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Impact of Arsenic trioxide on selected liver enzymes in *Oryctolagus cuniculus*

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Abstract : Arsenic is a long-known poison of environment and industrial origin. Prolonged exposure is associated with vascular disease, skin lesions and cancer. Transaminases are important enzymes in animal metabolism which are intimately associated with amino acid synthesis. The test animals were divided into three groups. Group I : treated as control. Group II: treated with 0.2mg/kg of As_2O_3 for 15 days and Group III : treated with 0.6mg/kg of of As_2O_3 for 7 days.In the arsenic treated groups there was a significant increase in ALP, SGPT and SGOT content. Therefore, it is suggested that water containing even low dose of arsenic should not be consumed.

Keywords : Arsenic trioxide, liver enzymes, SGOT, SGPT, ALP

INTRODUCTION

Arsenic poisoning is now considered as one of the biggest environment disaster and a major public health issue. Incidence of arsenic poisoning has been reported from many parts of the world. About 80% of ingested arsenic is absorbed and metabolized in liver and then excreted through urine and faeces, while upon chronic exposure, it is deposited in liver, kidney and skin. Liver is the most important site of arsenic methylation [1,2] but most organs show methylating activity.. Earlier findings reveals that SGOT and SGPT are reliable determinants of liver parenchymal injury[3].Because it targets widely dispersed enzyme reactions, arsenic affects nearly all organ systems. Acute arsenic toxicity may be associated with hepatic necrosis and elevated levels of liver enzymes. Arsenic intoxication may also result in toxic hepatitis with elevated liver enzyme levels. Case reports have also linked chronic high level arsenic exposure with hepatic angiosarcoma, a rare form of liver cancer. Arsenic exposure can affect hepatic vasculature and induce non cirrhotic portal hypertension[4]. Because of its widespread occurrence in animal and vegetable tissues, its toxicity, carcinogenicity and therapeutic use, arsenic should be studied extensively.

In previous studies it was seen that pulmonary absorption of soluble forms, such as arsenic trioxide, is rapid while less soluble forms may reside in the lower airways and be absorbed during a prolonged period of the time[5]. Pentavalent arsenic compounds are almost totally absorbed (till 90%) in most species. The absorption of trivalent arsenic is limited, although the toxicity is greater because of the high lipid solubility[6]. Experimental studies have indicated that the liver is an important site of arsenic methylation, especially following ingestion, when the absorbed arsenic initially passes through the liver[7]. The biomethylation of inorganic arsenic to Dimethylarsinic acid occurs via alternating reduction of pentavalent arsenic to trivalent and addition of methyl groups[8] .Arsenic methyltransferase activity has been detected in vitro in liver from rabbit, rat, mouse, hamster, pigeon and rhesus monkeys [9,10]. However it was suggested[11] that arsenic induced hepatic injury is caused by vascular and not hepatocellular damage.

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MATERIALS AND METHODS

Mature and healthy rabbits belonging to Order – Lagomorpha Family – Leporidae, taxonomically identified as *Oryctolagus cuniculus* were used to assess the effect of Arsenic toxicity. Rabbits weighing from 1.50 – 2.25kgs were obtained from the Veterinary College (Birsa Agricultural University), Kanke, Ranchi. They were kept in cages and supplied with dechlorinated tap water for acclimatization at 30.2 - 34.5^{0}C for fourteen days, during which they were fed with green leafy vegetables and grains *ad libitum*. The natural photo period was maintained during the period. Mortality during the experiment of acclimatization was less than 2%. Group I was maintained as control. Group II was exposed to 0.2mg/kg As_2O_3 for the period of 15 days. Group II was exposed to 0.6mg/kg As_2O_3 for the period of 7 days intraperitoneally. Blood samples for baseline data and of other treatments were collected from the ear vein of each rabbit with syringes and needles. Samples were stored in vials without EDTA and with EDTA (10%) in deep freeze and were analyzed in the laboratory for various liver parameters by standard techniques.

RESULTS

The data was statistically analyzed both by T-test and ANOVA through which it was observed that the complete picture (CP) of liver enzymes were significantly disturbed in arsenic feed groups.The ALP value to Group I rabbits were higher 64 IU/L±7 than the sham Control value of 12.5 IU/L whereas Group II value were recorded to be even higher 76 IU/L±3, Since the P-value of the F-test is less than 0.05, there is a statistically significant difference between the means of the 3 variables at the 95.0% confidence level.

Similarly significantly high values of SGPT and SGOT in Group I and Group II individual 77 IU/L±5 and 73 IU/L±8 whereas 72 IU/L±6 and 81 IU/L±10 respectively in each group as compared to control (63.5 IU/L and 44.5 IU/L for SGPT and SGOT) Observations shows the entire liver profile is conspicuous with statistically significant changes in all three experimental groups. For SGPT the P-value of the F-test is lower than 0.05, there is a statistically significant difference between the means of the 3 variables at the 95.0% confidence level. Whereas for SGOT the P-value of the F-test is less than 0.05, there is a statistically significant difference between the means of the 3 variables at the 95.0% confidence level.

