The Biobrio ISSN : 2393-9508
An International Quarterly Journal of Life Sciences
Website : www.thebiobrio.in
2 (1 & 2): 78 - 82, 2015

IMPACTS OF ARSENIC TRIOXIDE IN SOME RENAL PARAMETERS IN ORYCTOLAGUS CUNICULUS

MANISHA KUMARI
Department of Zoology, Nirmala College, Ranchi-834002

ABSTRACT

Arsenic is one of the most dangerous occupational and environmental toxins. Both natural and anthropogenic sources are responsible for the distribution of many toxicants, mainly heavy metals throughout the environment. Arsenic trioxide is a trivalent inorganic coumpound of arsenic. Nephrotoxicity was assessed by estimating the serum levels of Urea, Uric acid and Creatinine, the markers of renal dysfunctioning. The applied doses of arsenic trioxide administrered intraperitonially were 0.2mg/kg for 15 days and 0.6mg/kg for 7 days. Arsenic trioxide intoxication significantly increased the serum level of Urea, Uric acid and Creatinine in comparison to control due to renal dysfunctioning.

Key words: Arsenic trioxide, Urea, Uric acid, Creatinine.

Corresponding author: ranchimanishakumari@gmail.com

INTRODUCTION

Arsenic toxicity is a global health problem affecting many millions of people. Contamination is caused by arsenic from natural geological sources leaching into aquifers, contaminating drinking water and may also from mining and other industrial processes.

The arsenic contamination was also observed in three districts Ballia, Varanasi and Gazipur of UP in the upper and middle Ganga plain, India (Ahamed *et al*., 2006). Approximately 20 incidents of groundwater arsenic contamination have been reported from all over the world (Mukherjee *et al*., 2006). Arsenic compounds show toxicity in many organs of body as kidney, liver, lung, gastro intestinal tract and respiratory tract (Vahter, 2007). Kidney shows many renal functions as excretion of nitrogenous waste products, acid-base balance and balance of electrolytes and water. Arsenic trioxide toxicity disturb these renal functions. A disruption in kidney function has immediate effects on the composition of circulating blood (Martini, 1989). However to evaluate the effect of arsenic on kidney functions, it becomes a must to determine theurea, uric acid and creatinine levels in serum (Saxena *et al*., 2006).

Absorption occurs predominantly from ingestion from the small intestine, though minimal absorption occurs from skin contact and inhalation. Arsenic exerts its toxicity by inactivating up to 200 enzymes, especially those involved in cellular energy pathways and DNA synthesis and repair. Acute arsenic poisoning is associated initially with nausea, vomiting, abdominal pain, and severe diarrhoea. Human health effects of Chronic Arsenic Toxicity (CAT) are designated by the term arsenicosis which was first coined by WHO to imply a chronic disease caused by prolonged exposure in humans to arsenic.

Arsenic poisoning in animals is caused by several different types of inorganic and organic arsenical compound. Toxicity varies with factors such as oxidation state of the arsenic, solubility, species of animal involved and duration of exposure.

Its origin and mobilization in the environment, its biochemistry and bioavailability should be well understood to monitor arsenic resources and

formulate the ways to cope with it. Arsenic is the extensively studied of the metals and metalloids found in drinking water. The association between skin cancer and arsenic ingestion in drinking water was seen studies in Taiwan, Chile, Argentina and Mexico. Inorganic Arsenic as well as its organic metabolites are extensively absorbed (approximately 80%) and excreted in the urine. Accumulation of As in tissues is slow and occurs mainly in liver, kidney and skin. Withdrawal of exposure led to a decrease in tissue contamination (Underwood and Suttle, 1999). Liver and kidney are the primary target organs for toxic effects of As as evidenced by clinical manifestation and biochemical alterations (Santra et al., 2000). ATSDR also reported that chronic poisoning of as includes anemia, liver and kidney damage, hyperpigmentation and keratosis. In view of this, an attempt has made to study the effect of arsenic trioxide on the renal parameters of rabbit at sub-lethal concentration.

