RELEVANCE OF DUODENAL EOSINOPHILIA IN FUNCTIONAL DYSPEPSIA

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ABSTRACT

BACKGROUND

Functional dyspepsia is a relatively common disorder in gastroenterology practice. Even though symptom criteria (like ROME III consensus criteria) have been proposed for the diagnosis of functional dyspepsia, it remains a diagnosis of exclusion due to a lack of a diagnostic test.

The aim of the study is to find the prevalence of significant duodenal eosinophilia in functional dyspepsia. Rome III consensus criteria were used to diagnose functional dyspepsia and mucosal biopsies were taken from gastric antrum, D1 and D2 by gastroduodenoscopy. Gastroduodenal eosinophil counts and presence of Helicobacter pylori (H. pylori) after special staining were assessed by pathologist.

MATERIALS AND METHODS

The underlying pathophysiology of functional dyspepsia has been poorly understood. It has been thought as a motility disorder of the stomach and abnormal gastric emptying, failure of fundic relaxation and gastric hypersensitivity has been documented in subsets of patients.

RESULTS

Out of the 84 patients studied, 23 patients (26.3%) had H. pylori in antral biopsy. 9 (9.47%) and 19 (20%) patients had eosinophil count above the cut-off values in D1 and D2, respectively. No significant association between gastric H. pylori infection and eosinophilia in D1 (p=1) and D2 (p=0.37).

CONCLUSION

Prevalence of duodenal eosinophilia in patients with functional dyspepsia was noted to be low in this study.

KEYWORDS

Functional Dyspepsia, Eosinophilia.

HOW TO CITE THIS ARTICLE: Narayanan P, Philip A, Saifudhin AA. Relevance of duodenal eosinophilia in functional dyspepsia. J. Evid. Based Med. Healthc. 2017; 4(94), 5747-5749. DOI: 10.18410/jebmh/2017/1156

BACKGROUND

Functional dyspepsia is a relatively common disorder in gastroenterology practice. Even though, symptom criteria (like ROME III consensus criteria) have been proposed for the diagnosis of functional dyspepsia, it remains a diagnosis of exclusion due to a lack of a diagnostic test. There will be no structural abnormality seen in upper endoscopy in most of the patients, which leads to the diagnosis of non-ulcer dyspepsia. It substantially impair quality of life.[1] The collective healthcare costs for non-ulcer dyspepsia is very huge due to long-term medications and healthcare seeking attitude.[3] By definition, non-ulcer dyspepsia is not an organic disease; hence, the term functional dyspepsia has been recommended. But, the label of non-ulcer dyspepsia remains in wider use in clinical practice.[2] Management of non-ulcer dyspepsia is challenging. Helicobacter pylori are found in approximately one third of cases with non-ulcer dyspepsia. But, eradication of Helicobacter pylori infection only has a small symptom benefit over placebo. Acid suppression fails in approximately two thirds of cases and the efficacy of currently available prokinetic drugs are questionable.[2]

The underlying pathophysiology of functional dyspepsia has been poorly understood. It has been thought as a motility disorder of the stomach and abnormal gastric emptying, failure of fundic relaxation and gastric hypersensitivity has been documented in subsets of patients.[3]

In addition, for unexplained reasons, sensitivity to acid infusion and acid holdup in the duodenum has been observed.[4] Also, duodenal hypersensitivity to balloon distension[5] and abnormal duodenogastric reflex responses have been observed[6] implying that the duodenum has a role in the underlying pathophysiology. There is also a significant overlap of irritable bowel syndrome with non-ulcer dyspepsia.[7] A recent study of dyspepsia in 59 children, 71% had duodenal eosinophilia, but no control group was evaluated.[8] Also, dyspepsia can be a presenting symptom of

Financial or Other, Competing Interest: None.
Submission 24-11-2017, Peer Review 30-11-2017,
Acceptance 09-12-2017, Published 12-12-2017.
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DOI: 10.18410/jebmh/2017/1156

the very rare syndrome of eosinophilic gastroenteritis.[9] It is speculated that duodenal eosinophilia would be a positive pathologic marker for the diagnosis of nonnuclear dyspepsia, akin to eosinophilic oesophagitis. Eosinophil migration in the gastric mucosa is promoted in part by mast cells.[10] When mast cells are incubated with eosinophil mediators, MBP, eosinophil cationic protein and eosinophil peroxidase, degranulation occurs and histamine is released, which may modulate sensory-motor dysfunction.[11] Such a finding, not only would alter current concepts about the pathogenesis of nonnuclear dyspepsia, but also could have sweeping implications for diagnostic approaches and possibly therapy. So, we hypothesise that it may become possible to make a positive diagnosis of non-ulcer dyspepsia based on a positive duodenal biopsy specimen. These findings may give way to a new targeted therapy, since several drugs can inhibit eosinophil production or eosinophil-derived products. A study in Sweden[3] has shown that significant increase in duodenal eosinophil count occur in functional dyspepsia.

Aims and Objectives

The aim of this study is to examine the prevalence of duodenal eosinophilia in our patient population with functional dyspepsia.

MATERIALS AND METHODS

Study Design- The study was a prospective observational study conducted in Government Medical College, Kottayam.

