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Liver morphology changes in rats after high dose aluminium administration

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ABSTRACT

Background: Aluminum may get access to the human body through several different routes, including the gastrointestinal and the respiratory tracts. Furthermore, various medical interventions including aluminum-containing drugs such as antacids, phosphate binders, buffered aspirins; along with dialysis, vaccines, antiperspirants and injectable allergens also factor in the total human body consumption of aluminum. We investigated the effects of high dose aluminum administration in rats to examine the changes in hepatic and biliary morphology.

Materials & Methods: 50 rats of both genders were divided into 2 groups of 25 each. Group I received 0.5 mL of sterile physiological suspension of fine aluminum powder in the concentration of 100 mg mL^{-1} intraperitoneally (50 mg aluminum per rat). Group II did not receive anything. Liver aluminum was analysed using electrothermal atomic absorption spectrometry. For light microscopy the liver tissue was stained with haematoxylin and eosin, and for histochemical analysis with the triammonium salt of aurintricarboxylic acid (aluminon).

Results: The mean aluminum level in group I was 36.2 µg $g^{-1}$and in group II was 0.95 µg g^{-1} . The difference was significant ($P< 0.05$).Slight multiplied bile ductuli was seen in 15 rats in group I and 4 in group II. The difference was significant ($P< 0.05$).

Conclusion: The present investigation showed that aluminium injected intraperitoneally accumulates in the liver of experimental rats. In conclusion, aluminium administration appears to increase oxidant stress in the liver, as evidenced by mild proliferation seen in the biliary ductuli. These effects of aluminium toxicity may be directly related to the free radical generation.

Key words: Aluminum, liver, morphology, rat

Introduction

During recent years, the research surrounding the toxic effects of aluminum toxicity has considerably advanced and an increasing number of aluminum toxicity effects have been established. Exposure to aluminum is very common during daily life due to the fact that it is widely distributed in the environment, and extensively used in daily life. Major sources of aluminum exposure include, but are not limited to foods especially corn, yellow cheese, grain products (flour), salt and spices, vegetables and tea leaves, cosmetics, cookware and containers.[1] Also, it could be found in the drinking water, where it is usually added for purification purposes. Environmental pollution, especially wastewater, exposes people to a higher risk of aluminum toxicity. Aluminum can find its way into the human body via various routes, including the gastrointestinal and the respiratory tracts. Furthermore, various medical interventions including aluminum-containing drugs such as antacids, phosphate binders, buffered aspirins; along with dialysis, vaccines, antiperspirants and injectable allergens also factor in the total human body consumption of aluminum.[2, 3]

Aluminum-contaminated dialysis fluids and aluminum-containing phosphate-binding drugs are recognized to play a major role in hyperaluminemia.[4-9] Cessation of aluminum-contaminated water in the dialysis process along with selected prescription of aluminum-free phosphate binders have however, significantly reduced the prevalence of aluminum toxicity-related diseases. Aluminum has also been strongly implicated in the etiopathogenesis of various progressive and potentially fatal neurodegenerative disorders, such as Alzheimer's disease, amyotrophic lateral sclerosis and Parkinson's dementias along with osteomalacia and osteodystrophic lesions.[10-13] Despite the fact that aluminum build-up has been well-documented in macrophages and lysosomes, hepatotoxic effects of aluminum have so far been considered less significant. These findings compelled us to research the possible hepatotxic effects of aluminum. Furthermore, several recent studies have revealed occurrences of acute and, in some cases, fatal aluminum intoxication that draw attention to the fact that aluminum toxicity needs to be considered as a grave threat. [14,15] The toxic effects of aluminum appear to be mediated through free-radical generation. It may enhance Fe^{2+}-dependent membrane lipid peroxidation, thereby

possibly leading to increased lysosomal fragility.[16] Increased lipid peroxidation and thiobarbituric acid reactive substance (TBARS) levels along with reduced catalase activity has been noted following aluminum treatment. High serum superoxide dismutase and low serum catalase levels have also been reported following acute poisoning with aluminum phosphide.[17] We investigated the effects of high dose aluminum administration in rats to examine the specific changes in hepatic and biliary morphology.

Materials & Methods

The present study comprised of 50 rats of both genders. Ethical approval was obtained before commencing the study.

The rats were divided into 2 groups of 25 each. Group I received 0.5 mL of sterile physiological suspension of fine aluminum powder in the concentration of 100 mg mL-1 intraperitoneally (50 mg aluminum per rat). Group II (control) did not receive anything. After 7 weeks all animals were killed. In both groups rat's liver was dissected and one part used to determine aluminum mass fraction per gram of wet liver tissue and the other part was used for histological analysis. Liver aluminum was analysed using electrothermal atomic absorption spectrometry. For light microscopy the liver tissue was stained with haematoxylin and eosin, and for histochemical analysis with the triammonium salt of aurintricarboxylic acid (aluminon). Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

Results

Table I Distribution of rats

Groups	**Group I**	**Group II**
Method	50 mg Al	Control
Number	25	25

Table I shows that group I received 50 mg aluminum and group II was the control group.

Table II Assessment of aluminum level in both groups

Groups	**Mean (µg g^{-1})**	**P value**
Group I	36.2	0.01
Group II	0.95	

Table II, graph I shows that mean aluminum level in group I was 36.2 µg $g^{-1}$and in group II was 0.95 µg g^{-1}.The difference was significant (P< 0.05).

