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The influence of lithium on calcium and magnesium homeostasis in serum and tissues of rats

Lithium, known from the beginning of the 19^{th} century, was first used in the therapy of renal calculosis and rheumatic pathological states. But the turning point was obtaining positive results of lithium carbonate administration in cases of acute and chronic manic states (9, 13).

Lithium is used in psychiatry for the treatment of manic and depressive illness (4, 8) and for the potentialization of the action of other drugs (7, 10). The administration of this element must be associated with the monitoring of its level in organism, because its excess can have toxic effects (5, 11). It exerts teratogenic (3, 8) and cardio-toxicity influence (1, 8) and inhibits secretion of thyroid hormones (10). Lithium therapy can decrease negative side effects of chemotherapy used in cases of acute myeloid leukaemia (5). Lithium influences transport and intracellular concentration of calcium (14), and it can disturb water-electrolyte equilibrium of organism (13). It is excreted by kidneys (8). With the deficiency of Na^+, Li^+ are subject to resorption, which can lead to the poisoning. Li^+ take place of other ions of the first group and in this way influence excitability of central nervous system cells (4).

The relationships between lithium administration and water-electrolyte equilibrium made us investigate the effect of lithium intoxication on calcium and magnesium levels in serum and tissues of rats.

MATERIAL AND METHODS

Our study was carried out on 2-month-old, male Wistar rats (120–150 g). The animals were divided into two groups: control group - received redistilled water, tested group–received a water solution of $Li_2SO_4 \cdot H_2O$ in the form of drinking water, at the dose of 150 mg Li $\cdot$ dm^{-3}.

Half of the animals of each group were decapitated after three weeks and the rest after six weeks. Each time the rats were under ketamine narcosis and blood from the heart as well as the tissues of liver, kidney, femoral muscle, brain, spleen and heart muscle was collected. Serum was separated. 10% (w/v) tissue homogenates were prepared in 0.1 mol $\cdot$ dm^{-3} Tris-HCl buffer, pH = 7.4. Supernatants were obtained by centrifugation at 5000xg for 30 min.

In serum and supernatants calcium concentration by the reaction with o-cresolophtalein (diagnostic set Liquick Cor-CALCIUM 120) and magnesium concentration by the reaction with xylidyle blue (diagnostic set Liquick Cor-MG 60) were measured using colorimetric method. Wave lengths were 575 nm and 520 nm respectively. The assays were carried out with the help of SPECORD M40 (Zeiss Jena) spectrophotometer. Comparisons between control and tested groups were made using the Cochran-Cox test. The values were considered significant with $p<0.05$.

RESULTS

In serum the calcium level increased both after three and after six weeks of intoxication vs. control group. The level of magnesium in serum was increased very significantly at the time of administration (Tab. 1)

Table 1. Magnesium and calcium concentrations (mmol · dm^{-3}) in serum of rats receiving lithium in drinking water in relation to time

Group	Mg		Ca	
	after 3 weeks	after 6 weeks	after 3 weeks	after 6 weeks
Control	1.08 ± 0.16	1.46 ± 0.24	3.01 ± 0.43	2.36 ± 0.36
Tested group	2.24 ± 0.38↑*	3.22 ± 0.52↑*	3.81 ± 0.48↑*	3.20 ± 0.40↑*

* Significant differences in comparison to control

Tissue calcium concentrations in liver and kidney increased as a consequence of lithium intoxication during all the experiment (Tab. 2). In spleen and femoral muscle no significant changes were observed, however, in heart muscle the calcium level decreased both after three and six weeks. In the brain the Ca level at first increased and then decreased (Tab. 3,4).

Table 2. Magnesium and calcium concentrations (μmol · g^{-1} of tissue) in liver and kidney of rats receiving lithium in drinking water in relation on time

Group	Liver				Kidney			
	Mg		Ca		Mg		Ca	
	after 3 w	after 6 w	after 3 w	after 6 w	after 3 w	after 6 w	after 3 w	after 6 w
Control	9.2±1,4	12.5±1.9	2.5±0,4	4.8±0.9	7.2±1.4	11.2±1.9	2.3±0.5	7.5±1.5
Tested group	8.6±1,6 ↓	9.0±1,5 ↓*	2.7±0.5 ↑	6.9±1.1 ↑	6.0±1.2 ↓	8.9±1.5 ↓	4.5±0.8 ↑*	10.2±2.1 ↑*

* Significant differences in comparison to control

Table 3. Magnesium and calcium concentrations (μmol · g^{-1} of tissue) in brain and spleen of rats receiving lithium in drinking water in relation to time

