M. Pup, et al. Scientifical Researches. Agroalimentary Processes and Technologies, Volume XI, No. 1 (2005), 223-228

INFLUENCE OF ALUMINUM ON BLOOD SERUM GLUCOSE, TOTAL PROTEINS AND MAGNESIUM CONCENTRATION IN DOMESTIC RABBITS

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Abstract

Aluminum chloride was administered subcutaneous to domestic rabbits alone or in association with citrate (as citric acid) or fluoride (as NaF). This paper presents the modifications of carbohydrate, proteins and albumins in respect with control group C, for three experimental groups, E_1, E_2, E_3, in rabbit's blood serum. The blood serum glucose level varied between 119.6±7.1 mg/dL in-group C and 98.7±24.0 mg/dL in E_1, 108.6±7.4 mg/dL in E_2 and 101.7±4.6 mg/dL in E_3 group. The variation of proteins and albumins was not in very large limits for E_1 group comparing with control, but at the same dose of $AlCl_3$ administered, the presence of citrate in E_2 group and fluoride in E_3 group can decrease blood concentration of those. Modifications of blood parameters presented here could be explained in relations with the oxidative stress induced by aluminum.

***Keywords**: blood serum glucose, total proteins, magnesium, domestic rabbits.*

Introduction

In liver cells, appropriate enzymes are available to promote interconversion among the monosaccharide. The liver cells contain large amount of glucose phosphatase; therefore, glucose 6-phosphate can be degraded back to glucose and phosphate, and the glucose transported back into the blood. The transport is possible through protein carrier molecules from the lipid matrix of the cell. In biological systems, Al^{3+} will be competitive with Mg^{2+}. Both Al and Mg ions favor oxygen donor ligands, especially phosphate groups. This aspect was related by a study made by Carlisle in1984, cited by Nicolini et al, 1991 that aluminum binds strongly to ATP in place of the essential magnesium but which is removed by complexation with citrate. Aluminum inhibits enzymes with Mg^{2+} cofactors.

Three major types of protein present in the plasma are albumin, globulin, and fibrinogen. The principal function of the albumin is to provide colloid osmotic pressure, which in turn prevents plasma loss from the capillaries. Albumin and fibrinogen of the plasma proteins, as well 60-80 per cent of the globulins, are formed in the liver.

In carbohydrate metabolism, the liver performs the following specific functions: storage of the glycogen, conversion of galactose and fructose into glucose, gluconeogenesis and formation of many important chemical compounds from the intermediate products of carbohydrate metabolism.

One of the major functions of the liver in protein metabolism is formation of plasma proteins and interconversion among the different aminoacids and other compounds (Ryeuski et al, 1998).

Experimental

This experiment was made on three groups of young animals from species Oryctolagus Cunicullus, double hybrid three population, obtained through cross breeding between two lines of Big Chinchilla breed and White New Zeeland breed (the both of them are middle breeds of domestic rabbits), for meat production. The average mass of rabbit was of 0.700-0.800 Kg.

Aluminum as aluminum chloride was administered to three experimental groups of rabbits. Each group had 5 animals. For group E_1, $AlCl_3$ it has been administered by subcutaneous injection in concentration of 50 mg $AlCl_3$/kg b.w., for group E_2 it has been administered a solution containing 50 mg $AlCl_3$ and 2% v/v citrate /kg b.w and the third group E_3 received 50 mg $AlCl_3$ and 2 mg F as NaF/kg b.w. in the first and the third day of the experiment. The control group formed by 5 animals had not received any kind of injection. In the fifth day, after anesthesia, the animals were killed and blood samples were taken in order to determine some blood serum parameters: glucose, total proteins, and magnesium. The results are given as mean ($\overline{X}$) and standard deviation (S.D.).

Results and Discussions

Practically one can say that aluminum, in some conditions, may affect carbohydrate, lipid and protein metabolism in the same time (Dejica, 2000). Our results concerning the concentration of blood serum glucose, total proteins and albumins are revealed in table 1.