TABLE : Liver enzymes Data (All values are Mean + SEM)

LIVER ENZYMES	CONTROL	GROUP I	GROUP II
ALP [Alkaline phosphatase (IU/L)]	12.5± 0.7(5-20)	64± 7	76± 3
SGPT [Serum glutamate pyruvate transaminase (IU/L)]	63.5± 0.7(12-67)	77±5	73±8
SGOT [Serum glutamate oxaloacetate transaminase (IU/L)]	44.5±1.7(14-45)	72± 6	81±10

GRAPHS

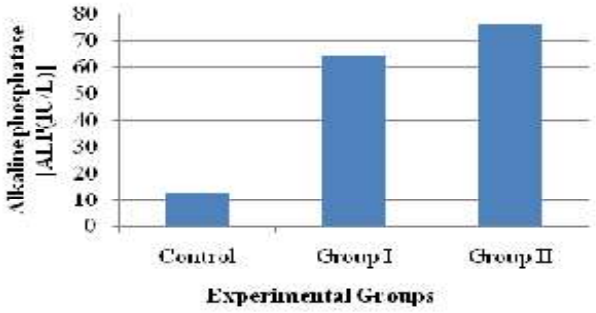

Fig2.1 Alkaline Phosphatase of Rabbit of three different groups. Control, Group I and Group II. Bars are Mean±(n=5) from the respective control group

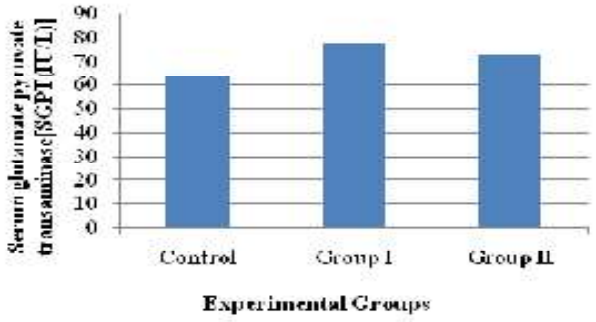

Fig.2.2: Serum Glutamate Pyruvate Transaminase of Rabbit of three different groups. Control, Group I and Group II. Bars are Mean±(n=5) from the respective control group.

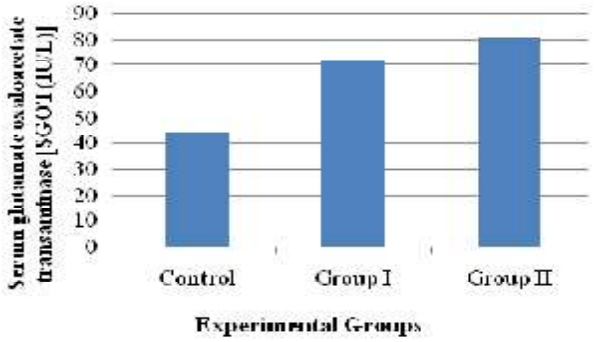

Fig.2.3: Serum Glutamate Oxaloacetate Transaminase of Rabbit of three different groups. Control, Group I, and Group II. Bars are Mean±(n=5) from the respective control group.

DISCUSSION

Arsenic toxicity is a health problem affecting millions of people all over the world, especially India and Bangladesh. Human exposure to arsenic is mainly represented by intake of food and drinking water contaminated with arsenic. Epidemiological studies show that a long time arsenic intake correlates with the occurrence of several illnesses: abnormal development, neurological and neurobehavioral disorders, cardiovascular and hematological diseases, diabetes, fibrosis of the liver and several types of cancers[12,13,14]. It is an important human toxic metalloid due to its presence in the environment and in workplaces. The present investigation revealed that arsenic induces significant increases in ALP, serum glutamate pyruvate transaminase and serum glutamate oxaloacetate transaminase activity. The SGPT and SGOT are chemicals that are made almost exclusively by liver cells. When the liver is irritated or inflamed it can leak SGPT and SGOT into serum where it can be measured. Arsenic intoxication significantly elevated the SGOT and SGPT activity in rabbit throughout the whole experimental period as compared to control animals. In the present study pathological alteration in hepatic cells is one of the major contributing factors for the change. The increase in SGOT and SGPT in serum may be due to hepatocellular necrosis, which causes increase in the permeability of the cell membrane resulting in release of transaminases in blood stream[15,16] .The present findings support those of previous study[17] . Chemicals such as ethanol has additive effects in marginally elevating blood SGOT and SGPT in arsenic intoxicated rats as shown by earlier finding[18]**.** Hepatocyte necrosis in acute hepatitis, toxic injury or ischaemic injury results in the leakage of enzymes into the circulation. However, in chronic liver diseases such as hepatitis C and cirrhosis, the serum SGPT level correlates only moderately well with liver inflammation.

The present study reveals increase in the activity of Alkaline phosphatase after arsenic exposure. Alkaline phosphatase in the liver is closely connected with lipid membranes in the canalicular zone. Arsenic induced hepatopathy causes increase in the activity due to hepatocyte damages. The present study is in agreement of the findings of previous studies[19,18] . Liver is the most important site of arsenic methylation[1,2] but most organs show methylating activity. Activities of both SGOT and

SGPT were significant higher in arsenic treated rabbits indicating liver dysfunction. Earlier findings reveals that SGOT and SGPT are reliable determinants of liver parenchymal injury[3]. The increment of the activities of SGOT and SGPT in plasma may be mainly due to the leakage of these enzymes from the liver cytosol into the blood stream[20], which gives an indication on the hepatotoxic effect of arsenic.

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