REVISTA ESPAÑOLA DE FISIOLOGIA, 47 (2), 87-90, 1991

Influence of Lithium and Exercise on Serum Levels of Copper and Zinc in Rats

A. Córdova and J. F. Escanero*

Departamento de Fisiología
Colegio Universitario de Soria
Universidad de Valladolid
42080 Soria (Spain)

(Received on October 19, 1990)

A. CÓRDOVA and J. F. ESCANERO. *Influence of Lithium and Exercise on Serum Levels of Copper and Zinc in Rats.* Rev. esp. Fisiol., 47 (2), 87-90, 1991.

The variations in serum levels of Cu and Zn induced by exercise in rats undergoing Li therapy are determined. The results show that exercise until exhaustion leads to a reduction in the Li concentration, which is more pronounced in rats subjected to training (to 50 % maximum capacity) in the week before the test. The serum levels of Zn and Cu increased significantly with exhaustion in untrained rats, while there were no significant alterations in trained rats, except for serum Zn in those not treated with Li. The modifications in serum induced by exhaustion are lower in rats treated with Li. It is likely that Li and exercise have opposite effects on the tissue distribution of the two ions studied.

Key words: Exercise, Training, Exhaustion, Li, Zn, Cu.

Lithium has been widely used to prevent the manic phases in manic-depressive illness (4). The alterations produced in plasma levels of the alkali metals Na and K, and of the alkaline-earth metals Ca and Mg, have been extensively studied (2, 3, 7, 12, 14); in contrast, the variation of the trace elements Cu and Zn are unknown. However, their variation in plasma after exercise has been widely studied (1, 5, 6, 16-18, 25), with contradictory results.

Taking into account the large number of patients who may be treated with Li, and who take exercise for professional or recreational reasons, the relation between Li therapy and exercise is of interest from the point of view of both medicine and sport. Therefore, this paper aims to analyze the modifications in the serum levels of Zn and Cu in rats treated with Li and subjected to physical exercise.

* To whom all correspondence should be addressed: Departamento de Biomedicina (área de Fisiología), Facultad de Medicina, Universidad de Zaragoza, 50009 Zaragoza (Spain).

Materials and Methods

Sixty male Wistar rats weighing 225-250 g, were divided into groups (n=10) as follows: 1. Control; 2. Rats performing exercise until exhaustion; 3. Rats treated with Li (3 mEq LiCl per kg b. w. in 250 µl, daily i.p. for 7 days); 4. Rats treated with Li (same dose as group 3), and per forming exercise until exhaustion; 5. Trained rats (15 min/day, for 7 days), and 6. Trained rats treated with Li, with the same time and dose as the above groups (3 and 5).

The exercise was performed in a tub (50 × 90 × 90 cm) containing water maintained at a constant temperature (20 °C) by a thermostat, with waves produced by bubbling air in order to induce regular swimming. The rats in groups 2 and 4 were exercised to exhaustion (determined by the moment they remained underwater for more than 15 s). The trained rats (groups 5 and 6) were trained in the same tub with water at 20 °C. The duration of training was determined by measuring the time taken to reach exhaustion (33 ± 4 min). It was estimated that 15 minutes at the temperature of the water was approximately 50 % of maximum capacity.

Lithium was administered at the above dose via intraperitoneum by daily injections for 7 days.

At the end of the experiment, the rats were anesthetized with sodium pentobarbital (5 mg/100 g b.w.) and a blood sample was taken from the peritoneal aorta. Polystyrene material (syringes and tubes) was used for collecting and centrifugating the blood.

The serum concentrations of Cu and Zn were determined by atomic absorption spectrophotometry (Perkin Elmer 272). Serum Li concentration was measured by emission photometry.

Student's test was used to compare the means of groups which had shown significant differences in ANOVA.

Results and Discussion

In rats treated with Li, exercise was found to provoke a significant reduction in lithemia, while the difference in rats exercised to exhaustion was not found to be significant.

