

IgE-mediated immune response to *Helicobacter pylori* examined by basophil histamine release in patients with dyspepsia

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Introduction

Helicobacter pylori (*H. pylori*) is an important pathogen in gastroduodenal inflammation and ulceration. Several mechanisms have been proposed to explain its role. One mechanism is the *H. pylori*-induced histamine release (HR) in the gastric mucosa, since a lower histamine content has been shown in patients with *H. pylori* infection compared to controls without *H. pylori* infection, and histamine content returns to normal after bacterial eradication [1, 2]. Here we studied whether such a HR depends on an IgE-mediated immune response to *H. pylori*, tested by homologous and heterologous *H. pylori* strains.

Materials and methods

The study (approved by local ethics committee) included 61 patients with peptic ulceration (28 females and 33 males; mean 54 years: range 21–81 years).

H₂-receptor antagonists and proton pump inhibitors were removed at least five days before, and antibiotics 1 month before gastroduodenoscopy. During gastroscopy biopsies were taken from antrum and corpus according to the Sydney classification of gastritis [3].

Paraffin embedded sections of the biopsies were stained with haematoxylin-eosin and examined for morphology and *H. pylori*. Biopsies were cultured on 7% lysed horse blood agar plates by incubation at 37°C under microaerobic conditions for < 7 days. *H. pylori* was identified as oxidase, catalase and urease positive curved rods. Sonicates of *H. pylori* for HR testing were produced from subcultures which were harvested, washed and resuspended in sterile distilled water. Bacterial suspensions were sonicated on ice, five times for 45 s at 20,000 Hz and adjusted to a protein concentration of 0.1 mg/ml by refractometry. Sonicates of a reference *H. pylori* strain, CH-20429, isolated from a patient with peptic ulceration and used in earlier studies [4] were included. Basophil HR induced by *H. pylori* in leukocyte suspensions from the patients was performed according to [5]. *H. pylori* was tested in final concentrations of protein from 10⁻¹² to 10⁻² mg/ml. A HR > 10% was considered a positive response (spontaneous releases = 6 ± 2%). Intact leukocytes and leukocytes stripped of IgE were run in

parallel. A reduced HR from stripped cells indicates an IgE-mediated reaction, which was defined by a > 50% reduction in maximum HR [5].

Results and discussion

Of 61 patients with dyspepsia, 37 patients were infected with *H. pylori*. No difference was found in gastritis and peptic ulcer between infected and noninfected individuals. Leukocytes from the *H. pylori*-infected patients stimulated with homologous *H. pylori* strains, i.e. the patients' own isolates, showed a positive HR response of 13% (Fig. 1a). Removal of surface IgE from basophils in 7 of the infected patients demonstrated a significantly reduced response from 11 to 4% (Fig. 1b₁ and b₂) indicating that the response to homologous strains was IgE-dependent. Conversely, a negative response of 6% was obtained by the heterologous *H. pylori* strain CH-20429 (Fig. 1c). When testing 8 of the infected patients with heterologous strains from the other infected patients only 2 patients showed a positive response (12 and 15%) and the group showed a HR of 7% (Fig. 1d). In the group of 24 non-infected patients a negative response of 6% was obtained to CH-20429 (Fig. 1e). When 11 of these individuals were tested with strains from the infected patients only 2 showed positive response (11 and 12%) and the group showed an 8% release (Fig. 1f).

The results demonstrate that *H. pylori* caused basophil HR only in individuals with gastric *H. pylori* infection, and only with the patient's own *H. pylori* strain. Stripping experiments showed that HR was caused by a specific IgE-mediated immune response to *H. pylori*. A negative response was obtained using the heterologous strains, except in a few patients. These cases may have involved strains with identical or cross-reacting bacterial epitopes or patients who may have had a previous *H. pylori* infection. Our results agree with those of Aceti et al. [6], using a standard mixture of surface components of *H. pylori* cells harvested from 10 different strains. They also agree with reports showing no HR response from control individuals or peritoneal mast cells

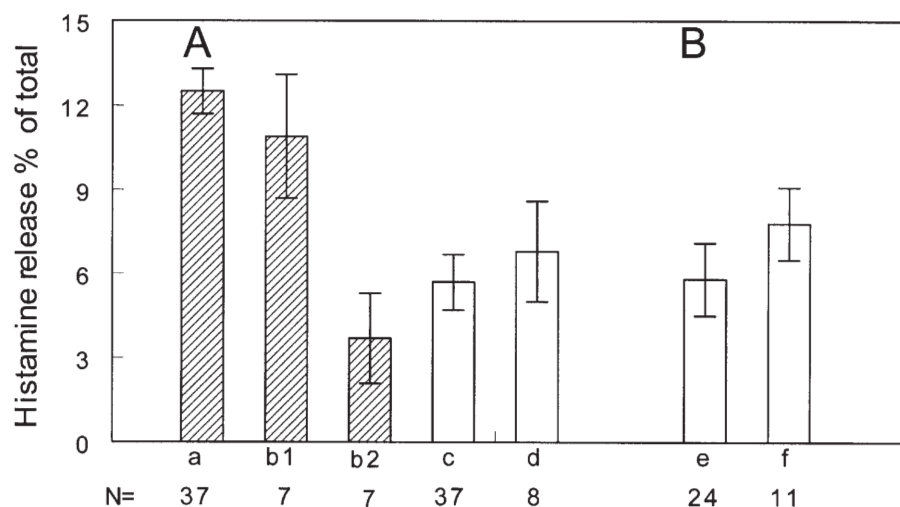


Fig. 1. Maximum histamine release caused by *H. pylori* in leukocyte suspensions from patients with dyspepsia: infected (A) and not infected (B) with this bacterium. Response to the patient's own *H. pylori* strain (a), before and after removal of IgE-molecules from the basophil cell surface (b₁ and b₂), in response to a heterologous laboratory strain of *H. pylori* (CH-20429) (c and e) and heterologous strains from the other patients (d and f). Mean $\pm$ SEM and N are given. $P < 0.01$ by Student's t-test for a/c, a/d and b₁/b₂.

from uninfected rats [7, 8]. Furthermore, specific IgE directed against *H. pylori* was demonstrated in serum from *H. pylori* infected patients but not noninfected patients [6]. A specific IgE-mediated immune response to *H. pylori* may be associated with gastric *H. pylori* infection. However, studies focusing on IgE-mediated secretion from histamine storing cells and other cells involved in gastric secretion are necessary.

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