ORIGINAL ARTICLE

Protective Role of Vitamin E on Sodium Arsenite Induced Histomorphological Changes of Liver in Albino Rat

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ABSTRACT

Background: Heavy metals and their chemical salts are source of great threat to human and animals alike.
Aim: To observe hepato-protection by vitamin-E on sodium arsenite induced histomorphological changes of liver on albino rats.
Study Design: Cross Sectional study.
Methodology: 90 adult albino male rats (30 in each group), weighing 140 to 180 grams were taken. They were housed in separate stainless steel cages and were kept under controlled temperature of 23+2 and humidity 50+5% in the experimental research lab of postgraduate medical institute Lahore. The night and day cycle was maintained for 12 hours each. Each animal of every group was labeled from 1-30 with different color for every group. Standard diet and tap water ad libitum was given to animals. Before starting the experiment animals were acclimatized for 10 days. Data analyzed by SPSS 22.0v.
Results: The initial and final body weights of animals in all the three study groups were shown in table-1 as mean ± SD. The relative tissue weight index (RTWI) of liver was measured and group wise comparisons were made for RTWI was found significant with p-value <0.001. The difference for diameter of hepatocyte among three groups was significant with p-value <.001.
Conclusion: This study concluded that there is clear evidence of improvement with vitamin E hence it can be safely stated that vitamin E provides hepatoprotection against arsenic induced hepatotoxicity.
Keywords: Vitamin-E, Hepato-protection, Relative Tissue Weight Index and Albino Rats.

INTRODUCTION

Heavy metals and their chemical salts are source of great threat to human and animals alike. Among heavy metals, arsenic contamination in ground water has become a geo-environmental problem because of its toxicological concern, which is affecting more than 100-million people across the globe.[1]

Drinking water and agricultural products are amongst the main source of intoxication for general population.[2] Seafood is also an important source of arsenic.[3] Its use in many industrial processes is widespread as in purifying industrial gases, electronics manufacturing products, hardening metal alloys, bronze plating, and clarifying glass and ceramics. It becomes a part of air during processes like burning fossil fuels, burning wood treated with arsenic preservatives. The use of arsenic for medicinal purpose cannot be ignored being used in Fowler's solution (potassium arsenite), antiparasitic drugs (carbasone), Donovan's solution, folk remedies ("Asiatic pill," kushtay, yellow root), and some naturopathic remedies.[4]

Arsenic exists in water as oxyacids in two oxidation states, trivalent (Arsenite - As^{+3}), and pentavalent form (Arsenate - As^{+5}), the former is more toxic.[5] World Health Organization (WHO) has established a level of 10 micrograms/litre (µg/L) as safety limit and a maximum limit of 50 µg/L in drinking water[6] but many areas of Pakistan have exceeded this limits especially Eastern Punjab. According to a survey conducted by Swiss Federal Institute of Aquatic Science and Technology concentrations of arsenic is extremely high in ground water that is 200 along Indus river valley, the major source of water to Pakistan. 50 to 60 million people are using water that contains more than 50µg/L of arsenic, the values being five times more than WHO's safety limit.[7]

Oxidative stress is the main mechanisms of its toxicity. Oxidative stress is defined as the imbalance between the generation of reactive oxygen species (ROS) and antioxidant defense, and leads to the damage of DNA which causes disturbances in cellular biology[8]. In humans generally liver is the primary site for metabolism of arsenic. Ingested inorganic arsenic is mostly absorbed in the gastrointestinal tract. On absorption, majorly arsenic is stored in liver, kidney, heart, and lungs.[9] In humans acute arsenic poisoning is associated with nausea, vomiting, abdominal pain, and severe diarrhea.[10]

With this background, it is important to find a suitable therapeutic agent to control the effects of arsenic poisoning. An agent with high content of powerful antioxidants could prove beneficial in chelating arsenic, as antioxidants facilitate in the methylation and excretion of heavy metals.[11] In an effort to explore the possibility of existence of such an agent which is easily available in its natural form with antioxidant properties could be a possible answer.

Vitamin E is widely accepted as one of the most potent antioxidants in nature. Vitamin E is a collective term to a group of lipophilic compounds that have antioxidant activities essential for health.[12] It is discovered as a dietary

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factor essential for normal reproduction, is now accepted as a major free radical scavenging antioxidant in humans and protects biological molecules from detrimental oxidative modifications.[13]

The objective of the study was to observe hepato-protection by vitamin-E on sodium arsenite induced histo-morphological changes of liver on albino rats.

METHODOLOGY

Ninety adult albino male rats (30 in each group), weighing 140 to 180 grams were taken. They were housed in separate stainless steel cages and were kept under controlled temperature of 23+2 and humidity 50+5% in the experimental research lab of postgraduate medical institute Lahore. The night and day cycle was maintained for 12 hours each. The cages were labeled according to the group and number of animals. Each animal of every group was labeled from 1-30 with different color for every group. Standard diet and tap water ad libitum was given to animals. Before starting the experiment animals were acclimatized for 10 days.

Grouping of animals: The animals were divided into 3 groups. They were designated as:

Group A: Control group: were given only distilled water according to weight of the animal by oral gavage method for 30 days.

Group B: Arsenic group: were given sodium arsenite 0.5 mg/100gm/day dissolved in distilled water by oral gavage method for 30 days.

Group C: Arsenic +Vitamin E**:** Sodium arsenite was given as 0.5 mg/100gm/day and Vitamin E were given to each animal as 5 mg/100gm/day by oral gavage method for 30 days.