Inclusion and Exclusion Criteria- The study included patients with functional dyspepsia above 18 years of age, diagnosed by Rome III consensus criteria. All patients with any history of peptic ulcer disease or H. pylori eradication treatment were excluded.

Investigations

Symptom Questionnaire- The self-administered abdominal symptom questionnaire assessed symptoms of the abdomen and has been validated in earlier studies.[12] A standardised procedure for the administration of the questionnaire at the visit was used. The questionnaire includes questions describing the presence or absence (yes/no) of troublesome gastrointestinal symptoms over the preceding 3 months.

A complete clinical examination and routine laboratory workup was done to exclude other diagnosis.

Oesophagogastroduodenoscopy- Upper endoscopies were performed and endoscopists were unaware of the symptoms of the subjects before and during endoscopy. Current H. pylori infection was defined as a positive histological finding.

Definitions of Symptom Groups- Subjects were classified according to their symptom patterns as defined.

Non-ulcer dyspepsia- Dyspepsia was defined by the Rome III criteria, which must be fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis, which must include one or more of the following-

a. Bothersome postprandial fullness.
b. Early satiation.
c. Epigastric pain.
d. Epigastric burning.

Also, these cases were required to have no evidence of peptic ulcer disease, reflux oesophagitis (based on the Los Angeles classification) or malignancy.

Gastroesophageal reflux symptoms- Gastroesophageal reflux symptoms were defined as the presence of any troublesome heartburn and/or acid regurgitation over the past 3 months.[13]

Irritable bowel syndrome- Irritable bowel syndrome was defined concordant with the Rome III criteria as troublesome abdominal pain at any site plus concomitant bowel habit disturbances (constipation, diarrhoea or alternating constipation and diarrhoea).[14]

Cases- A group of 100 patients randomly selected was studied over a period of 3 months.

Histopathology- At endoscopy, biopsy specimens were taken from the following sites- fundus, body, antrum, duodenal bulb (D1) and second portion (descending part) of duodenum (D2).

Biopsy specimens were fixed in formalin and routinely processed to paraffin wax. Sections were stained with H and E and the Warthin-Starry stain (for H. pylori).

Two pathologists independently assessed the biopsy specimens. The pathology at each site (fundus, body, antrum, D1 and D2) was noted. osinophil counts were obtained from fundus, body, antrum, D1 and D2, and the H pylori status was defined as either positive or negative according to whether the bacteria was visible on the Warthin-Starry stain. Eosinophils were quantified by counting the number per high-powered field and 5 high-powered fields were selected randomly in each section. The sum, mean and median over the 5-field counts then were calculated in every subject. Based on median values of eosinophil count in the previous study by Talley et al,[3] duodenal eosinophilia was defined as eosinophil count more than 22 per 5-HPF in D1 and more than 21 per 5-HPF in D2.

RESULTS

Total number of cases studied was 95. The mean age was 42.93 years (range 19-78 years). Male patients were 42 (47.62%). 25 patients (26.3%) had H. pylori in antral biopsy. No subjects had intestinal parasites or celiac disease in biopsy. Mean eosinophil count was 9.1 per 5-HPF in D1 and 12.4 per 5-HPF in D2.

Nine (9.47%) and 19 (20%) patients had significant eosinophilia in D1 and D2, respectively. No significant association between gastric H. pylori infection and eosinophilia in D1 ($p=1$) and D2 ($p=0.37$). D1 eosinophilia was higher in females ($p=0.041$), but there was no significant association between sex and D2 eosinophilia ($p=0.18$).

DISCUSSION

We did not find a significant positive association for an eosinophil infiltrate in the duodenum with non-ulcer (functional) dyspepsia. Little other data on the possible relevance of duodenal eosinophilia exist in the literature. Toukan et al[11] from Turkey evaluated 31 cases with non-ulcer dyspepsia and 32 healthy controls; they found a slight, but significant increase in the eosinophil count of the duodenal bulb mucosa, but H. pylori status was not considered. In a study by Friesen CA et al[8] with 59 paediatric cases with non-ulcer dyspepsia, 71% were diagnosed with possible duodenal eosinophilia, but no control group could be evaluated and atopy may have confounded these results. Another study by DeBrosse et al[15] reported a mean of 9.6 eosinophils per 1 high power in the duodenum in healthy paediatric cases (maximum, 26), which is higher than the results we observed in healthy adults. A Swedish case-control study by Talley et al[3] showed that duodenal eosinophil counts were increased significantly in subjects with non-ulcer dyspepsia vs. controls and this was not related to their H. pylori status. Our study shows that the prevalence of duodenal eosinophilia in D1 and D2 is low in our population when compared to the study done by Tally et al[3] where the prevalence higher in functional dyspepsia compared to controls. The duodenal eosinophilia if present was not related to H. pylori infection in the antrum in our study. The difference in prevalence of duodenal eosinophilia in different studies shows that a local allergen or undiagnosed parasite infection may account for duodenal eosinophilia and it may not be the pathognomonic marker of functional dyspepsia.

CONCLUSION

There was no significant increase in duodenal eosinophilia in our patient population with functional dyspepsia. So, the finding of duodenal eosinophilia must be regarded cautiously and cannot be generalisable as a marker of functional dyspepsia.

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