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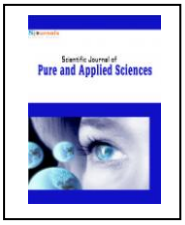

Original article

Some liver function indicators in guinea pigs injected with cyanide

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ABSTRACT

To determine the lethal effect of cyanide poisoning on the liver cells using ALP, AST, ALT and Bilirubin (Total and Conjugated) as test indicators, eighteen (18) male guinea pigs, age matched were used for this study. This included 12 guinea pigs which served as test groups and injected with different concentrations of potassium cyanide saline solution while 6 guinea pigs without cyanide injection served as control group. Blood samples were collected from the guinea pigs three hours after the injections of the cyanide saline solution. The blood samples were analysed for liver enzymes and bilirubin using standard methods. The result of the plasma AST and ALT at the different concentrations showed decreased levels which were significant when compared with the controls. The plasma levels of Total and Conjugated bilirubin were also significantly decreased when compared with controls. However, the levels of the ALP in both test and control groups showed no significant difference. This study therefore highlighted the need to determine the levels of these liver function indicators in cases of cyanide poisoning to ensure efficient management of patients who are exposed to the cyanide.

1. Introduction

Cyanide is any chemical compound that contains the cyano group (C≡N), and consists of a carbon atom triple bonded to a nitrogen atom. Inorganic cyanides are generally salts of the anion CN- (Greenwood and Earnshaw, 1997). The different kinds of cyanide exist in different forms which include; gaseous, liquids and solids. Those that can release the cyanide ion (CN-) are highly toxic (International Cyanide Management Institute, 2006).

Cyanide is generally considered to be rare source of poisoning. However, cyanide exposure occurs relatively frequently in patients with smoke inhalation from residential or industrial fires. Cyanide poisoning may also occur in industries, particularly in metal trades, mining, electroplating, jewellery manufacturing and X-ray film recovery.

Cyanides have been used as suicide agents, particularly among healthcare and laboratory workers and they can potentially be used in terrorist attack. The deleterious effects of cyanide majorly affect the respiratory organs. The effects of cyanide on the liver have been alluded to by Yamamoto et al, 1982.

The liver is one of the major organs in the body that performs several different functions in the body. However, the main function of the liver is the barrier-cleansing, but could also serve as powerful filter, remove and destroy bacteria, neutralizing toxins which are produced by metabolic reactions. The liver could be adversely affected in cases of poisoning, drug overdose and poor nutrition, although it rarely makes itself felt at the beginning of the disease because of its high functional reserve. Usually, when the symptoms manifest, it is obvious that the damage has been done and extensive. One of the functions of the liver is the production of a large number of enzymes which when hepatocytes are destroyed they leak directly into the blood and serve as useful indicator of the degree of liver damage (Burtis et al, 2006).

Cyanide exerts its toxic effects by forming a complex with ferric ion of the mitochondrial cytochrome oxidase, the enzyme that catalysis the terminal step in electron transport chain, thereby preventing the use of oxygen by cells .The inhibition of this enzyme also leads to the disruption of cellular respiration and consequently producing cytotoxic hypoxia.

Adult rats exposed to 200mg/KCN/l drinking water for 21 days had significantly higher liver weights compared with controls but no effect on liver weight when KCN was administered in the diet at a dose of 200mg/kg diet (Baselt, 1979).

Yamamoto et al. (1989) reported that the concentration of cyanide in the liver was mostly determined by the route of the administration. They also opined that the lungs, spleens and brains of experimental rats had appreciable levels of cyanide after oral dose of 7mg/ml concentration of cyanide radical as sodium cyanide saline solution, but that the concentration of cyanide was highest in the liver. The present study was designed to investigate the possible effects of cyanide salt on the integrity and function of liver cells of normal guinea pigs in relation to dose of cyanide salt ingested.

2. Materials and methods

2.1. Experimental animals

Animals used in this study were male guinea pigs with an average weight of 260g. They were eighteen (18) in numbers and were obtained from the animal house of College of Medicine, Ambrose Alli University, Ekpoma, Edo State, Nigeria and allowed to acclimatize for a period of three (3) weeks in the histopathology laboratory. The guinea pigs were fed with grower's mash, elephant grass and fresh clean water.

