas include impaired oxidative phosphorylation, direct adrenal and cardiac muscle toxicity and circulatory collapse (Hegazy et al., 2019). AlP poisoning has grave consequences, with major effects including hypotension, ventricular tachycardia, heart failure, metabolic acidosis and multi-organ failure (Karimani et al., 2018).

Metabolic acidosis caused by ALP toxicity is the primary cause of fatality. However, maintaining blood pH levels at normal range can increase survival rates up to 27%. Erythrocyte anion-exchange transporters played a vital role in regulating ion movement across the RBC membrane, aiding in the maintenance of normal body PH (Rahimi et al., 2018).

This study aimed to evaluate and compare the effectiveness of fresh packed RBCs and sodium bicarbonate as remedies for ALP toxicity in rats via biochemical and histological examinations.

Materials and Methods

This experimental study was conducted in the laboratory of The Departments of Forensic Medicine and Clinical Toxicology at the Faculty of Medicine, Minia University during the period from 1st to 8th March 2022.

The study was carried out in accordance with the ethical guidelines and recommendations for the care and usage of laboratory animals authorized by the Faculty of Medicine's ethical committee, with approval number 279-2022.

Ethical consideration of the study:

The animals were kept in hygienic plastic cages. The name of the drug and the group number were clearly labeled on each cage to prevent any mixing. The rats were kept in a clean and well-ventilated environment with 12-hour light/dark cycles. They were provided with rat pellets and water to consume throughout the study period. Prior to the commencement

of the experiment, the animals underwent a week-long acclimatization process to ensure that they were accustomed to the laboratory conditions and free from any potential stress. Approval of pathology department, Faculty of Medicine, Minia University was obtained before the start of work.

Animal:

Fifty albino rats, weighing between 200-250 grams on average, were included in the study. The animals were sourced from the National Research Centre in Giza, Egypt and kept in plastic cages. To ensure compatibility, each cage housed two rats with the same blood type. One rat was designated as a donor of packed red blood cells for each rat in groups IV and V.

Chemicals:

Aluminum phosphide discs were procured from a local farm supply store in Matai, Minia governorate, Egypt. Each disc weighed 3 grams and was dissolved in almond oil (O′Neil, 2001). Ketamine HCL, xylazine HCL, sodium bicarbonate and Almond oil were purchased from Cooperative Society Pharmacy in Minia, Minia governorate, Egypt.

Preparation of fresh packed RBCs:

Blood was drawn from the heart of a deeply anesthetized rat using heparinized syringes, and then the rat was euthanized. One rat was selected for each rat in group IV and V for blood type compatibility. After cross-matching, the blood was centrifuged for 10 minutes at room temperature. Plasma and platelets were separated, and red cells were washed thrice in isotonic saline by centrifugation (Barshtein et al., 2020). Packed RBCs were separated and prepared for injection via tail vein using an infusion pump.

Study design:

Rats were divided into five groups (10 rats each). Group I (control group) received Almond oil orally through feeding needle. Group II, III, IV and V received single dose of AlP (12 mg/kg by feeding needle) (Mashayekhian et al., 2016) (the lethal dose of aluminum phosphide in human when ingested ranges between 0.15–0.5 g (Moghadamnia, 2012). Sodium bicarbonate ($NaHCO_3$) was injected intraperitoneally to group III (3 mmol/kg) (Stefanovic et al., 2006). Group IV received packed RBCs (1.5 ml) by intravenous infusion (Rahimi et al., 2018) and group V was treated by both packed RBCs infusion (1.5 ml) + $NaHCO_3$ injection (3mmol/kg). After one hour, electrocardiogram (ECG) was performed and an arterial blood sample was drawn from the heart in heparinized syringe for arterial blood gases (ABG). A venous blood sample was drawn from tail vein for cardiac troponin I (cTnI) level. Painful procedures were carried out under general anesthesia (ketamine 85mg/kg and xylazine 15mg/kg) (Parasuraman et al., 2010). All rats were sacrificed by cervical decapitation for histopathological studies.

Methods:

Blood samples were drawn via a polyethylene cannula and centrifuged for 15 minutes at 3000 rpm. For spectrophotometric analysis of cTnI level, serum was collected and kept as aliquots at 20°C using commercial ELISA kits (Bertinchant et al., 2003). Electrodes made of stainless steel were placed under the skin to monitor the ECG. A Power Lab (4/35) data gathering system was used. Data were analyzed by LabChart7 software. To assess blood gases, samples were taken from the heart and analyzed using the radiometer ABL 800 Flex at the pharmacology department in Minia University's medical school (Svorc et al., 2018).

