

IMPLICATIONS OF HISTAMINE IN THE MECHANISM OF ACID GASTRIC SECRETION

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Abstract

Histamine is an important factor stimulating the control of acid gastric secretion. Works, probably, regulating the local microcirculation and is involved in the inflammation pathogenesis It favours biochemical processes of growth and tissue repair. It Stimulates sensitive endings for pain and itching and acting as a modulator of the transmission pulse to some synapses in the brain, interfering in the arousal response in neuroendocrine regulation in thermoregulation and in regulating blood circulation.

Histamine stimulates bronchial and intestinal smooth muscle, dilates small vessels and capillaries, stimulates gastric secretion.

Key words: Histamine, Gastrine, Acid secretion

I. HISTAMINE

Histamine or beta imidazolyletilamina is a widespread biogenic amine. It starts in the body by histidine decarboxilation, and it is deposited in the majority in the mastocyte and basophile leukocytes. Its Depositing is in granular formations, together with heparin and chimyotactic factors for eosinophils and neutrophils. Mastocyte rich tissues - skin, bronchial mucosa, intestinal mucosa - contain relatively large quantities of histamine. Small quantities of histamine are found in epidermic cells and gastric mucosa, in some neurons and in fast rowing tissues.

The main pathways of histamine metabolism in humans consist of N-methylation, followed in part by oxidative desamination (under the monoaminoxidase influence), with formation of N-metiimidazolacetic; oxidative desamination (under the influence of diaminoxidase) with formation of imidazolacetic acid, which is in part riboconjugated. Histamine is an important factor stimulating the control of acid gastric secretion. Works, probably, regulating the local microcirculation and is involved in the inflammation pathogenesis It favours biochemical processes of growth and tissue repair. It Stimulates sensitive endings for pain and itching and acting as a modulator of the transmission pulse to some synapses in the brain, interfering in the arousal response in neuroendocrine regulation in thermoregulation and in regulating blood circulation.

Histamine stimulates bronchial and intestinal smooth muscle, dilates small vessels and capillaries, stimulates gastric secretion.

2. HISTAMINE RECEPTORS.

Histamine effects are due to the operation of specific receptors, belonging to three subtypes:

- H1 - whose stimulation is responsible for bronchoconstriction and vasodilatation.
- H2 - which causes gastric hypersecretion of hydrochloric acid, heart depression and vasodilation.
- H3 - which acts as presynaptic autoreceptors with inhibitory function at the level of histaminergic endings in the central nervous system.

Location and principal actions of agonists and antagonists at histamine receptors level are presented in *Table 1*.

Table 1

Receptor	Location	Action mech.	Actions	Agonists	Antagonists
H1	smooth muscle, brain, vascular endothelium	GQ ↑ PLC	Bronchoconstriction Vasodilatation and capillary permeability.	2-methyl-histamine	astemizole, clemastina, clorfenamin
H2	gastric mucosa, myocardium, brain, mastocyte	Gs ↑ Ac	Gastric secretion of hydrochloric acid	4(5)-methyl-histamine, impromidin, betazol	cimetidine, ranitidine
H3	Brain, plexus mienteric	GQ ↓ Ca ²⁺	Inhibition of some neurotransm. release	Α-methyl-histamine	Impomidin, tioperamida

3. IMPLICATIONS IN ACID GASTRIC SECRETION.

Stimulating effect of histamine on gastric acid secretion is known since 1920. Physiological role of histamine in gastric secretion was elucidated only after the discovery of histamine H2-blocker. Regarding the gastric acid secretion mechanism confrontations were summarized 2 approaches: 1. Final common mediator theory (theory of Code.), in which histamine is the

final mediator to other secretagogue (gastrine, acetylcholine), resulting that the parietal cell has receptors only for histamine.

2. Grossman's theory - Konturek, or receptor theory, which postulates that all three secretagogue (histamine, acetylcholine, gastrine) stimulate parietal cells directly and that each of them potentiates the other. According to this theory, these 3 receptors are in a dynamic interaction so that activation of one receptor increase sensibility to other specific receptors for agonists and inhibition of one receptor decreases sensitivity of other antagonist receptors.

It can be said after all the current data that histamine plays a central role in regulating gastric acid secretion. Recent research shows that histamine is produced and released from neuroendocrine cells (NEC) of the gastric mucosa of the fundus and gastrine and vagus nerve stimulate the formation and release of histamine from NEC.

Regarding the relationship with calcium, it is noted that high concentrations of calcium inhibit histamine release stimulated by gastrine inhibiting also the gastric acid secretion. At the same time, serum calcium levels did not influence gastric acid secretion stimulated by histamine.

H₂ receptor transduction is mediated by GTP linked to G protein with 3 subunits: alpha, beta, gamma. These subunits are associated or dissociated related to receptor occupation or vacancy. H₂ receptor G protein has not yet been isolated, but its existence is strongly suggested by the observation that GTP could mimic histamine stimulation of gastric acid secretion. This would be of subtype G_s (adenylate cyclase stimulator), in contrast to G_i protein associated with somatostatin PG inhibits adenylate cyclase. Histamine increases intracellular cyclic AMP considered the second messenger of H₂ receptor. Histamine increases the circulatory flow of gastric mucosa which is inhibited by cimetidine but not by omeprazole, and also serves as a vasodilator on gastric arterioles via H₁-receptor, or via the H₁-H₂-receptor.

4. CONCLUSION:

1. Histamine or beta imidazolyletilamina is a widespread biogenic amine.
2. Histamine is an important factor stimulating the control of acid gastric secretion.
3. It favours biochemical processes of growth and tissue repair.
4. It stimulates sensitive endings for pain and itching and acting as a modulator of the transmission pulse to some synapses in the brain, interfering in the arousal response in neuroendocrine regulation in thermoregulation and in regulating blood circulation.

5. Histamine stimulates bronchial and intestinal smooth muscle, dilates small vessels and capillaries, stimulates gastric secretion.

6. Histamine effects are due to the operation of specific receptors, belonging to three subtypes:

- H1 - whose stimulation is responsible for bronchoconstriction and vasodilatation.

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REFERENCES

1. Andersson K., Cabero J.L., Mattsson H., Hakanson R.-Gastric acid secretion after depletion of enterochromaffin-like cell histamine. A study with fluoromethylhistidine in rats. *Scand. J. Gastroenterol.*, 1996, 31:24.
2. Code C.F. -Histamine and gastric secretion. In :Wolstenholme GEW, O'Connor(eds.), London 1956, 181-219.
3. Emas S. - Effect of acetazolamide on histamine-stimulated and gastrin-stimulated gastric secretion. *Gastroenterology*, 1962, 43:557-563.
4. Feldman M.-Gastric secretion: normal and abnormal. In: *Gastrointestinal and Liver Disease. Pathophysiology/Diagnosis/Management*. Edited by Feldman M. Schrschmidt BF, Sleisenger M.H., WB.Saunders Company, 1998, 587-603.
5. Grossman M.I., Konturek S.j.-Inhibition of acid secretion in dog by metiamide, a histamine antagonist acting on H2 receptors. *Gastroenterology*, 1974, 66, 517-521.
6. Janovitz D.H, Cocker H, Hollander F.-Inhibition of gastric secretion in dogs by carbonic anhydrase inhibitor 2-acetylamino-1,3,4-thiadiazol-5-sulfonamide. *Ann J. Physiol.* 1952, 171, 325-330.
7. Soll A.H.-Physiology of isolated canine parietal cells: receptors and effectors regulating function. In : *Physiology of the Gastrointestinal Tract*. Edited by Johnson L.R., Raven Press, New York, 1981, 693-709.