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EFFECT OF LITHIUM HYDROXYBUTYRATE ON THE PARAMETERS OF ACUTE INFLAMMATION

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Lithium hydroxybutyrate, which is used in the treatment of several pathological conditions (shock, diseases of the nervous and cardiovascular systems, allergic reactions), attracts increasing attention [2]. The aim of this investigation was to study some models of acute inflammation and the effect of lithium hydroxybutyrate on them.

EXPERIMENTAL METHOD

Experiments were carried out on 81 male Wistar rats weighing 120-150 g. Lithium hydroxybutyrate, dissolved in isotonic sodium chloride solution, was injected subcutaneously into the dorsal region of the animals in a dose of 200 mg/kg, 30 min before administration of the inflammation-inducing agents. As one model of inflammation peritonitis developing in the animals 3 h after intraperitoneal injection of 1 ml of a 0.1% aqueous solution of silver nitrate was used. The animals were then decapitated and the volume of fluid in the peritoneal cavity was determined. The mesentery was fixed with 96° alcohol, stained with 0.05% toluidine blue, and the number of degranulated mast cells was counted among 100 cells in the preparation. Acute edema of the rats' hind limbs after subplantar injection of 0.1 ml of an aqueous solution of histamine ($1 \cdot 10^{-7}$ g/ml), serotonin ($1 \cdot 10^{-7}$ g/ml), or prostaglandin E_2 (PGE_2; from Upjohn Ltd., England) — which, in a concentration of 10^{-6} g/ml, can also induce an acute inflammatory reaction [4] — was used as the other models of inflammation. Control animals were given an injection of 0.1 ml of distilled water. The volume of the limbs was measured 1 h after injection of the phlogogene in a measuring cylinder, the skin temperature of the limb was measured with an electrothermometer (TPEM-1), and sensitivity to pain was measured with an "Analgesymeter for the rat paw" (Italy). The results were subjected to statistical analysis [5].

EXPERIMENTAL RESULTS

In the experiments of series I 3 h after injection of silver nitrate into the peritoneal cavity of the animals a reddish brown fluid appeared (diapedesis of erythrocytes) and total degranulation of the mast cells occurred in the mesentery (Table 1).

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TABLE 1. Effect of Lithium Hydroxybutyrate on Volume of Intraperitoneal Fluid and on Degranulation of Mast Cells in Mesentery of Rats with Peritonitis Induced by Silver Nitrate (M ± m)

Experimental conditions	Number of animales	Volume of intraperitoneal fluid, ml	Degranulation of mast cells, %
Intact animals	6	0,1±0,04*	3,0±1,3*
Control (distilled water)	6	0,2±0,09*	2,3±0,9*
Lithium hydroxybutyrate	6	0,1±0,01*	3,1±1,2*
Silver nitrate	6	1,3±0,07	99,8±1,2
Lithium hydroxybutyrate + silver nitrate	9	0,6±0,08*	67,0±1,1*

Legend. *P > 0.05 compared with injection of silver nitrate.

TABLE 2. Volume, Temperature, and Sensitivity to Pain of Rat Hind Limbs after Subplantar Injection of Histamine, Serotonin, and PGE_2, and after Preliminary Administration of Lithium Hydroxybutyrate (M ± m)

Experimental conditions	Volume of paw, ml^3	Temperature, °C	Pain threshold, g
Intact animals	1,0±0,05	24,3±0,95	294,5±12,8
Control (distilled water)	0,9±0,01	23,8±0,44	290,1±19,3
Lithium hydroxybutyrate	1,1±0,03	24,7±0,35	286,7±16,7
Histamine	1,8±0,06*	31,9±0,51*	117,8±15,9*
Lithium hydroxybutyrate + histamine	1,2±0,04	25,7±1,02	255,1±26,8
Serotonin	1,9±0,08*	30,2±0,89*	125,0±14,7*
Lithium hydroxybutyrate + serotonin	1,1±0,09	24,2±1,12	284,5±20,8
PGE_2	2,0±0,09*	30,9±1,04*	128,5±15,6*
Lithium hydroxybutyrate + PGE_2	1,0±0,06	25,9±1,08	299,5±19,4

Note. In each group 6 experiments were performed.
*Significantly different from control.

Leukocytic infiltration of the tissue surrounding the blood vessels was observed. Injection of distilled water and lithium hydroxybutyrate into the control animals did not induce a peritoneal reaction.

After preliminary injection of lithium hydroxybutyrate the volume of peritoneal fluid was significantly reduced by half compared with that in animals receiving silver nitrate alone. The liquid had an opalescent hue (the number of erythrocytes in it was greatly reduced). The percentage of degranulated mast cells in the mesentery was significantly less.

In the experiments of series II (Table 2) subplantar injection of histamine, serotonin, and PGE_2 increased the volume of the limbs, their temperature, and the threshold of sensitivity to pain. In all groups lithium hydroxybutyrate prevented the development of these reactions.

The investigations thus showed that lithium hydroxybutyrate, when given prophylactically, inhibits the development of certain types of acute inflammation. The action of this compound is evidently linked with a change in permeability of the blood vessels and a reduction of mast cell granulation; in turn, it delays the release of biologically active substances into the focus of injury.

This investigation showed for the first time that lithium hydroxybutyrate prevents the development of edema induced by histamine, serotonin, or PGE_2. The anti-inflammatory action of the compound may perhaps be linked with indirect inactivation of these biologically active substances, which are most frequently found in a focus of inflammation [4-6]. It may be expected that lithium hydroxybutyrate, in conjunction with other preparations, may be promising as a means of preventing the development of acute inflammatory changes, during which excessive formation of histamine, serotonin, or PGE_2 takes place.

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