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Original article

Exploring the Protective Effects of Vitamin C and D against Phosphine-Induced Kidney Damage

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ABSTRACT

Background: In Africa, Aluminium phosphide is commonly used for storage and transportation of food grains. Unfortunately, the chemical build up in the food we eat is poisonous without a specific antidote. We speculate that the antioxidant effects of vitamins C and D could mitigate the long list of side effects. Aim of the Work: To determine the possible protective effect of vitamins C and D against phosphine-induced kidney damage in Wistar rats Materials and Method: This is an experimental laboratory-based study. Twenty Wistar rats were assigned randomly into five groups (n=4). Group, I served as the normal control while Groups II-V were exposed to 2.5 mg/kg phosphine tablet. Group II was the positive control without treatment while Groups III-V were treated with vitamin C (100mg/kg/bw), vitamin D (10mg/kg/bw). Group V was co-administered with vitamins C and D. All treatments lasted for 30 days. Animals were euthanized and blood was collected via cardiac puncture for renal function parameter while excised kidney was processed histologically by the paraffin wax method. Result: There was a significant increase in the urea and creatinine levels in phosphine-induced animals, indicating the kidney was injured. Creatinine is a more reliable marker for assessing kidney function than urea. Moreover, a number of interstitial foci of haemorrhage and inflammatory cells observed on the kidney confirmed the renal toxicity of phosphine. However, the co-administration of vitamins C and D produced a dose-related improvements in the kidney parenchyma. Conclusion: Aluminium phosphide is toxic to the kidney parenchyma. However, co-administration of vitamins C and D ameliorates phosphine-induced kidney damage.

1. Introduction

Nowadays, environmental pollution is a common health problem confronting humans. Many pollutants interfere with our daily lives whether directly or indirectly, but the residual build up of pesticides in the food we eat is one of the most toxic contaminants. According to World Health Organization (WHO), millions of pesticide poisoning occur yearly accounting for over 250,000 deaths (1). Aluminum phosphide (ALP) alone account for over 10.5% suicidal cases in 2019 (2). Unfortunately, there is no specific antidotes for phosphine poisoning consequently accounting for the high morbidity and mortality rates particularly among the youths (3). Some of the palliative care for ALP poisoning include oral administration of charcoal, coconut oil, and intravenous magnesium sulphate (4).

Exposure to the toxic phosphine gas may reduce both humoral and cellular immune functions which causes oxidative stress, depletion of the antioxidant levels, and nephrotoxicity (5). In our previous study, we demonstrated and reported the mitigating effects of the co-administration of vitamins C and D in phosphine-induced liver damage (6). Moreover, Adikwu and Deo (7) reported that antioxidant supplementation especially vitamins C and vitamin D ameliorate the stress associated with metal poisoning. Similarly, in many experimental studies, vitamins C and D diminishes reactive oxygen species and heightens the antioxidant defence system (8,9,10). Besides, vitamin D is essential for a wide range of non-classical functions and its deficiency is associated to a number of chronic disorders including diabetes, cardiovascular and kidney diseases (11).

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Some clinical studies on humans have associated positive health outcomes with vitamins C and D ingestion (4), however their significance are inexhaustible. From the perspective that the kidney is susceptible to more than a few damage due to high volume of blood and toxins flowing through it and its ability to filter, there is paucity of information on the histopathology of phosphine-induced kidney damage and their possible antidote. It is against this background we determined the proctective effect of vitamins C and D on phosphine-induced kidney damage.

MATERIALS AND METHODS

Ethical approval

This study was carried out in accordance with the code of ethics for experiments involving the use of laboratory animals. The protocol was approved by The Ethics and Research Committee, Ondo State Ministry of Agriculture, Akure City, Ondo State, Nigeria as referenced (MNR/V384/9).

Experimental animals

This is an experimental laboratory-based study. Animals were obtained from the Animal Holding of the Department of Anatomical Science, Achievers University Owo, Ondo State, Nigeria. The animals were housed in ventilated cages at the Animal House and allowed access to a standard rodent diet and water ad libitum through out the experiment following the International Human-Animal Care Standard.

Study Design

This is an experimental study. Twenty Wistar rats were assigned randomly into five groups (n=4). Group, I served as the normal control while Groups II-V were exposed to 2.5 mg/kg phosphine tablet. Group II served as the positive control without treatment while Groups III-V were treated with vitamin C (100mg/kg/bw) and vitamin D (10mg/kg/bw). Group V was co-administered with vitamins C and D. All treatments lasted for 30 days and the animals were euthanized for sample collection.

Sample collection

Blood was collected via cardiac puncture into a lithium heparinized anticoagulant bottles and was centrifuged at 3000 rpm for 15 mins to obtain the plasma. The plasma obtained was used for biochemical analysis while the excised kidney was fixed in 10% neutral buffered formalin for histological investigation.

