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ASSESSMENT OF FUNCTIONAL OESOPHAGEAL MUCOSAL INTEGRITY IN BIOPSIES OF PATIENTS WITH REFRACTORY GORD

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Introduction Patients with non-erosive reflux disease (NERD) exhibit oesophageal mucosal epithelial dilated intercellular spaces (DIS), which can be reversed by PPI therapy and are not seen in patients with functional heartburn. Oesophageal mucosal functional integrity can be evaluated by measuring transepithelial electrical resistance (TER) and permeability to small molecules. Such functional changes may be relevant for symptom perception but are thus far not studied in NERD. We investigated oesophageal mucosal functional integrity in patients with GORD symptoms refractory to PPI.

Methods Oesophageal biopsies at 3 cm above the squamocolumnar junction were obtained from 17 patients with persistent typical reflux symptoms (heartburn, regurgitation) on PPI but with no erosions (mean age 52, range 35–76), and 10 control subjects (no upper GI symptoms; mean age 38, range 18–54). Biopsies were placed in micro-Ussing chambers and baseline TER measured after equilibration in KHBB pH 7.4 solution. The mucosal side of the biopsies was then exposed for 30 min to either: KHBB control solution at pH 7.4; weakly acidic solution pH 5 + 1 mg/ml pepsin + 1 mM sodium deoxycholic acid; or acidic solution pH 2 + 1 mg/ml pepsin + 1 mM taurodeoxycholic acid. % change in TER at the end of the exposure was recorded. Following this the mucosal chamber solution was replaced with KHBB pH 7.4 + 1 mg/ml fluorescein. Passage of fluorescein to the serosal chamber was measured after 2 h.

Results There was no significant difference between controls and NERD patients on PPI with regards to TER baseline ($74 \pm 6 \Omega/\text{cm}^2$ vs $99 \pm 11 \Omega/\text{cm}^2$) or permeability after exposure to the pH 7.4 solution. There was no reduction in TER after 30 min exposure to the pH 7.4 solution. Exposure to acidic solution resulted in a significant reduction in TER ($-25.0 \pm 2.9\%$, $p < 0.05$) for all subjects, with no significant difference between patient and control groups. Permeability to fluorescein after 2 h trended towards an increase in patients versus controls that did not reach statistical significance. Exposure to weakly acidic solution caused a smaller, significant, decrease in TER. This TER reduction was greater in patients than in controls ($-6.7 \pm 1.2\%$ vs $-1.4 \pm 2.4\%$, $p = 0.02$). There was no significant difference in permeability to fluorescein between groups after weakly acidic exposure.

Conclusion In basal conditions or after exposure to aggressive acidic solutions, oesophageal mucosal integrity of NERD patients refractory to PPI did not differ from controls. However, mucosal exposure to weakly acidic + bile acid solutions produced a distinct response in these patients, suggesting an increased susceptibility which may explain some patients' apparent hypersensitivity to weakly acidic refluxate and failure of PPI therapy.

Competing interests None.

Keywords Non-erosive reflux disease (NERD), Oesophageal mucosal functional integrity, Refractory GORD.