MATERIALS AND METHODS

Mature and healthy Rabbits belonging to Order- Lagomorpha, Family- Leporidae were used to assess the effect of Arsenic toxicity. Rabbits weighing from 1.50-2.25 kgs 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 - 34.50C 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 As2O3 for the period of 15 days. Group II was exposed to 0.6mg/kg As2O3 for the period of 7 days intraperitoneally. Blood samples for renal parmeters 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 renal parameters by standard techniques.

RESULT AND DISCUSSION

The data was statistically analyzed both by T-test and ANOVA through which it was observed that the complete pictures (CP) of renal parameters were significantly disturbed in arsenic feed groups. Renal function was evaluated in terms of Serum creatinine, Serum urea and Serum Uric acid values in both two experimental groups. As evident from the table the subsequent increase in all the three parameters in both Group 1 and Group 2 have been found which is statistically significant treatments ($p<0.05$) (Table 1). As for Creatinine 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. Like the liver, the kidneys will accumulate arsenic in the presence of repeated exposures. The kidneys are the major route of arsenic excretion, as well as major site of conversion of pentavalent arsenic into more toxic and less soluble bivalent arsenic. Site of arsenic damage in the kidney includes capillaries, tubules, and glomeruli (Schoolmeester and White, 1980; Squibb and Fowler, 1983; Winship, 1984). In kidney ,arsenic exerts its toxic effects through several mechanisms, the most significant of which is the reversible combination with sulflydryl group of proteins present in glomerular filteration membrane (Yoon et al., 2008). It causes oxidative stress by producing reactive oxygen species (Flora et al., 2007; Vahter, 2007) which damage proteins. Due to lipopilic nature, arsenic also attaches to lipid, increases the lipid droplets in the slit pores of glomerular filteration membrane. Both the above reasons are responsible for decreased glomerular filteration rate (GFR), causing retention of nitrogenous waste products into the blood. The increased level of serum creatinine after arsenic trioxide intoxication is due to inhanced formation of metabolic waste product of muscle metabolism. Further, creatinine is anhydride of creatine. Muscle contains phosphocreatine which undergoes spontaneous cyclization with loss of inorganic phosphorous to form creatine. Conversion of creatine to creatinine is a non enzymatic

irreversible process. Due to affinity for thiol group of various proteins found in the cell membrane of muscles, arsenic damages the cells due to which the enzyme CPK (Creatinine phosphokinase) gets released from the cells which is responsible for the conversion of phosphocreatine into creatine. Thus increases the level of creatinine. For Urea 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. Urea is end product of protein metabolism, gets inceaed and serum level of urea increases (Aphosian, 1989). Anetor (2002) revealed that production of oxygen free radicals by arsenic induces tubular necrosis which in turn increases tubular permeability, resulting in diffusion and backleak of the filterate across the tubular basement membrane back into the interstitium and circulation, leading to an apperent decreases in GFR. Under these circumstances, backleak of filterate results in decreased excretion and increased retention of nitrogenous waste i.e urea in serum (Klassen, 1996; Verbeke *et al*., 1996). For Uric acid also the P-value of the F-test is less than 0.05, there is a statistically significant difference between the means of the 4 variables at the 95.0% confidence level. The serum uric acid concentration is determined largely by the efficiency of renal clearance and rate of purine metabolism (Anetor, 2002; Chandra Sekher *et al*., 2003; Dioka *et al*., 2004; Kalia and Flora, 2005). Uric acid is the final product of purine metabolism. Moreover, formed from guanine and hypoxanthine via xanthine in reactions catalyzed by guanase and xanthine oxidase of liver, small intestine and kidney. Arsenic intoxication changes the activity of guanase and xanthine oxidase which results into the increased serum level of uric acid.

Table -1. Renal parameters (all values are Mean+S EM)

	SHAM CONTROL	GROUP 1	GROUP 2
Serum creatinine (mg/dl)	1.3± 0.4 (0.8-1.8)	2.8±0.7	3.5± 1.01
Serum Urea (mg/dl)	5.4± 1.2 (4.2-6.8)	14 ±2.8	18 ± 5.3
Serum uric acid (mg/dl)	0.75 ±0.03 (0.6-0.9)	1.4 ± 0.76	2.18 ± 0.96

