ORIGINAL RESEARCH

ALUMINIUM RESIDUES IN THE TISSUES OF INTRAVENOUSLY AND ORALLY TREATED RABBITS

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Abstract

The tissue distribution and residue profile of aluminium chloride was investigated in rabbits treated intravenously and orally. Aluminium was administered at 0.08mg/kg and tissue and blood samples were taken at 48, 72, 120, 168 and 240 hrs after sacrifice. The aluminium was distributed to various organs and tissues of the body with high concentrations occurring in the liver, heart and brain. Higher aluminium levels were obtained in the tissues of intravenously administered rabbits when compared to orally treated animals. The level of aluminum in the tissues were significantly different ($p<0.05$) from those in the blood. The aluminium residues were still detectable in the tissues of rabbits 10 days after treatment.

Key words: Aluminium, Residue, Rabbits.

Introduction

Aluminium, a heavy metal, has been implicated in Alzheimer's disease and other neurological disorders such as dialysis dementia (Wills and Savory, 1983; McClure and Smith, 1984; Cowburn *et al*., 1990). The sources of aluminium to man and animals may include water treated with aluminium sulphate as a flocculating agent to clarify contaminated sources. In addition, many medications contain aluminium in some form and many food stuffs may contain aluminium (Marytn *et al*., 1989). Studies have shown that aluminium inhibits several metalloenzymes such as hexokinase and inositol triphosphatase (Birchall and Chapel, 1988), and adenosine triphosphatase (Cowburn and Blair, 1989; Cowburn *et al*., 1990). In an earlier study, aluminium was observed to cause severe anaemia, anorexia and degeneration of the liver, kidney and brain in treated rabbits (Kolo, 1996). Although animals and man are exposed to aluminium in various ways, the distribution and elimination of this metal from edible tissues and blood in domestic animals has not been established. Such information is desirable to avoid potential human health hazard which may follow the ingestion of animal tissues exposed to aluminium. The aim of the study, therefore, is to determine the extent of tissue distribution and residue profile of the agent in rabbits treated intravenously and orally. This is important because of the effects of aluminium on the body systems.

Materials and Methods

Experimental animals and treatments

Thirty-two clinically healthy rabbits of both sexes, weighing 0.8 to 1.5 kg and 10 - 12 months old purchased from Shehu Shagari Low Cost Estate Maiduguri, Nigeria were used. The animals were housed in clean rabbit cages in the Department of Veterinary Physiology and Pharmacology. The rabbits were fed on dry groundnut leaves, lettuce and concentrates, with drinking water provided *ad libitum*. The animals were randomly separated into two groups of 15 rabbits each. A 1% solution of aluminium chloride in distilled water was administered intravenously to group one at 0.08 mg/kg body weight, while group two received aluminium chloride at the same dose orally.

Sample collection

Two grams of tissue samples (liver, kidney, brain, heart and skeletal muscle) were taken postmortem from the animals at 48, 72, 120, 168 and 240 hrs following aluminium administration. Three rabbits from each of the groups were sacrificed at each period of sample collection. Two untreated rabbits were sacrificed for the

preparation of control tissues and tissue standards. The experimental work area and all utensils were cleaned thoroughly after each slaughter to prevent contamination. The tissue samples obtained were placed in appropriately labelled white plastic bags. Blood samples were collected prior to aluminium administration and at each period of sacrifice. All blood samples were collected in vials containing EDTA as anticoagulant. The blood samples were centrifuged immediately after collection at 2000 rpm for 10 min to obtain the plasma. The plasma and tissue samples were frozen until analysed.

Aluminium determination from plasma and tissue samples

Determination of free aluminium in plasma and tissues sampled was done using atomic absorption spectrophotometer. The method of Ramires-Munoz (1968) was adopted for the analysis. The concentrations of aluminium in the samples were obtained from the standard curves prepared for the various tissues.