Histopathological studies:

After scarification of rats by cervical dislocation, their hearts were carefully dissected under sterile conditions for histological analysis. The tissue samples were fixed in 10% neutral buffered formalin then dehydrated using increasing concentrations of alcohol. They were then infiltrated with paraffin wax to create firm blocks suitable for cutting uniform 5 μm thick sections. These sections were trimmed and stained with hematoxylin and eosin (H&E) dye to prepare them for examination under a light microscope (Gillespie et al., 2002). The heart samples were examined using a light microscope with an attached camera (Olympus BX51, Tokyo, Japan) to capture images. This analysis was conducted in the Pathology Department at the Faculty of Medicine, Minia University.

Statistical analysis

The collected data was statistically analyzed using SPSS program (Statistical Package for Social Sciences) software version 26. The quantitative data was expressed as mean ± SD with minimum and maximum range, Analysis of quantitative data was done using One Way ANOVA Test between the five groups followed by post hoc test between each two groups. Qualitative data was analyzed by Chi square test between groups. Difference was considered to be significant if P value was ≤ 0.05.

Results

The present study included fifty albino rats with an average weight 200- 250 gm. Rats were classified into 5 groups, 10 rats per each group. Group I received Almond oil (control group), while the others were exposed to aluminum phosphide (12 mg/kg). Group III was given $NaHCO_3$ (3 mmol/kg), group IV received packed RBCs (1.5 ml) and group V was treated by both packed RBCs and $NaHCO_3$.

ALP resulted in significant bradycardia in group II and III ($p=0.002$ and $p=0.010$ respectively) in comparison with control group. Both packed RBCs alone and packed RBCs with $NaHCO_3$ successfully averted the onset of bradycardia as illustrated in table (1).

As regard ECG in table (2, 3 and 4), ALP resulted in prolongation of QT interval ($p<0.001$), widening of QRS complex ($p<0.001$), elevation of ST segment ($p<0.001$) in comparison with control group. Administration of 1.5ml fresh packed RBCs or packed RBCs + $NaHCO_3$ prevented these effects significantly ($p<0.001$).

Aluminum phosphide resulted in significant decrease of blood PH and bicarbonate level (severe

metabolic acidosis) ($p<0.001$) with significant CO2 wash as compared with control group. Administration of 1.5ml fresh packed RBCs or packed RBCs + $NaHCO_3$ significantly increase of PH and HCO_3 thus decreasing acidosis ($p<0.001$) more than $NaHCO_3$ only as illustrated in table (5, 6 and 7).

Table (8) shows that ALP raised serum cardiac troponin I level significantly ($p<0.001$*) in comparison with control group. Treatment with fresh packed RBCs or packed RBCs + $NaHCO_3$ significantly prevented this effect ($p<0.001$*).

Histopathological results:

All rats of each group were sacrificed by cervical decapitation. After scarification, their hearts were carefully dissected and prepared for histopathological examination.

Histopathological examination of the heart of the control group showed normal cardiac muscle fibers that are long branched cells with one to two nuclei located centrally. The fibers are separated by collagenous tissue that supports the capillary network of cardiac tissue (Fig. 1). In group II and III histopathological examination revealed wavy cardiac muscle cells that represent dead or necrotic cells due to acute necrosis of most cardiac muscles (Fig. 2, 3). Group IV revealed mild necrosis (Fig. 4) but histopathological examination of heart of rats in group V were nearly similar to normal cardiac muscle fibers (Fig. 5).

Table (1): Analysis of the heart rate in all experimental groups using one way ANOVA followed by post hoc test (n: 50 rats).

	Group I n=10	Group II n=10	Group III n=10	Group IV n=10	Group V n=10	p value
HR Range Mean ± SD	(246-315) 289±27.65	(201-299) 254.87±40.1	(224-308) 261.27±25.68	(199-293) 270.73±25.76	(240-322) 279.07±21.75	**0.014 (S)**
P value (between each two groups)						
Group I		**0.002 (HS)**	**0.010 (S)**	0.088 (NS)	0.349 (NS)	
Group II			0.546 (NS)	0.137 (NS)	**0.025 (S)**	
Group III				0.372 (NS)	0.096 (NS)	
Group IV					0.432 (NS)	

Results are considered non-significant (NS) when p>0.05, significant (S) when p<0.05 and highly significant (HS) when p<0.01. n: Number. HR: heart rate. SD: standard deviation.

