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The influence of various metals on magnesium concentration in cellular subfractions of certain rat tissues

There is an increased interest in the role of magnesium in clinical medicine, physiology and nutrition. Magnesium is the main intracellular metal cation with a free concentration in a cytosol around 0.5 mmol·dm^{-3}. It is evident that magnesium, whose gradient over the plasma membrane is slight, and whose free extracellular concentration (ionized magnesium) is about 0.7 mmol·dm^{-3}, at most can play a complementary role of a more long-term regulatory element (5, 18). Magnesium is a cofactor in hundreds of enzymatic reactions and is especially important for those enzymes that use nucleotides as cofactors or substrates. In addition, magnesium is required for protein and nucleic acid synthesis, the cell cycle, cytoskeletal and mitochondrial integrity and for the binding of substances to the plasma membrane. Magnesium frequently modulates ion transport by pumps, carriers and channels and thereby may modulate signal transduction and the cytosolic concentration of calcium and potassium (5, 13, 18). Positively charged Mg^{2+} is able to bind electrostatically to the negatively charged groups in membranes, proteins and nucleic acids. Magnesium may influence the binding of other cations like calcium which depends upon their concentration; it may have antagonistic or co-operative effects (18). Magnesium is important for normal neurological and muscular function. Hypomagnesemia leads to hyperexcitability due mainly to cellular calcium transport and signalling (5, 18).

The adult body contains approximately 21–28 g (about 1 mole) of magnesium, muscle and soft tissues accounting for almost half of this and bone for slightly more than half. Only about 1 % of magnesium is present in the blood plasma and red cells (6, 18).

Magnesium is absorbed mainly in the ileum and in the colon. Approximately 75 % of the total plasma magnesium is filtered through the glomerular membrane. Under normal conditions only 3–5 % of the filtered magnesium is excreted in the urine. The development of magnesium deficiency is usually linked either to disturbances in the intestinal magnesium absorption and/or to an increased renal magnesium excretion. Disturbances in the metabolism of this macro-element may be also induced by the administration of some metals (5, 16, 18). Based on this fact, the purpose of our work was to estimate the influence of various metals on magnesium concentration in cellular subfractions of certain rat tissues.

MATERIAL AND METHODS

The experiment was conducted on Wistar rats, weighing 130–180 g. The animals were divided into five groups, each of 10 rats. The first group of animals was on a normal diet (LSM dry food and redistilled drinking water) and it was a control group. The other groups of animals were fed LSM dry food and they received redistilled drinking water with addition of: • lithium

sulphate ($Li_2SO_4 \cdot H_2O$) in the amount of 150 mg·dm^{-3} in the reduction to unalloyed metal (group II), • aluminium sulphate ($Al_2(SO_4)_3 \cdot 18\ H_2O$) in the amount of 500 mg·dm^{-3} in reduction to unalloyed metal (group III), • plumbum nitrate ($Pb(NO_3)_2$) in the amount of 500 mg·dm^{-3} in reduction to unalloyed metal (group IV), • chromium nitrate ($Cr(NO_3)_3 \cdot 9\ H_2O$) in the amount of 500 mg·dm^{-3} in reduction to unalloyed metal (group V).

After 3 weeks the animals were anaesthetized with 0.5 ml of 5 % ketamine. Liver, brain and kidneys were excised and homogenized in four-fold volumes of 100 mM Tris-HCl buffer pH 7.4.

The homogenates were centrifuged to obtain nuclear, mitochondrial and cytosol subfractions. Magnesium concentration was determined by the reaction with xylidine blue (Cormay-Mg). The results were submitted to statistical analysis with the Cochran-Cox test, accepting $p<0.05$ as significant.

RESULTS

The intoxication of various metals influenced magnesium concentrations in cellular subfractions of rat liver, brain and kidneys.

The changes in magnesium concentration in rats tissues are shown in Table 1.

The administration of lithium resulted in magnesium concentration decrease in all cellular subfractions of liver, brain and kidneys. The most significant changes were observed in mitochondrial subfraction of all tested tissues. There were statistically significant alterations, except hepatic mitochondria. Similar shifts concerned aluminium intoxication. Magnesium decrease was noticed in all subfractions of liver and brain; however, a less important decrease was found in all subfractions of kidneys. These alterations were statistically significant only with hepatic nuclear subfraction and brain cytosol subfraction.

The application of lead and chromium induced both decrease and increase of magnesium concentration, according to the subfraction and tissue. Magnesium concentration decrease caused by lead and chromium intoxication, in nuclear and mitochondrial subfractions of liver and kidneys and in mitochondrial and cytosol subfractions of brain took place. The largest changes were observed in mitochondrial subfraction of all tested tissues of animals treated with chromium. On the contrary, the increase of magnesium concentration was shown in cytosol subfraction of liver and kidneys and in nuclear subfraction of brain.

Both lead and chromium caused significant increase in magnesium concentration in cytosol subfraction of kidneys. The increase caused by chromium in cytosol subfraction of liver was statistically significant but that caused by lead in this subfraction of liver was statistically insignificant.

Generally, the most important changes on magnesium concentration were shown in animals intoxicated of chromium.

DISCUSSION

There are biological relationships between elements in human and animal organism. The changes in the homeostasis of essential elements, especially magnesium, by toxic metals were studied with a view to understanding the harmful action of these elements on the organism (20, 21). Disturbances in the metabolism of magnesium may be induced by intoxication of cadmium (7, 10), lead (1, 7, 8, 9, 10, 14, 15) and chromium (4). Antagonistic effect between magnesium and lead was reported. It was suggested that reduction of magnesium level resulted in an increase in intestinal lead absorption and in a decrease in renal lead excretion (5, 7, 8).