2.2. Experimental design

The guinea pigs were divided into three (3) groups A-C with six (6) guinea pigs in each group and were injected with different concentrations of the potassium cyanide-saline solution, except the group C which served as the control group. The study was carried out within a period of 3 months. The groups and dosages of potassium cyanide are as follow:

Group A injected with 5mg/ml, Group B injected with 10mg/ml and Group C, control group without cyanide.

2.3. Sample collection and analysis

Blood samples were collected after three hours from the heart of each guinea pig using sterile 5ml syringes. Prior to this, the guinea pigs were sedated with chloroform and an incision was made on the thoracic

cage to gain access to the heart. The collected blood specimens were dispensed into lithium heparinised bottles. The blood bottles were gently mixed and labelled properly and centrifuged for 5mins at 3,000 rpm. The plasma separated into corresponding labelled plain specimen containers and stored frozen until analysis time.

Plasma Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) were analyzed by method described by Reitman and Frankel (1957) using Randox reagents on spectrophotometer. Total and Conjugated bilirubin (TB and CB respectively) were analyzed by method described by Jendrassik and Grof (1938) using Randox Kit and then Alkaline Phosphatase (ALP) was analyzed using Phenolphthalein monophosphate reagents.

2.4. Statistical analysis

Results were presented in mean ± S.D. The paired sample t test was used to test the level of significance and $P<0.05$ was considered significant.

3. Results

Table 1 showed the mean and S.D of AST, ALT, ALP, TB and CB of control and test subjects at concentration of 5mg/ml of potassium cyanide saline solution. The mean of the results of AST, ALT, TB and CB levels of the test samples were significantly decreased than those of the controls ($p<0.05$) while the mean value of ALP showed no statistical significant difference ($p>0.05$) when compared with the controls.

Similarly, a comparison of the results of the controls with the test samples of the respective parameters at 10mg/ml concentration as shown in Table 2, all the values were statistically significant ($p<0.05$) except ALP.

Table 1
The mean ± SD Levels of AST, ALT, ALP, TB and CB of Test Subjects at 5mg/ml concentration of cyanide as compared with controls.

Parameters	Control subjects (m ± SD) n= 6	Test subjects (m ± SD) n= 6	T-value	P-value
AST (U/L)	347.5±7.6	143.17±3.54	59.79	<0.05
ALT (U/L)	94.83±25.56	62.33±2.50	3.146	<0.05
ALP (U/L)	43.66±12.83	43.33±3.39	0.062	>0.05
TB (mg/dl)	1.28±0.48	0.10±0.00	5.996	<0.05
CB (mg/dl)	0.83±0.31	0.75±0.03	0.013	<0.05

P<0.05 is significant.

Table 2
The Mean ± SD Levels of AST, ALT, ALP, TB and CB of Test Subjects at 10mg/ml Concentration of Cyanide as compared with Controls.

Parameters	Control subjects (m ± SD) n= 6	Test subjects (m ± SD) n= 6	T-value	P-value
AST (U/L)	347.5±7.6	119±2.73	69.34	<0.05
ALT (U/L)	94.83±25.56	60.50±3.62	2.973	<0.05
ALP (U/L)	43.66±12.83	45.33±2.66	-1.117	>0.05
TB (mg/dl)	1.28±0.48	0.27±0.10	5.123	<0.05
CB (mg/dl)	0.83±0.31	0.13±0.10	5.496	<0.05

P<0.05 is significant.

4. Discussion

Poisons generally, are harmful to all animals to include man. Poisons are basically chemical substances and most of which may be synthetic or biological in nature. The effect of cyanide on the animal is primarily targeted at the respiratory system. Cyanide, however can affect the functions of other organs in the body. This experiment was designed to determine the effects of cyanide on the liver of guinea pigs. The majority of the absorbed cyanide

reacts with thiosulphate in the presence of enzymes to produce thiocyanate which is excreted in the urine over several days. Owing to this rapid detoxification, animals can ingest high sublethal doses of cyanide over extended periods without harm (Eisler, 1991). Minute amounts of cyanide in the form of vitamin B12 (cyanocobalamine) are necessary requirement in the human diet.