Table (2): Comparison of QT interval between all groups using one way ANOVA followed by post hoc test (n: 50 rats).

	Group I n=10	Group II n=10	Group III n=10	Group IV n=10	Group V n=10	p value
QT Range Mean ± SD	(77-95) 85±6.54	(94-117) 104.93±5.34	(93-113) 101.4±6.24	(75-102) 90.27±8.8	(65-115) 85.27±15.99	**<0.001(HS)**
P value (between each two groups)						
Group I		**<0.001(HS)**	**<0.001(HS)**	0.130 (NS)	0.938 (NS)	
Group II			0.308 (NS)	**<0.001(HS)**	**<0.001(HS)**	
Group III				**0.002 (HS)**	**<0.001(HS)**	
Group IV					0.150 (NS)	

Results are considered non-significant (NS) when p>0.05, significant (S) when p<0.05 and highly significant (HS) when p<0.01. n: Number. SD: standard deviation.

Table (3): Comparison of QRS complex by one way ANOVA followed by post hoc test between all groups (n: 50 rats).

	Group I n=10	Group II n=10	Group III n=10	Group IV n=10	Group V n=10	p value
QRS Range Mean ± SD	(18-25) 21.13±2.26	(22-30) 27.4±2.8	(22-30) 26.13±2.7	(15-31) 21.2±5.25	(18-31) 23.07±3.81	**<0.001(HS)**
P value (between each two groups)						
Group I		**<0.001(HS)**	**<0.001(HS)**	0.959 (NS)	0.138 (NS)	
Group II			0.329 (NS)	**<0.001(HS)**	**0.001(HS)**	
Group III				**<0.001 (HS)**	**0.020 (S)**	
Group IV					0.152 (NS)	

Results are considered non-significant (NS) when p>0.05, significant (S) when p<0.05 and highly significant (HS) when p<0.01. n: Number. SD: standard deviation.

Table (4): Comparison of ST segment by one way ANOVA followed by post hoc test between all experimental groups (n: 50 rats).

	Group I	Group II	Group III	Group IV	Group V	p value
	n=10	n=10	n=10	n=10	n=10	
ST segment						
Normal	15(100%)	3(20%)	5(33.3%)	13(86.7%)	14(93.3%)	**<0.001(HS)**
Elevated	0(0%)	12(80%)	10(66.7%)	2(13.3%)	1(6.7%)	
P value (between each two groups)						
Group I		**<0.001(HS)**	**<0.001(HS)**	0.143 (NS)	0.309 (NS)	
Group II			0.409 (NS)	**<0.001(HS)**	**<0.001(HS)**	
Group III				**0.003(HS)**	**0.001(HS)**	
Group IV					0.543 (NS)	

Results are considered non-significant (NS) when p>0.05, significant (S) when p<0.05 and highly significant (HS) when p<0.01. n: Number. SD: standard deviation.

Table (5): Statistical analysis of blood PH values using one way ANOVA followed by post hoc test in all groups (n: 50 rats).

	Group I	Group II	Group III	Group IV	Group V	p value
	n=10	n=10	n=10	n=10	n=10	
PH						
Range	(7.33-7.38)	(7.25-7.3)	(7.25-7.38)	(7.31-7.38)	(7.32-7.37)	**<0.001(HS)**
Mean ± SD	7.36±0.02	7.28±0.01	7.29±0.04	7.34±0.02	7.35±0.02	
P value (between each two groups)						
Group I		**<0.001(HS)**	**<0.001(HS)**	0.125 (NS)	0.355 (NS)	
Group II			0.218 (NS)	**<0.001(HS)**	**<0.001(HS)**	
Group III				**<0.001(HS)**	**<0.001(HS)**	
Group IV					0.537 (NS)	

Results are considered non-significant (NS) when p>0.05, significant (S) when p<0.05 and highly significant (HS) when p<0.01. n: Number. SD: standard deviation.

