

THE ROLE OF H₂-RECEPTORS IN CH. PHARYNGITIS?

Pages with reference to book, From 25 To 26

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In a world overloaded with environmental pollution, suffering from the greenhouse phenomenon and a “hole” in the ozone layer, one is not in the least surprised to see the ever increasing number of cases of sore throat in a city like Karachi. Until a few years ago the major causes of sore throat used to be tonsillitis, rhino-sinusitis, aphthous ulcers and acute pharyngitis etc. One would seldom encounter a case of chronic granular pharyngitis and that too in smokers. However, in the last decade or so the incidence of intractable chronic pharyngitis seems to have dominated the scene. The essential features of this ailment being, soreness, dryness, rawness, persistent discomfort, hawking, coughing, repeated necessity to clear the throat and a sense of uneasiness. The appearance of pharynx may vary from generalized hyperaemia to prominence of the posterior pharyngeal bands, or the entire mucosa being studded with tiny mounts of granulation tissue, and palor in old and established cases, giving the pharyngeal mucosa appearance of a parchment membrane, devoid of any mucociliary or secretory activity. Though more commonly seen in adults, and not necessarily smokers of any age or sex is prone to develop it. Its incidence seems to rise during the month of Ramadan, due to obvious increase in consumption of spicy foods and cold drinks. Two factors have been identified and incriminated in its causation. The alteration of pharyngeal pH brought about by the gastro-oesophageal reflux and the defective mucociliary flow. Many people have studied the role of G.E. reflux on the aerodigestive system. It is known to account for varied pathologies, from mild heartburn to the development of the cancer of larynx and the hypopharynx¹. Amongst them is the development of acid pharyngitis which is particularly common in our population due to dietary, and postural reasons such as ‘ruku’ and ‘sajda’ as both these postures aggravate the G.E. reflux². Some other research workers have described that the reflux of gastric contents and acid may be carcinogenic in the oesophagus causing Barrett’s oesophagus² and Plummer-vinson syndrome⁴ non specific laryngitis, contact granulomas hypertrophy of the posterior commissure, crico-arytenoid arthritis, globus hystericus, latent asthma, spasmodic volatile non-specific cough, and numerous other changes in the tracheo-bronchial tree⁵⁻⁹. The second factor responsible for chronic pharyngitis maybe the defective mucociliary flow. The mucosal blanket combined with ciliary activity is responsible for providing a protective layer to the pharyngeal mucosa. Although interrelated mucosal blanket is independent of the ciliary flow, and Gaynor¹⁰ as well as Dalhamn¹¹ have observed that the ciliary activity may persist even after the cessation of mucociliary flow. Reduction of mucociliary activity may predispose to infection as observed by Sasaki et al¹² and variations in the pH of pharynx appears to have a direct effect upon the mucociliary transport. but not ciliary activity. In fact Hakansson¹³ and Gaynor¹⁰ consider the fall in pH to cause increased viscosity of the mucous blanket which may hinder transport. It is also suggested by Lutz et al¹⁴ that pepsin might directly affect the underlying cilia and perhaps the character of the mucous itself. Pharyngeal mucosal ciliary activity and mucous transport system are also influenced by humidity, temperature variation, chemicals and polluted air¹⁰. Karachi’s atmosphere is undoubtedly an ideal example of atmospheric pollution and indeed a certain cause of sore throat. In addition to these factors, the possibility of yet another cause cannot be overlooked, as it seems to be gaining grounds, lately. Until 1960’s there were only H₁ receptors that reacted to histamine and brought about clinical manifestation of what is generally, recognized as allergy or histamine sensitivity. However in 1966, Ash and Schild¹⁵ observed that the effect of histamine in guinea pig ileum and bronchus could be inhibited by the classical antihistamine mepyramine but that several other actions of histamine, for example stimulation of both gastric acid

