IS IT WORTHWHILE TO TREAT H PYLORI IN ALL DYSPEPTIC PATIENTS?

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ABSTRACT

To evaluate the efficacy of H pylori eradication in patients with nonulcer dyspepsia, an interventional study was carried out in the Dept of Gastroenterology, MH Rawalpindi from Jan to Feb 2004. Five hundred consecutive patients, who were referred for UGI Endoscopy, were studied. Out of these 500 patients, gastric biopsy was done in 245 patients. The patients in whom gastric biopsy was done, histopathology revealed gastritis in 187 patients and 129 (69%) were found H pylori positive. The subgroup of patients who were H pylori positive was further studied. These patients were given one week's course of eradication therapy and subsequently followed up. Sixty three percent (n=81) responded to treatment and reported improvement in their symptoms; whereas in thirty seven percent (n=48) of patients the dyspeptic symptoms persisted. In our set up where H pylori infection is pandemic, in the absence of alarm symptoms; all patients with nonulcer dyspepsia below 45 years of age should be considered for H pylori eradication.

Keywords: Nonulcer dyspepsia, gastritis, H. pylori eradication

INTRODUCTION

Helicobacter pylori is one of the most common bacterial infections of mankind. According to conservative estimates 50% of the world's population is infected with H pylori [1]. In the developing countries more than 80% among middle aged adults are affected [2]. In the industrialized countries, 20-50% of the adult population is infected [3].

Since the first recognition of H pylori by Warren & Marshall more than 20 years ago [4], the diagnosis and treatment of gastroduodenal diseases have changed dramatically. Peptic ulcer is now approached as an infectious disease, in which the elimination of the causative agent cures the condition. H pylori has been classified as a class I gastric carcinogen, and its role is well established in gastric cancer [5]. The risk of gastric cancer markedly decreases with eradication of H pylori [6]. Similarly H pylori increases risk of gastric MALT lymphoma. According to study H pylori has been present in 72-98% of cases of MALT lymphoma. Importantly, H pylori eradication leads to regression in 70-80% of MALT lymphoma cases [7].

The most common type of dyspepsia encountered in general medical and gastroenterology practice is functional (idiopathic) dyspepsia, also called nonulcer dyspepsia. The term dyspepsia is derived from Greek words dys (bad) and pepsis (digestion). It refers to symptoms originating in the upper gastrointestinal tract [8]. The prevalence of dyspepsia ranges from 26% in United States to 41% in England [9]. The prevalence in Pakistan is unknown, but it is thought to be high. 20-25% of patients with dyspepsia seek medical advice [10]. In patients with dyspepsia 40% are found to have an organic cause, and in the remainder 60%, no cause is found. These patients are classified as idiopathic/functional or nonulcer dyspepsia [11].

There are extensive and sometimes inconsistent data on the treatment of nonulcer dyspepsia. Treatment approaches that have been used are: antisecretory agents and prokinetic agents. In the current literature, eradication of H pylori in the treatment of nonulcer dyspepsia has been the subject of active research and much debate [12]. The present study was undertaken to evaluate the efficacy of H pylori eradication in nonulcer dyspepsia in our population.

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MATERIALS & METHODS

Five hundred consecutive patients referred to the Dept of Gastroenterology, Military Hospital (MH), RWP, for upper GI endoscopy in the months of Jan and Feb 2004 were evaluated for the study. These patients were referred from MH (general medical wards, general medical OPD, emergency room), Combined Military Hospital (CMH), RWP, and other peripheral hospitals. Endoscopies were performed by senior gastroenterologists and fellows in gastroenterology. The instrument used was Pentax Video, EG 2940. Biopsies were done based on clinical presentation and endoscopic findings; with interobserver variation. The biopsies were sent to the Depts. of Histopathology in Army Medical College and Armed Forces Institute of Pathology; where they were reviewed by experienced pathologists. The tissue samples were stained with hematoxylin & eosin preparations for general histopathology and giemsa stain for H pylori.

In a subset of the study, patients with dyspepsia, who had no other finding on endoscopy except gastritis and H pylori positive on biopsy, were further evaluated for H pylori eradication therapy. Their dyspepsia had ranged from 3 months to few years. The main exclusion criteria in this subgroup of patients were: documented peptic ulcer disease, GERD, gastritis on endoscopy but biopsy negative for H pylori. Those patients who fulfilled the inclusion criteria and after obtaining informed consent, were given one week's course of eradication therapy; and subsequently followed up after one month.