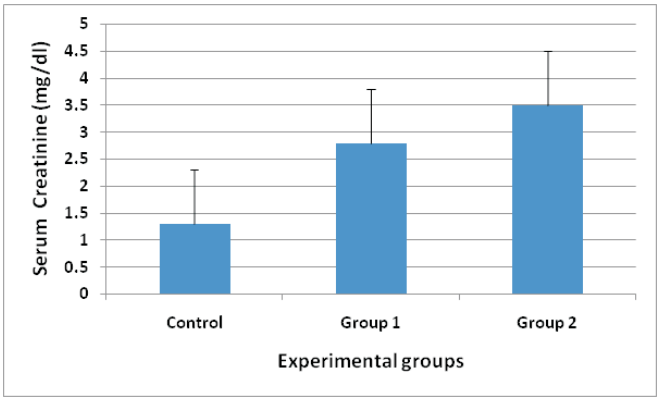

Fig. 1. Serum Creatinine of Rabbit of three different groups. Control, Group I and Group II. Bars are Mean±(n=5) from the respective control group.

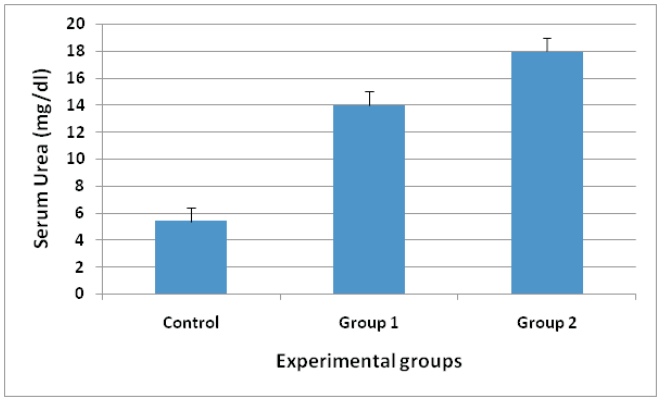

Fig. 2. Serum Urea of Rabbit of three different groups. Control, Group I and Group II. Bars are Mean±(n=5) from the respective control group.

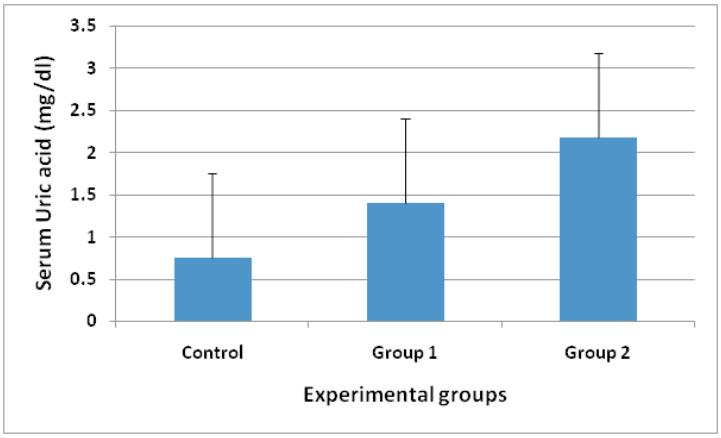

Fig. 3. Serum Uric acid of Rabbit of three different groups. Control, Group I and Group II. Bars are Mean±(n=5) from the respective control group.

In the present study there is a significant rise in serum creatinine, urea and uric acid level of arsenic treated rabbits as compared to control which is similar with the previous observation (Roger *et al.*, 2000; Islam *et al.*, 2009) where the significant increase in serum creatinine, urea and uric acid levels implies a relationship between the As level and the degree of chronic renal insufficiency.

REFERENCES

Ahamed, S., Sengupta, M.K., Mukherjee, M.A., Hossain, M.A., Das, B., Nayak,A., Mukherjee, S.C., Pati, S., Dutta, R.N., Chatterjee, A., Mukharjee, R. and Chakraborti, D. 2006. Arsenic groundwater contamination and its health effects in the state of Uttar Pradesh (UP) inupper and middle Ganga plain, India: A severe danger. Sci. Total Environ. 370: 310-322.

Anetor, J. I. 2002. Serum uric acid and standardized urinary protein : Reliable bio indicators of lead nephropathy in Nigerian lead workers. African J. Biomed. Res. 5: 19-24.

Aphosian, H.V. 1989. Biochemical toxicology of arsenic. Rev. Biochem. Toxicol.10: 265-299.

