SIGNIFICANT LIVER TOXICITY IN ALBINO RATS UPON ORAL ALUMINIUM ADMINISTRATION: A SERIOUS PUBLIC HEALTH IMPLICATION

Deepa Rani Agarwal, Shilpi Jain*

SMIMER, Near Sahara Darwaja, Surat, Gujarat
*Deptt. of Anatomy, Subharti Medical College, Meerut

ABSTRACT

Aluminium is widely used in medicines, as food additives, as water purification agent, as in the making of household cookware and storage utencils. Aluminium absorption depends on the chemical form of aluminium taken up. Aluminium hydroxide and chlorides are absorbed more efficiently than its phosphorus and fluorine compounds. As aluminium is stored mainly in the liver,[1] the present work is conducted to study the morphological and morphometric changes in the liver produced by aluminium chloride($AlCl^3$). 20 inbred adult albino rats weighing 150-200gm each were administered 37.5mg per day of aluminium chloride orally for 21 days with maintenance of 20 similar controls.A small piece of liver tissue was processed for paraffin sections. 7 μ thick sections were stained with hematoxylin and eosin stain and observed under light microscope. The changes were observed at tissue and cellular level along with general architectural derangement, degenerative changes and nuclear variations such as karryorrhexis, pyknosis. These findings are highly conclusive of toxic hepatitis.

Key words: Aluminium,Liver, Hepatocellular degeneration, Nuclear variations, Toxic hepatitis

INTRODUCTION

Aluminium is among the most plentiful element in the earths crust. In certain subtropical plants it may accumulate in high concentration. Most individuals consume 1-10 mg aluminium per day from natural sources[2]. According to WHO, provisional tolerable weekly intake of aluminium (PTWI) is 7 mg per kg body weight for adults[3].

The uses of metallic aluminium and its compounds are very extensive. Aluminium metal is an important structural material in the building, canning, automobile, aviation industries, paints, cracking of petroleum as lubricants, tanning agents, in wood preservation and in manufacture of synthetic rubber and paper. Higher levels of aluminium usually occur in freshwater and drinking waters treated with aluminium sulphate against turbidity[4]. UV rays may liberate the aluminium in waters toxic to aquatic organisms[5]. First case of encephalopathy was associated with high quantities of aluminium in brain cells[6].This encephalopathy was found in patients on chronic dialysis or in heavily exposed workers eg: welders. Besides brain, aluminium in high doses was also shown to damage the kidney, bones, heart and lungs.

Despite its toxic effects, aluminium remains a metal of choice in the making of various kinds of household cookware and storage utensils[7]. The usage of aluminium in packaging of food stuff is on the increase and is becoming a potential source of contamination. 10-15% production of aluminium compounds are utilized in processing, packaging and preservation of food such as aluminium foils[8]. As the aluminium vessels are the most commonly used cookware in rural and semiurban India, the major contribution of aluminium from Indian foods are through the dietary sources. A plethora of literature is available regarding the adverse effects of aluminium on liver of albino rats through parenteral route in comparision to oral route. Laske et at[9]; have reported lysosomal damage, hepatopathy, periportal inflammation, cholestasis in liver after parenteral administration of aluminium.

The aim of this study is to assess morphological and morphometric changes in the liver tissue after intragastric exposure to aluminium in albino rats: .

MATERIAL AND METHODS

40 inbred adult albino rats weighing 150-200 gm each were randomly divided into 2 groups. Group 1 served as the experimental and Group 2 as the control. The animals were group housed with ad libitum access to food and water.Group 1 rats received 37.5 mg per day

Correspondence
Dr. Deepa Rani Agarwal
SMIMER, Near Sahara Darwaja,
Surat, Gujrat
Ph. : 919427657229, 912616599015
Email : deepaagarwal99@yahoo.in

Comparision of mean diameter of the hepatocytes in the Experimental and Control Group				
Diameter	**Group**	**Mean(micron)**	**SD(micron)**	**significance**
Long Diameter	**Experimental**	**27.01**	**4.23**	**Both the diameters of the experimental group were significantly increased as compared to the control group.**
	Control	**21.01**	**3.11**	
Short Diameter	**Experimental**	**18.91**	**2.91**	
	Control	**11.13**	**2.39**	

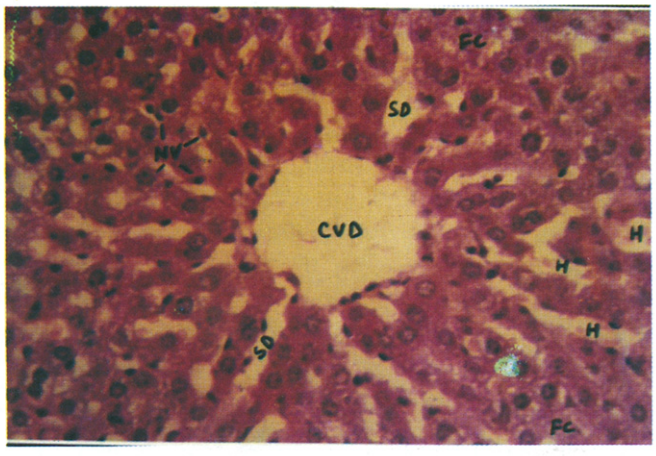

Fig 1 : Dialated Central vein and sinusoids having blood and Hepatocytic plated appeared disheveled H&E; X 400

