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Research Article

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Further Investigations into the Biochemical Effects of Aluminum on Protein Levels in Serum, Liver and Brain Homogenates of Wistar Albino Rats

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ABSTRACT

The protein levels in serum, liver and brain digests in aluminum intoxicated male wistar rats were investigated. Twenty-four male wistar rats weighing between 150- 205g were used. The rats were divided into four separate groups and were treated as follows: while group A received 0.2 ml normal saline groups B-D received 0.38 mg/kg, 3.8 mg/kg and 38 mg/kg body weight aluminum as aluminum chloride (AlCl3) respectively. Normal saline served as vehicle for the administration of the toxicant. The results of this study show that the aluminum-treated groups had significant reduction ($p<0.05$) in protein levels as compared to the control. The reduction in serum, liver and brain protein levels observed were dose and duration dependent suggesting that aluminum administration to rats probably interfered with protein synthesis.

Keywords: Aluminum; Liver; Brain and serum; Toxicity

INTRODUCTION

Aluminum, (Al) is ubiquitous being the third most prevalent element and the most abundant metal in the earth's surface mainly in the combined form- silicates, oxides, and hydroxides, and is considered to have no definite biological role [1].

Aluminum finds use in a variety of application such as in food industries (as a packaging foil, drying agents as well as additives and colorants), pharmaceutical industries (as anti-diarrheal and anti-cholinesterase agents) and engineering works, as in roofing of buildings and construction of vehicle parts. From the environment, it gets access to the human body via the gastrointestinal and the respiratory tracts. AL is a constituent of cooking utensils and medicines such as antacids, deodorants and food additives [2] and this has allowed its easy access into the body. All these uses of Al is probably because Al is light-weight and cheap, combines easily with other elements and corrosion free [3].

However, Al is an element with known toxicity in the human body, mainly in the central nervous system [4]. The toxic consequence in humans after Al exposure are now established [5,6]. Al is known as a neurotoxin that can cause diseases such as Alzheimer's, dementia, Parkinsonism, and amylotropic lateral sclerosis [7-9]. The role of Al in these disorders is not clear. Al is absorbed into the body cells through

receptor-mediated endocytosis by transferrin receptor similar to iron absorption [10]. The target tissues for Al burden include bone, liver, Kidney and brain [11].

Exposure to xenobiotics produces adverse effects which could take place through various mechanisms leading to toxicity and significant changes in the levels of biomolecules such as proteins, carbohydrates and lipids. Hence, there is need for further investigation into the biochemical effects of Al intoxication on the protein levels of some tissues such as serum, liver and brain, and this is the essence of the study. The objective of the study is to evaluate the protein concentration of some selected tissues: serum, liver and brain in male wistar albino rats following Al intoxication.

MATERIALS AND METHODS

Materials

Twenty-four (24) male wistar albino rats aged between 8-10 weeks with body weight range of 150-205 g were purchased from the animal house of the Faculty of Veterinary Medicine, University of Nigeria, Nsukka. The toxicant administered daily to the experimental animals was aluminum as in aluminum chloride ($AlCl_3$) at varying doses: 0.38, 3.8 and 38 mg/kg body weight while the control animals received the vehicle (normal saline, 0.2 ml). All chemicals used were of the analytical grade.

Methods

Four separate metabolic cages containing six animals each were used. The animals were differentially marked and acclimatized for five days. The groups were labeled i-iv while group i is the control administered 0.2 ml normal saline, groups' ii, iii and iv were given 0.38, 3.8 and 38 mg/kg body weight aluminum as aluminum chloride ($AlCl_3$). The route of administration was per oral (p/o). All animals were fed with commercial feed (grower's mash) and water *ad libitum* for 2 weeks. Each experiment was in triplicate and results were pooled. Blood was collected from each group after 7 and 14 days through the median cantus vein in the eyes of the rats with the aid of capillary tubes and transferred into plastic tubes. This was later centrifuged at 2000 xg and serum collected into separate test tubes. The sera were used for analysis. The rats were weighed on days 3, 7, 10 and 14 to observe weight gain/ lost during the treatment period.