Biochemical analysis

Plama urea (U) and creatinine (Cr) were analysed using diagnostic kits from Randox laboratory, United Kingdom while plasma electrolytes; potassium (K+), sodium (Na+), chloride (Cl-), and bicarbonate (HCO3) were estimated using "ARCHITECT c4000" Aboot automated chemistry analyser.

Histopathological analysis

Representative organs were processed histologically as described by Avwioro (12). Briefly, the grossed tissue was dehydrated in three changes of alcohol, xylene, and molten paraffin wax. Sections was cut at 4 microns on a rotary microtome (Leica RM2125 RTS, Leica Biosystems, Buffalo Grove, United States of America) and stained in hematoxylin-eosin (H & E).

Statistical analysis

Data were evaluated by one-way analysis of variance (ANOVA) using statistical package for social science (SPSS) Version 25 (SPSS, Cary, NC, USA) and expressed as the mean standard error of the mean, while the student t-test was used to assess if there is any difference in the data obtained, p values < 0.05 was considered statistically significant.

RESULT

Biochemical assessment

In this study, there was a significant increase in plasma urea and creatinine levels in phosphine-induced animals compared to the control group, indicating that the kidney was injured (Table 1).

Table 1: Effect of Vitamin C and D on kidney function markers:

Parameter	Group I	Group II	Group III	Group IV	Group V
Sodium (mmol/L)	137.4±2.06#	113.8±2.71*	126.8±1.17*#	128.2±1.72*#	130.4±1.02*#
Potassium (mmol/L)	3.84±0.16#	6.12±0.28*	4.92±0.25*#	4.9±0.35*#	4.36±0.27*#
Chloride (mmol/L)	104.4±2.73#	88±2.76*	96.8±1.17*#	98.8±0.75*#	98.8±2.04*#
Bicarbonate (mmol/L)	22.2±0.75#	14.4±1.85*	18.8±0.75*#	19.2±0.75*#	20.4±0.49*#
Urea (mmol/L)	4.06±0.24#	8.26±0.42*	6.16±0.40*#	5.82±0.67*#	5.18±0.74*#
Creatinine (µmol/L)	63.8±3.92#	176.6±9.24*	136.8±6.05*#	123.2±14.46#	94±8.60*#

Results were expressed as mean value ± standard deviation (SD).*mean values were significantly different compared to the Normal control at P≤ 0.05.#mean values were significantly different compared with the positive control (Aluminum Phosphate). Group I: Control, Group II: Aluminum Phosphate, Group III: Aluminum Phosphate + Vitamin C, Group IV: Aluminum Phosphate + Vitamin D, Group V: Aluminum Phosphate + Vitamin C and D.

Figure 1: The effect of Vitamin C and D on electrolytes and creatinine values. *mean values were significantly different compared to the phosphine group at P≤ 0.05.

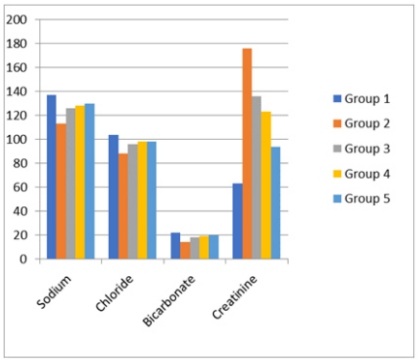
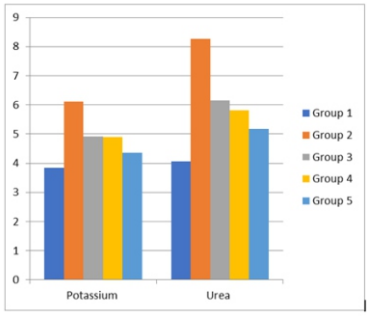


Figure 2: Effect of vitamin C and D on potassium and urea levels. *mean values were significantly different compared to the phosphine group at P≤ 0.05.



Histopathology assessment

There was inflammatory cells and foci of interstitial haemorrhage on the kidney parenchyma. However, co-administration of vitamins C and D produced a dose-related improvements in the kidney (Figures 3-5).

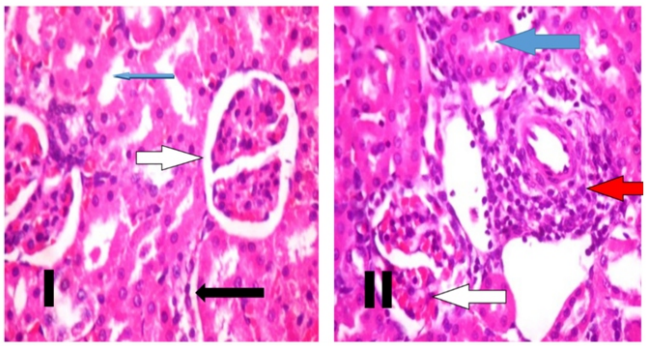


Figure 3 Normal kidney section (I): shows renal corpuscle (white arrow), renal tubule (black arrow), and proximal tubule (blue arrow). Phosphine induced degenerated kidney (II) exhibited severe inflammation (red arrow). (H&E. Mag. X 400).

