ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN – POLONIA
VOL. LXIII, N 1, 16 SECTIO D 2008

Medical Chemistry Department, Medical University of Lublin

MAŁGORZATA KIEŁCZYKOWSKA, IRENA MUSIK,
ANNA HORDYJEWSKA, ANNA BOGUSZEWSKA,
ANNA LEWANDOWSKA, KAZIMIERZ PASTERNAK

The effect of lithium administration in drinking water on silicon homeostasis in rats

Silicon, an element which belongs to 14th group of Mendeleev's table is a constituent of most rocks and soils. Its amount in animal organisms is small; however, it is the third most abundant trace element in humans (1). Silicon affects particularly connecting tissues (2), although it is also present in organs, muscles and blood (3). Disturbances of its level in serum were found in pathological states (2, 4, 5). Relationships between renal disturbances and silica exposure have been described (6). Silicon has also been found to play an important role in plants' metabolism (7). Despite numerous studies performed with the aim of complete understanding of the biochemical role of silicon, which have resulted in many interesting outcomes, this problem still remains unclear (3).

Lithium, the lightest metal, is known for almost two centuries. For the last fifty years the concern in the medical application of lithium salts has still been growing (8). The research regarding lithium's influence on metabolism and mechanism of its both beneficial and adverse effects has been carried out, but without final result (9). Among other things the effect of lithium on microelements' homeostasis has been revealed (10–12).

The purpose of our work was to contribute to the knowledge of lithium's action in the organism. We have been particularly concerned with the influence of oral administration of lithium on microelements' homeostasis. Aiming at unravelling this question we studied the effect of different doses of Li given in drinking water on silicon concentration in plasma and chosen tissues of rats.

MATERIALS AND METHODS

Our study was performed on two-month-old male Wistar rats (180–220 g), divided into six groups (six animals each). Five tested groups were provided with water solutions of lithium carbonate (Li_2CO_3) as the only drinking fluids. The Li_2CO_3 concentrations were as follows: 0.7; 1.4; 2.6; 3.6; 7.1 mmol Li^+dm^{-3}. The sixth group was control (C) and received redistilled water. The animals had free access to standard feed LSM and drinking fluids. Each animal was put in a separate cage and the consumption of the provided fluid as well as body weight were monitored every day. Using the obtained data the daily lithium intake was calculated for each rat: daily Li intake [mg $Li^+ \cdot kg^{-1}$ b.w.] = $V \cdot c \cdot m^{-1}$, V – consumption of the provided fluid [ml], c – concentration of the provided fluid [mg $Li^+ \cdot ml^{-1}$], m – body weight [kg]. After the experiment the average value was estimated for each rat and the mean of the daily Li intake in each group was calculated.

After four weeks the rats were killed under ketamine narcosis and blood from the heart as well as the tissues of kidney and spleen were collected. Plasma was separated and 10% (w/v) tissue homogenates were prepared in 0.1 mol dm^{-3} Tris-HCl buffer, pH = 7.4. Supernatants were obtained by centrifugation at 5000 x g for 30 min. The prepared material was stored in the temperature –18°C. In plasma and tissue homogenates the concentration of silicon was measured using the spectrophotometric method described by Wielkoszyński (13) and expressed in μmol dm^{-3} in plasma and in μmol g^{-1} of fresh tissue in kidney and spleen. The assays were performed with the help of spectrophotometer SPECORD M40 (Zeiss Jena).

Comparisons between the control and tested groups were made using c-Cochran-Cox test. Values were considered significant at $p < 0.05$. The correlations between Li daily intake and Si concentration were estimated with the help of the Pearson test.

The study was approved by I Local Ethical Commission of the Medical University of Lublin, acceptance 435/2003.

RESULTS

Lithium administration resulted in a significant decrease in silicon concentration in plasma except for the group receiving the lowest dose. On the contrary, in the studied tissues the observed results were considerably different. In kidney lower doses of lithium cased statistically significant depletion, whereas in groups receiving high doses no well-marked changes were found. In spleen Si concentration was not significantly altered as a consequence of administration of lower doses, while high doses caused significant enhancement (Table 1).

Analysis of correlations between Li daily intake and Si concentration displayed the existence of negative correlation (r = -0.645) in plasma (Fig. 1) and positive correlation (r = 0.794) in the spleen tissue (Fig. 2).