Statistical analysis

Linear regression analysis was performed on the mean tissue concentrations (three rabbits at each time interval) and the slope of the elimination curves determined. The results were expressed as mean " SD" Test for significance between mean parameters in respect of intravenously and orally treated rabbits were performed using Student's *t*- test and the "null" hypothesis was rejected at the 5% level of probability.

Table 1. The half-life and elimination rate constants in blood and tissues of rabbits treated orally and intravenously with single dose of aluminium chloride at 0.08 mg/kg body weight

Tissues	Intravenous route		Oral route	
	Half-life (hr)	Elimination rate constant (per hr)	Half-life (hr)	Elimination rate constant (per hr)
Blood	346.5	0.002	138.6	0.005
Liver	17.3	0.040	38.5	0.020
Heart	21.0	0.030	33.0	0.020
Skeletal muscle	38.7	0.020	38.7	0.20
Kidney	27.7	0.025	24.8	0.028
Brain	32.0	0.02	23.0	0.030

Results

Intravenous and oral administration of aluminium chloride to rabbits at 0.08 mg/kg body weight resulted in a measurable blood level for 240 hrs (i.e. 10 days). A mean plasma concentration of 13.2 ± 0.5 µg/ml was obtained following i.v. treatment while 9.3 ± 0.8 µg/ml was obtained in orally treated rabbits 48 hr post-treatment (Fig. 1). Two hundred and forty hours post-aluminium administration mean values of 4.5 ± 0.3 and 2.4 ± 0.3 µg/ml were recorded for intravenously and orally treated animals, respectively.

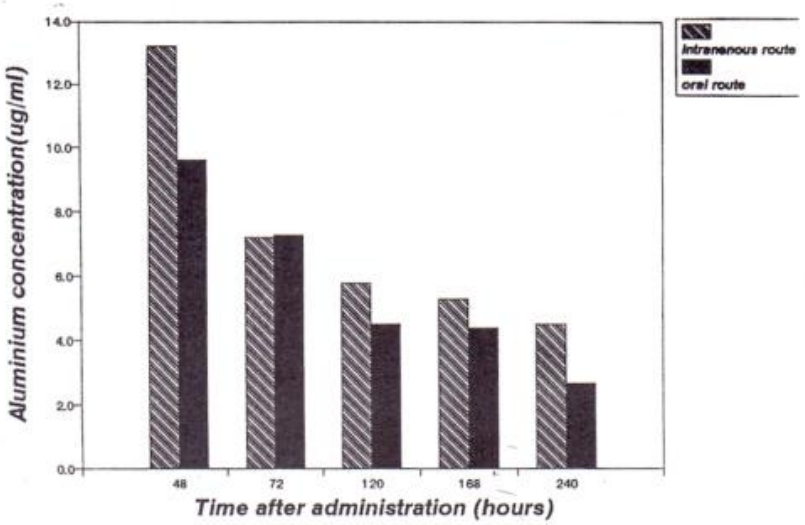

Fig. 1

Aluminium concentration (ug/ml) in blood of rabbits treated intravenously and orally with a single dose of aluminium chloride (0.8mg/kg).

The mean concentrations of aluminium in the liver of intravenously and orally treated rabbits are shown in Fig. II. The highest concentrations of 61 ± 4.5 and 42 ± 3.4 µg/g were obtained in intravenously and orally treated animals, respectively. The concentrations in the liver showed a continuous decrease and at 240 hr (10 days) post-treatment, the concentration had dropped to 10 ± 1.0 and 10.5 ± 0.9 µg/g, respectively in i.v. and orally treated rabbits.

