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Endoscopic findings of dyspeptic patients unresponsive to proton pump inhibitors

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ABSTRACT

OBJECTIVE: To evaluate the endoscopic findings of dyspeptic patients unresponsive to proton pump inhibitors (PPIs) and analyze if there is any correlation between these findings and dyspeptic symptoms via predetermined inquiry.

METHODS: Patients between 18 and 45 years of age were selected among those referred to our unit for upper GI endoscopy due to failure to achieve improvement in dyspeptic complaints with PPI. Patients who consent to participate in and eligible for the study were questioned for their symptoms using questionnaires.

RESULTS: A total of 446 patients with female preponderance (60%) were included in the study. Endoscopic results were listed as: 147 (32.9%) normal, 16 (3.6%) gastric ulcer, 36 (8.1%) duodenal ulcer, 216 (48.4%) gastritis, 7 (1.5%) duodenitis and 24 (5.4%) esophagitis. A total of 122 patients were classified as functional dyspepsia. While incidence of persistent bloating was distinctly higher in patients with gastritis compared to those with normal endoscopic findings (p:0.000), but its incidence was comparable between ulcer and normal patients. No statistical difference was detected between gastritis, ulcer and normal endoscopy patients considering incidence of early satiety. Compared to those with normal endoscopy patients, incidence of epigastric pain was significantly higher among patients with gastritis and ulcer (p: 0.002 and p: 0.000 respectively). Incidence of heartburn was higher in patients with gastritis compared to those with normal endoscopy findings, but it was similar to those with ulcer.

CONCLUSION: Most (67.1%) of the patients between 18 and 45 years of age with no alarm symptoms had diagnoses that required use of a PPI. Hence, the patients should be carefully evaluated before referring for endoscopy.

Key words: Dyspepsia; esophagogastroduodenoscopy; proton pump inhibitor- treatment.

Dyspepsia is a discomfort felt over the upper abdomen, and epigastrium. Dyspepsia is a group of symptoms including pain, bloating, early satiety, postprandial upper abdominal fullness, nausea, loss of appetite, pyrosis, regurgitation, and belching. Dyspepsia is an important clinical problem in that it is very frequently seen in the community which is also one the reasons for seeking medical help. Be-

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cause of recurrent complaints in half of the patients, patient's quality of life, and social life is affected directly or indirectly [1, 2]. In addition to medical services used for dyspeptic patients, loss of labour, and productivity lead to considerable financial burden. In Western countries estimated prevalence of dyspepsia among adults ranges between 10, and 20%, and it constitutes 5% of referrals to outpatient clinics, and nearly 40-70% of the consultations for gastrointestinal complaints [3, 4]. In studies performed in various parts of the world, the prevalence of dyspepsia has been reported to vary between 14.5, and 45 percent [5-10]. In a few studies carried on in our country the prevalence of dyspepsia was revealed to fluctuate between 30.8, and 39 percent [11, 12, 13].

Patients without alarm symptoms and history of chronic disease, GIS operation, thyroid dysfunction, accidental intake of corrosive material, and diseases causing gastroesophageal symptoms as scleroderma, cases who didn't use non-steroidal anti-inflammatory drugs, steroids or routine aspirin users, and those refractory to 8 weeks of treatment with proton pump inhibitors (PPIs) were considered to have dyspepsia unresponsive to PPI treatment. In our study, upper gastrointestinal system (GIS) endoscopic findings of the patients with PPI-refractory dyspeptic symptoms.were evaluated. The purpose of the study was to investigate if any correlation exists between findings of upper GIS endoscopic examination performed with the indication of initial diagnosis of dyspepsia, and dyspeptic symptoms using a preprepared questionnaire forms

MATERIALS AND METHODS

Patients without alarm symptoms and history of chronic disease, GIS operation, thyroid dysfunction, accidental intake of corrosive material, and diseases causing gastroesophageal symptoms as scleroderma, cases who didn't use non-steroidal anti-inflammatory drugs, steoids or routine aspirin users, and those refractory to 8 weeks of treatment with proton pump inhibitors (PPIs) were considered to have dyspepsia unresponsive to PPI treatment. Our study population was selected among patients aged 18-45 who were referred to our endoscopy unit for endocopic GIS examinations with the indication of dyspepsia unresponsive to PPIs. One week after endoscopic examinations, patients were called for a control in the polyclinics, and face-to-face interviews. Among patients who gave their consent for participation in the study, cases without any alarm symptoms, accidental corrosive substance intake, but with complaints priorly suggestive of dyspepsia (individuals describing heartburn and/or regurgitation were excluded), and those without history of chronic diseases (diabetes, chronic obstructive pulmonary disease, coronary artery disease, chronic renal failure, chronic renal failure or chronic hepatic failure), thyroid dysfunction, and scleroderma which might induce gastroesophageal symptoms, cases who didn't routinely use non-steroidal anti-inflammatory drugs, steroids or aspirin were included in the study. Patients whose first degree relatives had been diagnosed as gastric and/or esophageal cancer, and underwent endoscopic procedures for diagnostic purposes, cases with Barrett's esophagus, gastric, and esophageal tumors who were endoscopically monitored, and those with metastases who were screened for primary tumor foci were not included in the study.

