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CLINICAL REPORT

Is *Helicobacter pylori* Infection Associated with Chronic Urticaria?

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There have been controversial reports of an elevated prevalence rate of *Helicobacter pylori* infection in chronic urticaria patients. Furthermore, in some studies remission of chronic urticaria has been reported after eradication of *H. pylori*. The aim of this investigation was to evaluate the prevalence of *H. pylori* infection among chronic urticaria patients and to study the effect of eradication therapy on urticaria symptoms. Chronic urticaria patients (n= 235) were enrolled and *H. pylori* status was determined serologically. Thirty-five patients received antimicrobial triple therapy.

25% of the patients were positive for *H. pylori*. The prevalence of *H. pylori* infection was not significantly higher among urticaria patients compared with the normal Finnish population in any of the age groups studied. Of the successfully treated patients, 27% showed remission of urticaria. Our data suggest that the prevalence of *H. pylori* infection is not elevated among chronic urticaria patients and that *H. pylori* eradication does not appear to influence the course of chronic urticaria. *Key words: Helicobacter pylori; chronic urticaria; eradication therapy; seroepidemiology*.

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Chronic urticaria is a common immunological skin disorder, with a prevalence of 15–25% (1). Several exogenous and endogenous causes, e.g. hyperreactivity to foods, food additives or drugs, hidden and overt infections in the ear, nose and throat and dental areas and also in the gastrointestinal tract, have been proposed as causative agents. Despite thorough investigations, the etiology remains unresolved in >80% of the cases (1).

Helicobacter pylori is the cause of chronic gastritis and an important risk factor for peptic ulcers and gastric cancer as well as mucosa-associated gastric lymphomas (2). Persistent serum antibodies against *H. pylori* are characteristic of this common infection, and are present in perhaps half of the world's population. The prevalence of *H. pylori* increases with age (2–4); in developed countries this is mainly caused by the decreasing rate of childhood infections (5).

Since the discovery of *H. pylori*, the understanding and treatment of many gastrointestinal illnesses have changed and it is not surprising that this common pathogen has evoked the interest of researchers in many fields who have tried to link this pathogen with different disorders. Controversial reports of an elevated prevalence rate of *H. pylori* infection in chronic urticaria patients have been published. In 2 studies (6, 7) a high (55–62%) prevalence of this infection among chronic urticaria patients was demonstrated but there was no information on the prevalence rate in an age-matched sample of the general population. In some studies remission of chronic urticaria has been reported after eradication of *H. pylori* (8–10) but other studies have shown no clinical improvement after eradication (11, 12).

MATERIAL AND METHODS

Patients with chronic urticaria (n= 235; mean age 41.1 years; 147 females and 84 males) were studied. *H. pylori* status was assessed by serology. Standard investigations for urticaria were performed, i.e. white blood cell count, hemoglobin level, erythrocyte sedimentation rate and urine analysis. In suspected cases, teeth, sinus and thorax X-rays were obtained and analyses of serum antigliadin antibodies, antinuclear antibodies, thyrotropin, free tyroxin and C1-esterase inhibitor were also performed.

The *H. pylori* antibody prevalence rates of a Finnish semi-urban population have been reported previously (3). The serum IgG and IgA antibody titers to *H. pylori* were measured using an in-house enzyme immunoassay (3, 4). The antigen used was an acid glycine extract from *H. pylori* strain NCTC 11637. The absorbance readings were converted to end-point titers, which were dilutions of the serum at the cut-off level defined by the optical densities of positive reference serum pools at constant dilutions.

Thirty-five patients were treated with metronidazole 400 mg t.i.d. and lanzoprazole 30 mg b.i.d., combined with either amoxicillin 1000 mg b.i.d. or tetracycline 500 mg q.i.d., for 7 days. The success of eradication triple therapy was assessed by a decrease in antibody titers 5 months after the treatment (13). At this time patients were also examined by a dermatologist.

The informed consent of all the participants was obtained. The study was approved by the Ethical Committees of the University Hospitals of Helsinki and Kuopio.

