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Combined Effects Of Cadmium And Cyanide On Liver Enzymes And Kidney Function In Rats

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Abstract

The present study aims to evaluate the combined effects of cadmium (Cd) and cyanide exposure on liver enzymes (alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and Kidney functions (urea and creatinine) in rats. 16 male albino rats weighing between 100 and 150 g were utilized in the study. The rats were divided into 4 groups (n=4) as follows: Group 1 = Control; Group 2 = exposed to cadmium only (as cadmium chloride), Group 3 = exposed to cyanide only (as potassium cyanide); Group 4 = exposed to cyanide + cadmium .The exposure of the rats to the experimental treatment was done daily for 28 days. The serum liver enzymes, urea and creatinine were assayed using standard operating procedures (SOP). The results showed a significant ($p < 0.05$) increase in the levels of serum ALT, AST and ALP, Urea and creatinine in Group 2, 3 and 4 when compared with Group 1. However there was a significant decrease in AST and ALT activity in the rats in Group 4 when compared with Group 2 rats. In addition there was no significant difference in Urea and Creatinine activities among all the treated groups when comparing across the treated Groups. The result indicates that a combination of cyanide and cadmium is toxic to the liver and kidney of rats and could be deleterious to these organs, however, their combined effects was not synergistic.

Key words: Cadmium, cyanide, liver, kidney, synergy

INTRODUCTION

The increase in environmental pollution recently is a major global problem. This is due to the use of toxic chemicals or xenobiotic substances or by certain synthetic compounds such as heavy metals (Yousef and Salama, 2009). Cyanide and cadmium are very toxic elements and are important environmental pollutant which causes poisoning in different tissues of man and animals (Kumar et al 2010; Whittaker et al., 2011). Cadmium (Cd), is a toxic, non-essential transition heavy metal which has been considered capable of several health problems by the world health organization (Wu et al., 2012) also, various factors have been implicated in cadmium accumulation in the environment and the health challenges associated with its effects (Nwaogu et al. 2007; Whittaker et al. 2011; Mansour, 2014). In addition, due to its solubility cadmium can easily infiltrate the soil and water bodies where it is readily absorbed by plants resulting in storage in crops and crop products (Safar and Otaibi, 2016). Workers in the metal industries, battery manufacturing industries, electroplating industries as well as tobacco smokers have been found to be at a high risk of exposure to cadmium toxic effects because of the use of cadmium in these industrial processes (Lecerf and De Lorgeril, 2011). Cadmium waste water from industrial facilities channeled into rivers and lakes when taken by fish also pose a great danger to human consumption (Whittaker et al. 2011). Cd can also be released into the atmosphere from volcanic eruption. (WHO, 2008) Both long term and short term exposures to cadmium were found to cause various disease conditions such as osteomalacia, anaemia and cardiovascular diseases (Igwegbe et al. 2013). It has also been found to induce oxidative stress in various tissues of the body such as the brain, liver, testes, kidney, etc. by increasing membrane

lipid peroxidation and changing the antioxidant parameters of these tissues (Nwaogu et al. 2007). The peroxidation causes damage to the cell membrane thereby compromising its integrity and consequently damage to the cellular components (Nwaogu et al. 2007).

Cyanide is among the most potent cytotoxic poisons known to humans and animals. Besides acute cyanide poisoning, chronic intoxication is often documented. Studies suggest that some complications of cyanide toxicity are attributed to prolonged exposure to dietary, industrial and environmental sources of this toxic compound (Igwegbe et al. 2013). However, the precise mechanism by which cyanide exerts a damaging action on tissues is not clear, although some researchers proposed that oxidative stress may be implicated in the harmful effects of cyanide poisoning (Tulsawani et al. 2005). Cyanide has been shown to induce oxidative stress and damage in a number of biological systems such as kidney and the liver (Mansour, 2014). Cyanide-induced oxidative stress may be as a result of increase in reactive oxygen species (ROS) and nitric oxide as well as inhibition of antioxidant systems and mitochondrial function (Mansour, 2014). The present study thus aims to evaluate and compare the combined effect of cyanide and cadmium exposure on the liver and kidney of rats with implication to human health.

MATERIALS AND METHODS

Reagents

For the present study, cadmium chloride $CdCl_2$ (98% maximum limit of impurities, iron 0.0005% and sulfate 0.005%) produced by Himedia laboratories Pvt. Ltd Mumbai india and potassium cyanide KCN (96% maximum limit of impurities, chloride 0.1%, iron 0.02%, lead 0.002%, sodium 0.5%) produced by BDH chemicals Ltd Poole England was procured and used.

