# EFFECTS OF LITHIUM SALTS ON EXPERIMENTAL NEUROGENIC LESIONS OF THE STOMACH AND HEART

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Elucidation of the mechanisms of neurogenic lesions of the internal organs and the development of ways of their pharmacological correction are of the greatest importance for progress in problems in general pathology and biochemical pharmacology. It has been shown that an important role in the pathogenesis of these lesions belongs to the sympathetic nervous system and noradrenalin [1, 3] and that lithium salts – chloride and hydroxybutyrate – inhibit enhanced sympathetic activity [4, 5] and abolish the toxic effects of adrenalin [4, 11].

It was accordingly decided to study the effects of lithium chloride and lithium hydroxybutyrate on neurogenic lesions of the stomach and heart arising under conditions of acute stress.

## EXPERIMENTAL METHOD

Experiments were carried out on noninbred male albino rats weighing 180-220 g. Neurogenic lesions of the stomach and heart were induced by combined immobilization for 3 h and electrical stimulation of the hungry animals. Stimulation was applied through needle electrodes implanted beneath the skin of the forelimbs, as square pulses of direct current (50 Hz, 7.5 V, pulse duration 10 msec).

Lithium salts were injected intraperitoneally in doses of 50 mg/kg (chloride) and 90 mg/kg (hydroxybutyrate). The preparations were given prophylactically 30 min before the beginning of stimulation, and therapeutically twice a day for 3 days (the first injection was given immediately after stimulation). In each series of experiments (15 rats) intact animals served as the control. At the end of the experiment all animals were decapitated. The stomach was removed, opened along the greater curvature, washed out with cold physiological saline and, after quick visual inspection, was immersed in liquid oxygen. To estimate the severity of damage to the gastric mucosa, the mean number of tissue defects per animal was counted in each group. The heart was removed, washed in cold physiological saline, and immersed in liquid oxygen.

Changes in the level of creatine phosphate, a high-energy compound [16], were studied as an early sign of tissue changes in stress injuries of tissues.

TABLE 1. Effect of Lithium Chloride on Creatine Phosphate Concentration (μmoles/g) in Tissues of Stomach Wall and Myocardium of Rats during Electrical Stimulation for 3 h and Immobilization (M ± m; n = 15)

| Experimental conditions | Stomach | | Myocardium | |
|---|---|---|---|---|
| | prophylactic | therapeutic | prophylactic | therapeutic |
| Control | 0,52±0,03 | 0,47±0,04 | 1,60±0,12 | 1,60±0,15 |
| Electrical stimulation and immobilization | 0,16±0,02 | 0,24±0,05 | 1,00±0,13 | 1,00±0,10 |
| Electrical stimulation and immobilization, lithium chloride | 0,34±0,02 | 0,40±0,05 | 1,10±0,11 | 1,00±0,12 |
| Lithium chloride | 0,52±0,06 | 0,42±0,04 | 1,15±0,06 | 1,10±0,11 |

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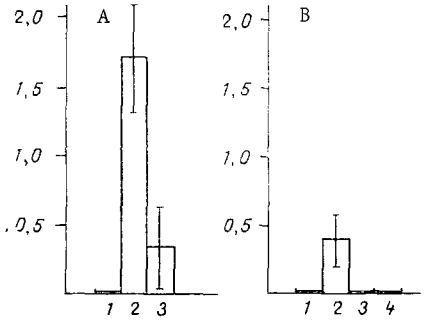


Fig. 1. Prophylactic (A) and therapeutic (B) effect of LiCl on ulcerations of gastric mucosa caused in rats by electrical stimulation for 3 h and immobilization. Abscissa, duration of action (in h); ordinate, number of regions of destruction of mucosa. 1) control (intact rats), 2) electrical stimulation and immobilization, 3) electrical stimulation and immobilization + LiCl, 4) LiCl.

TABLE 2. Effect of Lithium Hydroxybutyrate on Concentration of Creatine Phosphate (μmoles/g) in Tissues of Stomach Wall and Myocardium of Rats during Electrical Stimulation for 3 h and Immobilization (M ± m; n = 15)

| Experimental conditions | Stomach | | Myocardium | |
|---|---|---|---|---|
| | prophylactic | therapeutic | prophylactic | therapeutic |
| Control | 0,63±0,03 | 0,59±0,02 | 1,13±0,01 | 0,96±0,08 |
| Electrical stimulation and immobilization | 0,25±0,04 | 0,27±0,02 | 0,44±0,05 | 0,24±0,08 |
| Electrical stimulation and immobilization, lithium hydroxybutyrate | 0,57±0,05 | 0,52±0,12 | 0,84±0,10 | 0,75±0,08 |
| Lithium hydroxybutyrate | 0,52±0,05 | 0,46±0,05 | 0,79±0,08 | 0,92±0,06 |

## EXPERIMENTAL RESULTS

The results show that lithium chloride had a marked prophylactic action and prevented ulceration of the gastric mucosa due to stress (Fig. 1A). Its therapeutic effect was equally marked (Fig. 1B). A definite prophylactic and therapeutic effect of lithium chloride also was observed in a study of the creatine phosphate content in tissues of the stomach wall (Table 1). Lithium hydroxybutyrate had a similar, but more marked prophylactic and therapeutic action as reflected in the creatine phosphate level in tissues of the stomach and myocardium (Table 2).

Certain conclusions can be drawn from the results of these investigations. The fact that both lithium salts gave similar therapeutic and prophylactic effects against neurogenic lesions of the gastric mucosa and myocardium due to acute stress indicates a role of $Li^+$ ions in these effects. The ability of $Li^+$ to inhibit enhanced sympathetic activity, mentioned above, and to weaken the action of catecholamines [4, 5, 11] is connected with its many-sided action on the catecholaminergic system: It reduces catecholamine release [14, 25], increases their uptake [15, 22], activates monoamine oxidase, stimulates intraneuronal catecholamine metabolism [24], inhibits adenylate cyclase activity [15, 23], reduces the catecholamine concentration in the brain [17] and the sensitivity of catecholaminergic receptors [18, 20, 26], and it increases the GABA concentration in the brain [19].

Everything stated above confirms the conclusion that neurogenic lesions of tissues under conditions of acute stress are associated with involvement of the sympathetic (catecholaminergic) systems in the process. The results are in agreement with those obtained by many workers who have shown that the adrenergic system participates in the mechanism of stress injuries to tissues.

Lithium hydroxybutyrate has a stronger normalizing action than lithium chloride. This fact is in agreement with the results of investigations [2, 4, 5, 11, 12] into the effect of lithium chloride and lithium hydroxybutyrate on the disturbed cardiac rhythm, and also on other pathological processes [8, 10]. Sodium hydroxybutyrate can prevent stress injuries to the myocardium and stomach [6] and disturbances of myocardial energy metabolism [7].

It is interesting that under normal conditions $Li^+$ can itself lower the creatine phosphate level in tissues (Table 2). Meanwhile, under conditions of neurogenic stress lesions of the tissues, $Li^+$ increases the reduced concentration of this high-energy compound. Lithium thus possesses to some extent the properties of a normalizer of tissue processes. This action of lithium is exhibited at the membrane level in the form of its influence on the excited neuronal membrane, by inhibiting $Ca^{++}$ inflow [22].

The hydroxybutyrate anion, with its antihypoxic and trophic action, potentiates the normalizing effects of $Li^+$, and for that reason lithium hydroxybutyrate acquires even more marked and unique nootropic properties.

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