Patients who volunteered for the participation in the study filled up informed consent forms, and responded to the questions in questionnaire forms we prepared to evaluate symptoms. Questionnaire form is shown in Table 1. Following completion of questionnaire forms, heights, and weights of the patients were measured. Approval of the Ethics Committee of our hospital was obtained for the conduction of this study.

Endoscopic findings of the study participants were evaluated as normal, gastric ulcer, duodenal ulcer, gastritis, duodenitis, and esophagitis (suspect cases with short-segment Barret's esophagus were evaluated as esophagitis) Cases with esophagitis were classified based on Modified Los Angeles Classification.

A total of 579 patients were called by phone for polyclinic controls, and 517 of them attended the follow-up visits. Among 468 eligible patients, 21 of them did not want to participate in the study. One patient with GIS tumor detected during endoscop-

Table 1. Questionnaire form

Department of Gastroenterology, Dr. Lutfi Kirdar Kartal Training and Research Hospi□tal
Evaluation of the Patients who Underwent Endoscopic Examinations with the Indication of Dyspepsia

The first, and the last name of the patient: Date:
Age: ☐ Male ☐ Female
Alcohol use: cc/day Type of alcoholic drink: Duration: year
Smoking status: cigarettes/day Duration: year
Body weight: Kg Height: cm

1. Within the last 3 months, how often have you felt disturbing abdominal bloating after eating a normal amount of food?
   0. Never
   1. 8-20 days a month
   2. Every day
2. How long have you had this disturbing bloating?
   0. No bloating
   1. For the last 1 -6 months
   2. For more than 6 months
3. Within the last 3 months how often have you stopped eating your meal because of your stomach problems?
   0. Never
   1. 8-20 days a month
   2. Every day
4. How long have you had problems of stopping eating your meal because of your stomach problems?
   0. Early satiety is absent
   1. For the last 1-6 months
   2. For more than 6 months
5. Within the last 3 months, how often have you felt pain on the middle of your abdomen (not on your chest)?
   0. Never
   1. 8-20 days a month
   2. Every day
6. How long have you had this pain?
   0. Never
   1. For the last 1 -6 months
   2. For more than 6 months
7. Is this pain related to eating a meal?
   0. It does not change with eating?
   1. The pain worsens after eating a meal?
   2. The pain decreases after eating a meal?
8. Within the last 3 months, how often have you felt a burning pain at the middle of your abdomen (not on your chest)?
   0. Never
   1. For the last 1 -6 months
   2. For more than 6 months
9. How long have you had complaints of burning pain?
   0. Never
   1. For the last - 6 months
   2. For more than 6 months
10. Is this pain related to eating a meal?
   0. It does not change with eating?
   1. It worsens after eating .
   2. It decreases after eating
11. Within the last year how often have you used a PPI (omeprazole, lansoprazole, pantoprazole, rabeprazole, and esomeprazole etc.)?
   0. 1-3 times a day
   1. Every day
   2. Whenever I had complaints
12. How often have you had treatment for "Helicobacter pylori" infection?
   0. Never 2. Twice
   1. Once 3. Thrice
13. Have you ever undergone an endoscopic examination?
   0. None 2. Twice
   1. Once 3. Thrice

TABLE 2. Frequency of bloating

	Patients (n=446)	%
None	11	2.4
8-20 days a month	135	30.3
Every day	300	67.3

TABLE 3. Duration of complaints of bloating

	Patients (n=446)	%
None	11	2.4
1-6 months	36	8.0
≥6 months	399	89.6

TABLE 4. Frequency of early satiety

	Patients (n=446)	%
None	185	41.4
8-20 days a month	187	42.0
Every day	74	16.6

TABLE 5. Duration of early satiety symptoms

	Patients (n=446)	%
None	185	41.4
1-6 months	93	20.8
≥6 months	168	37.8

TABLE 6. Frequency of abdominal pain

	Patients (n=446)	%
None	9	2.0
8-20 days a month	141	31.6
Every day	296	66.4

TABLE 7. Duration of complaints of abdominal pain

	Patients (n=446)	%
None	9	2.0
1-6 months	37	8.4
≥6 months	400	89.6

ic examination was not included in the study. The study was completed with 446 patients.

