Dose and Duration Dependent of Aluminium in the Serum Liver and the Brain of Male Wistar Albino Rat

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Abstract

An atomic absorption spectrophotometric analysis on dose and duration dependent aluminum concentration in serum, liver and brain digests of three groups of male Wistar albino rats were investigated after seven and fourteen days of daily 0.38mg/kg, 3.8mg/kg and 38mg/kg aluminum administration respectively. The results showed that the test animals given the highest dose of (3.8mg/kg bw) of toxicant increase significantly ($p<0.05$) in aluminum concentration in serum, liver and brain digest after seven days when compared to the control animals. However, the mid and highest dose (38 and 38mg/kg bw) of toxicant significantly increased ($p<0.05$) in aluminum concentration in all the digest after fourteen days of exposure to aluminium. It is therefore concluded that increase in aluminum administration in male Wistar albino rats may predispose the animals to increase in aluminium concentration in the serum, liver and brain which is dose and duration dependent.

Keywords: Aluminum, Dose-and-duration dependent, Serum, Liver and brain digests

Introduction

Human systems have inorganic elements as their integral constituents. These inorganic elements may either be classified as bulk elements or trace elements, which aid in the growth and metabolism. Aluminum is neither classified as a bulk element nor does trace element yet find its way into the human system. However, it is considered to have no definite biological role (Devoto and Yokel, 1994).

The human dietary intake of aluminum averages about 30-50mg daily (Ganrot, 1986). This daily intake can be increased by aluminum containing drugs such as antacids, vaccines, aspirin, etc. (Greger, 1992)

Aluminum is released into the environment both by natural and anthropogenic sources. It is ubiquitous, being the third most prevalent element and the most abundant metal in the earth's surface mainly in the combined form as silicates, oxides and hydroxides (WHO, 1997).

Aluminum has a variety of applications such as in food industry (as a packaging foil and drying agents), pharmaceutical industry (as an anticholinesterase and antiperspirant) and engineering works (in construction of roof sheets, vehicle parts etc). Perhaps the numerous applications of aluminum is because of its light-weight, corrosion- free, and relative inexpensiveness (Kandiah and Kies, 1994).

Aluminum transverses across the cell membrane and enters into the blood circulation where it binds to the serum proteins, particularly transferrin (Moshtaghie and Ani, 1992). It is then absorbed by cells through transferrin receptors similar to iron absorption (Skillen and Moshtaghie, 1997). The target tissues for aluminum burden are bone, brain, kidney and liver (Ajoy *et al*., 1990).

However, aluminum is a known neurotoxin that can predispose to certain diseases such as Alzheimer's, dementia, Parkinsonism and amyotropic lateral sclerosis (Wurtman, 1985; Alferey *et al*., 1976). It also affects some body structures like the skeletal system, brain tissues and blood cells (Ajoy *et al*., 1990, Mestaghanmi *et al*., 2002). Aluminum is absorbed by cells through transferrin receptors similar to iron absorption (Skillen and Moshtaghie, 1997).

However, in spite of the known toxicity of aluminium until recently, there was little concern about dose and duration dependent of aluminium ingestion because it was assumed that aluminium was not orally bioavailable.

The objective of the study is to investigate the potentials of dose and duration of aluminium administration as a factor in aluminum accumulation in tissues of experimental animals. This study serves as a yardstick to find out whether aluminium accumulates faster in body tissues than the body's detoxification pathways can dispose of, resulting in a gradual build up of the metal in tissues.

Materials and Methods

Materials: Twenty-four (24) male Wistar albino rats aged between 8-10 weeks with a body weight range of 150-205g were purchased from the animal house of the Faculty of Vertinary 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 normal saline (0.2ml). All chemicals used were of the analytical grade.

Methods: The animals were housed and distributed randomly in four separate metabolic rat cages of six each differentially marked and acclimatized for five days. The four groups were labeled A to D. while group A is the control administered 0.2ml normal saline used in dissolving the toxicant, groups B, C and D were the treatment groups administered 0.38, 3.8 and 38mg/kg body weight daily of the aluminum as in aluminum chloride ($AlCl_3$) respectively. The route of administration was oral by means of gastric intubation. All animals were fed

with commercial feed (grower's mash) and water *ad libitum* for seven (7) and fourteen (14) days respectively. Each experiment was replicated thrice and results were pooled.

