SERUM PEPSINOGEN, A GENETIC MARKER IN DUODENAL ULCER

Pages with reference to book, From 23 To 24

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Role of genetic factors in the pathogenesis of ulcer has been suggested earlier[1]. The genetic markers used in the past were ABO blood groups[2], secretor and non-secretor st[3], HLA typing[4] and serum pepsinogen[5]. Of these, total serum pepsinogen is a better marker of ulcer disease and as reported earlier[6], higher values were found among patients with peptic ulcer disease.

Human pepsinogens belong to the group of aspartic proteases and are characterized into two main groups, pepsinogen A and pepsinogen C[7]. Pepsinogens are inactive forms of pepsins, the Proteolytic enzyme in gastric juice, synthesized in the chief cells of the oxyntic gland area and in. some cells of the pyroric gland area. The peptic cells of the stomach secrete pepsinogen directly into the circulation from which it is removed by the kidneys and excreted as uropepsin[8,9].

Analysis of serum pepsinogen is quite reproducible and the individual value fairly constant from day to day has littFe variation in relation to time of day[6]. The concentrations tends to rise with increasing age upto sixty years[10] above which the level declines probably due to increasing incidence of atrophic gastritis[11] Serum pepsinogen increases in most individuals after betazole[12] and pentagastrin stimulation[13] In hypersecretory states such as peptic ulcer disease the level increases whereas after total gastrectomy or pernicious anaemia, the concentration declines[6].

In duodenal ulcer, elevated concentration appears to be inherited as an autosomal dominant trait. Individuals with this trait have a frequency of duodenal ulcer eight times greater than the general population.[14]'Serum pepsinogen correlates positively with the level of pepsin in the gastric lumen and contributes to the pathogenesis of an ulcer while the genetically transmitted high levels of serum pepsinogen indicates the presence of an ulcer diathesis[15]

Serum pepsinogen levels among patients with duodenal ulcer show a bimodal distribution,[16] suggesting that the duodenal ulcer patients could be separated into two populations, on the basis of serum pepsinogen level. Duodenal ulcer with hyperpepsinogenaemia may be considered as 'primary duodenal ulcer' while an ulcer with normal level be considered as 'secondary duodenal ulcer'. Patients manifesting hyperpepsinogenaemia require further investigation in the family to indentify siblings and progeny carrying the trait and thus at higher risk[15] Studies among the first degree relatives of patients with duodenal ulcer show that an elevated serum pepsinogen level[1] is not only associated with duodenal ulcer but also inherited as an autosomal dominant trait. In these studies hyperpepsino-genaemia was found in about 50% of the offspring of family members with elevated serum level and in none of the offspring of normopepsinogenaemic family members. Clinical duodenal ulcer disease was encountered only in relatives with elevated serum pepsinogen level'. Duodenal ulcer patient with normopepsinogenaemia may safely be considered to be suffering from nongenetic or 'secondary duodenal ulcer' and these ulcers are the result of neuroendocrinological or environmental factors which are also known to cause ulcer disease[15]

Thus an elevated pepsinogen level may prove to be a valuable subclinical marker of duodenal ulcer disease.

REFERENCES

1. Rotter, J.l., Sones, J.Q. and Samloff, l.M. Duodenal ulcer disease associated with elevated serum pepsinogen-l. An inherited autosomal dominant disorder. N. Engi. J. Med., 1979; 300: 63.
2. Langman, MJ.S. Blood groups and alimentary disorders. Clin. Gastroenterol., 1973; 2 : 497.
3. McConnell, R.B. The genetics of gastrointestinal disorders. London, Oxford University Press, 1966; p.76.
4. Ellis, A. and Woodrow, J.C. HLA and duodenal ulcerS Gut, 1979;9:760.
5. Rotter, j.l Peterson, G. and Samloff, I.M. Genetic heterogeneity of hyperpepsinogenemic-l and normopepsinogenemic I duodenal ulcer disease. Ann. Intern. Med., 1979; 91 : 372.
6. Mirshy, A., Futterman, P., Kaplan, S. and Broh¬kahn, R.H. Blood plasma pepsinogen; I. The source, properties, and assay of the proteolytic activity of plasma at add reactions. 3. Lab. Clin. Med., 1952; 40: 17.
7. Westerveld, B.D., Pals, G., Defize, 3., Eriksson, A.E. and Meuwissen, S.G.M. Human pepsinogens; a review of clinical and genetic aspects. J. Gastroenterol.Hep.,1986;1 :401.
8. Bucher, G.R. Uropepsin; a review of the litera¬ture and report of some experimental findings. Gastroenterology, 1947;8 :627.
9. Mushy, l.A., Kaplan, S. and Broh-kahn, R.H. Pepsinogen excretion (Uropepsin) as an index of the influence of various life situations on gastric secretion. in life stress and bodily disease, Bal¬timore, Willians and Wilkins, 1950; p. 628.
10. Pals, G., Westerveld,B.D. and Defize, 3. Relations between serum pepsinogen levels, pepsinogen phenotypes, ABO blood groups, age and sex in blood donors. Ann. Hum. Biol., 1985; 12:403.
11. Ichinose, M., Miki, F. and Furihata, C. Radioim¬munoassay of group I pepsinogen (PGI) and the effect of food on serum PGI. Scand .J. Gastro¬enterol., 1979; 14 : 241.
12. Samloff, I.M., Secrist, D.M. and Passaro, E. Jr. The effect of betazole on serum group I pepsino¬gen levels; studies in symptomatic patients with and without recurrent ulcer after vagotomy and gastric resection or drainage. Gastroenterology, 1976; 70:1007.
13. Waldum, H.L., Burhol, P.G. and Straume, B.K. Serum group I pepsinogen during prolonged infusion of pentagastrin and secretin in man. Scand. 3. Gastroenterol.,1979; 14': 761.
14. Harrison, T.R. Principles of interml medicine. 10th ed. Editors: Robert G. Petersdrof et. al. London, McGraw-l-Hill 1983; p. 1697.
15. Habibullah, C.M., All, M.M., Ishaq, M., Prasad,' R., Pratap, B. and Saleem, Y. Study of duodenal ulcer disease in 100 families using total serum pepsinogen as a genetic maker. Gut, 1984; 25 :1380.
16. Samloff, I.M.,'Liebman, W.M. and Panitch, N.M. Serum group I pepsinogens by radioimrnuno-assay in control subjects and patients with peptic ulcer. Gastroenterology, 1975; 69 : 83.