RESULTS

A total of 446 patients (women, n=267; 60%, and men, n=179; 40%) with a mean age of 35.73±8.13 years were included in the study. Mean body heights, and weights of the patients were 168±8.51) cm, and 73.75 (±10.14) kg, respectively. Mean BMI (body mass index) of the patients was 26.18±3.8 kg/m^2 Among a total of 446 patients, 193 (53.2%) smokers, and 104 (23.3%) alcohol users were detected.

In the questionnaire form the item which questioned "bloating symptoms" was responded affirmatively by 435 (97.5%) patients. The responses to the question which inquired the frequency of bloating are shown in Table 2, while the patients' answers to duration of bloating are given in Table 3. Two hundred and sixty-one (58.6%) patients indicated that they had felt early satiety in response to the item of "early satiety" included in the questionnaire form. Frequency, and duration of early satiety indicated by the patients are shown in Tables 4, and 5. Frequency, and duration of the abdominal pain are shown in Tables 6, and 7. When the correlation of this complaint with meals was investigated, among

Table 8. Presence, and duration of complaints of epigastric pain

	Patients (n=446)	%
None	12	2.7
For 8-20 days	125	28.0
Every day	309	69.3

Table 9. Duration of complaints of epigastric burning

	Patients (n=446)	%
Epigastric burning is absent	12	2.7
Complaints of epigastric burning for 1-6 months	36	8.1
Complaints of epigastric burning for more than 6 months	398	89.2

Table 10. The frequency of PPI use by patients

	Patients (n=446)	%
1-3 times a week	105	23.5
Every day	149	3.,5
Whenever I had complaints	192	43.0

Table 11. Number of endoscopic examinations

Number of upper GIS endoscopic examinations	Patients (n=446)	%
None	362	81.2
Once	52	11.6
Twice	22	5.0
Thrice	10	2.2

Table 12. The number of patients who received treatment for "Helicobacter pylori" infection

	Patients (n=446)	%
*HP-treatment naive patients	277	62.1
HP treatment, once	103	23.0
HP treatment, twice	42	9.5
HP treatment, thrice	24	5.4

436 patients who were complaining of 'stomach pain' indicated that the intensity of their pains worsened with meals (51. 8% of the patients) or did not change (40.6%). Number of patients who described epigastric burning, and duration of their pains are shown in Tables 8, and 9. Frequency of PPI use, application of endoscopic procedures, and treatment for Helicobacter pylori infection are shown in Tables 10, 11, and 12, respectively.

Endoscopic findings of the patients are shown in Figure 1. During endoscopic examinations esophaghitis (n=18; 4%; Grade A, n=13; Grade B, n=5), and a suspect cases of short-segment (< 2 cm) Barret's esophagus (n=6; 1.3%) were detected.

The patients with normal endoscopic findings were classified according to their responses, and within the frame of Rome III diagnostic criteria, the diagnosis of functional dyspepsia (FD) was sought for. FD was detected in 122 (83%) out of 147 patients with normal endoscopic findings

Bloating symptoms, and endoscopic findings were evaluated, and higher rates of bloating were observed in patients with pathological endoscopic findings (p=0.015). Among 435 patients with bloating, gastritis was detected in 218 (48.9%) patients. Bloating complaints were more frequently experienced every day by patients with normal endoscopic findings or gastritis. (p=0.000). Any difference was not found in the frequency of bloating complaints in patients with and without ulcer. Still a significant difference was not found between patients whose endoscopies demonstrated normal

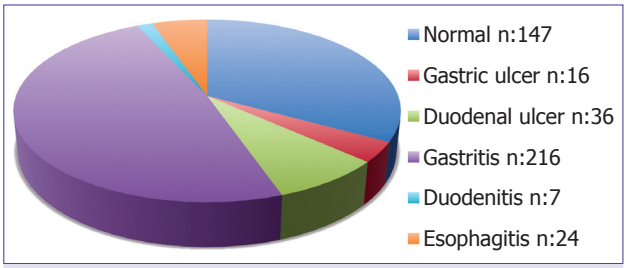

FIGURE 1. Endoscopic findings of the patients.

GIS, gastritis or ulcer. Epigastric burning was more frequently observed in patients with endoscopically detected ulcer or gastritis when compared with those normal GIS. (p=0.000, and p=0.002, respectively). Epigastric burning was more frequently experienced by patients with endoscopically detected gastritis relative to those with normal GIS (p=0.002). Frequency of epigastric burning did not differ between patients with normal endoscopic findings, and those with ulcer.

