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RAPID COMMUNICATION

Does *Helicobacter pylori* infection eradication modify peptic ulcer prevalence? A 10 years' endoscopical survey

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Abstract

AIM: To compare peptic ulcer prevalence in patients referred for upper gastrointestinal endoscopy in two Italian hospitals in pre-*Helicobacter* era and ten years after the progressive diffusion of eradication therapy.

METHODS: We checked all the endoscopic examinations consecutively performed in the Gastroenterology Unit of Padova during 1986-1987 and 1995-1996, and in the Gastroenterology Unit of Parma during 1992 and 2002. Chi Square test was used for statistic analysis.

RESULTS: Data from both the endoscopic centers showed a statistically significant decrease in the prevalence of ulcers: from 12.7% to 6.3% ($P < 0.001$) in Padova and from 15.6% to 12% ($P < 0.001$) in Parma. The decrease was significant both for duodenal (from 8.8% to 4.8%, $P < 0.001$) and gastric ulcer (3.9% to 1.5%, $P < 0.001$) in Padova, and only for duodenal ulcer in Parma (9.2% to 6.1%, $P < 0.001$; gastric ulcer: 6.3% to 5.8%, NS).

CONCLUSION: Ten years of extensive *Helicobacter pylori* (*H pylori*) eradication in symptomatic patients led to a significant reduction in peptic ulcer prevalence. This reduction was particularly evident in Padova, where a project for the sensibilization of *H pylori* eradication among general practioners was carried out between 1990 and 1992. Should our hypothesis be true, *H pylori* eradication might in the future lead to peptic ulcer as a rare endoscopic finding.

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Key words: Ulcer prevalence; *H pylori*

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INTRODUCTION

It is now well established that *Helicobacter pylori* (*H pylori*) eradication can significantly modify the natural history of peptic ulcer disease. Marshall *et al* first demonstrated in 1988 that when *H pylori* was cleared 92% of ulcers healed and only 21% relapsed during a 12 mo follow-up period[1]. Several studies have then confirmed these data over the years. Follow-up studies have in fact shown lower relapse rates of both gastric and duodenal ulcers after successful *H pylori* eradication, in the short term as in the long term[2-4]. So by the end of the eighties *H pylori* was generally accepted as a causal factor in the pathogenesis of chronic gastritis and peptic ulcer. Between the end of the eighties and the beginning of the nineties eradication of *H pylori* has become a widespread approach for acid-related disorders, first among GI specialists, then among general practitioners.

Leerdam *et al* (2003) described a reduction in the incidence of upper gastrointestinal bleeding between 1993/94 and 2000[5]. They hypothesized that the decrease in incidence might partly be explained by the fact that *H pylori* is more often eradicated in patients with dyspeptic complaints and peptic ulcer disease, thus reducing the possibility of development of complications as bleeding. Furthermore, it is often reported as an impression by endoscopists that we see fewer ulcers than we did years ago, but data on the real prevalence are still scanty. Xia *et al* (2001) studied the prevalence of *H pylori* infection, peptic ulcer disease and reflux esophagitis in consecutive patients referred for upper GI endoscopy in an endoscopy unit in Sydney in a three-month period in different years (1990, 1994 and 1998), reporting a decrease in peptic ulcer disease

(22%, 15% and 13%, respectively, $P=0.003$). They also described a lower prevalence of *H pylori* infection as well as a significant decrease in NSAIDs consumption, leading to the hypothesis that both these two risk factors likely contributed to the reduction of peptic ulcer disease[6].

Therefore, the aim of this study was to compare the prevalence of peptic ulcer disease among patients referred for upper GI endoscopy between the eighties and the nineties and after a period of 10 years, in two Italian GI units of two hospitals.

MATERIALS AND METHODS

Patients

We retrospectively analyzed all the upper GI endoscopies performed in the Gastroenterology Unit of Parma in two different years (1992 and 2002), and in the Gastroenterology Unit of Padova in two periods: from Feb 1, 1986 to Dec 31, 1987 and from Feb 1, 1995 to Dec 31, 1996. We selected the patients with a diagnosis of gastric or duodenal ulcer. Both the endoscopic units of Parma and Padova serve in-patients and out-patients, and are the major endoscopy centers of the area. Out-patients are directly sent by general practitioners or by specialists. Both the units have an informatic database (DB3 engine). We searched for gastric and duodenal ulcers both manually and informatically, with the strings "(gastrica or gastriche or angolare or antrale or del corpo-fondo) and/or (duodenale/i or bulbare or bulbari or del duodeno) and (ulcera or ulcere)".