Karczewski et al. (8) reported that magnesium content in the hair of workers occupationally exposed to lead was significantly decreased. Besides, higher lead levels were

Table 1. Magnesium concentration (μmol · mg^{-1} of tissue) in cellular subfractions of rat tissues

Tested tissue	Subfraction	Group I Control X ± SD	Group II 150 $mg \cdot dm^{-3}$ Li^{+} X ± SD	Group III 500 $mg \cdot dm^{-3}$ Al^{3+} X ± SD	Group IV 500 $mg \cdot dm^{-3}$ Pb^{2+} X ± SD	Group V 500 $mg \cdot dm^{-3}$ Cr^{3+} X ± SD
Liver	nuclear	1.28 ± 0.18	0.64 ± 0.10* ↓	0.60 ± 0.10* ↓	0.56 ± 0.08* ↓	0.72 ± 0.10* ↓
	mitochondrial	0.82 ± 0.12	0.60 ± 0.08 ↓	0.68 ± 0.10 ↓	0.62 ± 0.10 ↓	0.32 ± 0.06* ↓
	cytosol	6.60 ± 0.86	6.30 ± 0.98 ↓	5.20 ± 0.76 ↓	6.80 ± 1.06 ↑	10.80 ± 1.64* ↑
Brain	nuclear	0.64 ± 0.08	0.48 ± 0.08 ↓	0.44 ± 0.06 ↓	0.84 ± 0.14 ↑	0.76 ± 0.10 ↑
	mitochondrial	1.20 ± 0.18	0.48 ± 0.06 * ↓	0.88 ± 0.12 ↓	0.92 ± 0.14 ↓	0.68 ± 0.10* ↓
	cytosol	5.50 ± 0.62	3.30 ± 0.50 ↓	2.10 ± 0.22* ↓	1.80 ± 0.28* ↓	3.10 ± 0.46* ↓
Kidneys	nuclear	1.04 ± 0.16	0.72 ± 0.12 ↓	0.84 ± 0.12 ↓	0.68 ± 0.10 ↓	0.92 ± 0.14 ↓
	mitochondrial	0.50 ± 0.04	0.26 ± 0.04 * ↓	0.44 ± 0.04 ↓	0.20 ± 0.04* ↓	0.12 ± 0.02* ↓
	cytosol	4.80 ± 0.62	4.50 ± 0.66 ↓	4.40 ± 0.74 ↓	7.90 ± 1.21* ↑	8.90± 1.36* ↑

* Statistical significance in comparison with control ($p<0.05$)

found in the hair of children with magnesium deficiency (10). Another study showed a negative correlation between magnesium and lead, too. Recommended magnesium-lead ratios should amount to 25:1 at least, but in the examined population the mean ratio of magnesium to lead concentrations was lower in 90.7 % of cases (7).

Lead influenced magnesium concentration in the rat skin only to a small degree and it was statistically insignificant. This could be explained by the fact that antagonistic effect between magnesium and lead was seen mainly in soft tissues (14). On the contrary, Pasternak et al. (15) showed that lead intoxication of rats with experimental hyperthyroidism caused statistically significant magnesium increase in liver. These changes could result in metabolic disorder in rat organism. Similar changes were observed in a study on rats with experimental diabetes mellitus. In comparison with the control lead significantly increased magnesium concentration in liver (1).

Magnesium may also cause a reduction of chromium concentration in organism, as it was shown in hair examinations, increasing at the same time the its excretion with urine. During the intraperitoneal administration of potassium dichromate and magnesium chloride to experimental animals it was confirmed that magnesium counteracts the accumulation of chromium in the skin (4). Interactions are also reported between magnesium and lithium human and animal organism.

It was shown that the administration of lithium ions to rats resulted in an increase serum (3,11,12,17), muscle (12) and cerebellar (11) magnesium concentrations. However, Bellwinkel et al. (9) reported no changes due to the therapy in rats treated with lithium determinations of serum magnesium.

The effect of lithium administration on urine electrolyte excretion is controversial with reports of increased, unaltered and reduced excretion rates of magnesium. Thompson et al. (22) noticed that magnesium excretion was initially unaltered by lithium administration but than decreased during the final collection period. Thus, it is postulated that lithium ions exert their effect on renal electrolyte transport in a similar manner to that of sodium.

A physiological balance of elements is needed for a normal cellular function, and any changes like those observed in the present study in magnesium concentration may act on other ions and alter the animals and humans physiology (19).

CONCLUSIONS

1. Intoxication of various metals influenced magnesium concentration in cellular subfractions of rats tissues.

2. Changes in magnesium concentration were dependent on the kind of metal, tissue and cellular subfraction.

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SUMMARY

There are interactions between magnesium and other elements in human and animal organisms. Changes in homeostasis of this macro-element may be induced by intoxication of lead, chromium and the other metals. The purpose of our work was to analyze the influence of various metals (lithium, aluminium, lead and chromium) on magnesium concentrations of certain rat tissues. It was shown that the changes in magnesium concentration were dependent on the kind of metal, tissue and cellular subfraction.

Wpływ różnych metali na stężenie magnezu w subfrakcjach komórkowych tkanek szczura

W organizmie ludzkim i zwierzęcym stale zachodzą interakcje między magnezem i innymi pierwiastkami. Zmiany w homeostazie tego makroelementu mogą być spowodowane intoksykacją ołowiem, chromem lub innymi metalami. Celem pracy było wykazanie wpływu różnych metali (litu, glinu, ołowiu i chromu) na stężenie magnezu w subfrakcjach komórkowych tkanek szczura. Wykazano, że zmiany w stężeniu magnezu były zależne od podawanego metalu, od rodzaju tkanki oraz od subfrakcji komórkowej.