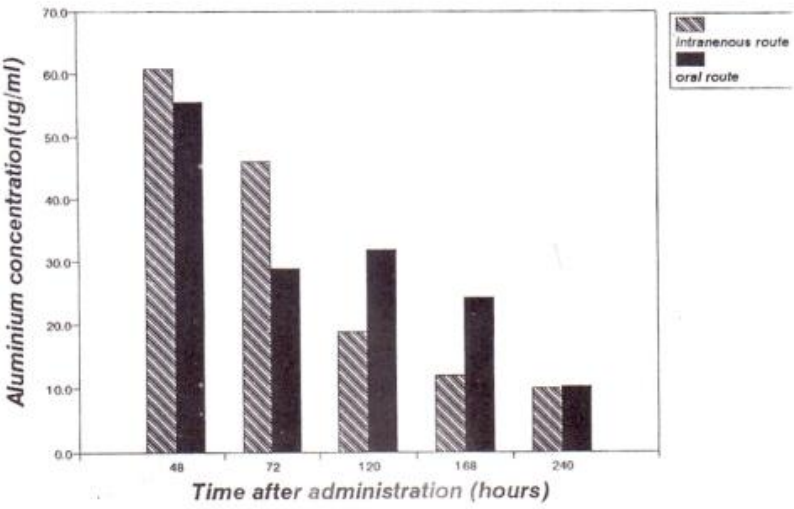

Fig. 2

Aluminium concentrations (ug/ml) in the liver of rabbits treated intravenously and orally with a single dose of Aluminium (0.08 mg/kg).

The highest concentrations (at 48 hr post-treatmegt) of 46 ± 6.3 and 39.5 ± 5.8 µg/g (Fig. III) were obtained respectively in the heart of i.v. and orally treated animals. The concentration decreased to 23 ± 3.4 and 15.8 ± 2.8 µg/g at 240 hr respectively in i.v. and orally treated rabbits.

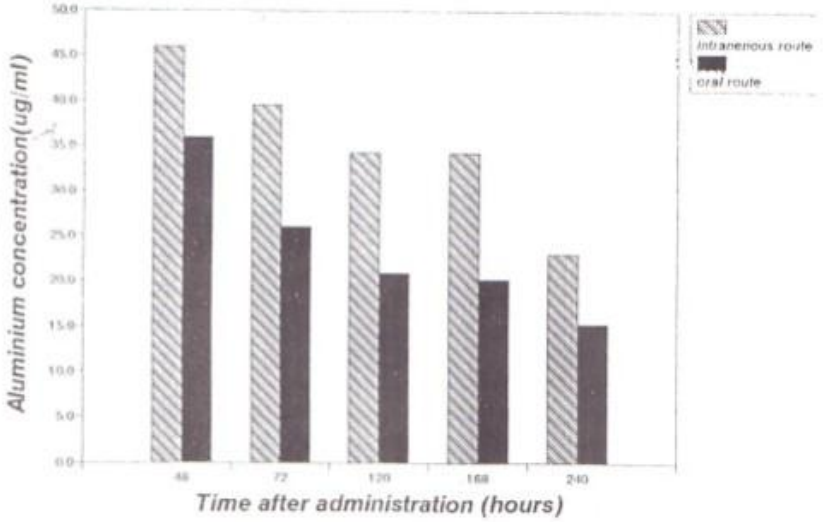

Fig. 3
Aluminium concentrations (ug/ml) in the heart of rabbits treated and orally with a single dose of Aluminium (0.08 mg/kg).

In the brain, concentrations of 61 ± 8.5 and 26.5 ± 3.2 µg/g were obtained 48 hr post-treatment in i.v. and orally treated rabbits (Fig. IV). The concentrations showed a continuous decrease and at 240 hr post-treatment, concentrations of 17 ± 1.5 and 2.5 ± 0.7 µg/g were obtained in i.v. and orally treated animals. The kidney at 48 hr had concentrations of 41 ± 5.4 and 39.6 ± 4.8 µg/g in i.v. and orally treated rabbits, and these decreased to 7.5 ± 0.9 and 21 ± 2.8 µg/g at 240 hr post-administration. Peak concentrations of 43 ± 4.4 µg/g (i.v. treated rabbits) and 37.5 ± 6.2 µg/g (orally treated rabbits) were obtained 48 hr after treatment. These amounts decreased to 12.0 ± 2.3 and 4.9 ± 1.2 µg/g at 240 hr post-administration.