After three hours exercise, renal clearance of Li was found to fall in rats, while that of Na, K and creatinine was unchanged (21). This result, together with theoretical speculation, helped to establish the belief that exercise until exhaustion produced a predisposition to Li intoxication, making it necessary therefore to reduce the dose of Li in psychotic patients who practised sport (11). From a clinical viewpoint, it has been accepted that patients taking Li can suffer intoxication if they perform strenuous exercise, particularly if they sweat abundantly (10, 13, 19, 20). In contrast, other authors (11, 15, 23) state that losses of Li in perspiration can be followed by reduced plasma concentrations of that element. The results of this study suggest that, since there is no perspiration in this experiment due to the water temperature, the reduction in serum levels of Li may be due to a redistribution of the element in tissue (11), migrating from the blood to the tissues. From this viewpoint, the fall in Li in serum would be connected with water and electrolyte changes produced during prolonged exercise, especially due to the fact that the volume of plasma appears to be maintained at the expense of the incracellular volume (8), as corroborated by the hematocrit values found in normal and trained groups (35 % and 44 %, repectively).

Table I also shows the serum concentrations of Zn and Cu in the different groups used in this study. Exercise to exhaustion raises the concentration of these ions, the increase being greater in untreated rats. The administration of Li in the control situation was not found to produce significant variations in the serum concentrations.

Table I. *Serum concentrations of Li, Zn and Cu in the different groups.*
Exhaustion (one session until exhaustion) and trained (15 min/day, 7 days) and the same groups with a lithium supplement (3 mEq/kg b.w.). Values are media ± SD, n=10. The serum concentration of Li in untreated rats was negligible.

	Li (mEq/l)	Zn (µg/100 ml)	Cu (µg/100 ml)
Control	—	102 ± 5.9	158 ± 6.2
Exhaustion	—	145 ± 6.5[a]	198 ± 21.4[a]
Treated with Li	0.122 ± 0.011	106 ± 10.8	154 ± 15.4
Exhaustion + Li	0.115 + 0.017	128 ± 8.3[a]	165 ± 7.3[a]
Trained	—	113 ± 7.9[b]	163 ± 13.6
Trained + Li	0.097 ± 0.005[a]	118 ± 9.3	159 ± 11

[a] $p \leq 0.001$; [b] ≤ 0.01.

There is no agreement in the literature as regards the variations of Zn in serum after exercise. VAN RIJ *et al.* (25) reported a fall in Zn concentration immediately after finishing exercise; in contrast, ANDERSON *et al.* (1) reported that this fall did not appear until 12 hours after finishing the exercise, and reported a 1.5 fold increase in urinary excretion of Zn compared with subjects who had not exercised; finally, other authors (5, 17) found increases in the plasma concentrations of Zn after exercise, which coincides with the results of this study. In this line, OHNO *et al.* (17) observed that the changes reversed 30 minutes after finishing exercise. The variations in Zn during exercise have been shown to be time-dependent (7).

With regard to training, the results presented here reveal significant differences in serum Zn levels. In rats treated with Li, training also increased the serum concentration of Zn, though not significantly, probably due to the greater dispersion of the results. OHNO *et al.* (18) reported that training did not increase the overall concentration of Zn in plasma, although it did increase the Zn bound to albumin.

Copper behaves in a similar way. Our results agree with those of NASOLODIN (16), who showed that the concentration of Cu in plasma increased after intense exercise, although ANDERSON *et al.* (1) reported that no such variation occurred. With regard to training, no variation in serum Cu levels was observed in the control group, or in those treated with Li.

Since some authors (22, 24) have described modifications in various bodily fluids, including plasma, due to treatment with Li, it could be assumed that the two variables studied here, exercise and Li, have opposing effects on the distribution in tissue. In this regard, a similar effect in rats undergoing exercise after treatment with Sr has been reported (9).

Resumen

Se determinan las variaciones en los niveles séricos de Cu y Zn, inducidas por el ejercicio, en ratas sometidas a tratamiento con Li. Los resultados muestran que el ejercicio hasta el agotamiento provoca descensos en las concentraciones de Li, más pronunciados en las ratas que previamente han estado sometidas a entrenamiento (50 % de su capacidad máxima) durante la semana anterior a la prueba. Las tasas séricas de Zn y Cu se incrementan significativamente con el agotamiento en ratas no entrenadas, mientras que en las entrenadas sólo es significativa la alteración del Zn sérico en las no tratadas con Li. Las modificaciones séricas inducidas por el agotamiento son menores en las ratas que toman Li. Probablemente, los

efectos provocados por el Li y el ejercicio sobre la distribución tisular de ambos iones estudiados sean de sentido contrario.