Total protein in serum, liver and brain were obtained with a Folin-Ciocalteau reagent according to the method of Lowry et al. and bovine serum albumen (BSA) was used as standard protein. The absorbance was measured at 750 nm against the blank using the SP 500 spectrophotometer. The protein concentration in (mg/ml) of the sample were read off from the standard curve.

Statistical Analysis

Significant differences were assessed by one-way analysis of variance (ANOVA) while differences between treatment animals were calculated using student's independent t-test. The acceptance level of significance was ($P<0.05$) using a two-tail distribution.

RESULTS AND DISCUSSION

Mean Body Weight Gain/ Loss of Rats

The results from this study Table 1, show no significant difference ($p>0.05$) between the body weight gain of control and all the test animals given 0.38, 3.8 and 38 mg per kilogram body weight of $AlCl_3$, while the aluminum- treated group given 38 mg/kg body weight of $AlCl_3$ had the least body weight gain, which was significantly lower ($p<0.05$) than that of 3.8 mg/kg group after three days of exposure.

Table 1: Mean body weight of control and test animals after aluminum administration

Groups / Days	3rd	7th	10th	14th
Control	18.23 ± 5.85	35.72 ± 4.22	44.60 ± 6.07	41.43 ± 8.6
0.38mg	17-67 ± 5.72	34.80 ± 6.40	42.90 ± 8.06	35.30 ± 9.0
3.8mg	20.08± 4.40	18.33 ± 2.56*	16.77 ± 2.40*	15.53 ± 2.97*
38mg	16.40 ± 1.30	12.08 ± 1.92*	9.80 ± 3.50*	9.53 ± 3.01*

There was no significant difference (P>0.05) observed in the mean body weight of control and that of the aluminum-treated group given 0.38 mg/kg $AlCl_3$, while body weight of test groups (3.8 and 38 mg/kg) were significantly lower (p<0.05) than that of the control animals after the seven days of exposure. The mean body weight of test groups given 3.8 and 38 mg/kg $AlCl_3$ decreased significantly (P<0.05) compared to the control group after the tenth and fourteenth days of aluminum exposure. The aluminum-treated group given 0.38 mg/kg $AlCl_3$ had the highest mean body weight among the other aluminum-treated groups after 7, 10 and 14 days which was non-significantly lower (p>0.05) than the control group.

Mean body weight in all the aluminum-treated groups (0.38, 3.8 and 38 mg per kilogram body weight) were significantly lower (P<0.05) at seven, ten, and fourteen days of exposure as compared to that of three days of exposure, while no marked difference was observed in the mean body weight of test animals given 0.38 mg per kilogram body weight of $AlCl_3$ throughout the days of exposure when compared with that of control.

Table 2: Total serum, liver and brain protein concentrations (mg/ml)

7 days			
Tissues / Groups	**Total serum protein (mg/ml)**	**Total liver protein (mg/ml)**	**Total brain protein (mg/ml)**
Control	0.96 ± 0.03	1.59 ± 0.21	0.92 ± 0.09
0.38 mg/kg	0.95 ± 0.05	0.50 ± 0.35	0.90 ± 0.20
3.8 mg/kg	0.92 ± 0.04	1.47 ± 0.15	0.76 ± 0.10*
38 mg/kg	0.86 ± 0.05*	1.30 ± 0.13*	0.71 ± 0.04*
14 days			
Tissues / Groups	**Total serum protein (mg/ml)**	**Total liver protein (mg/ml)**	**Total brain protein (mg/ml)**
Control	0.92 ± 0.01	1.63 ± 0.16	1.20 ±0.10
0.38 mg/kg	0.89 ± 0.02*	1.60 ± 0.18	1.02 ± 0.07*
3.8 mg/kg	0.29 ± 0.04*	1.50 ± 0.29	0.98 ± 0.01*
38 mg/kg	0.59 ± 0.05*	1.40 ± 0.10*	0.86 ± 0.02*

Results in Table 2, show significant decrease (p<0.05) in serum and liver protein concentrations of the aluminum-treated group (38 mg/kg) after seven days relative to the control group. However, the brain homogenate showed a significant decrease (p<0.05) in the test groups given 3.8 mg/kg and 38 mg/kg $AlCl_3$ after seven days relative to the control. After fourteen days, the liver protein concentration decreased significantly (p<0.05) in the aluminum-treated group (38mg/kg) while serum and brain protein concentrations decreased significantly (p<0.05) in all the test groups when compared with the control group.