Experimental animals

A total of 16 albino rats eight weeks old male weighing between 100 and 150 g were obtained from the Emmanuel laboratory animal house Delta State, Abraka, Nigeria. The rats were fed on rat pellets and were given water *ad libitum*. The rats were housed in cages constructed of aluminum and wire gauze under control condition of 12 h light/ 12 dark cycle. These rats were divided into 4 groups of 4 rats per group as follows:

Group 1: Control: Rats in this group received tap water daily throughout the experiment.

Group 2: Cadmium only : animals in this group were given cyanide solution as potassium cyanide at concentration 0.72 mg /500 ml in the drinking tap water every day for 28 days..

Group 3: Cyanide only: animals in this group were given cadmium solution as cadmium chloride at concentration 11.6 mg /500 ml in the drinking tap water every day for 28 days.

Group 4: Cyanide + Cadmium: animals in this group were given cadmium and cyanide mix solution every day for 28 days.

Biochemical analysis

The activities of serum aspartate aminotransferase (AST) and alanine amino transferase (ALT) were carried out using the Randox kit as described by Reitman and Frankel (1957) while the activity of alkaline phosphatase (ALP) was done using the Randox kit as described by Kaplan and Righetti (1955). The levels of creatinine were carried out using the Randox kit as described by Bartels and Bohmer (1972) and urea were assayed using the methods of Tietz (1995).

Statistical analysis

The data obtained in the experiment was expressed as means ±SD and analyzed using analysis of variance and the group mean were compared by least significant difference (LSD). The SPSS-PC programme package (version 16.0) was used for statistical analysis.

RESULTS AND DISCUSSION

Table 1. The combined effect of cyanide and cadmium on Body weight and Organ to body

Group	Bodyweight gain	Liver/bodyweight gain	Kidney/bodyweight gain
1-CONTROL	18.28±7.94[a]	0.24±0.09[a]	0.05±0.02[a]
2-CADMIUM	-1.31 ± 11.60[b]	0.43±0.17[b]	0.53±0.03[b]
3-CYANIDE	-1.63 ± 6.61[b]	0.48±0.12[b]	0.66±0.04[b]
4-CADMIUM + CYANIDE	-1.26 ± 9.87[b]	0.47±0.13[b]	0.55±0.03[b]

Values are expressed in mean ± SEM (standard error of mean). Values and means not having similar superscript in the same row differs significantly at $p<0.05$. Means sharing a common superscript (a, b) in the same column do not differ significantly at (p? 0.05).

Table 2: The combined effect of cyanide and cadmium exposure on the activity of AST, ALT and ALP levels in rats

Group	ALT (U/L)	AST (U/L)	ALP(U/L)
1-CONTROL	10.50 ± 4.14[a]	25.25 ±18.78[a]	30.16±11.15[a]
2-CADMIUM	18.00 ±4.05[b]	57.25±19.36[b]	70.38±12.09[b]
3-CYANIDE	13.50 ± 6.05[c]	34.75±11.52[c]	57.28±7.04[c]
4-CADMIUM + CYANIDE	16.50 ±6.02[c]	39.00±17.57[c]	63.28 ± 21.53[c]

Values are represented in means, (n=4). Values are represented as mean ± standard deviation where n=4. Means not sharing a common superscript letter (a, b) in the same column differ significantly at (p? 0.05). Means sharing a common superscript (a, b) in the same column do not differ significantly at (p? 0.05).

Table 3: The combined effect of cyanide and cadmium exposure in the level of urea and creatinine in the kidney of infected rats

GROUPS	UREA	CREATININE
1-CONTROL	2.07 ± 0.74[a]	4.64 ± 3.26[a]
2-CADMIUM	7.33 ± 0.49[b]	14.21 ± 6.22[b]
3-CYANIDE	6.39 ± 0.45[b]	13.48 ± 8.36[b]
4-CADMIUM + CYANIDE	7.21 ± 1.58[b]	15.92 ± 8.14[b]

Values are represented as mean ± standard deviation where n=4. Means not sharing a common superscript letter (a, b) in the same column differ significantly at (p? 0.05). Means sharing a common superscript (a, b) in the same column do not differ significantly at (p? 0.05).

No mortality was recorded throughout the experiment. The percentage body weight gain of rats intoxicated with the toxicants (cyanide and cadmium) singularly and in combination was significantly decreased when compared with control (Table 1). There was a significance increase liver and kidney/body weight ratio in rats intoxicated with cyanide and cadmium (Groups 2, 3, and 4) relative to control. However when comparing within the intoxicated Groups (2, 3 and 4) there was no significant difference in

percentage body weight gain and liver and kidney/body weight ratio. The significant decrease in body weight gain in rats intoxicated with cadmium is consistent with the studies of Ayyah et al. (2017), while the significant decrease in percentage body weight gain in rats exposed to cyanide is consistent with earlier reports by Avaias et al. (2014). In this present study the no significant difference in percentage weight gain and organ weight gain when comparing the combined treatment with individual treatment is an indication that the combined toxicant does not have any synergistic effect.