Blood was collected from each group on the days 7 and 14 through the median cantus vein in the eyes of the rats with the aid of a capillary tube and transferred into plastic test tubes. This was later centrifuged at 2000 x g in separate test tubes. The animals were later sacrificed, and dissected. The organs such as the liver and brain were removed, washed with normal saline, weighed and digested by the method of Taylor and Walker (1992). The absorbance of the clear supernatant was read at 375nm against the blank using atomic absorption spectrophotometer. The aluminum concentrations in µg/l of the samples were extrapolated from a standard curve.

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

Results

Figure 1 below shows no significant increase ($P > 0.05$) in the aluminium concentration in serum, and liver for the test groups administered 0.38mg/kg and 3.8mg/k g body weight while the test group administered 38 mg/kg increased significantly ($P < 0.05$) relative to the control group after day seven. The aluminium concentration in brain digest was significantly higher ($P < 0.05$) in the test groups administered 3.8mg/kg and 38mg/kg body weight of $AlCl_3$ after the seven days compared to the control group.

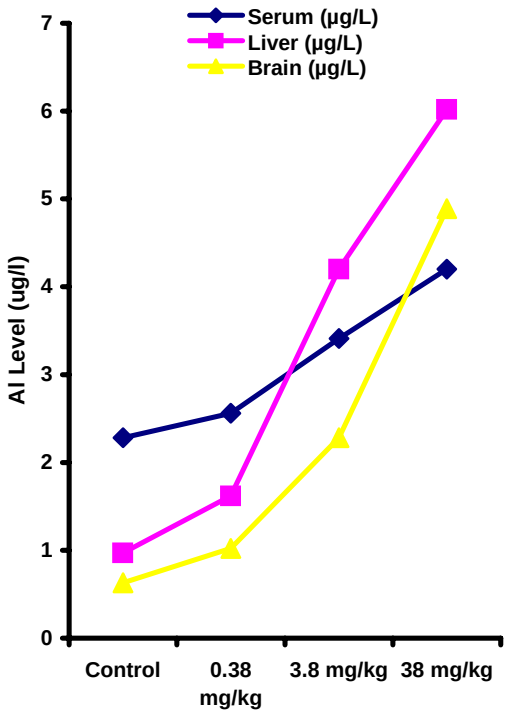

Fig. 1: Mean Aluminium concentration in Serum, Liver and Brain digest (ug/L) after 7 days

After fourteen days of aluminum exposure, the aluminum concentration in the brain of all the test groups were significantly higher ($P<0.05$) compared to the control group. However, aluminum concentration in the serum and liver were significantly higher ($P< 0.05$) in the test groups administration 3.8mg/kg and 38mg/kg relative to the control group. Results from figures 1 and 2 indicate that aluminum concentration in the serum; liver and brain digests increased markedly from the 7th day to 14th day in all the test animals.

Discussion

A search for the understanding on dose and duration depends of aluminium administration as a basis of its toxicity has stimulated very many experimental studies. In the present study, an attempt was made to delineate the potentials of dose and duration dependent of aluminium administration as a factor in aluminium accumulation in tissues of experimental animal. The results showed that aluminum concentration was more in the brain digest after days 7 and 14 respectively when compared to the serum and liver digests of other test animals at varying doses. The result may support the findings of Julka and Gill (1996) on the neurochemical effects of aluminum. The author said that aluminum inhibits cholinergic functioning as well as synaptic uptake of dopamine, norepinephrine and 5-hydroxytryptamine as well as inhibits Na-K ATPase and hexokinase activities. Hence aluminum decreases spontaneous nervous discharge, thereby reducing nervous activity. All these neurological effects of aluminum may be linked up with the bioavailability of aluminum in the brain tissues through aluminum intoxication. Aluminum accumulation has been implicated in neurological diseases such as Alzheimer's. dementia, Parkinsonism and amyotrophic lateral sclerosis (Alferey *et al*., 1986). Results from figures I and 2 indicate that aluminum concentration in the serum, liver and brain digests increased markedly from the 7th day to 14th day in all the test animals. Statistically, aluminum concentrations were significantly higher ($p<0.05$) in the digests of the test animals given the three doses of the toxicant after fourteen days when compared with that of seven days. This elevation dependent on the dose and duration of exposure. Sampson *et al*., (1989) found that serum aluminium concentration in renal patients maintained on haemodialysis was high and correlates with the intake and duration of aluminium consumption in chronic renal failure.

Conclusion: On the basis of these findings, it is concluded that aluminium accumulation in tissues of experimental animals were dose and duration dependent

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