Serum and brain protein homogenates decreased significantly (p<0.05) in the test animals given 3.8 mg/kg and 38mg/kg body weight after fourteen days compared to seven days. Liver protein decreased in all the test animals after fourteen days, compared to seven days but were not statistically significant (p>0.05).

CONCLUSION

A search for the understanding of the molecular basis of Aluminum toxicity has stimulated numerous experimental studies. Yet the actual molecular mechanism of Aluminum toxicity is not well elucidated. In the present study, efforts were made to investigate the biochemical effects of Aluminum on protein levels in serum, liver and brain tissues.

The results of this study show that administration of aluminum by oral intubation to rats produced some signs of toxicity such as reduction in the body weight and protein levels. Paternain et al. reported that administration of aluminum as $AlNO_3$ caused weight loss [12]. The observed loss in weight for the rats exposed to aluminum thus suggests that aluminum probably interferes with normal metabolic (biosynthetic) processes. The growth of an organism integrates a range of physiological, biochemical and cellular processes. Thus, loss in body weight should be a sensitive indicator of a toxic impact. Body weights of the rats exposed to aluminum decreased with increase in concentration of aluminum. This is in line with the

observation made by Donkin and Widdows, who stated that body weights of exposed organisms, decline in a predictable way with respect to the concentration of toxicant and duration [13].

Results from this study show a significant decrease ($p<0.05$) in total serum, brain, and liver protein concentrations of the test groups given 38 mg/kg body weight of $AlCl_3$ after seventh, and 3.8 mg/kg, 38 mg/kg after fourteenth days respectively as compared to the control group. The reduction in total serum, liver and brain proteins observed in this study increased with increased concentration and duration of exposure, suggesting that aluminum administration may interfere with protein synthesis. This interference may also have exposed proteins to a wide range of free radical species capable of oxidizing protein thiols, thus promoting the formation of disulphide bridges and even induction of protein fragmentation and catabolism. These will affect normal protein metabolism and growth, thus, leading to the observed body weight loss. In another work, Abubakar et al. [14], reported decreases in serum, liver and brain proteins during aluminum administration. However, this work is contrary to the report of Bondy et al. [15] who reported an increase in protein after aluminum administration. He placed the rats on a special food, selenium supplement, however. The antibiotic known as puromycin inhibits protein synthesis and thus causes a fatty liver and marked reduction in the concentration of very low density lipoprotein (VLDL) in rats. Other substances that act similarly include ethionine (α-amino-mercaptobutyric acid), CCL_4, chloroform, phosphorous, lead, aluminum, and arsenic [16]. The observed low levels of protein in serum, liver and brain may be attributed to protein oxidation and catabolism caused by the toxicant (aluminum). Al promotes the formation of amyloid-β protein plaques [17,18], by aggregating tau proteins in Alzheimer's disease [19].

Aluminum ion (Al^{3+}) is a trivalent cation, and has a high affinity for negatively charged groups. It has been proposed that aluminum preferentially interacts with phosphate groups such as nucleic acids and phosphorylated proteins. In this way, aluminum remarkably decreases DNA synthesis [20,21], and inhibits protein synthesis. Aluminum can also interfere with phosphate absorption and calcium deposition in the body, thus leading to phosphatemia and osteomalacia. Reports have shown an association between aluminum accumulation in the brain and antisocial behaviour in learning and development. There are also other cellular mechanisms by which aluminum is thought to exert its toxicity, including increasing the blood brain barrier permeability, interference with phosphorylation-dephosphorylation reactions, altered iron metabolism with subsequent free – radical production, and disruption of second messenger systems [22].

On the basis of our study, it is concluded that aluminum exposure to male Wistar albino rats produced a major biochemical effect- oxidation of protein which was time and dose dependent. This effect may lead to some metabolic and tissue dysfunctions.

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