The Importance of *Helicobacter Pylori* in Patients with Partial Gastric Resection

Kısmi Mide Rezeksiyonlularda *Helicobacter Pylori*'nin Önemi

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ABSTRACT Objective: Before the discovery of the relationship between peptic ulcer and *Helicobacter pylori* (Hp); partial gastric resection was performed frequently for ulcer treatment. Our aim was to establish the long term prevalence and the effects of Hp gastritis in patients who had undergone partial gastrectomy for peptic ulcer treatment and to find out the changes over years. **Material and Methods:** Patients who had partial gastric resection operation due to peptic ulcer disease, minimum 10 years ago, were chosen from clinic archieves of years 2000-2006. Thirty-five patients matching with these criteria (24 men, 11 women) took part in the study. Gastroscopies with biopsy were performed and the latest endoscopic and pathologic findings were compared with the previous data; both in the groups and between the groups. **Results:** There is no statistically significant difference between Hp positivity or negativity and atrophy, inflammation and stomatitis. In the previous endoscopies; Hp positivity drops significantly as alcaline reflux gastritis incidence increases. Again at the initial endoscopies, alkaline reflux gastritis frequency decreased significantly as the duration of time since the operation increased. There was no statistically significant relationship between reconstruction methods (B I, B II), Hp positivity and alkaline reflux gastritis frequency. As dysplasia or cancer was not observed in any of the patients, no relationship could be established between Hp and gastric resection. **Conclusion:** In patients with partial gastrectomy; dyspeptic complaints are readily attributed to alcaline reflux but here we point that Hp can be responsible as well. Therefore, biopsies for Hp are mandatory in the follow-up of this subgroup of patients.

Key Words: Gastrectomy; *Helicobacter pylori;* gastritis

ÖZET Amaç: Peptik ülser ile *Helicobacter Pylori* (Hp) arasındaki ilişkinin keşfinden önce, ülser tedavisi için sıklıkla kısmi mide rezeksiyonuna başvurulurdu. Amacımız, peptik ülser nedeniyle kısmi mide rezeksiyonu yapılmış hastalarda yıllar içerisinde Hp gastritinin prevalansını ve meydana getirdiği değişiklikleri ortaya koymaktı. **Gereç ve Yöntemler**: 2000-2006 yıllarına ait klinik arşivlerinden, peptik ülser sebebiyle enaz 10 yıl evvel kısmi mide rezeksiyonu yapılmış hastalar seçildi. Kriterlere uyan 35 hasta (24 erkek, 11 kadın) çalışmada yer aldı. Hastalara gastroskopi yapılarak biyopsiler alındı; yeni endoskopik ve patolojik bulgular, eski verilerle karşılaştırıldı. **Bulgular:** Hp pozitifliği veya negatifliği, atrofi, inflamasyon ve stomatitis açısından istatistiksel anlamlı fark saptanmadı. Eski endoskopilerde; alkalen reflü gastrit sıklığı arttıkça Hp pozitifliği anlamlı şekilde düşmektedir. Keza operasyon süresi uzadıkça, alkalen reflü gastrit sıklığı anlamlı biçimde azalmaktadır. Rekonstrüksiyon yöntemi (B I, B II), Hp pozitifliği, alkalen reflü gastrit sıklığı açısından anlamlı fark saptanmadı. Hiçbir hastada displazi veya kanser gelişimi saptanmadığından, Hp ve gastrik rezeksiyon ile aralarında bir ilişki tespit edilemedi. **Sonuç:** Kısmi gastrektomili hastalarda, dispeptik yakınmalar peşinen alkalen reflüye bağlanır ama biz burada, Hp' nin de sorumlu olabileceğini işaret ediyoruz. Dolayısıyla bu hasta kümesinde, Hp için biyopsi alınması ihmal edilmemelidir.

Anahtar Kelimeler: Gastrektomi; *Helicobacter pylori*; gastrit

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Gastric resection operations are performed for various reasons. Before the discovery of the relationship between peptic ulcer and *Helicobacter pylori* (Hp); partial gastric resection for peptic ulcer was a routine operation. When it became clear that Hp eradication leaded to peptic ulcer healing; this operation became seldom.[1]

Hp gastritis is one of the most common human bacterial infections and the organism is associated with gastritis, peptic ulcer disease, gastric adenocarcinoma and gastric B-cell lymphoma.[2-8] Bu it is readily accepted that; Hp colonisation is much more harder in the partially resected stomach, because bile reflux makes up an anti-Hp effect.[9,10]

Once it was understood that the eradication of Hp also eradicated peptic ulcer, the need for these operations has decreased substantially. Gastrectomy actually makes Hp colonization difficult because bile reflux destroys the natural habitat of Hp. Our first aim in this study was to determine the long term prevalance of Hp gastritis in patients after partial gastric resection due to peptic ulcer, through the years. Comparison of Hp (+) and Hp (-) operated stomachs; is noted.

