Jagua Publication

www.jpub.org

Current Research in Interdisciplinary Studies 2(2) (2023): 1 –5

Research Article

Ameliorative Effect of Vitamin E on Paraquat Induced Nephrotoxicity in Rat

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Received:
January 15, 2023
Accepted:
February 10, 2023
Published:
February 18, 2023

How to cite:
Okolonkwo et al. 2023. "Ameliorative Effect of Vitamin E on Paraquat Induced Nephrotoxicity in Rat". Current Research in Interdisciplinary Studies 2(2): 1 – 5. https://doi.org/10.58614/cris221

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Abstract: The kidney is a very vital organ required for excretion of metabolic waste products in the body and when the kidney is damaged, this function is compromised. Paraquat is a toxicant that is known to have toxic injuries in different organs. Therefore, the aim of this study was to uncover the treatment effect of vitamin E in paraquat inflicted kidney injury. The experimental animals (male rats) were 200 and they were classified into 4 groups designated as A, B, C and D. The A served as the control group, B, C and D were test groups classified based on dose of paraquat administered. A was not treated with paraquat, B, C and D were treated with 0.02g, 0.04g and 0.06g of paraquat respectively every two weeks for three months. Each group mentioned had subgroups designated "0" and "VE"; "0" subgroups were subgroups not treated with vitamin E while "VE" were subgroups treated with 500mg of vitamin E. Treatment of vitamin E occurred weekly for one month. Both vitamin E and paraquat treatments occurred orally. After treatment period rats were sacrificed and blood sample collected via cardiac puncture for urea and creatinine assay. The results showed that there was no significant difference in urea levels among paraquat alone treated groups but there was a significant increase in creatinine levels among paraquat alone treated groups. There was a significant decrease in creatinine level after paraquat treatment. This study has shown that vitamin E is a therapeutic hope for paraquat inflicted nephrotoxicity in rats.

Keywords: kidney, paraquat, rat.

1. Introduction

The kidney has some functions that are best remembered using the mnemonics "A WET BED". "A" represents maintaining acid-base balance, "W" stands for maintaining water balance, "E" represents maintaining electrolyte balance, "T" represents toxin removal, "B" represents blood pressure control "E" stands for making erythropoietin, "D" stands for vitamin D metabolism (Lisa *et al.*, 2016). The ability of the kidney to perform all of these roles depends on the three fundamental functions which are; filtration, reabsorption and secretion. Furthermore, the renal physiology is divided into three; glomerular filtration, tubular reabsorption and tubular secretion. They explain the transport systems involved in the kidney. The nephron, the functional unit of the kidney is divided into the following; proximal convoluted tubule, proximal straighted tubule, loop of henle, distal convoluted tubule and collecting duct. The loop

of henle has three compartments; thin descending, thin ascending and thick ascending. (Hook and Hewitt, 1977).

A commercially available herbicide called paraquat has been used globally to improve agricultural yields by way of destroying weeds that may interfere or compete with same nutrient with the plants (Akram 2014). It has a no discriminating or selective approach in green plant destruction. It kills and plant is touches. While it is beneficial in weed management in the agricultural sector, its high toxic effect has been reported to be harmful to animals and humans who get exposed to it. Human exposure to paraquat was reported to cause organ failure due to involvement in the generation of reactive oxygen species (ROS) which describes the pathogenesis of organ failure (Akram 2014).

Over time, the management of oxidative damage due to free radicals or reactive oxygen species is the administration of antioxidants (Ranjbar *et al*., 2002). Studies have reported the therapeutic role of antioxidants in the treatment of oxidative stress. Hence, antioxidants are referred to as antidotal therapy for oxidative induced tissue damage (Ray *et al*. 2007; Abdollahi *et al*. 2004).

Vitamin E is generally known as antioxidant and by virtue of antioxidative role, it may be very beneficial in the treatment of oxidative induced organ failure. Since studies by Block (1979) and Bus et al. (1975) reported that vitamin C, an antioxidative counterpart of E ameliorated the toxicity effect of paraquat exposure in rats and deficiency of vitamin E has reported to potentiate rise in free radical and decrease in survival rate, this study focused on evaluating the therapeutic effect of vitamin E supplementation in rats kidneys poisoned with paraquat.

2. Materials and Methods

2.1. Experimental Design

This was an experimental study designed with 200 rats which were divided into four groups based on dosage of paraquat such that the A group represents the group without paraquat treatment and served as the control group while B group represents group with 0.02g of paraquat treatment, C group represents group with 0.04g of paraquat treatment, and D group represents group with 0.06g of paraquat treatment. All the groups were further subdivided into two groups; those without vitamin E treatment and those with vitamin E treatment. Exactly 500mg of vitamin E was administered orally. The choice of doses used in this study was obtained from previous work (Okolonkwo *et al*., 2022a).

For paraquat treatment, it was given their respective paraquat doses once every two weeks for three months while vitamin E was administered once every week to the respective groups.

Both paraquat and vitamin E were administered orally according to their frequencies and duration.

After the duration of the treatment period, the rats were sedated using chlorofoam, sacrificed and blood sample was collected my means of cardiac puncture (Okolonkwo *et al*., 2022b).

2.2. Laboratory Analysis

Urea – Berthelot enzyme – colorimetric test method as applied by Fyneface et el. (2018).

