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Effect of Strenuous Exercise on Serum Lithium Level in Man

BY JAMES W. JEFFERSON, M.D., JOHN H. GREIST, M.D., PETER J. CLAGNAZ, M.D., ROGER R. EISCHENS, M.S., WILLIAM C. MARTEN, M.S., AND MERLE A. EVENSON, PH.D.

The authors examined the effect of strenuous exercise on the serum lithium levels of four healthy, conditioned athletes who were stabilized on lithium carbonate for 7 days and who ran a 20-km race under hot, humid conditions. The subjects became substantially dehydrated during the race, and their serum lithium levels decreased, suggesting that sweat lithium loss may be substantial. (The sweat-to-serum ratio for lithium exceeded that for sodium by a factor of 4.) The authors conclude that contrary to widely held belief, heavy sweating may not increase the risk of lithium intoxication. (Am J Psychiatry 139:1593–1595, 1982)

It is widely believed that patients taking lithium risk lithium intoxication when undergoing strenuous exercise, especially if they sweat copiously (1–4). Similar concern has been expressed about non-exercise-related thermal stressors, such as sauna exposure (5) or fever (1980 official package insert for lithium carbonate). It is felt that sweating would cause an increased serum lithium level through both dehydration (volume contraction) and sodium loss (resulting in compensatory renal retention of sodium and lithium). A minority opinion is that lithium lost through the process of sweating may actually lead to lower serum lithium levels (6, 7).

This present study was prompted by requests to the Lithium Information Center from clinicians concerned about the dangers of long-distance running in patients being treated with lithium. Considering the number of people currently being treated with lithium and the number of people either vocationally or recreationally engaged in strenuous activity, the population at risk seemed sizable. Consequently, we examined the effect of strenuous exercise on the serum lithium levels in four volunteers who ran a 20-km race under hot, humid conditions (temperature, 29°C; relative humidity, 75%).

METHOD

Four healthy, heat-acclimated, experienced male runners (age range, 38–43 years; weight range, 71.9–85.8 kg; distance range of weekly training, 42–100 km) took 300 mg t.i.d. of lithium carbonate for 7 days before a 20-km race. The subjects' food and fluid intake

Received July 15, 1981; revised Oct. 6, 1981; accepted Oct. 20, 1981. From the Department of Psychiatry, University of Wisconsin Center for Health Sciences, Madison. Address reprint requests to Dr. Jefferson, Department of Psychiatry, University of Wisconsin, CSC, 600 Highland Ave., Madison, WI 53792.

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during the period of the experiment was not restricted, and they followed their usual dietary routines.

On the day preceding the race three sets of blood samples were drawn from each subject while he was resting at 45-min intervals beginning 12 hours after the last previous lithium dose (control sample). The followng day blood samples were drawn at the start, midpoint, and finish of the race at time intervals corresponding to the control drawings. On the day of the race the first sample was drawn 12 hours after the last lithium dose. Sweat was collected as it dripped off the subjects at the end of the race. All samples were then analyzed for lithium, sodium, potassium, and chloride. The weight of each subject was recorded at each sampling point. Data were subjected to a repeated measures analysis of variance with further comparisons of trends (linear and quadratic) and selected comparison of means (Scheffé test).

RESULTS

Under control (resting) conditions, the subjects showed a slight decrease over time in their serum lithium levels, although during exercise the decrease in their serum lithium levels was more pronounced (table 1). The initial level on the day of the race was significantly higher than the initial control sample (Scheffé test, $F=22.80$, $df=5, 15$, $p<.01$). The decrease over time during the race was greater than during the control period. Repeated measures analysis of variance showed a significant interaction between conditions (control, race) and time (0 min, 45 min, and 90 min) ($F=33.51$, $df=2, 6$, $p<.001$) for lithium and a significant linear trend difference for this interaction ($F=43.03$, $df=1, 3$, $p<.01$).

Under control conditions, the subjects' serum sodium, potassium, and chloride values remained stable over the three sampling periods. During exercise, their serum sodium and chloride levels increased over time with maximum values occurring at 90 min. Serum potassium levels did not vary significantly over the period of exercise (table 1). Repeated measures analysis of variance showed significant interactions between conditions (control, race) and time (0 min, 45 min, and 90 min) for sodium ($F=6.42$, $df=2, 6$, $p<.03$) and chloride ($F=48.65$, $df=2, 6$, $p<.001$).

