

Chronic Idiopathic Urticaria: Natural Course and Association with *Helicobacter pylori* Infection

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Key Words

Urticaria · Chronic idiopathic urticaria · *Helicobacter pylori*

Abstract

Background: Chronic urticaria is a common disease, though only few data on its natural course are available. In most cases the cause cannot be determined. Recently a relationship of chronic urticaria to infection with *Helicobacter pylori* (HP) has been postulated, but no controlled study has been performed to prove this association. **Methods:** In this prospective study the clinical course and rate of HP infection in 46 patients with chronic 'idiopathic' urticaria were investigated. Infected patients were treated in a double-blind placebo-controlled crossover study with amoxycillin and lansoprazol. Eradication and clinical course were followed up 2 months after each treatment, respectively, 3 and 6 months after the first consultation. **Results:** In 19/46 (41%) the chronic 'idiopathic' urticaria resolved within 6 months. 12 patients (24%) were infected with HP, which corresponds to the infection rate of the population at comparable ages without urticaria in Switzerland. Eradication of HP was achieved in 3, but only in 1 was the eradication associated with the resolution of urticaria. **Conclusions:** Our data show that in young patients with a rather short history of chronic urticaria frequently a rather favourable natural course of chronic idiopathic urticaria can be seen. No association between HP infection and chronic urticaria could be demonstrated.

Introduction

Urticarial disease is a cutaneous reaction evoked by multiple factors. Chronic urticaria, usually defined as weekly recurrent attacks of hives over a >6-week period, can be a troublesome dermatologic disorder. Only few data on prevalence and natural course of chronic urticaria are available [1]. In contrast to acute urticaria causal factors of chronic urticaria are usually elusive [2, 3] and therefore the disease is often labelled as chronic idiopathic urticaria (CIU). Recently a relationship of CIU and *Helicobacter pylori* (HP) has been postulated (table 1), however no prospective and controlled study has been performed to prove this association.

In this study we investigated prospectively the clinical course and the rate of HP infection in patients with CIU in our outpatient clinic between June 1996 and April 1998. All patients with a positive ¹³C urea breath test indicating an active HP infection were treated in a double-blind, placebo-controlled crossover study with amoxycillin and lansoprazol. Eradication and clinical course were followed up 2 months after each treatment, respectively, 3 and 6 months after the first consultation.

Methods

Patients and Definitions

Patients referred to the allergy and immunology outpatient clinic of the University Hospital of Bern with chronic urticaria were assessed between June 1996 and April 1998 by a standardised protocol. The study protocol was reviewed and approved by the local ethical

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1018–2438/99/1191–0060 \$17.50/0

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Table 1. Association of chronic urticaria and HP infection in the literature

	Total patients	HP-infected	HP-eradicated	Urticaria resolved
Kolibaxova et al. [4]	30	21/30	21/21	20/21
Rebora et al. [5]	7	4/7	?	3/4
Bohmeyer et al. [6]	10	8/10	?	8/8
Tebbe et al. [7]	25	17/25	14/17	8/14
Kalas et al. [8]	40 ^a	17	17/17	no change
Wedi et al. [9]	100	26 ^b	21	14/21

^a In 40 out of 95 patients the chronic urticaria was accompanied by gastrointestinal complaints.

^b 47 patients were seropositive for HP, 27 of them underwent endoscopy and in 26 antral HP infection was found.

committee and all patients gave informed consent to the study and investigations. Potential causes were evaluated by a detailed history, physical examination and laboratory tests (table 2). 115 patients were classified as chronic urticaria. The age of the patients ranged between 15 and 78 years. CIU was considered if no aetiological or triggering factor could be found. In the case of the presence of urticarial dermographism and the infestation of *Blastocystis hominis* (an endoparasite with unclear clinical significance) the urticaria was also classified as idiopathic.