Chandra , S. K., Chary, N. S., Kamala, C. T., Rao, V. J., Balaram, V and Anjaneya, Y. 2003 Risk assessment and pathway study of arsenic in industrially contaminated sites of Hyderabad: A case study. Environ. Int. 29: 601-611.

Dioka, C. E., Orisakwe, O. E., Adeniyi, F. A., and Meludu, S. C. 2004. Liver and renal function tests in artisans occupationally exposed to lead in mechanism village in Nigeria. Int. J. Env Res. Pub. Hlth. 1: 21-25.

Farombi, E. O., Adelow, O. A. and Ajimoko, Y. R. 2007. Biomarkers of oxidative stress and heavy metal levels as indicators of environmental pollution in African cat fish (Clarias gariepinus) from Nigeria Ogun river. Int. J. Environ. Res. Pub. Hlth. 4: 158-165.

Flora, S. J .S., Bhadauria, S., Kanan, G. M and Singh, N. 2007. Arsenic induced oxidative stress and the role of antioxidant supplementation during chelation: A review. J. Environ. Biol. 28: 333-347.

Islam, M. Z, Awal, M. A., Mostofa, M., Ghosh, A. and Khair, A. 2009. Effect of Spinach against Arsenic Toxicity in Rats. Bangladesh Journal of Veterinary Medcine. 7(2): 358363.

Kalia, K and Flora, S. J. S. 2005. Strategies for safe and effective therapeutic measures for chronic arsenic and lead poisoning. J. Occup. Hlth. 47: 11-21.

Klassen, C. D. 1996. Heavy metals and heavy metal antagonists. In: Good manand Gilman's the pharmacological basis of therapeutics (Eds.: J.G.Hardman, A.G. Gilman and L.E. Limbird).

McGraw- Hill, New York. pp. 1649-1672.

Martini, F. 1989. Fundamentals of Anatomy and physiology. Prentice Hall, Englewood Cliff s, New Jersey. p . 944.

Mukherjee, A., Sengupta, M. K and Hossain, M. A. 2006. Arsenic contamination in groundwater: A global perspective with emphasis on the Asian Scenario. J. Hlth. Popul. Nutri. 24: 142-163.

Roger, D. M., Ayal-Fierro, F. and Carter, D. E. 2000. Systemic indicators of inorganic arsenic toxicity in four animal species. Journal of Toxicology and Environmental Health. 59(2): 119-134.

Santra, A., Maiti, A., Chowdhury, A. and Mazumder, D.

N. 2000. Oxidative stress in liver of mice exposed to arsenic contaminated water. Indian J Gastroenterol. 19: 112-115.

Saxena, P. N., Mahour, K. and Kumar, A. 2006. Protective effect of Panax ginseng extract on renal functions altered by mercuric chloride in albino rats. J. Ginseng Res. 30: 100-105

Schoolmeester, W. L., and White, D. R. 1980. Arsenic poisoning. South Med. J. 73: 198-208.

Squibb, K. S and Fowler, B. A. 1983. The toxicity of arsenic and its compounds. In B. A.Fowler (Ed.), Biological and Environmental Effects of Arsenic. Elsevier, New York. pp 233-269.

Underwood, E. and Suttle, N. 1999. The mineral nutrition of livestock. 3rd Ed. CABI Publ., Wallingford.

Vahter, M. E.2007. Interactions between arsenic induced toxicity and nutrition in early life. J. Nutr. 137: 2798-2804.

Verbeke, M., Van De Voorde, J. and Lameire, N. 1996. Prevention of experimental acute tubular necrosis; current clinical applications and perspectives. Adv. Nephrol. 25: 177-216 .

Winship, K. A. 1984. Toxicity of inorganic arsenic salts. Adv. Drug. React. Acute poisoning Rev. 3: 129-160.

Yoon, S., Han, S. S and Rana, S. V. S. 2008. Molecular markers of heavy metal toxicity– A new paradigm for health risk assessment. J. Environ.Biol. 29: 1-14. Santra, A., Maiti, A., Chowdhury, A. and Mazumder, D. N. 2000. Oxidative stress in liver of mice exposed to arsenic contaminated water. Indian J Gastroenterol. 19: 112-115.