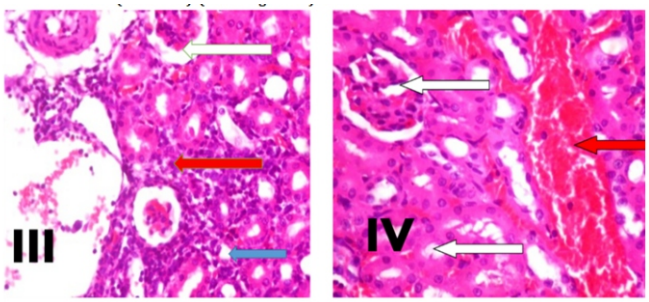


Figure 4 Phosphine induced degenerated kidney (I) treated with Vitamin C exhibited severe inflammation (red arrow) while animals treated with Vitamin D (IV) exhibited extravasion of blood (red arrow). (H&E. Mag. X 400).

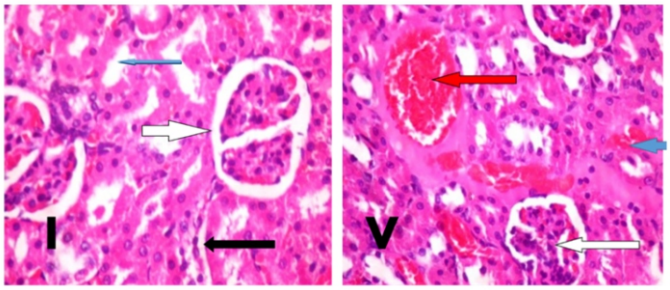


Figure 5 Phosphine induced degenerated kidney (V) treated with Vitamin C and D shows mild interstitial haemorrhage (red arrow) with improved histological features compared to normal control (I). (H&E. Mag. X 400).

DISCUSSION

The protective effect of antioxidants against the many deleterious effects of ALP have been reported (13). We determined the protective effects of vitamins C and D against phosphine-induced kidney damage. In this experimental study, ALP caused significant changes in both the biochemical and anatomic structures of the kidney. There was a significant decrease in sodium (Na2+) levels in the phosphine-induced group whereas vitamin supplementation restored the Na2+ values with the most significant improvement detected in the group co-administered vitamins C and D. There was also significant restoration of potassium, chloride, and bicarbonate values to normalcy in the group. Previous studies has suggested that electrolytes abnormalities, such as high or low sodium and potassium levels may be present in phosphine poisoning (14,15,16).

According to Mokhtari et al., (11), vitamin D improves the antioxidant defence system such as glutathione, glutathione peroxidase, and superoxide dismutase. Normal redox homeostasis would break down when their intracellular scavenging capacity is abridged. In some cases of metabolic stress, the levels of intracellular oxidants may rise with toxic effects indiscriminately damaging proteins, lipids, and DNA and activating specific signaling pathways that is linked to the onset of a number of diseases (4). In addition, some studies have also indicated the significance of vitamin C in reducing the oxidative effect of phosphine (17,18). Creatinine is a reliable marker than urea to assess kidney function (19), a significant increase in both creatinine and urea in the present study shows that the animals suffered nephrotoxic changes. The alleviating effect of vitamins when administered individually, as well as the co-administration of vitamins C and D was apparent in this study with a significant reduction in urea and creatinine values. Moreover, free radicals interacts with normal cellular components leading to tissue-breakdown (14,20). The histopathological changes in the present study is similar to previous reports (21,22) that documented interstitial haemorrhage in the kidney of experimental animals.

A number of studies have reported the role of vitamin D supplementation in oxidative stress (23,24,25,26,27). The present study revealed for the first time that vitamins C and D supplementation improved the kidney function as well as histologic features in phosphine induced damaged in tandem with previous studies which established phosphine-induced kidney damage (28,29).

CONCLUSION

In this study, ALP significantly increased the plasma urea and creatinine levels, indicating that the kidney was injured. A number of inflammatory cells and interstitial haemorrhage proved the kidney was injured. However, co-administration of vitamins C and D produced a dose-related improvements in the kidney.

Declarations:

Ethics Approval: The protocol was approved by The Ethics and Research Committee, Ondo State Ministry of Agriculture, Akure City, Ondo State, Nigeria as referenced (MNR/V384/9).

Consent for publication: Not applicable

Availability of data and material: Data are available from the corresponding author upon request.