Design of the Study

All patients with CIU (n = 50) were screened for HP by ELISA-IgG. Subjects with a positive serology for HP were tested by the ¹³C urea breath test. If the ¹³C urea test was positive, an active HP infection was assumed [10]. These patients were randomised into two study arms receiving either the drug or placebo each for 2 weeks. Two months after therapy with the drug or placebo, the patients were reassessed with a ¹³C urea breath test and treated with the reciprocal drug (placebo or drug). 2 months later a new reevaluation with the ¹³C urea test and the clinical course was done. The study end points were the eradication of HP as assessed by the ¹³C urea breath test and the clinical course of the CIU. The CIU was considered as resolved if no attacks of hives occurred for a period of at least 2 weeks. The clinical course of patients with CIU and negative serology or negative ¹³C urea breath test was followed up by a phone call 3 and 6 months later.

Treatment of HP

Lansoprazol 30-mg capsules and amoxicillin 1-gram tablets twice daily postprandially for 2 weeks were used as treatment of the HP infection. A similar regime (omeprazole and amoxicillin) was described as highly effective in one study with patients with chronic urticaria and HP infection [6]. Symptomatic treatment with short acting antihistamines was allowed in both study arms.

Results

Clinical Course

50 of 115 patients (43%) with chronic urticaria were considered having CIU since the investigations (table 2) did not yield causal factors such as allergy, autoimmune or infectious diseases. In 65 subjects the constellation of labora-

Table 2. Investigations in patients with chronic urticaria

<i>History regarding influencing factors</i>
General factors observed by the patient
Physical factors
Delayed pressure (> 4 h)
Physical exercise
Cold/heat
Exposure to sunlight
Contact (e.g. latex, pets)
Drugs
Food (e.g. dye, preservatives such as sodium benzoate)
<i>Physical tests</i>
Dermographism
Immediate skin tests with common aero-allergens, foods and methacholine
<i>Laboratory investigations (only performed in nonphysical urticarias)</i>
<i>Haematology</i>
CRP
Protein electrophoresis
Screening for hepatitis B/C infection
IgG antibodies to HP
Thyroid function (TSH)
ANA scinting
Total IgE level
Urinalysis
Stool examination for endoparasites

tory analysis and history was compatible with a possible cause or triggering factors (physical factors in 15, focal infections in 11, autoimmune disorders in 10, food intolerance in 7 and various diseases in 22). 46 out of the 50 patients (92%) with CIU were followed up for 6 months. In 19 of these 46 subjects (41%) CIU resolved within 6 months. Patients with or without immediate pressure urticaria did not show any difference in their clinical course, whereas age

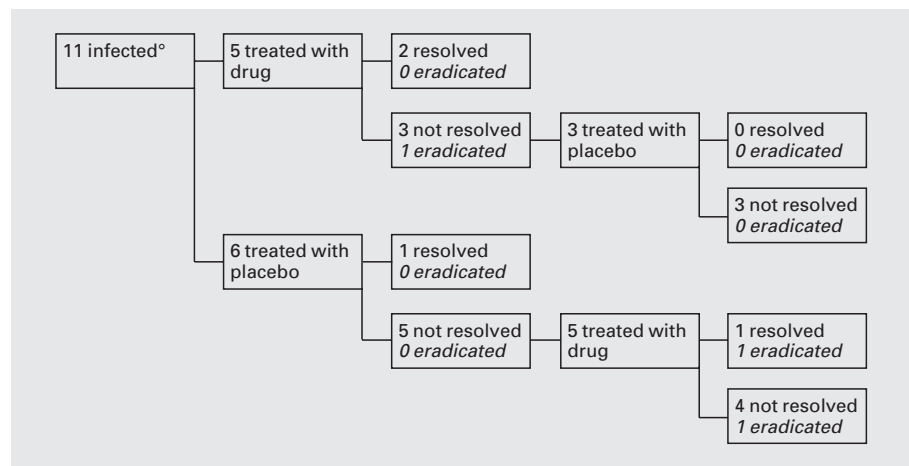


Fig. 1. Clinical course of chronic urticaria in HP-infected patients ○ = 1 out of 12 patients with HP infection refused an eradication treatment but was followed up. The number of patients in whom the treatment led to an HP eradication is indicated in italics.