Between 1990 and 1992 a project was performed in Padova in order to stimulate the aptitude towards the *Helicobacter pylori* (*H pylori*) eradication among physicians. It involved both specialists and general practitioners.

H pylori status was obtained for all patients accessing the hospital, through the dosage of serum antibodies. Data about upper GI symptoms and history of acid-related disorders were also collected. All patients positive for *H pylori* infection were treated with a triple one week therapy ("ulcer-free hospital" project).

Several meetings were held by the Gastroenterology Clinic of Padova between 1990 and 1992, with the participation of groups of 30 general practitioners. Statements discussion and interactive clinical case analysis were conducted, with initial and final testing of *H pylori* . General practitioners were sensibilized to test all patients suffering from upper GI symptoms or with a history of gastritis or peptic ulcer, diagnosed with a structured questionnaire ("ulcer-free ambulatory") and eradicate *H pylori*, when positive.

Statistical analysis

Chi Square test was applied on the changes of prevalence of peptic ulcers (total), gastric and duodenal ulcers after a decade. $P<0.05$ was considered as significant.

RESULTS

In Parma we analyzed a population of 3779 subjects in 1992 (2185 out-patients and 1594 in-patients), with a mean age of 69.4 years (range 5-94 years) and a sex distribution of 54.4% males and 45.6% females, as well as a population of 3828 subjects in 2002 (1985 out-patients and 1843 in-patients), with a mean age of 62.3 years (range 12-97 years) and a sex distribution of 53.4% males and 46.6% females. We found 588 ulcers in 1992 (239 GU and 349 DU), 459 ulcers in 2002 (223 GU and 236 DU). *H pylori* status was evaluable only for 28.7% of patients with peptic ulcer in 1992 and 47.7% in 2002, so it could not be useful for statistical analysis. Among gastric ulcers, we found neoplastic lesions in 56 subjects in 1992 and 20 subjects in 2002.

In Padova we analyzed a population of 3703 subjects during 1986-1987, with a mean age of 54 years (range 15-91 years) and a sex distribution of 53.5% males and 46.5 females, as well as a population of 5727 subjects during 1995-1996, with a mean age of 51 years (range 14-98 years) and a sex distribution of 39.7% males and 60.3% females. We found 470 ulcers during 1986-87 (144 GU and 326 DU), 361 ulcers during 1995-1996 (86 GU and 275 DU). *H pylori* status was available only for patients with peptic ulcer during 1995-1996 and showed a prevalence of 83.6% (68.6% for GU and 88.4% for DU). It was determined by histology of mucosa, with appropriate staining.

Table 1 and Table 2 summarize the changes in prevalence of peptic ulcer after ten years in Parma and in Padova. Table 3 and Table 4 describe the epidemiological characteristics of the populations we studied.

Both the endoscopic centers showed a statistically significant decrease in the prevalence of ulcers: 12.7% to 6.3% ($P<0.001$) in Padova, 15.6% to 12% ($P<0.001$) in Parma. The decrease was greater for duodenal ulcer (8.8% to 4.8%, $P<0.001$ in Padova, 9.2% to 6.1%, $P<0.001$ in Parma) than for gastric ulcer (3.9% to 1.5%, $P<0.001$ in Padova, 6.3% to 5.8%, NS in Parma).