Because the collection technique was not standardized, sweat lithium and electrolyte concentrations could not be reliably measured. It was possible, however, to calculate a sweat-to-serum ratio for each ion. This ratio was 3½ to 4 times higher for lithium and potassium than for sodium and chloride, suggesting that proportionately more lithium than sodium is lost in sweat.

The extent of the subjects' dehydration during the race was substantial, as evidenced by their weight loss, ranging from 1.9 to 3.75 kg (2.6%–4.7% of total body weight).

All subjects completed the race without difficulty, and their finishing times were consistent with past performances. None experienced neurological, gastrointestinal, or other symptoms suggestive of lithium toxicity.

TABLE 1. Serum Lithium and Electrolyte Levels in Four Men Over Time at Rest and During Strenuous Exercise

Condition and Time After First Drawing[a]	Lithium (mEq/liter)		Sodium (mEq/liter)		Potassium (mEq/liter)		Chloride (mEq/liter)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
At rest								
0 min	.48	.10	142.3	1.5	4.0	.3	106.0	1.8
45 min	.46	.10	141.8	1.5	4.3	.6	105.3	1.3
90 min	.46	.10	141.0	.8	4.4	.5	105.0	1.2
Strenuous exercise								
0 min	.52	.10	143.0	1.4	3.9	.5	105.0	.8
45 min	.44	.08	143.8	1.5	4.0	.1	108.5	1.3
90 min	.42	.08	146.0	2.2	4.0	.2	109.3	2.2

[a]First blood sample was drawn 12 hours after last previous dose of lithium.

DISCUSSION

Smith (8) showed in rats that 3 hours of strenuous exercise in a motor drum activity wheel caused a significant ($p<.001$) decrease in renal lithium clearance, although sodium, potassium, and creatinine clearance remained unchanged. He implied that strenuous exercise in man might produce similar results and that lithium dose reduction might be necessary to avoid toxicity. His study, together with theoretical speculations, has led to the widespread, but unsubstantiated, belief that strenuous exercise predisposes one toward lithium intoxication.

On the other hand, Miller and associates (6) found that the lithium content of pilocarpine-stimulated forearm sweat ranged from 1.2 to 4.6 times (mean, 2.3 times) higher than the serum lithium concentration, and they suggested (as did Amdisen [7]) that under conditions of heat-induced sweating, lithium loss through the skin may be of clinical importance. This view is supported by our finding that exercise-induced sweating and dehydration were associated with a decrease in serum lithium level. This decrease must be contrasted to the slight yet significant exercise-related increase in serum sodium and chloride concentration.

Further support for an exercise-related reduction in serum lithium level is provided by comparing the zero-time lithium levels on the control and race days. The lower value (.48 mEq/liter) on the control day was obtained following a day of strenuous exercise (training), and the higher value (.52 mEq/liter) followed a day of rest (prerace training break).

The inaccuracies of "in the field" sweat collection did not allow a reliable determination of absolute sweat lithium loss. However, because sweat sodium (especially in heat-acclimated individuals) is hypotonic to serum while sweat lithium appears to be hypertonic, the observed decrease in serum lithium levels during exercise may well be explained by this mechanism. Our finding that the sweat-to-serum ratios for lithium and potassium were about 3½ to 4 times greater than those for sodium and chloride are in keeping with ratios calculated from the data of Amatruda and Welt (9), which showed a potassium ratio 2–10 times greater than the sodium ratio.

Exercise-related shifts among body compartments of water, electrolytes, and lithium could also contribute to the variation in serum lithium level, especially because plasma volume appears to be maintained at the expense of intracellular volume during prolonged exercise (10). It is also possible that changes in intracellular lithium level do not parallel those in serum, and, conceivably, tissue lithium levels could remain unchanged or even increase.

We advise caution in extrapolating our findings to all clinical situations, stressing that our subjects were healthy, conditioned athletes who had taken lithium for 7 days, who had ad libitum access to food (including dietary sodium) and fluids over the course of the experiment, and who were restricted to 90 min of strenuous exercise. For example, lithium intoxication has been reported in association with marked dietary restriction and thermal sweating (sauna) over a 3-day period (5).

Nonetheless, it would seem that strenuous exercise in hot weather is more likely to cause a decrease rather than an increase in serum lithium level and that patients under such conditions may require either no change or an increase in lithium dose to maintain therapeutic levels. The prior assumption that heavy sweating increases the risk of lithium intoxication no longer appears valid, and prophylactic reduction in lithium dose in anticipation of such an event would be ill advised. However, because of the many variables associated with any alteration in fluid and electrolyte balance, careful monitoring of serum lithium level is strongly recommended under such conditions.

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