(>35 years) and longer duration of the urticaria (>1 year) were unfavourable prognostic factors (27 and 24% resolution, respectively).

Association with HP Infection

14 of the 50 patients with CIU had a positive serology for HP and 12 (24%) of them an active HP infection as demonstrated by the ^{13}C urea test. The mean age of subjects with active HP infection was 45 years (range 34–73 years). 11 of these 12 individuals participated in the double-blind crossover study. Eradication could be achieved in 3 subjects (27%) and in 4 individuals (36%) a resolution of the chronic urticaria could be observed. However, no correlation of HP eradication and resolution of urticaria could be demonstrated, as the urticaria resolved only in 1 patient after successful eradication treatment whereas in 3 patients the urticaria disappeared without eradication of HP (fig. 1). The resolution rate of patients who received a drug eradication treatment ($3/10 = 30\%$) was thus similar to that of age-matched patients without eradication treatment ($4/14 = 29\%$).

Discussion

In this study, 50 of 115 patients (43%) with chronic urticaria were classified as CIU. This proportion seems rather low compared to the literature [2, 11], and may reflect the relatively extensive investigations done in our study group. 19 of 46 individuals (41%) became symptomless within 6 months without any or only symptomatic treatment (mainly non sedating antihistamines). Patients under the age of 35 years had a more favourable clinical course with a 60% res-

olution. These results are in agreement with Harris et al. [11], showing a fairly high rate of spontaneous resolution of CIU in young people, particularly if the CIU had not lasted longer than 1 year. 12 of 50 patients (24%) with CIU had an active HP infection. This proportion of HP infection is in the range of a population at comparable ages but without urticaria in Switzerland (19% asymptomatic people, 39% in dyspeptic people [12]). Thus, HP infection does not appear to be more frequent in patients with CIU, indicating no strong association of HP infection with chronic urticaria.

In only 3 of 11 patients with active HP infection and CIU, an HP eradication was achieved following a 2-week treatment with lansoprazol and amoxicillin. This treatment, chosen because it led to resolution of the chronic urticaria in 8 of 8 in one study [6], was not sufficiently effective in our series as well as in other recent studies [13, 14]. Urticaria was resolved only in 1 of 3 patients, in whom eradication was successful. This corresponds to the natural course of the disease, since 3 of the remaining 8 subjects in whom eradication treatment failed also experienced resolution of CIU. Thus, in our study neither the frequency of HP infection nor the response to treatment indicates a causal relationship between chronic urticaria and HP infection.

This 'negative' finding is in contrast to other reports postulating a causal relationship between HP infection and chronic urticaria [4, 6, 7, 9]. Our data, however, are in agreement with a recent study failing to demonstrate an association between HP infection and CIU [8]. These contradictory findings may have various reasons. (1) HP eradication regimens were different. In our study only a few patients have been successfully treated. A more effective treatment may have yielded a higher success rate. But this does not explain the discrepancy in the prevalence rate of

HP infections in our study and by Wedi et al. [9]. (2) There was a lack of appropriate controls in most previous studies. Since the natural course of CIU might be rather favourable, resolution may have occurred even without eradication of HP. (3) Selection of patients is probably the main reason why results are contradictory. While our analysis was prospective, other published studies relied on retrospective data.

In summary, the association of HP infection and chronic urticaria remains controversial. Thus we consider a recommendation for the general screening for HP infections as

first-line investigation in patients with chronic urticaria as not justified until more data from prospective, double-blind placebo-controlled studies are available [9].

Acknowledgement

This work was supported by Swiss National Foundation No 32-46798.96 (to A.H.) and the Inselspital Bern. Drug and placebo were given to us by Grüenthal, Mitlödi, Switzerland.

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