

Histamine content, synthesis and degradation in human nasal mucosa

Y. ABE, S. OGINO, M. IRIFUNE, I. IMAMURA*, H. FUKUI*, H. WADA* and T. MATSUNAGA

Departments of Otolaryngology and *Pharmacology II, Faculty of Medicine, Osaka University, Osaka 553 and *Suita 565, Japan

Summary

Histamine content and enzyme activities of histamine metabolism, histidine decarboxylase (HDC), histamine *N*-methyltransferase (HMT) and histaminase (diamine oxidase, DAO) in human nasal mucosa were determined with a highly sensitive and specific fluorescent method which was combined with high performance liquid chromatography. Histamine content and HDC activity were determined in 10 specimens of nasal polyp, nine specimens of maxillary sinus and five specimens of inferior turbinate. HMT and histaminase activities were determined in 15 specimens of nasal polyp, nine specimens of maxillary sinus and five specimens of inferior turbinate obtained during surgical therapy. Histamine and activities of HDC, HMT and histaminase were detected in all specimens except the case of histaminase activity in one specimen of nasal polyp. The mean values of histamine content and activities of HDC, HMT and histaminase of human nasal mucosa were 137.3 nmol/g wet weight, 26.3 fmol/min/mg protein, 26.4 pmol/min/mg protein and 0.5 pmol/min/mg protein, respectively. Histamine content in the mucosal tissue of the maxillary sinuses was significantly higher than that of nasal polyps or inferior turbinates. There were no significant differences in HDC activities among three kinds of nasal mucosa. Activities of HMT and histaminase, including their kinetic constants (K_m and V_{max} values for histamine) indicated that HMT has a greater potential than histaminase for histamine degradation in the human nasal mucosa. The presence of these enzymes suggests that these activities constitute an important modulating factor in histamine mediated allergic and inflammatory reactions in human nasal mucosa.

Clinical and Experimental Allergy, Vol. 23, pp. 132–136. Submitted 31 March 1992; revised 9 July 1992; accepted 15 July 1992.

Introduction

Histamine, an important chemical mediator in nasal allergy [1,2], is synthesized from histidine, an amino acid, with histidine decarboxylase (HDC, L-histidine carboxylase, EC 4.1.1.22) [3] and stored in a preformed state in mast cells and basophils. In nasal mucosa, histamine which is released from mast cells, diffuses into the surrounding tissues and induces nasal symptoms mainly through its H_1 receptor subtypes. Nasal congestion is induced by the effect of its intense vasodilatation and increased vasopermeability [1,2], whereas pruritus, sneez-

ing and mucus secretion are caused by sensory nerve stimulation [4]. Subsequently, some histamine is degraded in the nasal mucosa, and the remainder is eliminated from the nasal mucosa into nasal discharges or blood flow. Histamine is degraded rapidly *in vivo*, and its degradation mechanisms have been ascertained in terms of two alternative pathways. One is transmethylation to trimethylhistamine, catalysed by histamine *N*-methyltransferase (HMT, S-adenosyl-L-methionine: histamine-*N*-methyltransferase, EC. 2.1.1.8), and the other is oxidative deamination to imidazole acetaldehyde, catalysed by diamine oxidase (DAO, diamine: oxygen oxidoreductase, EC 1.4.3.6) which is also called histaminase (Fig. 1) [3]. Tissues so far examined contain both or at least one of

Correspondence: Dr Y. Abe, Department of Pharmacology II, Faculty of Medicine, Osaka University, 2-2, Yamadaoka, Suita 565, Japan.

and enzyme activities between healthy and diseased nasal mucosa.

In vivo blockade of histamine degrading enzymes brings about marked potentiation of the passive cutaneous anaphylactic reaction in guinea pigs [21]. The presence of histamine synthesizing and degrading enzyme activities suggests that these activities may modulate nasal allergy and inflammatory reactions.