Transferrin is the preeminent protein carrier of Al(III) in the plasma. The same authors conclude that citrate is the low molecular weight carrier and transferrin is the high molecular weigh carrier of Al (III) in rat serum. Albumin (administered to patients) has shown to be highly contaminated

with aluminum, which results from the procedures used to separate it from other serum proteins and store it (Quagliaro D.A et al., 1988, cited by Nicolini et al, 1991). Cell membranes contain transport systems and one of this is the channel-forming protein. Metal ions such as aluminum could interfere with finely tuned systems such as gated membrane channels if they bind these proteins. Experiments show that Al (III) open up channels in the surface membranes. These channels were normally closed and induced to open by the addition of the metal. In case of our experiment, the variation of albumins for E_1 group was not significant. Albumin is expected not to bind Al (III), with anywhere near the strength of transferrin or citrate (Martin, 1986 - cited by Nicolini et al, 1991), but seems that the citrate affect the level of albumin in the blood serum in this experiment.

Table 1. Modification of glucose, total proteins and albumins in blood serum

Specification	Glucose mg/dL	Protein total g/dL	Albumins g/dL	Globulins g/dL
	$\overline{X} \pm SD$	$\overline{X} \pm SD$	$\overline{X} \pm SD$	$\overline{X} \pm SD$
Group C	119.60 ± 7.10	5.83 ± 0.07	4.24 ± 0.29	1.59 ± 0.29
Group E_1 ($AlCl_3$)	98.70 ± 24.00	5.52 ± 0.20	4.37 ± 0.16	1.15 ± 0.16
$\Delta \overline{X}$	-20.90	-0.31	-0.13	-0.44
GroupE_2 ($AlCl_3$+citrate)	108.60 ± 7.40	5.18 ± 0.08	3.17 ± 0.14	2.01 ± 0.14
$\Delta \overline{X}$	-11.00	-0.65	-1.07	+0.42
Group E_3 ($AlCl_3$+NaF)	101.70 ± 4.60	5.03 ± 0.10	3.45 ± 0.06	1.58 ± 0.06
$\Delta \overline{X}$	-17.90	-0.80	-0.79	-0.01

Aluminum forms coordinated complexes between carboxyl groups of collagen fibers in association with oxygen cross linking the collagen fiber and inhibiting bone induction properties. In that case we can presume that aluminum react with carboxyl groups of the aminoacids in proteins and with oxygen can induce an oxidative stress on the protein. According to Dejica (2000) aminoacids, the main components of peptids and proteins are the target of the oxidative stress, especially to their lateral chains. The protein oxidation determines some physical modification of the protein: fragmentation, cross-linking, proteolytic digestion. In vitro, Al^{3+} promoted oxidative damage to lipids and proteins in membranes isolated from rat brain (Oteiza, 1995). Over the last years, numerous reports from

China, India and elsewhere indicate that fluoride in varying concentrations induces free radical toxicity in both animals and people living in areas of endemic fluorosis. There is much evidence that superoxide free radicals are reactive and may lead to chemical modifications and impairment of proteins, lipids, carbohydrates, and nucleotides in living cells (Dejica, 2000). The decrease of total protein and albumin in E_2 and E_3 group can be provoked by an oxidative stress caused by aluminum - citrate and aluminum - fluoride salts.

Oxidative stress also affects carbohydrates (Dejica, 2000). Glucose oxidation is posible in condition of metalic ions presence. Carbohydrates oxidation is necessary for energy production, but is also the cause of anenzymatic glycation of proteins. In growing animals, deficiency of thyroxine causes growth to be greatly inhibited because of lack of protein synthesis (Nicolini et al, 1991).

The ability of aluminum fluoride to activate G proteins that can affect membrane channels has been established, but the high levels of fluoride needed are not physiological. Aluminum has a high affinity for phosphate groups, which must surely form the basis of binding to many proteins (Panchalingam K., et al.1987 - cited by Nicolini et al, 1991). Suttie, 1970, cited by Ghergariu, 1980, showed that the excess of fluoride decrease the level of plasmatic aminoacids. Total proteins in this experiment have the same evolution when the fluoride is administered.