Table (6): Statistical analysis of CO2 levels using one way ANOVA followed by post hoc test in all groups (n: 50 rats).

	Group I	Group II	Group III	Group IV	Group V	p value
	n=10	n=10	n=10	n=10	n=10	
CO2						
Range	(33-38)	(25-30)	(25-38)	(31-38)	(32-37)	**<0.001(HS)**
Mean ± SD	35.8±1.86	27.93±1.49	29±3.74	34.47±2.07	35±1.93	
P value (between each two groups)						
Group I		**<0.001(HS)**	**<0.001(HS)**	0.125 (NS)	0.355 (NS)	
Group II			0.218 (NS)	**<0.001(HS)**	**<0.001(HS)**	
Group III				**<0.001(HS)**	**<0.001(HS)**	
Group IV					0.537 (NS)	

Results are considered non-significant (NS) when p>0.05, significant (S) when p<0.05 and highly significant (HS) when p<0.01. n: Number. SD: standard deviation. CO2: carbon dioxide

Table (7): Statistical analysis of HCO3 levels using one way ANOVA followed by post hoc test in all groups (n: 50 rats).

	Group I	Group II	Group III	Group IV	Group V	p value
	n=10	n=10	n=10	n=10	n=10	
HCO3						
Range	(22.5-27.6)	(7-11.8)	(8-14.2)	(21.7-26)	(21.3-25.9)	**<0.001(HS)**
Mean ± SD	25.21±2.05	9.17±1.8	10.11±1.86	24.29±1.41	24.34±1.24	
P value (between each two groups)						
Group I		**<0.001(HS)**	**<0.001(HS)**	0.146 (NS)	0.167(NS)	
Group II			0.137 (NS)	**<0.001(HS)**	**<0.001(HS)**	
Group III				**<0.001(HS)**	**<0.001(HS)**	
Group IV					0.940 (NS)	

Results are considered non-significant (NS) when p>0.05, significant (S) when p<0.05 and highly significant (HS) when p<0.01. n: Number. SD: standard deviation. $NaHCO_3$: Sodium bicarbonate

Table (8): One way ANOVA analysis of troponin values followed by post hoc test in all groups (n: 50 rats).

	Group I	Group II	Group III	Group IV	Group V	p value
	n=10	n=10	n=10	n=10	n=10	
cTnI						
Range	(0.021-0.035)	(0.209-0.32)	(0.207-0.315)	(0.025-0.04)	(0.02-0.038)	**<0.001(HS)**
Mean ± SD	0.029±0.005	0.263±0.041	0.261±0.035	0.032±0.005	0.029±0.005	
P value (between each two groups)						
Group I		**<0.001(HS)**	**<0.001(HS)**	0.747 (NS)	0.994 (NS)	
Group II			0.828 (NS)	**<0.001(HS)**	**<0.001(HS)**	
Group III				**<0.001(HS)**	**<0.001(HS)**	
Group IV					0.741(NS)	

Results are considered non-significant (NS) when p>0.05, significant (S) when p<0.05 and highly significant (HS) when p<0.01. n: Number. SD: standard deviation. cTnI: cardiac troponin I