Group	Brain				Spleen			
	Mg		Ca		Mg		Ca	
	after 3 w	after 6 w	after 3 w	after 6 w	after 3 w	after 6 w	after 3 w	after 6 w
Control	4.5±0.8	9.4±1.4	2.9±0.4	3.8±0.7	6.5±0.8	12.1±2.1	2.1±0.3	6.2±0.8
Tested group	3.4±0.7 ↓	11.0±1.7 ↑	5.5±0.9 ↑*	2.5±0.4 ↓*	6.9±-.7 ↑	13.5±2.4 ↑	2.4±0.4 ↑	7.3±0.9 ↑

* Significant differences in comparison to control

Tissue magnesium concentrations decreased in liver and kidney (Tab. 2). In spleen there were no significant changes (Tab. 3). In heart muscle the magnesium level increased throughout the experiment (Tab. 4). The changes of its level in the brain and the femoral muscle were dependent on time – after three weeks decreased and after six weeks increased.

In the tested group magnesium concentration increased and associated calcium concentration decreased in the brain and the femoral muscle depending on time.

Table 4. Magnesium and calcium concentrations (μmol · g^{-1} of tissue) in femoral muscle and heart muscle of rats receiving lithium in drinking water in relation to time

Group	Femoral muscle				Heart muscle			
	Mg		Ca		Mg		Ca	
	after 3 w	after 6 w	after 3 w	after 6 w	after 3 w	after 6 w	after 3 w	after 6 w
Control	9.2±1.4	9.9±1.6	5.2±0.9	4.2±0.6	5.3±0.8	10.2±1.9	3.8±0.5	5.5±0.7
Tested group	6.4±1.1 ↓	14.5±1.9 ↑*	6.7±0.8 ↑	4.8±0.6 ↑	8.5±1.1 ↑*	14.4±2.1 ↑*	3.3±0.4 ↓	3.9±0.5 ↓

* Significant differences in comparison to control

DISCUSSION

Lithium use in psychiatry is connected with the treatment of maniac and depressive states. In our experiment animals receiving lithium showed a significant increase of Ca and Mg levels in blood serum associated simultaneously with the great reduction of strength. Lewandowicz (6) reported that lithium causes magnesium retention in blood. It should be noticed that in the tested group a significant increase of magnesium level accompanied with calcium level decrease was observed during the experiment. It is connected with the fact that magnesium and calcium are antagonists.

Lithium administration to rats for the period of one month, undertaken by Tandon et al. (12) also resulted in an increased serum calcium level. Cordova et al. (2) observed an increased calcium and magnesium levels in serum of rats caused by lithium intoxication.

The results show that very significant increase of serum magnesium level was accompanied by its decrease in liver, kidney, brain and femoral muscle after three weeks. After six weeks an increase of magnesium concentration vs. control group was observed in the brain and the femoral muscle. It can prove that the amount of magnesium rose in some tissues when its serum level still significantly increased.

CONCLUSIONS

1. Lithium caused increase of calcium and magnesium level in serum.
2. Lithium, administered in diet, influenced tissue concentrations of magnesium and calcium. It was associated with tissue displacement of these elements and their mutual interactions.

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SUMMARY

Lithium is used in medicine. However, its administration can have negative side effects, disturb the water-electrolyte equilibrium and affect the level of essential elements. For these reasons the influence of oral lithium intoxication at the dose of 150 mg Li · dm^{-3} on magnesium and calcium levels in serum and tissues of rats was investigated. The concentration of Mg and Ca in serum increased throughout the experiment. The concentration of magnesium in tissues decreased after three weeks in liver, kidney, brain and femoral muscle. The trend of the changes of calcium tissue concentration was opposite to the one observed in the case of magnesium.

Wpływ litu na homeostazę wapnia i magnezu w surowicy i tkankach szczurów

Lit jest pierwiastkiem stosowanym w medycynie. Może jednak wywierać negatywne skutki uboczne, zaburzać gospodarkę wodno-elektrolitową i wpływać na poziom zasadniczych biopierwiastków. Z tego powodu podjęliśmy badania nad wpływem doustnej intoksykacji litem w dawce 150 mg Li · dm^{-3} na poziom wapnia i magnezu w surowicy i tkankach szczurów zależnie od czasu. Stężenie Mg i Ca w surowicy wzrosło podczas całego okresu trwania eksperymentu. Stężenie magnezu w tkankach wykazywało tendencję spadkową, szczególnie po trzech tygodniach intoksykacji. Dotyczyło to wątroby, nerki, mózgu i mięśnia uda. Kierunek zmian tkankowego stężenia wapnia był przeciwny do tendencji obserwowanych w przypadku magnezu.