EFFECT OF LEAD ACETATE SOLUTION ON REACTIVITY OF THE SMALL INTESTINE TO HISTAMINE IN NORMAL CONDITIONS AND IN LEAD POISONING

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A factor which may be of great importance in the mechanism of pathogenesis of lead colic is the change in reactivity of the neuromuscular apparatus of the intestine to mediators of the nervous system and to other active substances of endogenous origin arising in lead poisoning.

The object of the present investigation was to study the reactivity of the small intestine of animals with lead poisoning to histamine.

EXPERIMENTAL METHOD

Two series of experiments were carried out. In the series I the reactivity of the small intestine of 45 healthy animals and 36 animals with lead poisoning to histamine was compared against the background of the action of lead acetate solutions of different concentrations on the intestine. In series II the thresholds of sensitivity of the isolated intestine of 15 healthy warm-blooded animals and 20 animals with lead poisoning to histamine were studied.

The experiments were carried out on isolated atropinized segments of the small intestine of guinea pigs. The intestine was atropinized (by injection 0.1 ml of atropine) sulphate solution in a concentration of 10^{-5}, equivalent to the histamine concentration, into a blood vessel) was carried out to prevent the possible action of acetylcholine present in the tissues of the intestine and to weaken the spontaneous contractions of the isolated intestine. The injection was given 30 sec before injection of the histamine solution.

In the experiments of series I histamine (dihydrochloride) was given in the standard optimal concentration of 0.2×10^{-5}. After studying the effects of histamine, the drug was washed out and the lead solution injected into the vessel (exposure 15 min); the lead was then washed out and the effects of histamine again studied.

TABLE 1. Reaction of the Isolated Intestine to Histamine during Perfusion with Tyrode Solution (I) and after Exposure of the Intestine of Healthy (II) and Poisoned (III) Animals to Lead Acetate Solution (difference between initial reaction and reaction after treatment with lead acetate, in %; M ± m)

Series of experiments	time (in min) from beginning of perfusion of intestine and concentration of lead acetate (in %)			
	76; 0,1	99; 0,25	133; 0,5	158; 1,0
I	7±1,6	6±1,0	6±0,3	9±2,6
II	5±1,5	19±2,7	48±5,0	87±4,0
P	<0,5	<0,001	<0,001	<0,001
III	23±9,0	39±7,0	65±6,0	99±0,3
P	<0,2	<0,001	<0,001	<0,001

Altogether 7 concentrations of lead acetate were tested: 0.02, 0.05, 0.1, 0.25, 0.5, 0.75, and 1% solutions. Not more than 3 or 4 tests were carried out on each segment of the intestine.

In the experiments of series II histamine solutions were used in decreasing concentrations from 10^{-5} to 10^{-16} or less. The criterion chosen was a reaction corresponding to 50% of the initial magnitude—ED_{50} (the reaction measured 1.0-1.5 cm). Comparative analysis of the data obtained in the experiments on both groups of animals was carried out on the basis of the ED_{50} values.

Some guinea pigs (15) were used in control experiments to test for how long the reaction of the isolated

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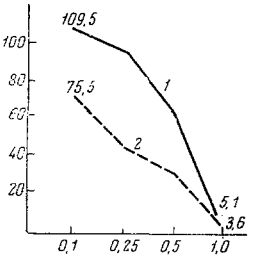
TABLE 2. Reaction of the Isolated Intestine of Healthy and Poisoned Animals to Histamine after Exposure to Lead Acetate Solution (in % of magnitude of initial reaction; M ± m)

Test object	concentration of lead acetate (in %)					
	0,02	0,05	0,1	0,25	0,5	1,0
Isolated intestine of healthy guinea pigs	—	—	109,5±5,7 (25)	99,8±5,9 (17)	64,3±5,7 (25)	5,1±1,3 (21)
Isolated intestine of poisoned guinea pigs	82,1±3,3 (7)	88,8±4,1 (16)	75,5±5,8 (7)	47,1±5,7 (15)	35,9±1,7 (21)	3,6±0,9 (21)
p	—	—	<0,001	<0,002	<0,001	>0,05

Note. Number of animals given in parentheses.



Reaction of isolated intestine of healthy (1) and poisoned (2) animals to histamine (0.2×10^{-5}) during the action of different concentrations of lead acetate. Abscissa—concentration of lead acetate (in %), ordinate—reaction to histamine (in % of initial level).

intestine to histamine persisted during perfusion of the organ with pure Tyrode solution and to test the action of distilled water out on the basis of the ED_{50} values.

The animals were poisoned by daily oral administration of 5% lead acetate solution for 2.5-3.5 months in a dose of 1 ml/kg body weight (50 mg/kg). In all the animals the characteristic changes of lead poisoning were found in the blood: the hemoglobin concentration fell by 1.6-4.4 g% from the original level, the reticulocyte count rose by 31-102% compared with its initial level, and the number of erythrocytes with basophilic granules increased to 26-168 in 50 fields of vision. Most guinea pigs developed clonico-tonic convulsions.

EXPERIMENTAL RESULTS

The control experiments showed that perfusion of the isolated intestine with pure Tyrode solution for 2. 5 h (76, 99, 133, and 158 min from the beginning of perfusion) caused little or no change in its reaction to histamine (Table 1). The reaction of the isolated intestine was independent of the action of water. After injection of 0.1 ml distilled water into the vessel no reaction of the isolated intestine was observed, and only after injection of 1 ml water were weak contractions of the intestine found in 60% of the experiments, with a mean amplitude of 1 mm.

In the experiments in which the isolated intestine was exposed to lead acetate solutions the reaction to histamine was considerably depressed. The degree of depression of the reaction increase with an increase in the concentration of the lead acetate solution. The difference between the initial and subsequent reactions of the isolated intestine to histamine (in %) after exposure to lead acetate solutions in the case of the healthy animals was 3-8 times greater than the reaction of the intestine when perfused with pure Tyrode solution, compared with 6-10 times greater in the case of the poisoned animals (see Table 1). This difference, caused by depression of the reaction of the isolated intestine to histamine under the influence of lead acetate, was statiscally significant and was more marked in the animals with lead poisoning (Table 2).

In the case of the healthy animals,weak solutions of lead acetate (0.1%) caused a slight increase in the reaction to histamine. In the poisoned animals, depression of the reaction to histamine took place without a phase of intensification (see figure). Lead acetate solution (1%) caused marked depression of the reaction of the isolated intestine of the animals of both groups to histamine.

The study of the reactivity threshold of the isolated intestine to histamine in healthy and poisoned animals showed (from the difference of the ED_{50} of the reaction) that in the animals with lead poisoning the thresholds of the reactions to histamine were about ten times higher than in the healthy animals (0.1 and 0.01 μg respectively).

The authors showed previously that relatively concentrated solutions of lead acetate increased the tone of the smooth muscle of the isolated intestine, developing into a contracture. The degree of depression

of the reaction to histamine was directly dependent on the degree of contracture. Against the background of a marked contracture, the reaction of the isolated intestine to histamine was completely absent. Lead poisoning predisposed to spasms with the character of contracture. In the poisoned animals contracture of the isolated intestine developed in response to lower concentrations of lead acetate (ED_{50} 2.8 g/liter) than in the healthy animals (ED_{50} 4.2 g/liter). This accounts for the increase in the thresholds of sensitivity to histamine in these animals. The facts described above may be attributed to the spasms and contracture of the isolated intestine developing under the influence of lead acetate.