Palabras clave: Ejercicio, entrenamiento, agotamiento, Li, Zn, Cu.

References

1. Anderson, R. A., Polansky, M. M. and Bryden, N. A.: *Biol. Trace Elem. Res.*, 3, 327-336, 1984.
2. Aronoff, M. S., Evens, R. G. and Durell, J.: *J. Psychiat. Res.*, 8, 139-159, 1971.
3. Birch, N. J. and Jenner, F. A.: *Br. J. Pharmacol.*, 47, 586-594, 1973.
4. Cade, J. F. J.: *Med. J. Aust.*, 2, 349-352, 1949.
5. Córdova, A., Giménez, M. and Escanero, J. F.: *J. Trace Elem. Electrol. Health Dis.*, 4, 189-193, 1990.
6. Córdova, A., Soteras, F., Castellano, M. C., Elósegui, L. M.ª and Escanero, J. F.: *Arch. Ftad. Zarag.*, 29, 56-159, 1989.
7. Córdova, A., Soteras, F., Elósegui, L. M.ª and Escanero, J. F.: *Actas Luso Esp. Neurol. Psiquiatr. Cienc. Afines*, 18, 103-109, 1990.
8. Costill, D. L.: *Ann. N. Y. Acad. Sci.*, 301, 160-174, 1977.
9. Escanero, J. F., Córdova, A. and Giménez, M.: In "Nutrition et Sport" (H. Monod, ed.) Masson et Cie, París, 1989, pp. 138-146.
10. Granoff, A. L. and Davis, J. M.: *J. Clin. Psychiatry*, 39, 103-107, 1978.
11. Jefferson, J. W., Greist, J. H., Clagnaz, P. J., Eischens, R. R. Marten, W. C. and Evenson, M. A.: *Am. J. Psychiatry*, 139, 1593-1595, 1982.
12. Lapeña, M. F., Muñoz-Tejedor, D. and Escanero, J. F.: *IRCS Med. Sci.*, 6, 404, 1978.
13. McSigan, C.: *Med. J. Aust.*, 1, 89-92, 1979.
14. Mellerup, E. T., Plenge, P. and Rafaelsen, O. J.: *Acta Psychiat. Scand.*, 53, 360-370, 1976.
15. Miller, E. B., Pain, R. W. and Skripal, P. J.: *Br. J. Psychiatry*, 133, 477-478, 1978.
16. Nasolodin, V. V.: *Gig. Sanit.*, 12, 21-24, 1985.
17. Ohno, H., Yamashita, K., Doi, R., Yamamura, K., Kondo, T. and Taniguchi, N.: *J. Appl. Physiol.*, 58, 1453-1458, 1985.
18. Ohno, H., Yamashita, K., Ogawa, K. and Taniguchi, N.: *Bull. Phys. Fitness Res. Inst.*, 65, 29-37, 1987.
19. Saran, B. M.: Br. J. Phsychiatry, 134, 445, 1979.
20. Schou, M.: In "Lithium treatment of manic-depressive illness". S. Karger A. G., Basel, 1980, p. 48.
21. Smith, D. F.: *Int. Pharmacopsychiatry*, 8, 217-220, 1973.
22. Suva, J. and Musil, F.: *Pharmacochem. Libr.*, 8, 413-418, 1985.
23. Tonks, C. M.: *Br. Med. J.*, 2, 1396-1397, 1977.
24. Turpin, J. P., Schlagenhauf, C. K. and Creson, D. L.: *Am. J. Psychiatry*, 125, 536-542, 1968.
25. Van Rij, A. M., Hall, M. T., Lynis, G., Bray, J. and Pories, W. J.: *Biol. Trace Elem. Res.*, 10, 99-205, 1986.