Hp infection is strongly linked to the development of gastric carcinoma in the intact stomach.[9,11] But there are conflicting opinions about carsinogenesis in the patients with partial gastric resection.[5,12,13] We also focused on this topic.

MATERIAL AND METHODS

This is a retrospective cohort study, which was held in Haydarpaşa Numune Research and Education Hospital (İstanbul, Turkey) with the collaboration of Gastroenterology and Pathology clinics in year 2006. The study was approved by the local ethics committee. Patients who had partial gastric resection operation due to peptic ulcer disease, minimum 10 years ago, were chosen from clinic archieves of years 2000-2006. Thirty-five patients matching with these criteria (24 men, 11 women) took part in the study.

Demographic data and medical histories of the patients, were taken into record. Patients taking acetylsalycilic acid and non-steroidal anti inflammatory drugs were excluded. Operation date, indication-surgical method and complications of the operation were questioned. Previously performed gastroscopies' reports and pathology blocks of biopsies were obtained; these blocks were revised, comparing them with the newly taken biopsies. History of Hp eradication therapy was also noted.

Hemogram, iron, total iron binding capacity (TIBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), carcinoembryogenic antigen (CEA) and CA-19-9 results were obtained for all patients. HNEAH Medical Biochemistry Laboratory values were taken into account. All patients were performed ultrasonographic examination of the abdomen for a possible intraabdominal malignancy. No intraabdominal malignancy was detected so all the chosen patients completed the study.

Written informed consents were taken and oesophagogastroduodenosopy was performed for all patients. Alcaline reflux gastritis was recorded. Stomatitis was reported as the presence of hyperemia, edema and/or erosions at the stoma; an endoscopic observation. According to the number of loops and anatomy of the residual stomach; type of reconstruction [Billroth (B) I-B II] was also noted. We looked for gastric cancer; if present, for its association with Hp.

Biopsies from four quadrants of anastamosis and from any possible suspect macroscopic lesion were routinely obtained. For grading gastritis and finding out any possible gastric atrophy or displasia; biopsies were also obtained from middle gastric stumpf and fundus. Patients were divided into two groups as: Hp(+) and Hp(-) ones. The latest endoscopic and pathologic findings were compared with the previous data; both in the groups and between the groups. Results were discussed on statistical significance basis.

PATHOLOGY

Biopsies were fixed in 10% formoline solution. Then parafine blocks and lam preparations of these blocks were made. We treated them with Haemotoxilen-Eosin (HE), MGG (Tissue Giemsa), PAS-Alcian Blue paints. Preparations painted with

HE were examined under the light microscope for dysplasia, inflammation, alcaline reflux and other findings. MGG paint was for demonstrating Hp and PAS-Alcian Blue was for demonstrating intestinal metaplasia. All the old and new pathology blocks were examined by the same pathologist.

Pathological grading of the gastric mucosa was made according to the Sydney System. In this system; the intensity of the inflammmatory cells (lymphocytes, plasma cells and granulocytes) are graded as follows:

Absent…….0

Low intensity..1

Intermediate…2

Intense…….3

The final grade of inflammation is determined according to the combination of the grades of the inflammatory lesions in antrum and corpus mucosa.[14] Hp in gastric mucosa and intestinal metaplasia, atrophy were expressed as positive or negative. Dysplasia, precancerous lesions and frank cancer in partially resected stomachs was also investigated. Standard for his evaluation is the Padova İnternational Classification.[15]

Another topic we took into consideration was alcaline reflux gastritis. As a definition, it explains the changes due to the reflux of duodenal content into the stomach. We evaluated it both as an endoscopic finding and as a pathologic definition. Endoscopic definition is the co-existance of hyperemia,edema or/and erosions with excess biliary secretion. Pathologically, gastrites are classified into three:

1-Acute gastrites.

2-Chronic gastrites.

3-Specific gastrites.