RESULTS

Out of total of 500 patients, 337 were males and 163 females. They ranged in age, from 13 years to 78 years. The reasons for referral are outlined in table-1. It will be noted that the vast majority of cases presented with dyspepsia 295 (59%), followed by hematemesis and melena 92 (18.4%). Pain epigastrium was present in 35 (7%) of patients.

A very sizeable portion of patients were diagnosed with Gastritis no 336 (67.2%). The second common diagnosis was Esophageal varices no 51 (10.2%). Duodenal ulcer and gastric ulcer were diagnosed in 43 (8.6%) and 11 (2.2%) patients respectively fig. 1.

Biopsy was done in 245 patients. Out of these 187 were found to have gastritis, and 129 (69%) of patients were H pylori positive. A breakdown of severity of gastritis and respective presence of H pylori is presented in table-2.

Patient's were given one week's eradication therapy; Clarithromycin 500 mg orally bd, Amoxycillin1g orally bd, and omeprazole 20 mg orally bd. Subsequently patients were followed up for improvement in their symptoms.

Those who were treated, 63% (no 81) noted improvement in their symptoms, while 37% (no 48) patients did not respond fig. 2. The patients who responded, we believe H pylori had contribution towards dyspepsia, and those patients who did not respond; we postulate that their dyspepsia could possibly be from various other non-motility and motility disorders table-3 which have been proposed as causes of dyspepsia.

DISCUSSION

Currently, one of the most important unresolved questions concerning Helicobacter pylori is whether eradication of the organism leads to a substantial improvement in symptoms in patients with nonulcer dyspepsia. In this review, we will try to answer the question, briefly discuss H pylori, nonulcer dyspepsia, and analyze the contemporary literature regarding relevance of H pylori in nonulcer dyspepsia.

Helicobacter pylori is a slow growing, microaerophilic, highly motile, gram negative, spiral urease producing organism [13]. It has predilection for gastric mucosa (native or heterotopic) [14]. It induces lifelong inflammatory response, unless infection is cured. Infection is acquired from person to person via fecal oral, oral oral and gastro oral routes [15]. Transmission is inversely proportional to socioeconomic status and prevalence increases with age [16].

Nonulcer dyspepsia is defined as recommended by Rome II criteria, "Chronic or recurrent abdominal pain or discomfort for a period of at least one month, with symptoms present more than 25% of the time, and an absence of clinical, biochemical, endoscopic, and ultrasonographic evidence of organic disease that would account for the symptoms"[17].

Nonulcer dyspepsia results in substantial health care costs, both direct costs of visits to doctors, expensive tests, and medications, and indirect costs of absenteeism from work and diminished productivity in work place. It is broadly classified into nonmotility and motility disorders [18] table-3.

The recognition of the pathogenic role of H pylori infection in patients with peptic ulcer disease and the benefits of eradicating infection has led to suggestions that infection may be the cause of dyspepsia in some patients with nonulcer dyspepsia.

Intentional self infection with H pylori has caused dyspeptic symptoms [19]. Some cases of dyspepsia may represent various stages of H pylori infection and may subsequently progress to ulcer disease [20]. Age related prevalence of H pylori is higher in patients with nonulcer dyspepsia [21].

In the local literature, the incidence of gastritis in nonulcer dyspepsia has been reported in 61% [22], 75% [23], and 94% [24] of gastric biopsies. H pylori antibodies have been detected in 78.87% of gastritis cases [22]. H pylori has been detected in biopsies from 69% [25] to 81% [24] of subjects with dyspepsia. It has been suggested that majority of patients with dyspepsia have H pylori related problem and could be put on therapy for H pylori without doing endoscopy [22].

Some studies from international literature have demonstrated an improvement in dyspeptic symptoms after eradication of H pylori [26], while an equal number of studies have not [27]. Generally studies done in areas/countries with a higher background prevalence of H pylori infection and peptic ulcer disease reported improvement in symptoms [28].

Amidst all this debate, the 1994 National Institute of Health consensus conference concluded that H pylori should NOT be eradicated in patients with nonulcer dyspepsia [29]. However some investigators and clinicians subsequently recommended that this directive be reconsidered due to following reasons: Self infection with H pylori has caused dyspeptic symptoms [19]. The frequency of H pylori infection is higher among patients with nonulcer dyspepsia than among age matched controls [21]. Some patients with dyspepsia may have antral gastritis, which can

Table-1: Indications for UGI endoscopy in 500 patients.

Reasons for referral	No	Percentage
Dyspepsia	295	59%
Hematemesis/melena	92	18.4%
Pain epigastrium	35	7%
Anemia	23	4.6%
Recurrent vomiting	16	3.2%
Chronic diarrhea	12	2.4%
Dysphagia	10	2%
Weight loss	8	1.6%
Gastric outlet obs	8	1.6%
Achalasia	1	0.2%
Total	500	100

Table-2: The severity of gastritis on endoscopy and presence of H pylori.

