

EFFECT OF QUATERON ON THE HISTOAMINOPEXIC POWER OF THE DEGENERATING STOMACH WALL

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Experiments on rats have shown that quateron reduces the frequency and intensity of reflex degenerative changes in the stomach wall. This effect is accompanied by a relative increase in the histaminopexic power of the stomach tissue; the content of total and free histamine varies within normal limits.

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The work of S. V. Anichkov and co-workers [1, 3, 7] showed that degenerative changes take place in the gastric mucous membrane during injury to the duodenum.

The most effective agents for preventing and abolishing neurogenic degeneration of the stomach wall are central cholinolytics and ganglion-blocking drugs [2, 5, 15], and the mechanism of the therapeutic action of quateron [4, 16, 17] is largely attributable to its depressant effect on secretion of adrenal hormones. With respect to interaction between central and local mechanisms regulating the function and tissue nutrition of the stomach, the discovery of certain mediators and biogenic amines in the secretion and wall of the stomach is of definite importance [6, 13, 19]. One aspect of this problem which deserves attention is the intensity of histamine formation [22], largely dependent on acetylcholine. It has also been shown that the histamine-forming power of the tissue is appreciably increased by adrenalin, noradrenalin, DOPA, and dopamine [21].

Parrot and co-workers [11, 23] showed that the blood serum of healthy persons and of some animals, and also other animal tissues, possess the ability to fix added histamine, whereas the blood serum of patients with allergic diseases [10] possesses almost no histaminopexic power. The histaminopexic power of the tissue was also confirmed in experiments using labeled histidine- C^{14} [24] and with inactivation of the histaminase - histidine decarboxylase system [12].

The results of investigations demonstrating an increased histamine concentration in the blood and gastric juice of patients with gastric ulcer [18], the absence of histaminopexic power of their blood serum during a relapse [9], and an increase in histaminopexy during administration of "Dzhermuk" mineral water to patients with neurogenic degeneration of the stomach [14] paved the way to a more profound study of histamine metabolism in gastric ulcer.

The object of the present investigation was to study changes in the histaminopexic power and histamine content during the onset and development of degeneration of the stomach wall and to establish a relationship between the preventive action of ganglion-blocking substances, especially quateron, and changes in the histaminopexic power of the stomach tissues.

EXPERIMENTAL METHOD

Experiments were carried out on albino rats by I. S. Zavodskaya's method [7]. Quateron was injected intramuscularly into the experimental animals in a dose of 10 mg/kg 20 min before stimulation, and again 6, 12, and 24 h after trauma. The animals were decapitated 24 h later, the stomach was extracted and opened along the lesser curvature, and the state of the mucous membrane and the intensity and number of visible hemorrhages, erosions, and ulcers were determined. The free histamine and the histaminopexic power of the stomach tissues were determined chromatographically [25], with the introduction of a slight modification [14], and the total histamine was determined by hydrolysis for 3 min with concentrated HCl [20].

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TABLE 1. Changes in Histamine Content and Histaminopexic Power of Tissues of the Rat Stomach Wall during Experimental Ulcer Formation

Animal	No. of animals	Histamine (in $\mu\text{g/g}$ tissue)		Histaminopexic power (in %)
		total	free	
Normal	30	19.36 ± 1.27	9.8 ± 0.77	73.1 ± 1.9
With experimental ulcer	40	28.4 ± 0.8	16.1 ± 1.27	48 ± 2.4
		$P < 0.001$	$P < 0.02$	$P < 0.001$

TABLE 2. Effect of Quateron on Intensity and Number of Degenerative Lesions of the Stomach in Rats and Histamine Content and Histaminopexic Power during Experimental Ulcer Formation

Animal	No. of animals	% of animals affected	Mean No. of degenerative lesions per animal	Histamine (in $\mu\text{g/g}$ tissue)		Histaminopexic power (in %)
				total	free	
Normal	30	—	—	17.4 ± 1.12	10.5 ± 0.9	70.6 ± 1.1
With experimental ulcer	50	92	6.7	30.4 ± 1.8	18.3 ± 1.3	54.5 ± 1.6
				$P < 0.001$	$P < 0.02$	$P < 0.001$
With experimental ulcer and receiving quateron	50	52	1.4	15.2 ± 1.14	9.4 ± 0.95	75.3 ± 1.1
				$P < 0.001$	$P < 0.01$	$P < 0.001$

EXPERIMENTAL RESULTS

During production of a reflex ulcer in rats, extensive degenerative changes were found in the gastric mucous membrane in 90–100% of cases. In the animals of the control group, when the stomach was opened 24 h after trauma, marked edema of the mucous membrane was observed, with obliteration of the folds, hyperemia, lividity, diffuse and petechial hemorrhages, and also erosions and multiple ulcers.

It is clear from Table 1, that during production of a reflex ulcer a definite increase was observed in the content of free and total histamine, accompanied by a sharp decrease in the ability of the stomach tissues to fix histamine.

In the next series of experiments some of the experimental animals received quateron in accordance with the scheme described above.

Table 2 shows that quateron caused a marked decrease in the morbidity of the animals and a particularly sharp decrease in the mean number of degenerative lesions per animal. At the same time, the histaminopexic power of the stomach tissues was appreciably reduced in the animals not receiving quateron. This was accompanied by an increase in the content of total and free histamine in the stomach tissues. Meanwhile, in the stomach tissues of the experimental animals receiving quateron not only were the protective mechanisms not inhibited but, as the slight increase in histaminopexic power showed, they were actually strengthened.

To determine the significance of the tissue histaminopexic power in experimental gastric ulcer formation, in a special series of experiments the ability of the tissues to fix histamine was determined in animals receiving quateron, which were subdivided into two groups: animals with a completely positive effect (in which no changes whatsoever took place in the stomach), and animals with a negative effect after administration of quateron. The results of this series of experiments are given in Table 3.

It may be concluded from the results of these experiments that when quateron has no marked preventive effect on development of experimental ulcer, the histaminopexic power of the tissues of the injured stomach is much below normal, and differs only slightly from the level observed in animals not treated with quateron. This fact is evidence of the protective role of the histaminopexic power of the stomach tissues under pathological conditions. Consequently, histaminopexy is an effective defensive mechanism of the body, disturbance of which may be of definite importance in the pathogenesis of peptic ulcer.

TABLE 3. Changes in Histaminopexic Power of Tissues of the Rat Stomach Wall Depending on Effect of Quateron

Animals	No. of animals	Mean No. of degenerative lesions per animal	Histaminopexic power (in %)
Normal	20	—	71.5±1.7
With experimental ulcer	20	7.2	50.3±1.13 P < 0.001
With positive effect from quateron	27	—	77.1±0.92 P < 0.001
With absence of effect from quateron	30	1.5	56.6±2.1 P' > 0.05

Note. P' relative to the group of animals with experimental gastric ulcer.

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