Absence of antibodies stimulating H₂-receptor mediated cyclic adenosine monophosphate (cAMP) production in peptic ulcer disease

Str,- We read with great interest the paper by Burman et al (Gut 1991; 32: 620–3). Using porcine gastric mucosal cells as an in vitro test system, the authors could not find any stimulatory effect on cyclic adenosine monophosphate (cAMP) production by sera or immunoglobulin (Ig) fractions of 57 patients with relapsing ulcer disease. As the authors reported, their results are in contrast with data obtained by De Lazzari et al. This group found in duodenal ulcer patients antibodies stimulating cAMP production in enriched guinea pig parietal cells. Thus, De Lazzari et al have suggested that duodenal ulcer disease may be caused by an increased tansaminating antibody to H₂-receptors, which therefore are proposed as 'a new addition to the growing list of receptor antibodies in human diseases'.

By using another in vitro test system, we have also investigated the possible role of cAMP stimulating antibodies in peptic ulcer disease. We tested the effects of Ig preparations on cAMP production in cultured human gastric tumour cells (HGT-1); kindly provided by De C Greenfield Institute, U 55, Paris. These cells have H₂-receptors and are considered to be a useful tool for studies of cAMP mediated gastric acid secretion. Igs were derived from sera of 36 peptic ulcer patients. The patients were classified as adequate (AR; n=16) and inadequate responders to ranitidine (IR; n=20) by intragastric pH monitoring. Sera were not tested directly because of several undefined conditions which decreased cell viability from 91 to 52% after four hour incubation of the cells with 20% serum. IgG was isolated by column chromatography on protein G-sepharose and concentrated by micro-ultrafiltration. Other proteins were removed and non-IgG was precipitated by ammonium sulfate (1.6 mol/l). The Igs were tested at concentrations of 4 (IgG) and 1 (non-IgG) mg protein/ml medium. HGT-1 cells were grown as monolayers and incubated for 10, 30, 60, 180, and 360 minutes with Igs in the presence of 1 mmol/l phosphodiesterase inhibitor (IBMX). Standard IgG (Behringwerke) was used as control. The total amount of cAMP was measured by radioimmunoassay (Amerham Buchler).

The basal value of cAMP production in HGT-1 cells was mean (SD) 10.7 (1.7) pmol/ml protein and was stimulated after 10 minutes incubation (10 mg IgG/ml) to 80.4 (15.0) pmol/mg protein in all experiments (n=36). The stimulation could be blocked by the H₂-receptor antagonists cimetidine and ranitidine with IC50 values of 0.400 and 0.034 μmol/l, respectively, confirming the presence and specificity of H₂-receptors on this cell type. No statistically significant stimulation of cAMP production could be obtained after incubation of HGT-1 cells with any Ig preparation tested (see Table).

Our results agree with those of Burman et al. In neither in vitro test systems was there evidence for cAMP stimulating antibodies in peptic ulcer patients. In addition, we conclude that antibodies to H₂-receptors do not cause an inadequate response to H₂-antagonists as has been assumed. However, despite these results, it can not be totally ruled out that auto-immunological processes have a role in specific subpopulations of patients with peptic ulcer disease. Moreover, the differing results of Burman et al and our group on one hand and De Lazzari et al on the other may be caused by the different in vitro test systems used. In particular, De Lazzari et al failed to detect any cAMP stimulating effects on antibodies, unless the parietal cell content in cell suspensions was at least 50%.

A SAREM-ASLANICH
CH BERGMANN
S VILKER
H DIRAGE
U KLOTZ
CH WISSE

Department of Clinical Chemistry,
and Gastroenterology, Robert-Bosch Hospital,
Dr Margaret Fischer-Bosch Institute of
Clinical Pharmacology,
Stuttgart, Germany