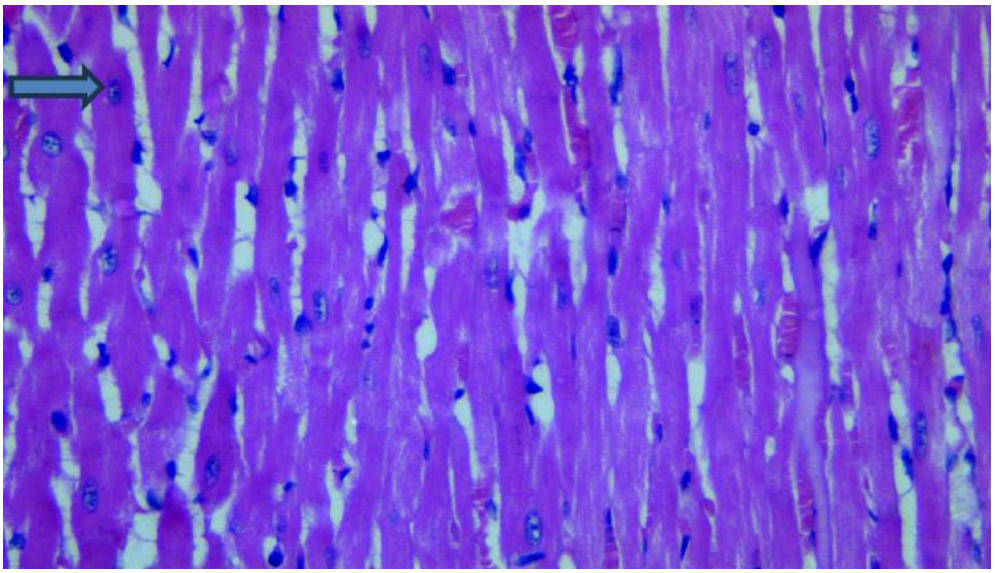

Figure (1): Longitudinal section in mice heart showing normal cardiac muscle fibers that are long branched cells with one to two nuclei located centrally (arrow). The fibers are separated by collagenous tissue that supports the capillary network of cardiac tissue (group I) (H&EX200)

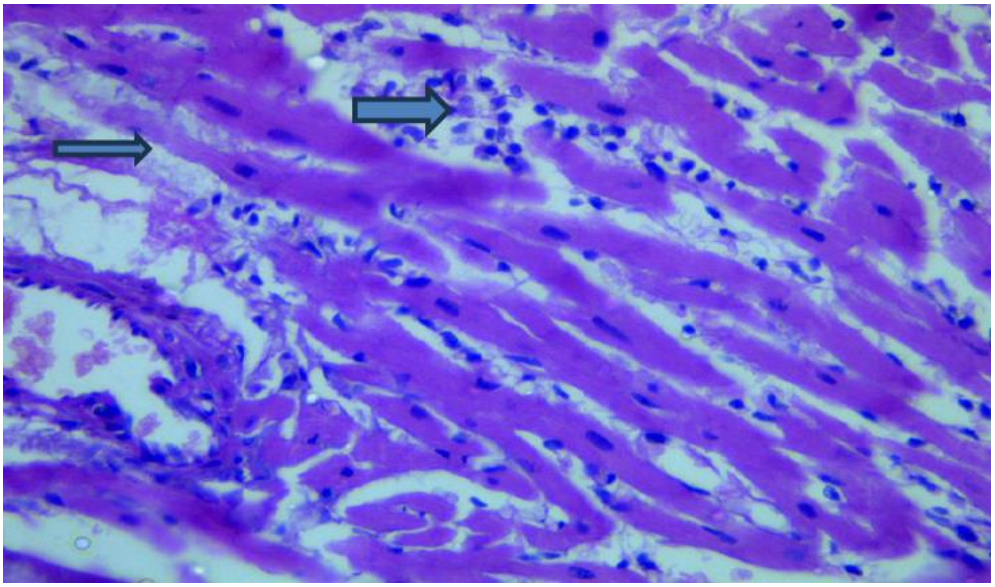

Figure (2): Section in mice heart in aluminum phosphide group revealed Acute myocardial infarction (wavy cardiac muscle cells that represent dead or necrotic cells) (thin arrow). Inflammation due to necrosis is also evident (thick arrow) (group II) (H&EX200)