The half-lives and elimination rate constants of aluminium in plasma and other tissues of rabbits following i.v. and oral aluminium administration is shown in Table 1. The half-lives of aluminium in blood of 346.5 and 138.6 hr after i.v. and oral administration, respectively were significantly ($p<0.05$) higher than those obtained for the other tissues.

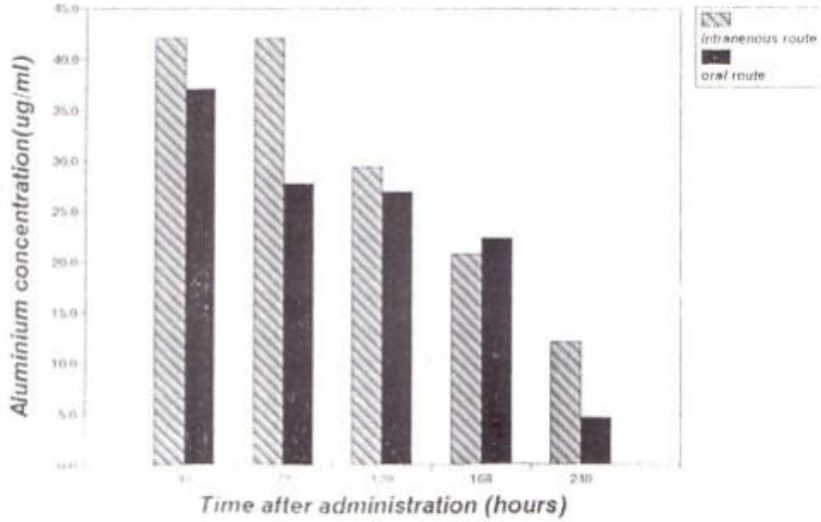

Fig. 4
Aluminium concentrations (ug/ml) in the skeletal muscle of rabbits treated intravenousl and orally with a single dose of aluminium (0.08mg/kg).

Discussion

Aluminium was observed to be well distributed to the organs and tissues of the body. The high concentration of aluminium present in the organs and tissues of the body may be reflective of the blood vascular supply to those organs and tissues. The highest concentration of aluminium occurred in the liver and brain. The high amount in the liver was expected since the liver is the main organ of bio-transformation. Very high amount of aluminium was obtained in the brain following i.v. administration compared to oral treatment. This high amount may have resulted from the breakdown of the blood brain barrier due to increased aluminium load resulting in enhanced penetration into the brain. Kolo (1996) also reported high concentration of aluminium in the brain of rabbits exposed for a period of two weeks in drinking water.

The high concentration of aluminium in the kidney following i.v. and oral aluminium administration is not considered unusual since kidney apparently is the primary organ of elimination. The mechanism of excretion via the kidney is unknown but may include such mechanisms (considering the molecular size of aluminium) as passive diffusion or active secretion.

The results also indicate that aluminium persisted in tissues for more than 240 hr (10 days) after intravenous and oral administrations. This should be given due consideration in the estimation of the residue profile of the agent.

The results reported in Fig. 1 indicate that aluminium is readily absorbed by the oral route. A mean plasma concentration of 9.3 ± 0.8 µg/ml was attained in 48 hr after oral route while a concentration of 13.2 ± 0.5 µg/ml was obtained at the same time following i.v. route. Aluminium is known to be absorbed through the gastro-intestinal tract especially in lipid forms, although ionic forms are also known to pass through intercellular spaces (Cowburn *etal*, 1990). The fall in plasma aluminium concentration is attributed to the rate of elimination by the kidneys or other excretory organs (Baggot, 1977). There was slow elimination of aluminium from the plasma. This is substantiated by the fact that the rate of elimination was 0.002 and 0.005 per hour for i.v. and orally administered aluminium. The slow elimination of aluminium from the plasma may be due to the binding of aluminium in body tissues and the slow re-entry of this metal into the central compartment (blood) for clearance from the body (Baggot, 1977).

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