References

- 1 Mygind N. Mediators of nasal allergy. *J Allergy Clin Immunol* 1982; 70:149-59.
- 2 Otsuka H, Okuda M. Important factors in the nasal manifestation of allergy. *Arch Oto-Rhino-Laryngol* 1981; 223:227-35.
- 3 Gilman AG, Goodman LS, Rall TW, Nies AS. Goodman and Gillman's the pharmacological basis of therapeutics, 8th edn. New York: Pergamon Press, 1990:575-88.
- 4 White VW. The role of histamine in allergic diseases. *J Allergy Clin Immunol* 1990; 86:599-605.
- 5 Watanabe T, Taguchi Y, Sasaki K, Tsuyama K, Kitamura Y. Increase in histidine decarboxylase activity in mouse skin after application of the tumor promotor tetradecanoylphorbol acetate. *Biochem Biophys Res Commun* 1981; 100:427-32.
- 6 Yamada M, Watanabe T, Harino S, Fukui H, Wada H. The effects of protease inhibitors on histidine decarboxylase activities and assay of enzyme in various rat tissues. *Biochem Biophys Acta* 1980; 615:458-64.
- 7 Yamatodani A, Fukuda H, Wada H. High-performance liquid chromatographic determination of plasma and brain histamine without previous purification of biological samples: cation-exchange chromatography coupled with post-column derivatization fluorometry. *J Chromatogr* 1985; 344:115-23.
- 8 Watanabe T, Yamatodani A, Maeyama K, Wada H. Pharmacology of α -fruolomethylhistidine, a specific inhibitor of histidine decarboxylase. *Trends Pharmacol Sci* 1990; 11:363-7.
- 9 Beaven MA, Shaff RE. New inhibitors of histamine-N-methyltransferase. *Biochem Pharmacol* 1979; 28:183-8.
- 10 Blaschko H, Freidman PJ, Hawes R, Nilsson K. The amine oxidases of mammalian plasma. *J Physiol (Lond)* 1959; 145:384-404.
- 11 Lowry OH, Rosebrough NJ, Farr AR, Randall RJ. Protein measurement with the folin phenol reagent. *J Biol Chem* 1951; 193:265-75.
- 12 Recsei PA, Snell EE. Pyruvoyl enzymes. *Ann Rev Biochem* 1984; 53:357-87.
- 13 Eady RAJ, Cowen T, Marshall TF, Plummer V, Graves MW. Mast cell population density, blood vessel density and histamine content in normal human skin. *Br J Dermatol* 1979; 100:623-33.
- 14 Pipkorn U, Karlsson G, Enerback L. Secretory activity of nasal mucosa mast cells and histamine in hay fever. *Int Arch Allergy Appl Immunol* 1988; 87:349-60.
- 15 Naclerio RM, Meier HL, Kagey-Sobotka A, Adkinson NF Jr., Meyers DA, Norman PS, Lichtenstein LM. Mediator release after nasal airway challenge with antigen. *Am Rev Respir Dis* 1983; 128:597-602.
- 16 Schayer RW, Cooper JAD. Metabolism of C¹⁴ histamine in man. *J Appl Physiol* 1956; 9:481-4.
- 17 Imamura I, Watanabe T, Maeyama K, Kubota A, Okada A, Wada H. Effect of food intake on urinary excretions of histamine, N¹-methylhistamine, imidazole acetic acid and its conjugate(s) in humans and mice. *J Biochem* 1984; 96:1931-7.
- 18 Fransis D, Greavis MW, Yamamoto S. Enzymatic histamine degradation by human skin. *Br J Pharmacol* 1977; 60:583-7.
- 19 Kay AB. The role of the eosinophil. *J Allergy Clin Immunol* 1979; 64:91-104.
- 20 Handall CH, Mack P, Fogerty FJ, Baenziger NL. Role of receptors in metabolic interaction of histamine with the human vascular endothelial cells and skin fibroblasts. *J Biol Chem* 1987; 262:10220-8.
- 21 Yamamoto S, Fransis D, Greavis MW. Enzymatic histamine metabolism in guinea-pig skin and its role in immediate hypersensitivity reactions. *Clin Exp Immunol* 1976; 26:583-9.