SHORT COMMUNICATION

Rectal mucosal histamine release in ulcerative colitis

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(Received 1 May 1980; accepted 7 July 1980)

Summary

1. Rectal dialysis in vivo was used to assess rectal mucosal release of histamine in patients with ulcerative colitis and in control subjects.

2. Rectal mucosal histamine release was significantly increased in ulcerative colitis, whether the patients were in remission or relapse. The highest values were found in active colitis, but in several such patients histamine release was within the control range. Measurement of rectal mucosal electrical potential difference suggested that increased mucosal histamine release in this group of patients was not due to enhanced epithelial permeability.

3. Rectal dialysis appears to be a useful method for assessing mucosal histamine production and the results obtained are consistent with the hypothesis that immediate hypersensitivity reactions could be of importance in some patients with ulcerative colitis.

Key words: histamine, rectum, ulcerative colitis.

Introduction

Increased numbers of mast cells and eosinophils have been found in the rectal mucosa of patients with ulcerative colitis (Bercovitz & Sommers, 1966; Heatley, Calcraft, Rhodes, Owen & Evans, 1975; Heatley & James, 1979) and disodium cromoglycate, which is thought to prevent the release from sensitized mast cells of various inflammatory mediators including histamine (Cox, 1971), is reported by some authors to benefit patients with proctocolitis (Heatley et al., 1975; Mani, Lloyd, Green, Fox & Turnberg, 1976). It has therefore been suggested that an immediate hypersensitivity reaction might contribute to the pathogenesis of this disease.

However, in the only published study of rectal mucosal concentrations of putative mediators of type I hypersensitivity reactions, Binder & Hvidberg (1967) found no difference between mucosal histamine contents in controls and in colitic patients with or without active disease. To re-evaluate this apparent discrepancy we have applied the technique of rectal dialysis in vivo (Edmonds, 1971) to the investigation of rectal mucosal histamine release in patients with proctocolitis in remission or relapse. Disease activity was assessed sigmoidoscopically (Baron, Connell & Lennard-Jones, 1964) and a guide to mucosal functional integrity was obtained by measurement of rectal mucosal electrical potential difference (Edmonds & Pilcher, 1973; Rask-Madsen, 1973).

Methods

Patients

We studied 24 patients in whom ulcerative proctocolitis had been diagnosed by conventional clinical, histological and radiological criteria. Disease activity in the distal colon and rectum was scored according to sigmoidoscopic appearance (Baron et al., 1964); patients with a normal appearance or mucosal oedema were classified as being in remission, and those with contact or spontaneous bleeding as being in relapse. Twelve patients (seven in remission and five in relapse) were on treatment with oral sulphasalazine and/or rectal corticosteroids when studied. Nine subjects with irritable bowel syndrome served as controls.
All patients gave informed consent for the study, approval for which was obtained from the Guy's Hospital Ethical Committee.

Rectal dialysis

After determination of rectal potential difference (Rampton, Sladen & Youlten, 1980) rectal mucosal histamine release was assessed by measurement of the amount of histamine appearing in the dialysis bag during a 1 h period of rectal dialysis in vivo. Rectal dialysis was performed with a PVC cannula on which was mounted a Visking 8/32 dialysis tube (diameter 6 mm, length 8 cm) containing 2-5 ml of isotonic dialysate (Na+, 120 mmol/l; K+, 30 mmol/l; Cl−, 120 mmol/l; HCO3−, 30 mmol/l) and with its tip 12 cm from the anal verge (Rampton et al., 1980). After the 1 h dialysis period volume change was measured by weighing. Dialysates, other than those discarded because of contamination by faeces, were frozen at −20°C for up to 6 months until analysis.

Dialysis bag permeability

To assess the permeability of the dialysis membrane to histamine in vitro dialysis bags containing a histamine-free solution were placed in a large stirred volume of a similar fluid containing histamine; the amount of histamine in the bags and in the surrounding fluid was assayed after incubation periods of 10, 20, 30, 40, 60 and 90 min at 37°C.

Histamine assay

Histamine was assayed fluorimetrically after extraction into highly alkaline salt-saturated butanol and acidified heptane followed by condensation with o-phthalaldehyde by using an automated continuous-flow system (Technicon Auto-Analyzer II) with a modified manifold (Siraganian, 1974). The coefficient of variation of duplicate estimations of 10 samples of dialysate was 1.4% and the recovery of histamine added to the dialysate was 101 ± 5.3% SEM (n = 4).

Calculations and statistics

A standard formula (Edmonds, 1971) was used to calculate the rate of flux of histamine into the dialysis bag. Results are expressed as medians with ranges and numbers of patients in parentheses and were compared by Wilcoxon's rank-sum test (two-tailed).

Results

Experiments in vitro

The half-life of entry of histamine into the dialysis bags was 25 min, compared with 18 min for sodium.

Studies in vivo

Median rectal mucosal histamine release was 1.7 ng h−1 cm−2 in control subjects (Fig. 1). In patients with proctocolitis histamine release was significantly greater both in remission (median 8.2 ng h−1 cm−2, P < 0.01 from controls) and in relapse (16 ng h−1 cm−2, P < 0.05 from controls). The highest values of histamine release were found in patients with active colitis, but histamine release in this group as a whole did not differ significantly from that of patients with quiescent disease. Within each group of colitic patients histamine release was not clearly related to treatment with sulphasalazine and/or topical steroids (Fig. 1).

Rectal potential difference was −49(42–64) mV (n = 9) in the control subjects, −43(31–58) mV (n = 13) (P < 0.05 from control subjects) in the patients with quiescent colitis and −34(10–49) mV (n = 11) (P < 0.01 from control subjects, P < 0.05 from patients with quiescent disease) in those in relapse. There was no evidence of a direct correlation between potential difference and the widely varying mucosal histamine release of the patients with active colitis (Spearman's rank correlation coefficient −0.40, P < 0.3).

Discussion

The use of rectal dialysis for the measurement of rectal mucosal solute transport depends on
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...of the apparently beneficial effect of cromoglycate in patients with high rectal eosinophil counts (Healey et al., 1975), it would also be of interest, in such a study, to evaluate the relationship between mucosal histamine release and eosinophil content.

Finally, the demonstration that histamine modifies human colonic mucosal transport in vitro towards secretion, and that this effect can be inhibited by H_2-receptor blockade (Linaker, McKay, Higgs & Turnberg, 1979), raises the possibility that treatment with antihistamines might alleviate the diarrhoea of patients with ulcerative colitis in whom rectal mucosal histamine release is increased.

Acknowledgment

We are grateful to the Wellcome Trust for financial support.

References