Table 1. Average Li daily intake in the group and silicon concentration in plasma and tissues of rats provided with lithium in drinking water

Li concentration (mmol Li^+ dm^{-3})	Average Li daily intake in the group (mg/kg b.w.)	Si (μmol dm^{-3})	Si (μmol g^{-1} of wet tissue)	
		plasma	kidney	spleen
	$\bar{x}$ ± SD	$\bar{x}$ ± SD	$\bar{x}$ ± SD	$\bar{x}$ ± SD
C	-	160.0 ± 43.9	3.5 ± 0.3	2.3 ± 0.4
0.7	0.6 ± 0.1	115.0 ± 47.0	1.9 ± 0.2 * ↓	2.7 ± 0.4
1.4	1.1 ± 0.2	39.2 ± 5.1 * ↓	1.9 ± 0.4 * ↓	2.0 ± 0.2
2.6	2.4 ± 0.6	46.1 ± 19.0 * ↓	2.0 ± 0.3 * ↓	2.6 ± 0.4
3.6	3.2 ± 0.7	50.0 ± 22.2 * ↓	3.1 ± 0.9	3.0 ± 0.3 * ↑
7.1	5.1 ± 0.6	43.7 ± 13.1 * ↓	3.1 ± 1.1	3.9 ± 0.7 * ↑

Values are mean ± standard deviation

* Statistical significance vs. control $p < 0.05$

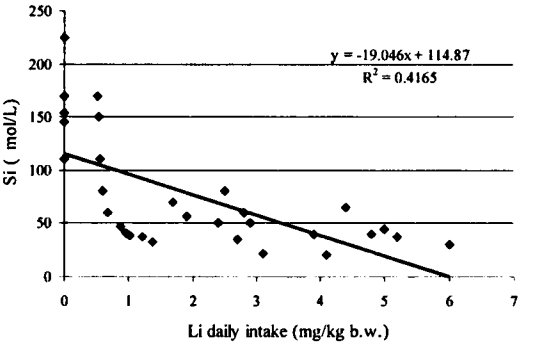

Fig. 1. Negative correlation between Li daily intake and Si concentration in plasma

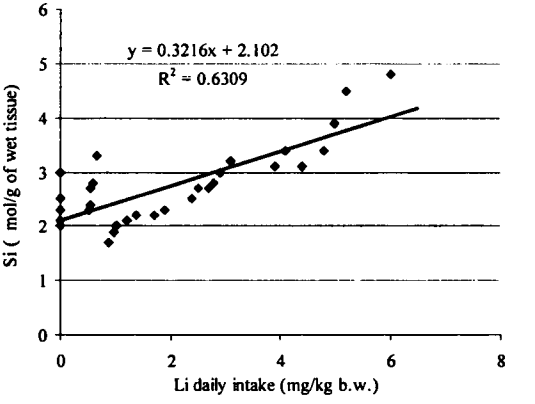

Fig. 2. Positive correlation between Li daily intake and Si concentration in spleen

DISCUSSION

Lithium salts have a significant beneficial effect in cases of psychiatric diseases (8), but Li therapy can also result in serious adverse effects. Blood and urine are the only materials available for studying biochemical parameters in human. However, Li administration causes complex changes in organs (10). We applied the animal model to evaluate lithium effect on silicon level in tissues. Our special concern was to find out if changes of serum Si reflect Li effect on tissue silicon content.

Kidney was shown to be one of the main storage organs for silicon in rats (14). Both spleen (15) and kidney (10) could be influenced as a consequence of exposure to lithium. For these reasons these two organs were chosen for studying.

Lithium administration to rats resulted in a significant decrease of silicon concentration in plasma and negative correlation between Li daily intake and plasma Si was shown. Such results are consistent with observations made by Bocca et al. (4) who reported that in patients suffering from Alzheimer's disease lower Li concentration in blood and higher Si concentration in serum in comparison with healthy persons were noticed. This effect does not reflect Li influence on Si content in tissues.

Our observations regarding changes of Si content in kidney are unexpected. The Si depletion observed in groups given low doses accompanied by restoration of Si in the animals provided with higher doses is difficult to explain. The same Li doses given for a period of eight weeks caused no significant changes (12). It proves that lower doses of lithium exert a transient effect in the first period of exposure, which in some time can be overcome by organisms. More data should be obtained to this question resolve. Observations concerning the tissue of spleen have also revealed that lithium effect on Si homeostasis in this organ depends strongly on the applied dose.

Concluding, the Li effect on Si metabolism is both time- and dose-dependent but further studies concerning this problem should be carried out.

CONCLUSIONS

1. Changes of plasma silicon concentration do not reflect lithium's effect on Si homeostasis in tissues of kidney and spleen.
2. Lithium exerts complicated, dose-dependent influence on Si homeostasis in the tissue of kidney and spleen.