Statistical analysis: Data analyzed by SPSS 22.0v. For initial and final weight of rat, relative tissue weight index and diameter of hepatocytes mean +/- SD were described along with one way ANOVA. Tukey's test was used for post hoc analysis. P-value ≤ 0.001 was taken as statistically significant.

RESULTS

The initial and final body weights of animals in all the three study groups were shown in table-1 as mean ± SD.

The group wise comparison for final body weight at the end of experiment was found significantly different for groups with p-value <0.001 as shown in table-2.

Liver weight and relative tissue weight index of animals in all the three study groups were shown in table-3 as mean ± SD.

The relative tissue weight index (RTWI) of liver was measured and group wise comparisons were made for RTWI was found significant for groups with p-value <0.001 as shown in table-4.

Analysis for microscopic observations like diameter of hepatocytes was done as mean ± SD in table-5.

The difference for diameter of hepatocyte among three groups was significant with p-value <0.001 as shown in table-6.

Table-1: The initial and final body weight of animals in three study groups

Groups	Initial Weight			Final Weight		
	N	Mean	SD	N	Mean	SD
Group A (Control group)	30	153.03	8.01	30	201.43	9.90
Group B (Arsenic group)	30	154.60	8.27	30	179.57	8.50
Group C (Arsenic+ Vit E)	30	155.47	11.82	30	199.17	14.09

Table-2: Group wise comparison for Final body weight among three groups

(I) group	(J) group	Mean Diff. (I-J)	Std. Error	Sig.	95% CI	
					LL	UP
Group A	Group B	21.87*	2.86	<0.001*	15.04	28.69
Group A	Group C	2.27	2.86	0.709	-4.56	9.09
Group B	Group C	-19.60	2.86	<0.001*	-26.43	-12.77

*Statistically Significant

Table-3: The Liver Weight and Relative Tissue weight index and Weight of animals

	Liver Weight			RTWI Weight		
	N	Mean	SD	N	Mean	SD
Group A (Control group)	30	7.45	0.48	30	3.70	0.11
Group B (Arsenic group)	30	7.47	0.58	30	4.16	0.18
Group C (Arsenic+ Vit E)	30	7.41	0.67	30	3.72	0.14

Table-4: Group wise comparison for RTWI among three groups

(I) group	(J) group	Mean Diff. (I-J)	Std. Error	Sig.	95% CI	
					LL	UL
Group A	Group B	-.459*	.037	<0.001*	-.5491	-.3696
Group A	Group C	-.017	.037	.896	-.1065	.0729
Group B	Group C	.442*	.037	<0.001*	.3529	.5323

*Statistically Significant

Table 5: The Diameter of hepatocytes (µm) of animals in three study groups

	Diameter of hepatocyte (µm)		
	N	Mean	SD
Group A (Control group)	30	13.74	1.39
Group B (Arsenic group)	30	23.19	1.62
Group C (Arsenic+ Vit E)	30	15.55	2.12

Table 6: Comparison for diameter of hepatocytes among 3 groups

	Sum of Squares		Mean Square		Sig.
Between groups	1508.720	2	754.360	249.535	<0.001*
Within groups	263.006	87	3.023		
Total	1771.726	89			

*Statistically Significant

DISCUSSION

This study was conducted to explore the protective role of Vitamin E against the toxic effects of sodium arsenite on liver of albino rat. One of the parameters of the present study was the weight of the animals. Weight gain may be taken as an indicator of general wellbeing of animal. In the present study, there was weight gain in all animals but the final weight at the end of experiment was found significantly different among three groups. There was more increase in weight of animals of group A (control) and C (Arsenic + vitamin E) as compared to group B (Arsenic only). Although there was weight gain in animals of arsenic treated group as well, but the extent of weight gain was less in comparison to control.

This finding was comparable to the study of Sayed S et al. who studied on mice to find the Protective effects of phyllanthus emblica leaf extract (PLE) on sodium arsenite-mediated adverse effects in the duration of 4 weeks. In that study sodium arsenite treated group animals gained less weight as compared to other groups (control and PLE treated group).[14] This study supports the fact that animals treated with sodium arsenite gained less weight. Contrary to that in 2016 B.B Baltaci reported in his 15 days experiment that there is no difference between control group and arsenic group in body weight gain[15] this difference in results could be due to difference in duration of experiment.

In the present study, difference in diameter of hepatocytes was statistically significant among three groups. Due to fat accumulates within hepatocytes, there is increase in their size. This change was well documented in our results. Similar results have been seen in various other experiments.[16] There is a clear cut evidence in result of present study that Vitamin E prevented ballooning of hepatocytes. In 2018 a study was published by Hegazy et al. on hepatotoxicity of zinc oxide nanoparticles and protective role of vitamin E on it and similar results were found.[17]

Limitations: Present study had number of limitations like small sample size, financial contrains and limited resources. This study just observed hepato-protective effect of vitamin-E only.

CONCLUSION

This study concluded that there is clear evidence of improvement with vitamin E, it can be safely stated that vitamin E provides hepatoprotection against arsenic induced hepatotoxicity. Therefore use of vitamin E to counter hepatotoxic effects of arsenic can be considered by health providers. However further studies are required for determination of appropriate dose for said purpose.

Author's contribution: AI: Overall supervision, write up and literature review. MT: Statistics application analysis literature review, help in write up. ST, RTK & TL: Literature review help in write-up.

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