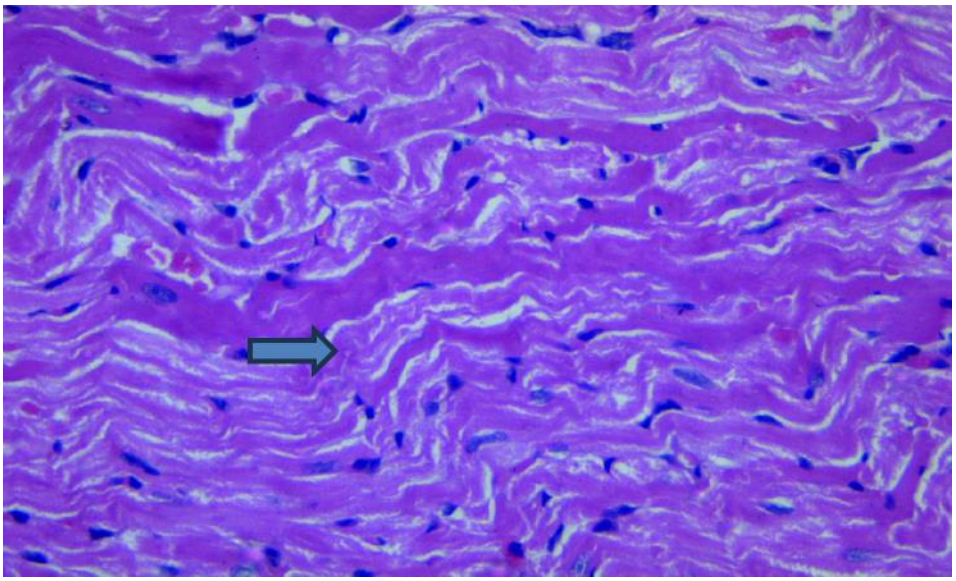

Figure (3): Section in mice heart revealed Acute myocardial infarction (wavy cardiac muscle cells that represent dead or necrotic cells (arrow) (group III) (H&EX200)

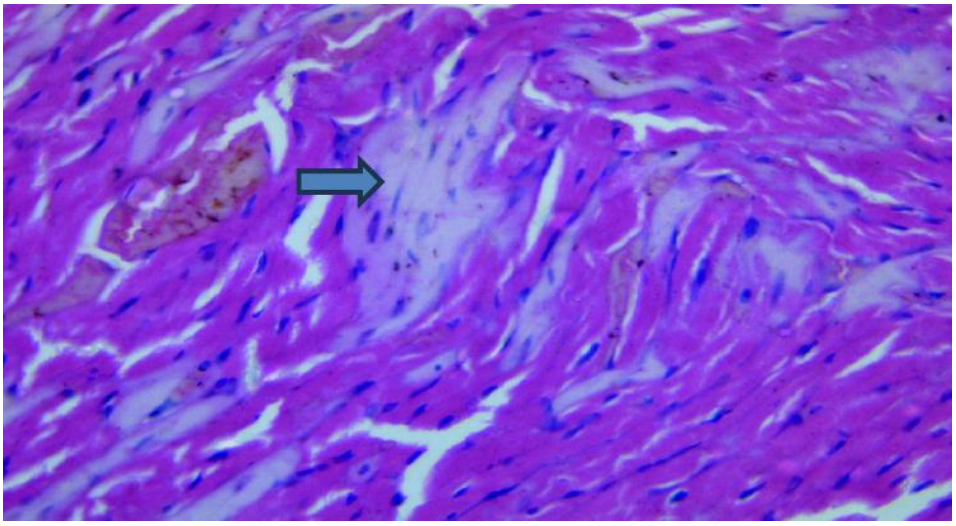

Figure (4): Section examined in mice heart revealed mild necrosis of cardiac muscles (group IV) (arrow)(H&EX200)

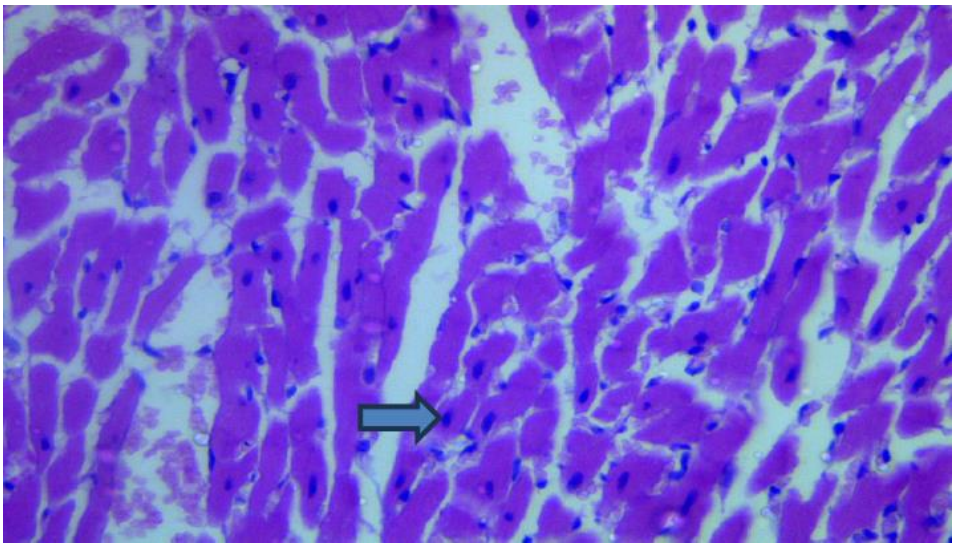

Figure (5): section in mice heart showing bundles of normal cardiomyocytes (group V) (arrow)(H&EX200)

Discussion

In Egypt, farmers usually use aluminum phosphide to safeguard stored grains, as it absorbs humidity from the grains. It is cheap and easily obtained, hence its accessibility for suicide attempts. Aluminum phosphide can be absorbed dermally or via the GIT, and the phosphine gas can be absorbed via inhalation (Hena et al., 2018). ALP causes severe toxicity with very high mortality and to date, no antidote is available. Management depends mainly on symptomatic and supportive treatment (Anand et al., 2011).