AST and ALT are very active in the liver, hence they are marker enzyme. Any damage to the liver will therefore lead to their increase in the serum. In this present study, the serum AST and ALT activities were increased in all the groups of rats (Groups 2, 3 and 4) exposed to cadmium and cyanide (Table 2) when compared with the control (Group 1). This increase in AST and ALT in rats exposed to cyanide level is in line with the study conducted by Okolie and Osagie (2000) who stated that sub lethal cyanide poisoning increases serum AST and ALT activities in rats. Elsaid and Elkomy (2006) also observed similar results, where they observed significant increases in AST and ALT enzyme activities in rat's drinking water contaminated with cyanide. The increase in AST and ALT activities in rats induced with cadmium toxicity in this present study is also in agreement with previous studies that Cadmium induces toxic lesions in various tissues, the largest amount of this metal is deposited in the liver and kidney tissues (Vinodini et al. 2014) and it also causes functional changes in the liver (Safar and Otaibi, 2016). However a significant decrease in AST and ALT activities was also indicated in the combined Group 4 when compared with the Group 2 given cadmium only. The decrease in serum AST and ALT, in the combined Group may due to the antagonistic effect of these two metals. This is line with the study of Doudoroff (1956) who indicated that simple cyanide solutions are detoxified by the addition of metals in quantities sufficient to precipitate most of the cyanide in to the insoluble metal-cyanide salt.

Alkaline phosphatase (ALP) plays an important role in metabolism within the liver and in down regulating secretory activities of the intra hepatic biliary epithelium (Shiddappa and Muniswamy 2015; Kadiri, 2016). Serum ALP activity was significantly increased in all treated groups (Groups 2,3 and 4) when compared with control (Table 1). This is in line with the study of Shiddappa and Muniswamy**,** (2015) and by Kadiri (2016) who reported increase in serum ALP activity in rats exposed to cyanide. Abedi *et al*. (2013) and Sousa et al. (2002) also reported an increase in serum ALP in rats exposed to cadmium. However ALP was significantly decreased in the combined Group (Group 4) when compared with Cadmium only (Group 2) and not significantly different to Groups 2 rats exposed to cyanide only. This indicates that the damage imparted to the liver by this combined compounds is not significantly higher than that imparted by the individual compounds.

Serum parameters such as urea and creatinine are useful in early deduction of toxicity induced by exogenous compounds such as cyanide and cadmium (Igwegbe et al. 2013). Serum cratinine and Urea levels are used as index of renal damage in living organisms (Igwegbe et al. 2013). A significantly higher urea and creatinine activity was indicated (Table 3) in all treated rats (Group 2, 3 and 4) when compared with the control (Group 1). This indicates that compounds, cyanide and cadmium either individually or in combination induced damage on the kidney of the rats. This confirms earlier studies by Kadiri (2016) carried out on cyanide toxicity in rats and the studies of Rana et al. (2018) who carried out on cadmium toxicity on rats. However there was no significant difference in urea and creatinine activity when comparing the Groups 4 that was treated with the combined compounds with Group 2 and 3 that were treated with only one compound. This indicates that the combined cyanide and cadmium did not increase the damage caused to the kidney. Studies indicates that cyanide as well as cadmium promotes the generation of reactive oxygen species in animals thereby inhibiting the anti-oxidative activities of various body antioxidants either by aiding their depletion or by inhibiting their activities. (Sousa et al.2002; Abedi *et al.* 2013). In addition the inability of the body to strike a balance between the generation of these free radicals and the

ability of the body defense mechanism to detoxify and repair their oxidative damage leads to an oxidative stress which is the hallmark of oxidative damage resulting from cyanide and cadmium induction. (Sharma, 1989; Cuypers, 2010; Sharma 2012; Rana et al. 2018).

CONCLUSION

This present study indicates that a combination of cyanide and cadmium is toxic to the liver and kidney of rats and could be deleterious to these organs.

RECOMMENDATION

Histopathological studies of the liver and kidney will be needed to confirm if the combined toxicant causes damage to the microanatomical architecture of the liver and kidney. In addition, because ALP is an isoenzyme which can be of diverse origin such as the liver, red blood cells, bone and placenta, there is also need to show differential diagnosis of the source of the enzyme to know if it is from the liver. This may include inactivating the ALP from other sources and analyzing only that from the liver.

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