RESULTS

All the standard investigations for urticaria were negative for these patients. Of the chronic urticaria patients, 25% (57/231) were positive for *H. pylori*. The prevalence rate of *H. pylori* infection rose with age similarly to that of the control subjects. In the age groups ω15, 15–24, 25–34, 35–44, 45–54, 55–64 and >65 years the prevalence rates were 0%, 11%, 14%, 22%, 32%, 42% and 57%, respectively (Fig. 1). The prevalence rate of *H. pylori* infection in urticaria patients was not significantly higher in any age group than that of the normal Finnish population (Fig. 1).

Thirty-five *H. pylori*-positive patients received eradication triple therapy. The eradication therapy was successful in 30/35 (86%) of the patients. Eight out of 30 (27%) patients in whom *H. pylori* was successfully eradicated showed remission of urticaria. Three out of five (60%) of the treatment failures also showed remission of urticaria. Five of the 18 (28%) *H. pylori*-

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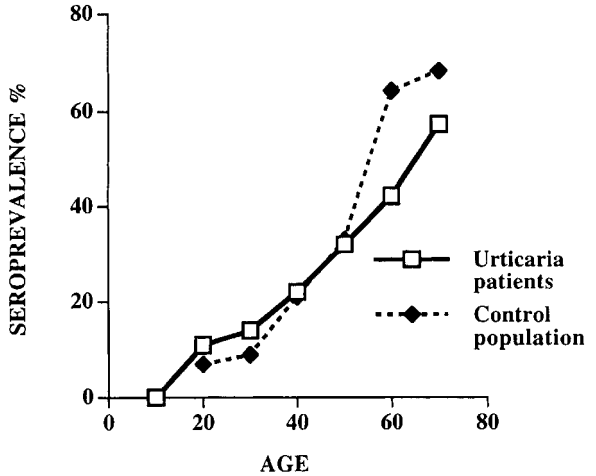

Fig. 1. Prevalence of *Helicobacter pylori* antibodies (IgG and IgA results combined) in chronic urticaria patients compared with the Finnish control population.

positive patients who were not treated showed remission of urticaria. Four of the *H. pylori*-positive patients did not complete the treatment or did not attend the control visit. The treatment failures and non-treated patients combined showed remission of urticaria in 8/24 (33%) cases; thus there is no statistically significant difference between the *H. pylori*-positive and -negative patient groups in terms of the outcome of urticaria.

DISCUSSION

Our study of 231 patients, to our knowledge the largest study so far on *H. pylori* and chronic urticaria, revealed no difference between the prevalence rates of this infection in chronic urticaria patients and control subjects. The number of patients included in earlier studies on *H. pylori* and chronic urticaria has been small, and comparisons with the prevalence of *H. pylori* infection in age-matched samples of the general population have not always been reported (6, 7). Two population studies indicated that the prevalence of *H. pylori* infection in Finland is the same as that in other Western countries (3, 4). The prevalence of this infection increases concomitantly with age (3, 4), implying that age should be taken into consideration in studies linking *H. pylori* to any disorders. This point of view has also been expressed in a recent letter (14).

According to our study, *H. pylori* eradication does not appear to have a marked influence on the course of chronic urticaria. Two other groups have come to the same conclusion (11, 12) but different results have also been reported (6–9). The small number of patients and different follow-up times in these studies have made it difficult to draw any firm conclusions and may partly explain the contradictory results. Spontaneous remission of chronic urticaria may occur in up to 50% of patients 6 months after onset (1), which suggests that the follow-up time should be fairly long. It was quite common in our study to see a temporary relief of urticaria symptoms after treatment, but symptoms recurred after a few weeks or months.

None of these studies, our included, have been carried out blinded. Thus, the treatment of *H. pylori* could favor the reporting of reduced urticaria symptoms in patients' assessment of their symptoms. A placebo-controlled study design might not solve this problem, as it is not known what the eradication therapy might eradicate besides *H. pylori*. This is indicated by the fact that the eradication therapy was associated with the rapid relief (within 2–3 days) of urticaria symptoms in some of our patients even though *H. pylori* was not eradicated. Even alterations in the gut flora caused by triple treatment could be of importance. A part of the dilemma could be solved by treating *H. pylori*-negative chronic urticaria patients with triple treatment; however, this is ethically questionable. A large, double-blinded, placebo- controlled study design including both *H. pylori*-positive and -negative patients may be the only way to conclusively demonstrate the role of *H. pylori* in chronic urticaria.

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