Yamamoto et al (1982), reported that the concentration of cyanide in the liver was most sensitive to the route of administration and also that the liver, lung, spleen and brain of experimental rats had oral dose of 7mg/ml concentration of cyanide radical as sodium cyanide saline solution and the results showed that the concentration of cyanide was higher in the liver. In our study, cyanide was administered intramuscularly to the guinea pigs and the results showed that most of the enzymes were significantly decreased ($p<0.05$) when compared with the control samples. This could be ascribed to the effect of cyanide on the liver.

Baselt (1979), reported that even though the respiratory system is the main site of initial action of cyanide, it could rapidly be distributed to other organs and tissues as the cyanide is transported through the blood and the lymphatics. Our experiment has shown that the decrease in levels of AST, ALT, total and conjugated bilirubin were statistically significant except for ALP when compared with the controls.

Ansell and lewis (1970), reported that cyanide levels of up to 3.2mg% was detected in the stomach contents, brain and urine, 30 minutes after death in a woman who ingested 25g NaCN, unfortunately, the liver enzymes were not determined.

This study showed that the hepatocytes were poisoned by the presence of cyanide as a result, the activities of the liver enzymes studied were affected hence the decrease in values. When the liver is damaged, some liver enzymes in the blood are decreased while others increase (Burtis et al, 2006) depending on the stage of liver damage. Our findings were in agreement with this claim as our results showed significantly decreased levels of AST and ALT. Furthermore, this study also showed that bilirubin levels were significantly reduced ($p<0.05$) when compared with the control samples. This is not surprising because the liver functions which include conjugation of bilirubin could be affected when the enzymes which are involved in these processes have been interfered with or prevented from performing this function due to cyanide poisoning. The activities of cyanide is not only restricted to the respiratory system, it is rapidly distributed to other organs of the body and indeed Yamamoto et al (1982), stated in their work that the liver had the highest concentration of cyanide when rats were fed orally.

Some controversies have risen over the use of sodium nitroprusside metabolite (cyanide) for elective induction of hypotension during general anaesthesia (Tinker and Minchenfelder, 1976). It was previously thought that sodium nitroprusside was ideal for this practice because of pharmacological efficacy but subsequently, it was realized that metabolic acidosis developed in some patients who received sodium nitroprusside as a result of disturbed aerobic metabolism (Tinker and Minchenfelder, 1976).

Furthermore, Tinker and Minchenfelder, (1976) stated that blood adenosine triphosphate (ATP) levels were depressed in patients following the use of sodium nitroprusside metabolite-cyanide. ATP is involved in the generation of energy and in metabolic processes and therefore, an incapacitated liver would be depressed and would not generate the enzymes which are necessary for the liver functions. This study is in support of this assertion as it has shown that the liver enzymes were significantly reduced ($p<0.0.5$) due to toxic action of cyanide. Therefore cyanide poison is not only restricted to the paralyses of the respiratory system but also affects enzyme activities of the liver. The marked decrease in alanine aminotransferase, aspartate aminotransferase and bilirubin levels in cyanide poison suggest that the liver is affected by cyanide. Therefore, when it is necessary to determine whether cyanide was ingested, injected or inhaled, at least the liver must be investigated in addition to the blood and stomach for cyanide contents or effects.

However, the results of oral intoxication with cyanide must be interpreted with caution because the presence of food in the digestive tract may retard absorption. It is therefore recommended that in the determination of cyanide poisoning, the activities of liver enzymes in blood samples should be routinely done to determine the status of the patient in cyanide poisoning as this would be facilitate proper and effective management of patients diagnosed with cyanide poisoning.

5. Conclusion

In cyanide poisoning, it was observed that AST and ALT were significantly decreased while the ALP was unaffected. Additionally, bilirubin levels were also decreased.

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