	Gastritis	H pylori
Mild	37	24
Moderate	102	70
Severe	48	35
Total	187	129 (69%)

Table-3: Causes of nonulcer dyspepsia.

CAUSES OF NONULCER DYSPEPSIA
Nonmotility disorders
Peptic ulcer diathesis
Gastritis
H pylori infection
Hypersecretion of acid
Bile reflux
Duodenitis
Malabsorption of carbohydrates
Small intestine parasite (Giardiasis)
Chronic pancreatitis
Psychiatric disorder
Motility disorders
Nonerosive reflux disease
Idiopathic gastroparesis
Small intestine dysmotility
Gall bladder and biliary tract disease

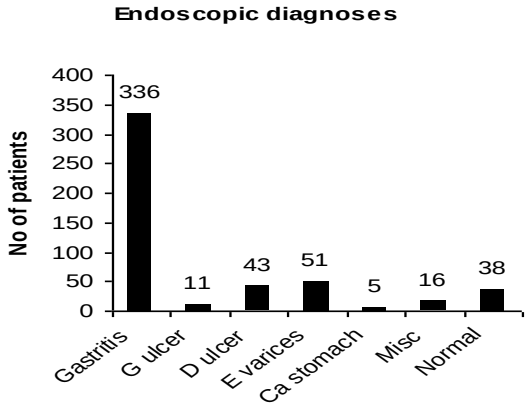

Fig. 1: Endoscopic diagnoses of 500 referred patients.

eventually progress to peptic ulcer disease [30]; this progression may be prevented by the eradication of H pylori. It is associated with the development of gastric adenocarcinoma [5] and MALT lymphoma [7].

A survey of British gastroenterologists reported that: although only 25% of the respondents considered H pylori infection a major etiologic factor in nonulcer dyspepsia, 69% were in favour of eradication [31]. In the interventional studies; improvement in dyspeptic symptoms has been noted after eradication of H pylori [26]. According to a large, well conducted, randomized, double blind, placebo controlled trial; 21% reported improvement in dyspepsia who received H pylori eradication, and 7% reported improvement in the placebo group [32]. The combined data of ORCHID and OCAY studies; two multinational, multicenter, randomized, double blind, placebo controlled trials, concluded that; in a subgroup analysis patients with reflux like and ulcer like dyspepsia showed a benefit from treatment over the control group [33]. The Cochrane review suggested that eradication of H pylori improved symptoms in 9% of patients with nonulcer dyspepsia, but this end point may miss other potential benefits of H pylori treatment [34]. Meta-analysis is used to resolve the uncertainty in magnitude of effect between studies. Several meta-analyses investigating the association between Helicobacter pylori infection and nonulcer dyspepsia report contradictory results. To address this issue, analysis of five meta-analyses was performed. It concluded that: in a subgroup of patients with nonulcer dyspepsia H pylori eradication is useful for the relief of symptoms [35].

These recommendations however should be accepted with some reservations, which are: Prevalence of H pylori infection is falling as is the incidence of peptic ulcer disease due to infection in the developed countries. Idiopathic peptic ulcer disease is on the rise. There is no clear cut link between H pylori and symptom profile. Then, there are issues regarding resistance to antibiotics and their side effects.

CONCLUSION

Nonulcer dyspepsia is a common disorder. In a developing country like ours, more than 80% of adult population is infected with H pylori. In symptomatic patients with nonulcer dyspepsia, the potential therapeutic benefit of curing a chronic disorder with a single course of antibiotics would support this approach. Not only will it help induce symptom resolution, but will also prevent further disease progression to peptic ulcer and gastric cancers.

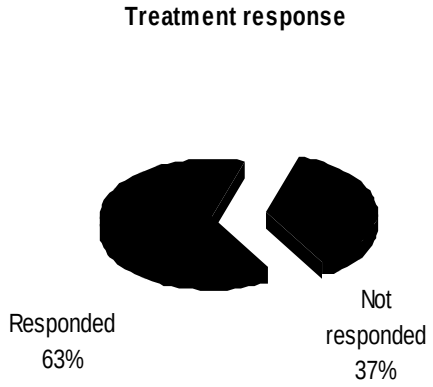

Fig. 2: Response to H pylori eradication (no 129).

In the absence of alarm symptoms, all patients with nonulcer dyspepsia below 45 years of age should be considered for H pylori treatment.

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