Graph I - Assessment of aluminum level in both groups

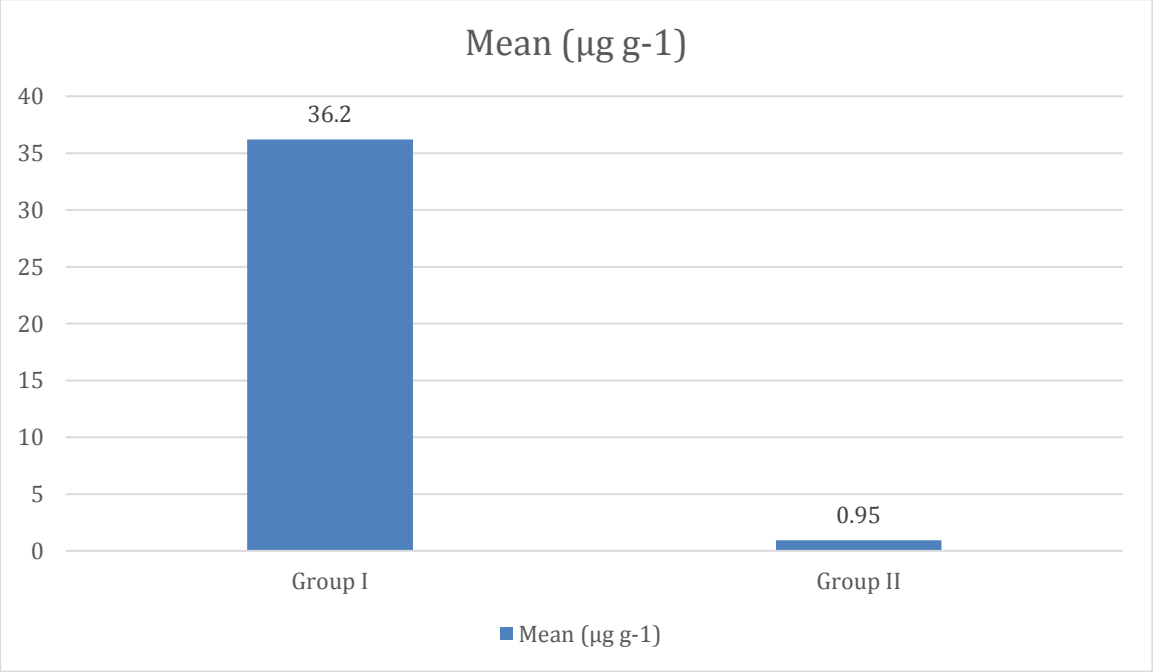

Table III Morphological changes

Groups	Group I	Group II	P value
Multiplied bile ductuli	15	5	0.01

Table III shows that slight multiplied bile ductuli was seen in 15 rats in group I and 4 in group II. The difference was significant (P< 0.05).

Discussion

Aluminum is widely present in the environment today, both in natural products as well as in man-made. Hence, the total daily consumption of aluminum in humans differs in such a way that it makes it tedious to be assessed. It has been definitively demonstrated that aluminum consumption, such as with antacids or compounds that bind phosphate, may lead to aluminum absorption and potential aluminum accumulation and toxicity. [18] Higher doses of aluminum could increase the risk of renal aluminum retention and hence, induced nephrotoxicity. It has also been reported that aluminum can cause degeneration of the renal tubular cells through generation of reactive oxygen species (ROS) which cause oxidative damage to cellular lipids, proteins, and DNAs.[19, 20]Aluminum intoxication lowers the intracellular levels of reduced glutathione. Also, aluminum salts may inhibit enzymes like acid and alkaline phosphatases and phosphodiesterase.[21, 22] In addition, it has also been reported that calcium homeostasis could be compromised by aluminum toxicity, as evidenced by positive correlation between higher concentration of aluminum found in the degenerated areas of the central nervous system in systemic degenerative diseases like amyotrophic lateral sclerosis.[23] The present study was conducted to assess changes in rat liver after a single high dose of aluminum.

We found that mean aluminum level in group I was 36.2 µg g^{-1} and in group II was 0.95 µg g^{-1}. Vandervoet et al[24] studied the storage of aluminum in the liver as a whole and in subcellular liver fractions, and its association with soluble cytosolic molecular species. Experimental rats were loaded with aluminum prior to liver fractionation by ultracentrifugation, and equilibrium gel filtration chromatography of the cytosol for aluminum speciation in serum. Aluminum was found to have been accumulated in a dose-dependent manner in liver and subcellular liver fractions, the lowest levels occurring in the cytosol. A dose-dependent elevation of aluminum in the blood was also observed. Gelfiltration of the cytosol indicated that aluminum was associated with a low molecular weight form which was not a citrate complex, and a high molecular weight form, which was larger than transferrin. No induction of and association with metallothionein occurred.

The results of our study showed that intraperitoneal aluminum administration in rats gave rise to adverse effects, which were dose dependent. We found that slightly multiplied bile ductuli was seen in 15 rats in group I and 4 in group II. Xie et al[25] have shown that aluminum is hepato and neurotoxic and that this may be due to a pro-oxidant effect. However, it is unclear as to what extent aluminum can participate in redox reactions in the absence of Fe^{3+}.

Aluminum appears to accumulate in the liver rapidly after an acute load in both animal models and clinically, whether given intravenously, or orally.[26] Aluminum accumulation within the liver is associated with a number of biochemical changes; these include the release of enzyme markers of liver injury, and alterations in oxidant status.[27] It has been reported previously that some of these changes are abrogated by concomitant treatment with dietary vitamin E. According to Galle et al[28], aluminum does not produce toxic effects in the liver because it is eliminated from hepatocytes into the bile together with lysosomes.

The limitation of this study is a relatively small sample size.

Conclusion

The present investigation showed that aluminium injected intraperitoneally accumulates in the liver of experimental rats. In conclusion, aluminium administration appears to increase oxidant stress in the liver, as evidenced by mild proliferation seen in the biliary ductuli. These effects of aluminium toxicity may be directly related to the free radical generation.

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