In our study any correlation between obesity, and dyspepsia was not found. Scarce number of patients in our study were smokers or using alcoholic beverages, so we couldn't establish any correlation between them, and dyspeptic symptoms.

DISCUSSION

Due to its chronic and /or recurrent nature, and its harmful effects on routine daily life of the patients, dyspepsia generally is an indication for endoscopic evaluation. Nearly 20% of our study participants had undergone upper GIS endoscopy at least once because of prolonged duration of their symptoms more than 6 months. In our study, upper GIS endoscopic findings of dyspeptic patients unresponsive to PPI treatment were evaluated. In previous studies where dyspeptic complaints, and endoscopic findings were analyzed, 15-26.7% of endoscopic findings were not indicative of gastritis. [14, 15, 16]. In our study its rate was 17.1 percent. We think that because of exclusion of the patients with alarm symptoms, and those older than 45 years of age from our assessments, our rate was lower than cited in the literature.

Dyspeptic symptoms of the patients were evaluated using our questionnaire forms. In 83% of the patients with normal endoscopic findings, FD was detected based on Rome III criteria. Park et al. [17] detected median FD rate as 40.9% in patients with chronic dyspeptic complaints according to Rome III criteria. In a population-based study performed in Japan, median FD rate was found to be 14.2% in patients with dyspeptic symptoms based on Rome III criteria [18]. In a study realized in Asia prevalence of FD was detected within a wide spectrum ranging between 7.4, and 70% [19, 20]. However, these studies were evaluated based on different criteria, and a heterogenous distribution of patients' ages was reported. Therefore, incidence of FD differed widely in these studies.

In our study similar rates of bloating (87.6%), epigastric pain (98%), and epigastric burning (97.3%) were detected. In studies performed in Europe, and Asia rates of epigastric pain were detected as 36.6-66.3%, and 25-44.5%, respectively [18, 21, 22]. In studies realized in Turkey epigastric pain was reported at an incidence rate of 77.9-95%, and frequency of epigastric burning was indicated as 95% [11, 23, 24]. We think that, our relatively higher rate of dyspeptic complaints is related to our evaluation of young-middle aged group of patients, PPI-unresponsive dyspeptic cases, and those without alarm symptoms. Symptoms of early satiety in studies on dyspepsia have demonstrated variations between 9.1, and 67.5 percent [21, 22, 25]. Studies realized in our country reported its incidence as ranging between 36.8, and 45 percent [11, 24]. In our study symptoms of early satiety was the least (58.8%) encountered complaint relative to the frequencies of other 3 symptoms.

Apart from other studies, in our questionnaire survey we evaluated the association between frequency of dyspeptic complaints, and endoscopic findings. Significantly higher number of patients with gastritis complained of bloating, epigastric pain or burning every day (p=0.000, p=0.002, and p=0.002, respectively). In cases with ulcer, as a striking finding, epigastric pain was felt every day. (p=0.000). These outcomes suggest that in patients complaining of dyspeptic symptoms in general,

gastritis may be present, and GIS ulcer may be detected in individuals suffering frequently from epigastric pain.

In our study, endoscopic examinations of dyspeptic patients unresponsive to PPIs revealed the presence of gastritis in half, normal findings in one-third, gastric ulcer or esophagitis in nearly one-fifth of the these cases. In 83% of the patients with normal endoscopic findings FD was detected. Great majority of the patients with FD can not benefit only from PPI treatment, however in the treatment of other diagnoses PPI has been used. In nearly 70% of the dyspeptic patients younger than 34 years of age without alarm symptoms, upper GIS endoscopy reveals diagnoses requiring PPI treatment. Therefore, before ordering endoscopy, the patients should be evaluated in detail to disclose problems which may arise from disuse or misuse of the drug Besides in our study we evaluated frequency of dyspeptic complaints, and endoscopic findings, and detected higher number of patients with gastritis among those who had dyspeptic complaints every day.

Median BMI value of the study participants was 26.1 kg/m^2. In a TEKHARF survey study where the prevalance of obesity in Turkey was investigated, median BMIs in the age group of 30-79 years of age were found to be 26.85 kg/m^2 in men, and 29.22 kg/m^2 in women [26]. In our study, a correlation between obesity, and dyspepsia was not found. However, in our study, we had scarce number of obese patients, and median BMI of our patients was lower than that estimated for Turkish population.

In conclusion, in dyspeptic patients without alarm symptoms younger than 45 years of age and unresponsive to PPIs, upper GIS endoscopy detects diagnosis which necessitates high doses of PPIs, Besides the incidence of gastritis is higher in patients experiencing dyspeptic symptoms every day. Therefore patients' complaints, and findings should be meticulously evaluated.

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