An important mechanism is the competition of aluminum with magnesium for binding at key sites in which magnesium is an essential co-factor (Meiri et al. 1993 - cited by Imray et al, 1995).

In table 2 are presented the variation of magnesium concentration in blood serum, the modifications of this metal can be linked by the variation of carbohydrates, because one of the major role of magnesium in biological systems is the participation of this metal in biochemical reactions with compounds containing phosphate ion implicated in the phosphate metabolism. (Ghizdavu, 2000). Otherwise, the phosphate has a structural role in carbohydrate-phosphate interaction systems in nucleic acids, and is the universal source of energy in biological systems. In the condition of the present experiment, the modifications of blood serum glucose are important for E_1 group where is registered a decrease comparing with control group C.

In 1984 Carlisle (cited by Nicolini et al, 1991) shown that aluminum binds strongly to ATP in place of the essential magnesium. In these

conditions, glucidic compounds cannot be degraded because of the blockage of ATP and Mg.The effect of glucide modifications is much important to aluminum administration in E_1 group than that of association aluminum chloride – citrate in E_2 group. Moshtaghie, in 1991, observed that the accumulation of aluminum in the cell organelles could therefore disturb many biochemical processes including carbohydrate and lipid metabolism. The same author observed that glucose enhanced aluminum uptake (Moshtaghie A.A., 1988). Aluminum also stimulates NADPH oxidation and takes parts in the process of free radicals formation (Zaman, 1995).

Table 2. Modification of magnesium (mg/dL) in blood serum

Specification	Group C	Group E_1 ($AlCl_3$)		Group E_2 ($AlCl_3$+citrate)		Group E_3 ($AlCl_3$+NaF)	
	$\bar{X}$±SD	$\bar{X}$±SD	$\Delta\bar{X}$	$\bar{X}$±SD	$\Delta\bar{X}$	$\bar{X}$±SD	$\Delta\bar{X}$
Mg-serum	3.52 ± 0.11	4.59± 0.89	1.07	3.46± 0.19	-0.06	3.57 ± 0.06	0.05

Fluoride affects protein, glycogen and lipid content of various tissues. Toxicity of fluoride is specific to different tissues and doses/concentration. The experiment was made on freshwater Indonaia caeruleus to 0.5; 2.0; and 5.0 ppm fluoride exposure for 12 hours. In our experiment the glucose and protein is not very much affected by the fluoride added to aluminum chloride and the conclusion is that the 2 mg/kg b.w. dose of fluoride administered in one injection have not disturbed the protein and carbohydrate metabolism as it is shown in the case of a continuous exposure (Mane et al, 1987).

Low magnesium in diet significantly enhanced fluoride absorption. Fluoride retention values simply reflected absorptive changes; which indicates that the site of the interaction between magnesium and fluoride is at the intestinal level, most likely involving insoluble complex formation (Cerklewski F.L., 1987).

Conclusions

Carbohydrate metabolism is affected by the presence of aluminum. Aluminum chloride decreases the amount of blood serum glucose in the case of the acute intoxication, which is simulated here. Observing the augmentation of Mg level in serum, an important ion in the process of

glucidic degradation we can say that in the conditions of the present experiment aluminum chloride create an imbalance, which disturb the mechanism of glucidic degradation. An amount of 2 mg/b.w. of fluoride administered does not affect carbohydrate and protein metabolism as shown in other experiments, where the metabolism was affected after a long term exposure to the same amount of fluoride. Carbohydrate metabolism seems not to be affected very much by fluoride in E_3 group as compared with E_1 group, the amount of aluminum chloride administered appear to be the cause of blood serum glucose modification. Comparing with control group, it seems that the variation of glucose, total proteins, and albumins in blood serum can be caused by an increase of oxidative stress of the animals in the present study.

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