Table 1 Changes in prevalence of peptic ulcer after ten years in Padova

Padova	1986-1987 *n* (%)	1995-1996 *n* (%)	*P*
Population	3703	5727	
Total of ulcers	470 (12.7)	361 (6.3)	< 0.001
Duodenal ulcer	326 (8.8)	275 (4.8)	< 0.001
Gastric ulcer	144 (3.9)	86 (1.5)	< 0.001

Table 2 Changes in prevalence of peptic ulcer after ten years in Parma

Parma	1992 *n* (%)	2002 *n* (%)	*P*
Population	3779	3828	
Total of ulcers	588 (15.6)	459 (12)	< 0.001
Duodenal ulcer	349 (9.2)	236 (6.1)	< 0.001
Gastric ulcer	239 (6.3)	223 (5.8)	NS

Table 3 Characteristics of the population from Parma

	1992	2002
Population (*n*)	3779	3828
Origin	2185 out-patients, 1594 in-patients	1985 out-patients, 1843 in-patients
Age (yr)	69.4 (range 5-94)	62.3 (range 12-97)
Sex (M/F)	54.4%/45.6%	53.4%/46.6%

Table 4 Characteristics of the population from Padova

	1986-1987	1995-1996
Population (*n*)	3703	5727
Age (yr)	54 (range 15-91)	51 (range 14-98)
Sex (M/F)	39.7%/ 60.3%	53.5%/ 46.5%

DISCUSSION

The study suggests that the incidence of peptic ulcer among patients referred for upper GI endoscopy significantly decreased through the years. Our hypothesis is that *H pylori* eradication could have changed the natural history of peptic disease. Eradication of the bacterium by the general practitioners in symptomatic subjects has become a common approach through the nineties. So we identified those patients who have not been eradicated or who were still symptomatic after the therapy.

One limit of the present study is the examination of a selected population, which was referred for upper GI endoscopy and probably had been given antisecretory drugs during the weeks preceding the access to the endoscopy. We have asked ourselves if the reduced prevalence of ulcer after ten years could be related with differences in drug prescription of anti-secretive agents among general practitioners. We did not collect data on drug intake, however, we thought this finding might only play a secondary role in the observed trend. In fact, significant differences in drug prescription could be seen when comparing the early eighties to the nineties, and since the late eighties histamine H2-receptor antagonists (anti-H2s) and proton pump inhibitors (PPIs) have been widely used in both the Italian areas we examined.

Capurso *et al* (1996)[7] retrospectively analysed upper gastrointestinal endoscopies performed in their center in Rome between January 1981 and December 1991. They reported an incidence of 4.1%±0.6% and a mean annual prevalence of 6.9%±0.7%. These data are quite similar to those in our center at the beginning of the observation period.

Data in Parma for peptic ulcer prevalence are quite similar to those reported by Xia *et al* in Sidney during the same decade. The authors concluded that both the decreased use of NSAIDs and the decline of *H pylori* infection have likely contributed to the reduction of peptic ulcer disease. Regretfully we did not have data about the *H pylori* status and the NSAIDs use of the population we examined. A reduced use of NSAIDs during the last decade has, however, not been reported in our areas, so we do not think it could have played a significant role.

The two populations examined in the present study showed different prevalence of both duodenal and gastric ulcer. We are not sure if this reflected a really different prevalence in the general populations of Parma and Padova, since no available data were collected on this subject. On the other hand, it must be underlined that the organization of both endoscopic units was similar; they tested both in-patients and out-patients, directly sent by general practitioners or by specialists.

Padova showed a greater significant decrease in the prevalence of ulcers through the decade. This might be due to the fact that the Gastroenterology Department of the University of Padova performed during those years a diffuse sensibilization of general practitioners about the eradication of *H pylori*, by means of the so called "Ulcer Free Project", as above described.

The decrease in prevalence was greater for duodenal ulcer than for gastric ulcer in both the studied populations. This is probably related to the different role played by *H pylori* in gastric and duodenal ulcer pathogenesis: it is known that more than 90% of duodenal ulcers but only 70% of gastric ulcers are associated with *H pylori* infection. This is in line with the results of the meta-analysis conducted by Ford *et al*[8]. They showed a reduction of relative risk of 54% in the recurrence of duodenal ulcer after *H pylori* eradication, and a still significant but smaller reduction of relative risk of 37% for gastric ulcer.

Additionally, it must be stressed that the role of anti-inflammatory drugs in the pathogenesis of gastric ulcer could be important in trying to correctly explain these data, but as previously mentioned, we lack at present epidemiological data on this subject.

In conclusion, we think *H pylori* eradication may in the future lead to peptic ulcer as a rare endoscopic finding, particularly in areas where a diffuse information program among general practitioners is performed. By now, the absolute number of ulcers we have diagnosed is still high, and there is need for more prevention strategies.

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