Procedures

Exactly 1.0ml working reagent was dispensed into three tubes labeled 'Blank', 'Standard' and 'Sample', after which 10µl each of standard reagent and sample was dispensed into their respective tubes. The tubes were mixed and incubated for 5 minutes at 37^0C. At the end of the incubation, 1.0ml of sodium hydroxide/sodium hypochlorite solution was then dispensed into the three tubes, mixed and incubated again for another 5 minutes at 37^0C, at the end of which, the absorbance (A) of the sample and standard was read against the blank. The colour was stable for at least 30 minutes at room temperature.

Creatinine (Jaffe colori–kinetic method) as applied by Fyneface et el. (2020).

Procedure

A working reagent (WR) was produced by mixing equal volumes of Picric acid (17.5mmol/L) and Sodium hydroxide (0.29mol/L). 1.0ml of WR was dispensed into each of the three tubes labeled 'Blank', 'Standard' and 'Sample'. 100µl of standard reagent and sample was then added to the respective tubes, mixed and the stopwatch started. The absorbance (A_1) was read after 30 seconds and after 90 seconds (A_2) of the sample addition at 492nm (490 – 510) wavelength.

Results

The result presented in table 1.0 shows the comparison of urea and creatinine levels across paraquat dose-dependent groups. The results show that there was no significant difference (p-value>0.05) in urea levels among the groups but there was a significant dose-dependent increase (p-value<0.05) in creatinine levels among the groups.

Table 1. Changes in some biochemical data after one month treatment period.

Sub-groups	Urea (mmol/L)	Creatinine (µmol/L)
A_0	3.10 ± 0.05	1.07 ± 0.03
B_0	4.65 ± 0.07	21.52 ± 0.60
C_0	4.97 ± 0.06	51.95 ± 1.53
D_0	5.33 ± 0.08	98.22 ± 2.49
p-value	>0.05	<0.05

The resulted shown in table 2 is a comparison in urea and creatine levels between subgroups. The results show that there was no significant difference (p-value>0.05) in urea level after vitamin E treatment but there was a significant decrease (p-value<0.05) in creatinine levels in all groups after vitamin E treatment.

Table 2. Comparison of urea and creatinine levels between subgroups

Sub-group	Urea (mmol/L)	Creatinine (µmol/L)
A_0	3.10 ± 0.05	1.07 ± 0.03
A_{VE}	4.33 ± 0.03	1.40 ± 0.04
B_0	4.65 ± 0.07	21.52 ± 0.60
B_{VE}	5.18 ± 0.02	12.33 ± 0.44[b]
C_0	4.97 ± 0.06	51.95 ± 1.53
C_{VE}	4.65 ± 0.07	17.83 ± 0.60[b]
D_0	5.33 ± 0.08	98.22 ± 2.49
D_{VE}	4.22 ± 0.08	48.54 ± 1.12[b]

P-value<0.05

"b" means significant difference between subgroups in main group.

3. Discussion

This study evaluated the effect of vitamin E treatment of paraquat induced nephrotoxicity in rats with the intention of answering the research question, "Is Vitamin E an effective antidotal therapy in renal-implicated paraquat intoxication?"

The finding from this study revealed that paraquat inflicted renal damage in rats in a dose-dependent manner such that the rats with the highest dose of paraquat had the highest nephrotoxicity while the rats with the least dose of paraquat had the least nephrotoxicity. However, in all paraquat treated groups, it inflicted nephrotoxicity in all doses in the rats. Similarly to the work carried out by Garba, *et al*. (2007), the significant increase in creatinine levels were classical indications or signs of adverse effect of PQ administration on kidney. This was also supported by Wershana (2011), who reported increased urea and creatinine values of PQ treated animals. However, the result differed from the work done by Ogbama, *et al*. (2010) on fish, where they reported decreases in urea and creatinine levels in gills of *Clarias gariepinus* when administered increasing concentration of PQ-dichloride. The renal markers studied were urea and creatinine but only creatinine showed significant increase with increasing doses of paraquat but urea did not show any significant level difference among the groups. The significant change in urea level may not necessary depict optimal kidney health because study conducted by same author and other colleagues revealed that paraquat intoxication resulted in significant decrease in total protein levels. Since urea is the by-product of protein metabolism, urea may not rise because protein levels are usually low in paraquat intoxication (Okolonkwo et al., 2022a; Okolonkwo et al., 2022b).

After paraquat intoxication, the rats were treated with vitamin E to assess the ameliorative potential of the vitamin. The result showed that in all groups treated with different doses of paraquat, vitamin E restored renal function by way of decrease creatinine levels in all groups. Irrespective of the paraqaut intoxication or dose administered, a weekly treatment with vitamin reversed the kidney injury inflicted by

paraquat. This was evidenced by the laboratory results present in table 2.0. This study is in agreement with the study of Wershana (2001) who stated that vitamin prevents impairment of renal function.

4. Conclusion

In view of the question, "Is Vitamin E an effective antidotal therapy in renal-implicated paraquat intoxication?" The finding of this study has demonstrated that vitamin E is effect in treating or ameliorative nephrotoxicity in rats inflicted by paraquat intoxication within a month of weekly vitamin E treatment.

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