secretion and isolated atria, or inhibition of rat uterus could not be inhibited by mepyramine. The observation led them to believe that histamine acted on two types of receptors, those that responded to mepyramine or classical antihistamine, were called H₁-receptors and those that were mepyramine insensitive were labeled as H₂-receptors. Black et al¹⁶ were later able to report synthesis of specific H₂-receptor antagonist, which are now frequently used to inhibit histamine-stimulated gastric acid production in peptic ulcers. In vivo and in vitro studies have shown the presence of H₂-receptors in the human bronchial system, responsible for mediation of bronchodilation¹⁷. Primitive pharynx is the birth cradle for the development of the entire aero-digestive system in human beings. In the fourth week of embryonic life an endodermal in folding develops in the floor of the primitive pharynx called the laryngo-tracheobronchial groove, from which subsequently develop the lining bronchial groove, from which subsequently develop the lining epithelium and associated glands of the larynx trachea, bronchi and possibly the respiratory epithelium of the alveoli themselves¹⁸. Although preliminary evidence is insufficient to claim it but encouraging results were obtained in a study conducted by the author, where in vivo use of Ranitidine for 4 weeks dramatically improved the state of chronic intractable pharyngitis¹⁹ which leads to the presumption of presence of H₂-receptors in the pharyngeal mucosa, since the aero-digestive system has a common embryological origin. Further studies are required in vitro with animal preparations of the pharyngeal mucosa, as well as in vivo clinical trials, to establish the real role of H₂-receptors in the causation of chronic pharyngitis. If so, then the entire philosophy of management of this otherwise resistant to treatment condition would require a review.

REFERENCES

1. Ward, H.P. and Hanson, G.D. Reflux as an aetiological factor of carcinoma of the laryngopharynx. *Laryngoscope*, 1988;98:1195.
2. Zaidi, S.H. and Jafri, R. Gastro-oesophageal reflux a cause of chronic intractable pharyngitis. *Pakistan J. Otol.*, 1989; 6:20.
3. Radigan, L.R., Glover, J.L., Shipley, F.E. and Shoemaker, R.E. Barrett's esophagus. *Arch. Surg.*, 1977;112:486.
4. Smiley, T.B. Cricopharyngeal complications of G.E. reflux, in the functions of the oesophagus. Edited by H.R. Sorensen, O. Jepsen and S.A. Pederson. Odense, Odense University Press, 1972, p.175.
5. Ward, P. H. Contact granulomas of the larynx, in current therapy in otolaryngology- Head & Neck Surgery. Edited by (J. Gates. Decker, 1984, p. 400.
6. Ward, P. H. and Barci, G. Observations on the pathogenesis of chronic non-specific pharyngitis and laryngitis. *Laryngoscope*, 1982;92:1377.
7. Gabriel, C. E. and Jones, D.G. The importance of chronic laryngitis. *J. Laryngol. Otol.*, 1960;74:349.
8. Gautz, H. and Kleinsasser, O. Chronic laryngitis and carcinoma. *Arch. Otolaryngol.*, 1986; 212:57.
9. Bray, P.F., Herbst, J.J., Johnson, D.G. et al. Childhood gastro oesophageal reflux. Neurologic and psychiatric syndromes mimic ed. *JAMA.*, 1977; 237:1342.
10. Gaynor, E.B. Gastro-oesophageal reflux as an etiologic factor in laryngeal complications of intubation. *Laryngoscope*, 1988; 98: 972.
11. Dalhamn, T. Studies on tracheal ciliary activity. Special reference to the effect of cigarette smoke in living animals. *Am. Resp. Dis.*, 1964; 89: 870.
12. Sasaki, C. T., Horinchi, M. and Koss, N. Tracheostomy related subglottic stenosis. *Laryngoscope*, 1979; 89: 857.
13. Hakansson, C. H. and Toremaim, N. G. Studies on the physiology of trachea. Histology and mechanical activity of the smooth muscles. *Ann. Otol.*, 1968; 77: 255.
14. Lutz, R. J., Litt, M. and Chakrin, C. W. Physical - chemical factors in mucosa-rheology, in rheology

of biological systems. Edited by H. L. Gablenick and M. Litt. Springfield Thomas, 1973, p. 119.

15. Ash, A.S.F. and Schild, H. O. Receptors mediating some actions of histamine. Br. J. Pharm. Chemotherap., 1966; 27:427.

16. Black, J. W., Duncan, W. A., Durrant, C. J. et al. Definition and antagonism of histamine H₂-receptors. Nature, 1972; 236: 385\

17. Chakrin, L. W. and Krell, D. Histamine receptors in the respiratory system; a review of current evidence, In H₂-receptor antagonists. European symposium proceedings, edited by A. Tor solli and P. B. Luchelli. Amsterdam Excerpta Medica, 1984, p. 338.

18. Hamilton, W.J. and Harrison, R.J. Anatomy of the mouth, pharynx and oesophagus in Scott Brown's diseases of the ear, nose and throat. 3rd ed. London, Butterworths, 1971, p. 189.

19. Zaidi, S. H. A study of H₂-receptor antagonists in treatment of chronic intractable pharyngitis. JPMA., 1990; 40: 9: 217.