Mechanism of toxicity in humans and animals is due to liberation of phosphine gas from ALP after being swallowed in presence of water or gastric HCL (aluminum phosphide react with water to release hydrogen ions and phosphine gas) (Gurjar et al., 2011).

In agreement with results published by Singh et al. (2006), phosphine gas inhibits cytochrome C oxidase thus inhibiting oxidative phosphorylation resulting in anaerobic metabolism, enormous metabolic acidosis and multi organ failure especially heart failure, circulatory collapse and death.

Inhibition of oxidative respiration in mitochondria results in lipid peroxidation which responsible for harmful free radicals formation as malondialdehyde (MDA) and superoxide dismutase that lead to protein denaturation, cell damage and more organ failure (Berry et al., 2015).

Schotola et al. (2012) reported that metabolic acidosis diminishes cardiac contractility because hydrogen ions decrease releasing of calcium and decrease sensitivity of cardiac muscles to calcium, also Mathai and Bhanu, (2010) revealed that alteration in permeability of ions (calcium, sodium and magnesium) leads to cardiac necrosis, ECG abnormalities and cardiac arrhythmias.

Correction of metabolic acidosis has an important role in clinical management of ALP toxicity and decreasing mortality rate. When metabolic acidosis is corrected with $NaHCO_3$, a substantial dosage of sodium bicarbonate is required, resulting in hypernatremia and hypercapnia (Swietach et al., 2010). Ion transport across the RBC membrane encouraged the buffering capacity of hemoglobin, so RBCs used in maintenance of acid base balance. Also RBCs can interact with phosphine gas and prevent its action so packed RBCs can be used in treatment of ALP induced metabolic acidosis as reported by (Mashayekhian et al., 2016).

The current result showed that ALP toxicity led to intense decrease in PH and HCO_3 in rats, fresh packed RBCs or fresh packed RBCs + $NaHCO_3$ prevented development of this metabolic acidosis significantly, but $NaHCO_3$ alone has no significant role. This is in agreement with Rahimi et al. (2018) who revealed that administration of $NaHCO_3$ to rats poisoned with ALP resulted in moderate elevation of HCO3 levels but couldn't elevate PH to normal level.

Coinciding with results published by Hu et al. (2012) current study showed that ALP toxicity resulted in negative chronotropic effects. Treatment with fresh packed RBCs + $NaHCO_3$ significantly improved hemodynamic state and prevented bradycardia of intoxicated rats. Fresh packed RBCs alone improved bradycardia but insignificant with ALP group.

As regard ECG parameters, ALP toxicity caused many ECG changes like (prolonged QT interval, widened QRS complex and elevated ST segment). Treatment with $NaHCO_3$ + packed RBCs or with fresh packed RBCs only resulted in significant improvement of these effects in comparison with ALP group and retuned all parameters to normal values that were concordant with data published by (Xenocostas et al., 2010).

In agreement with these results Sweilum et al. (2017) and Louriz et al. (2009) reported that ALP toxicity in rats caused elevated cardiac troponin I levels significantly compared with control group. Treatment with fresh packed RBCs and fresh packed RBCs + $NaHCO_3$ returned cardiac troponin I to normal level significantly with ALP group (Louriz et al., 2009). Regarding histopathology of heart, ALP group (II) showed wavy cardiac muscle cells that represent dead or necrotic cells and features of inflammation due to necrosis were also evident. Group III that received ALP + $NaHCO_3$ also revealed features of acute ischemia, but group IV that treated with packed RBCs revealed mild ischemia. The last group that treated with packed RBCs + $NaHCO_3$ appeared as normal heart of control group.