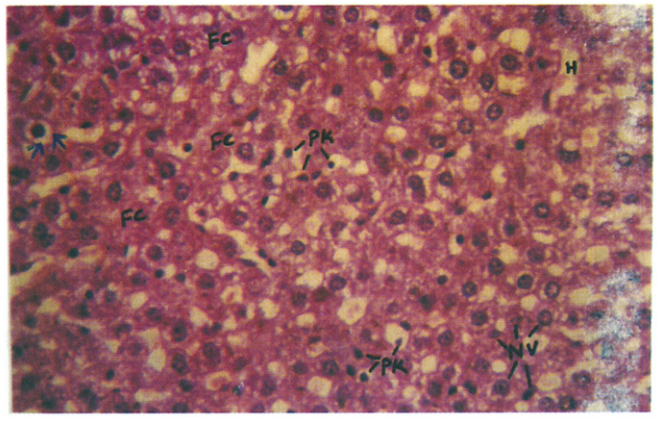

Fig 3 : Showing dark and highly eosinophillic cytoplasm and a pyknotic nucleus, surrounded with a clear halo (marked by arrow) H&E; X 400

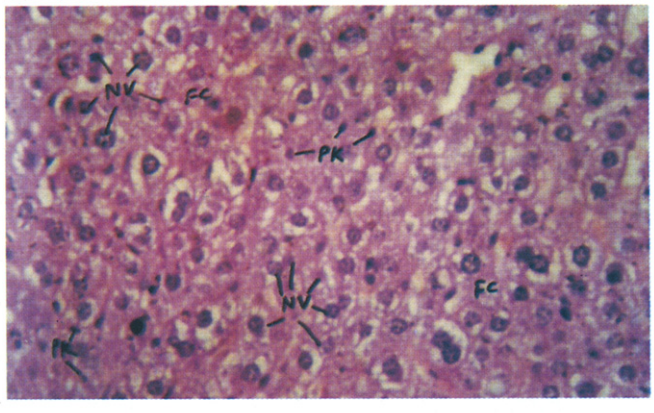

Fig 2 : Showing increased cytoplasmic basophillia and a large euchromatic nucleus having a prominent nucleolus H&E; X 400

of aluminium chloride through intragastric route for 21 days. The control group received equal quantity of the vehicle by the same route. The animals were sacrificed with in 24 hr. of the last dose. The liver was dissected and processed. Sections 7 μ were cut and stained with haematoxylin and eosin stain.

OBSERVATIONS

Microscopically, the constant finding was fatty changes. Affected areas showed large blood filled spaces which replaced the normal liver parenchyma and the haemorrhagic blood was seen in the central vein and the neighbouring sinusoids, which had become dilated. The hepatocytic plates appeared disheveled (Fig 1). The hepatocytes varied greatly in size. In most areas they appeared hypertrophied with increased cytoplasmic basophilia and a large euchromatic nucleus having a prominent nucleolus (Fig 2). The mean long and short diameters of these hepatocytes was 27.01 ± 4.23 μ and 18.91± 3.11 μ respectively in the experimental group and

21.01± 2.91 μ and 11.13± 2.39 μ respectively in the control group. Thus we obtained a significant increase in the mean diameter in experimental group as compare to control group (Table-1).

There were foci of hepatocellular degeneration. Degenerating hepatocytes appeared shrunken with dark and highly eosinophilic cytoplasm and a pyknotic nucleus, surrounded with a clear halo (Fig 3).

DISCUSSION:

Ebina et al[10] reported that even a low dose of aluminium is toxic to parenchymal cells of liver, kidney and brain when given in a chelated form with Nitrilotriacetic acid (NTA). It showed extensive midzonal coagulation, hepatocytic necrosis, inflammatory cells infilteration, degenerating hepatocytes . Ellis et al.[11] injected aluminium chloride intraperitoneally to rats, and noticed osteomalacia in bones. There are a relatively small number of data related to aluminium toxicity on the liver functionally and morphologically. According to Galle et al.[12], aluminium does not produce toxic effects in the liver because it is eliminated from hapatocytes into the bile together with lysosomes. On the other hand, Abubakar et al.[13], ascertained that aluminium in hepatocytes, even in small quantities is associated with an increase in reactive oxygen species and peroxidation. According to Somova et al.[14] liver showed high affinity for aluminium when injected intravenously. Galle and Guidicelli[15] reported ultrastructural localization of aluminium in hepatocytes. Constant finding in our experimental study is fatty changes. This can be explained on the basis that aluminium propogates the reaction between cytochrome C and succinyl dehydrogenase[16]. Since cytochrome C is an important enzyme in respiration at cellular level, interference with metabolic pathways involving this enzyme may lead to biochemical and histological changes.

Berlyne et al.[17] in an experimental study found that oxygen consumption in liver cells decreased by 25% in aluminium treated rats leading to hypoxia, which in turn leads to necrosis and fatty changes.

In the present study, aluminium was seen to cause an increase in diameter of the hepatocytes associated with large euchromatic nucleus and a cytoplasmic basophilia, indicative of an increase in cellular activity.

CONCLUSION

This study reveals that even oral administration of aluminium results in the disheveled pattern of the hepatocytes, increased cellular metabolism, inflammatory cells infiltration, nuclear variations such as pyknosis, karryorrhexis. These findings are conclusive of toxic hepatitis and point to the need of creating awareness among the population of the hazards associated with the extensive use of aluminium . It would be prudent to conduct further research in this area given its wide usage and subsequent publice health implications.

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