REFERENCES

1. Bissé E. et al.: Reference values for serum silicon in adults. Anal. Biochem., 337, 133, 2005.
2. Bulikowski W., Lingas W.: Wstępne badania stężenia krzemu w surowicy w zespołach reumatyzmu tkanek miękkich i wybranych chorobach skóry. Biul. Magnezol., 1, 50, 1996.
3. Sripanyakorn S. et al.: Dietary silicon and bone health. Nutr. Bull., 30, 222, 2005.
4. Bocca B. et al.: Monitoring of chemical elements and oxidative damage in patients affected by Alzheimer's disease. Ann. Ist. Super. Sanita, 41, 197, 2005.
5. Visconti A. et al.: Concentration of elements in serum of patients affected by multiple sclerosis with first demyelinating episode: A six-month longitudinal follow-up study. Ann. Ist. Super. Sanita, 41, 217, 2005.
6. Governa M. et al.: Variability of biological effects of silicas: Different degrees of activation of the fifth component of complement by amorphous silicas. Toxicol. Appl. Pharmacol., 208, 68, 2005.
7. Fauteux F. et al.: Silicon and plant disease resistance against pathogenic fungi. FEMS Microbiol. Lett., 249, 1, 2005.
8. Fawcett J. A.: Lithium combinations in acute and maintenance treatment of unipolar and bipolar depression. J. Clin. Psychiatry, 64 (suppl. 5), 32, 2003.
9. Gould T. D., Manji H. K.: Glycogen synthase kinase-3: a putative molecular target for lithium mimetic drugs. Neuropsychopharmacology, 30, 1223, 2005.
10. Chmielnicka J., Nasiadek M.: The trace elements in response to lithium intoxication in renal failure. Ecotoxicol. Environ. Saf., 55, 178, 2003.
11. Kiełczykowska M. et al.: The influence of different doses of lithium administered in drinking water on zinc and copper in chosen tissues of rats. Pol. J. Environ. Stud., 15, 94, 2006.
12. Kiełczykowska M. et al.: The influence of different doses of lithium administered in drinking water on silicon concentration in plasma and chosen tissues of rats. Pol. J. Environ. Stud., 15, 74, 2006.
13. Wielkoszyński T.: Zmodyfikowana, spektrofotometryczna metoda oznaczania krzemu w materiale biologicznym. Diagn. Lab., 36, 377, 2000.

14. Almeida T. et al.: Silicon and iron levels in tissues of animals treated with a "ferromagnetic ceramic" with oncotherapeutic potential (anti-tumor) value. J. Trace Elem. Med. Biol., 16, 255, 2002.
15. Shah M. S., Hassan G.: Structural changes in rat spleen after lithium therapy. Jk. Practitioner, 4, 215, 1997.

SUMMARY

The experiment aimed at determining the effect of different doses of lithium administered in drinking water on silicon homeostasis in plasma and chosen tissues of rats. For a period of four weeks rats were administered water solutions of Li_2CO_3. The concentrations were: 0.7; 1.4; 2.6; 3.6; 7.1 mmol Li^+ dm^{-3}. In plasma and tissue supernatants silicon concentration was determined spectrophotometrically using the Wielkoszyński method. Lithium treatment resulted in a significant decrease of silicon concentration in plasma. In kidney the administration of lower doses resulted in a significant Si depletion, whereas higher doses caused no changes. In spleen lower doses caused no changes, whereas administration of high doses resulted in a well-marked increase. Negative correlation between Li daily intake and plasma Si concentration (r = -0.645) as well as positive one (r = 0.794) in spleen were found. The changes of Si concentration in plasma do not correspond with lithium's effect on Si content in tissues. Further studies are needed to explain lithium's effect on Si homeostasis in kidney and spleen.

Wpływ podawania litu w wodzie pitnej na homeostazę krzemu u szczurów

Doświadczenie zostało przeprowadzone w celu określenia wpływu różnych dawek litu podawanego w wodzie pitnej na homeostazę krzemu w osoczu i wybranych tkankach szczurów. Przez okres czterech tygodni szczurom podawano wodne roztwory Li_2CO_3, których stężenia wynosiły: 0,7; 1,4; 2,6; 3,6; 7,1 mmol Li^+ dm^{-3}. W osoczu i homogenatach tkankowych oznaczono stężenie krzemu metodą spektrofotometryczną opisaną przez Wielkoszyńskiego. Podawanie litu spowodowało znaczny spadek stężenia krzemu w osoczu. W tkance nerki niższe dawki spowodowały znaczące obniżenie, natomiast podawanie dawek wyższych nie spowodowało istotnych zmian. W tkance śledziony niższe z zastosowanych dawek nie spowodowały znaczących zmian, natomiast w grupach otrzymujących wysokie dawki zaobserwowano znaczny wzrost Si. Zanotowano ujemną korelację pomiędzy dziennym pobraniem litu a stężeniem krzemu w osoczu (r = -0,645) oraz dodatnią w tkance śledziony (r = 0,794). Zmiany stężenia krzemu w osoczu nie odzwierciedlają wpływu litu na zawartość krzemu w tkankach. Kontynuowanie prac jest konieczne w celu wyjaśnienia wpływu litu na homeostazę krzemu w tkankach nerki i śledziony.