These effects occurred due to liberation of phosphine gas (after ingestion of ALP) which caused decrease in cardiac contractility and circulatory failure (Sogut et al., 2011) and impairment of mitochondrial function due to hypoxia (Karami-Mohajeri et al., 2013). In agreement with the current results, Rahbar et al. (2011) reported that histopathological features like infiltration of leukocyte were observed in the heart of rats received ALP. Shah et al. (2009) revealed that myocardial injury and infarction could occur due to ALP poisoning.

Conclusion and Recommendations

Aluminum phosphide (ALP), being affordable and readily available, is often misused for suicide attempts, particularly by young adults. ALP-induced cardiotoxicity and metabolic acidosis with very high mortality is a major health issue nowadays. The current study reported that treatment with packed RBCs alone or with $NaHCO_3$ resulted in significant correction of metabolic acidosis, ECG parameters and cTnI level. These findings suggest that using of packed RBCs alone or with $NaHCO_3$ boosts survival rates in ALP poisoning and significantly improving chemical and histopathological changes. However, the combination therapy demonstrated greater benefits compared to packed RBCs alone.

It is imperative to educate the public about the limitations and dangers of using aluminum phosphide. This highly toxic pesticide, while effective for grain preservation, poses severe risks when misused. Further research on humans is necessary to assess the effect of packed RBCs in improving survival rates in ALP poisoning cases. This could potentially revolutionize treatment methods.

Declaration of Conflicting Interests

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خلايا الدم الحمراء المعبأة مقابل بيكربونات الصوديوم في علاج السمية القلبية والحماض الأيضي الناجمة عن فوسفيد الألومنيوم في الفئران

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الملخص العربى

الخلفية العلمية: عادة ما ترتبط السمية البشرية بفوسفيد الألومنيوم بالحماض الأيضي الشديد ونقص تروية القلب والتي تعد السبب الرئيسي للوفاة. **الهدف من البحث:** تقييم ومقارنة تأثير إعطاء كرات الدم الحمراء المعبأة وبيكربونات الصوديوم في علاج سمية فوسفيد الألمنيوم. **طريقة البحث:** أجريت هذه الدراسة التجريبية في الفترة من الأول وحتي الثامن من مارس ٢٠٢٢ على ٥٠ فأراً، تم تقسيمهم عشوائياً إلى خمس مجموعات: المجموعة الأولى تلقت زيت اللوز (مجموعة التحكم)، بينما تعرضت المجموعة الأخرى لفوسفيد الألومنيوم (١٢ ملجم/كجم). المجموعة الثالثة تم إعطاؤها بيكربونات الصوديوم ($NaHCO_3$) بجرعة ٣ مليمول/كغ، المجموعة الرابعة تلقت كريات الدم الحمراء المعبأة (١.٥ مل)، والمجموعة الخامسة تم علاجها بكل من كريات الدم الحمراء المعبأة وبيكربونات الصوديوم. تم إجراء تخطيط القلب الكهربائي و قياسات غازات الدم الشرياني وقياس مستويات تروبونين القلب، بالإضافة إلى الفحص النسيجي المرضي للقلب لجميع الفئران. **النتائج:** أدى استخدام ALP إلى حدوث بطء القلب بشكل ملحوظ($p=0.002$) ، وإطالة في فترة QT ($p<0.001$) وتوسيع QRS ($p<0.001$)و ارتفاع ST ($p<0.001$) والحماض الأيضي المقاوم ($p<0.001$) وارتفاع مستوى التروبونين ($p<0.001$). أظهر الفحص النسيجي المرضي تغييرات إقفارية شديدة في القلب نتيجة التعرض لـ ALP. أدت كريات الدم الحمراء المعبأة مع بيكربونات الصوديوم ($NaHCO_3$) إلى تحسين ملحوظ في بطء القلب ($p=0.025$). كما أن كريات الدم الحمراء المعبأة وحدها وكريات الدم الحمراء المعبأة مع بيكربونات الصوديوم أدت الي تحسن التغيرات الكيميائية والنسيجية المرضية. ومع ذلك، أظهر العلاج المركب فوائد أكبر مقارنة بخلايا الدم الحمراء المعبأة وحدها. **الخلاصة:** تشير هذه النتائج إلى أن استخدام كريات الدم الحمراء المعبأة وحدها أو مع NaHCO3 يعزز معدلات البقاء في حالات تسممALP.

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