

CONTENT OF HISTAMINE AND SEROTONIN IN STOMACH WALL OF RATS DURING DEVELOPMENT OF NEUROGENIC ULCERATION

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UDC 616.33-009.85-092.9-008.93

The larger the number of gastric ulcers in rats, the higher the content of histamine and serotonin in the stomach wall.

Disturbance of nutrition of the gastric mucous membrane with the formation of ulcers is closely connected with disappearance of the tissue reserves of catecholamines which takes place after application of an "extraordinary" stimulus [1].

In the present investigation the content of two other monoamines (histamine and serotonin) in the gastric mucous membrane was studied during the development of gastric ulcers in rats.

EXPERIMENTAL METHOD

Experiments were carried out on 140 male albino rats weighing 180-260 g. Ulcers were produced in the gastric mucous membrane by immobilization of the animals accompanied by electrical stimulation for 3 h [2]. The animals were deprived of food for 24 h before the experiment. Some rats were decapitated 3 h after the experiment, the rest 24 h thereafter. Corresponding control animals were sacrificed at the same times.

At autopsy 3 h after the end of stimulation, ulcers were found in the mucous membrane of the rats' stomach in a mean number of 4.8 ± 3.9 per animal, while the corresponding number 24 h after stimulation was 2.8 ± 1.4 . In the control rats (deprived of food) only solitary lesions were found — on the average 0.7 ± 0.2 per animal.

The rats' stomachs were immersed in liquid oxygen and ground in a mortar. Samples of tissue weighing 60-200 mg were homogenized with perchloric acid (0.4 N). Fluorimetric determination of histamine was carried out by Shore's method [14], and of serotonin by Bogdanski's method [7]. The Soviet BIAN 130 fluorimeter was used.

EXPERIMENTAL RESULTS AND DISCUSSION

Histamine (Table 1). The mean content of histamine in the stomach wall of the rats 3 h after the experiment was 92.6 ± 4.1 $\mu\text{g/g}$, rather higher than in the control animals (87.2 ± 3.8 $\mu\text{g/g}$). This difference was not significant ($P > 0.05$). However, in rats with 0-2 ulcers per animal the histamine content was significantly lower (88.2 ± 0.9 $\mu\text{g/g}$) than in animals with 3-20 ulcers (102.0 ± 1.1 $\mu\text{g/g}$).

The histamine concentration fell sharply 24 h after the experiment to 64 ± 7.1 $\mu\text{g/g}$, i.e., 27% below the control level.

Department of Pharmacology, Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, Leningrad. (Presented by Academician of the Academy of Medical Sciences of the USSR S. V. Anichkov.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 69, No. 3, pp. 31-33, March, 1970. Original article submitted September 15, 1969.

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TABLE 1. Content of Histamine in Stomach Wall of Rats during Development of Neurogenic Ulcers ($M \pm m$)

Group of animals	Content of histamine (in $\mu\text{g/g}$)					
	3 h after stimulation			24 h after stimulation		
	number of experiments	number of ulcers per animal	content of histamine	number of experiments	number of ulcers per animal	content of histamine
Experimental. . . .	19	4.8 ± 3.9	$92.6 \pm 4.1^*$	18	2.8 ± 1.4	64.1 ± 7.1
Control.	19	0.7 ± 0.06	87.2 ± 3.8	8	0.5 ± 0.1	85.1 ± 2.8

*Difference not significant ($P > 0.05$).

TABLE 2. Content of Serotonin in Stomach Wall of Rats during Development of Neurogenic Ulcers ($M \pm m$)

Group of animals	Content of serotonin ($\mu\text{g/g}$)					
	3 h after stimulation			24 h after stimulation		
	number of experiments	number of ulcers per animal	content of serotonin	number of experiments	number of ulcers per animal	content of serotonin
Experimental. . . .	22	3.5 ± 1.6	10.7 ± 3.1	16	2.5 ± 0.9	7.7 ± 2.0
Control.	21	0.8 ± 0.1	5.6 ± 0.8	9	0.6 ± 0.2	5.0 ± 1.1

Serotonin (Table 2). The serotonin content 3 h after the experiment was more than doubled ($10.7 \pm 3.1 \mu\text{g/g}$ compared with $5.6 \pm 0.8 \mu\text{g/g}$ in the control). No definite relationship could be found between the serotonin concentration and the severity of ulceration of the stomach.

The serotonin content fell to $7.7 \pm 2 \mu\text{g/g}$ 24 h after the experiment, but this was still above the control level.

The role of histamine in the secretion of gastric juice has now been experimentally demonstrated, and many workers are inclined to regard it as the physiological stimulator of the parietal cells [8, 13]. However, under certain conditions, endogenous histamine can become a harmful factor. In rats with experimental gastric ulcers, histidine-decarboxylase activity increases sharply in the mucous membrane, and pharmacological blocking of this activity prevents the development of ulcers [11]. Ulceration of the stomach is accompanied by lowering of the histaminopexic property of the tissues [4].

The role of endogenous serotonin in physiological and pathological processes in the gastric mucous membrane has received less study [10].

The results of the present investigation give further evidence of the participation of histamine and serotonin in the formation of experimental gastric ulcers in animals. In fact, the concentration of these monoamines in the gastric mucous membrane reaches a maximum at the time of the maximal number of ulcers in the stomach, and in those animals with the largest number of ulcers. This hypothesis is supported by data in the literature according to which administration of large doses of histamine and serotonin to animals leads to the formation of multiple lesions in the stomach [3, 5, 6, 9, 12].

LITERATURE CITED

1. S. V. Anichkov, I. S. Zavodskaya, and I. S. Moreva, *Byull. Éksperim. Biol. i Med.*, No. 11, 89 (1967).
2. O. N. Zabrodin, in: *Annual Report of the Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, for 1961-1962* [in Russian], Leningrad (1963), p. 212.
3. I. S. Zavodskaya, in: *Annual Report of the Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, for 1956* [in Russian], Vilnius (1957), p. 271.
4. S. A. Mirzoyan and R. A. Nazaretyan, *Byull. Éksperim. Biol. i Med.*, No. 2, 55 (1968).
5. A. Bel, R. Levrat, J. Nesmoz, et al., *Rev. Inst. Hapat.*, 17, 65 (1967).
6. J. G. Blackman, D. S. Campion, and F. N. Fastier, *Brit. J. Pharmacol.*, 14, 112 (1959).
7. D. F. Bogdanski, A. Pletscher, B. B. Brodie, et al., *J. Pharmacol. Exp. Ther.*, 117, 82 (1956).
8. C. F. Code, *Fed. Proc.*, 24, 1311 (1965).
9. S. Franco-Browder, G. M. Masson, and A. C. Corcoran, *J. Allergy*, 30, 1 (1959).
10. S. Garattini and L. Valzelli, *Serotonin*, Amsterdam (1965), p. 82.
11. R. J. Levine and E. C. Saney, *Am. J. Physiol.*, 214, 892 (1968).
12. F. J. Lewis and O. H. Wangensteen, *Proc. Soc. Exp. Biol. (New York)*, 74, 20 (1950).
13. W. Lorenz and K. Pfleger, *Klin. Wschr.*, 46, 57 (1968).
14. P. A. Shore, A. Burkhalter, and V. H. Cohn, *J. Pharmacol. Exp. Ther.*, 127, 182 (1959).