Alcaline reflux gastritis belongs to the specific gastrites group and chemical (reactive) gastrites subgroup and again classified according to the Sydney system.[16,17]

In our study, surgical type of the resection and reconstruction were also noted and associated with other findings.

RESULTS

This study was performed on 24 male 11 female, totally 35 patients. Patient ages varied between 43 and 80; median age was 61. Median operation time was 24 years (Table 1).

Esophagogastroduodenoscopies were performed, standard biopsies were taken. Previous and new biopsies were compared pathologically. The time between the previous and latest endoscopies was mean 3.7 years (Table 1).

Excess bleeding from biopsy sites was observed nearly in all patients. In one patient, we even had to apply sclerotherapy with diluted Adrenalin, to the biopsy site.

The leucocyte, haematocrit and platelet counts of the 35 patients were within normal ranges.

All of the patients had ESR, CRP, CEA, CA-19-9 values within normal ranges. Iron was low at 6 patients and 3 patients had high TIBC values.

Thirty (%85.7) patients had B II, 5 (14.3%) patients had B I reconstruction. For all the patients with endoscopic alcaline reflux diagnosis; pathological criteria were also fulfilled.

No statistically significant difference was detected between B I and B II reconstructions, in means of alcaline reflux gastritis (p= 0.656). Hp positivity persentages in B I and B II groups were not statistically significant in comparison (p= 0.771). There was no statistically significant difference between the two groups for inflammation (p= 0.75).

When pathological findings (alcaline reflux gastritis, atrophy, inflammation, intestinal metaplasia, Hp) are compared between the previous and

TABLE 1: General characteristics

	N	Minimum	Maximum	Mean±SD
Operation year	35	6	40	23.6±10.3
Age	35	43	80	60.66±9.39
Interval between endoscopies	28	0,5	6	3.71±1.85

Note: We have a total of 35 patients in the study and they all had new gastroscopic examination but only 28 of them had previously performed gastroscopies; which can be clearly seen in Table 1.

latest endoscopies; no statistically significant difference is found. This is also true for the endoscopic finding, stomatit.

Alcaline reflux and stomatit are frequent findings at operated stomachs (94.3% and 68.6% respectively). Hp positivity of all the operated patients is 34.3%.

Atrophy is a rare finding in both the previous and latest endoscopies. Intestinal metaplasia positivity is nearly 25% in both groups.

No patient had dysplasia or cancer. So we couldn't set a relationship between Hp positivity and gastric cancer. There was no correlation between inflammation and Hp positivity.

As operation time increases, alcaline reflux gastritis incidence drops (p= 0.009) at the previous endoscopies.

At previous endoscopies; there was no statistically significant difference for atrophy, stomatit and inflammation between the Hp positive and negative groups. But alcaline reflux gastritis and Hp positivity are found to be reversely proportional and this is statistically significant (p= 0.018).

DISCUSSION

Opinions regarding the development of cancer in the resected stomach are controversial.[5,12,13] Although the procedure is not performed in the recent years, it is obvious that gastric resections performed in the older times create a risk for cancer. It has been absolutely established that Hp infection is precancerous in intact stomachs.[9,11] For this reason, we performed gastroscopy to investigate the development of cancer and its relationship with Hp in a group of patients who had undergone partial gastric resection for peptic ulcer at least 10 years ago.

In many studies investigating the relationship between Hp infection and gastritis following gastric surgery; a clear relationship could not be established between Hp infection and residue gastritis. The reason for this is because the most important cause of residue gastritis developing following distal partial gastrectomy is biliary enterogastric reflux. As a matter of fact, some of the investigators even think that this reflux has the capacity of totally eradicating Hp infection.[10]

In 1998, Shigetaka Yamamoto et al performed a study aiming to investigate the relationship between Hp and residue gastritis in 28 gastric cancer patients who had undergone distal partial gastrectomy and Billroth I reconstruction within the last 13 months. The endoscopic and pathological evaluations performed at the 3rd, 6th and 12th months following operation showed that inflammatory changes in the gastric mucosa developed in both Hp (+) and Hp (-) patients. No significant difference was found between these two groups at any point. Hp plays a destructive role over the gastric mucosa by reducing mucine and is a cause of residue gastritis; but, it is not the only cause of residue gastritis that develops following distal partial gastritis.[10]

In our study, we also found no statistically significant difference between Hp positive and negative groups regarding inflammation, but we established that as alcaline reflux increased, Hp positivity decreased. This is in accordance with the classical data that; alcaline reflux eradicates Hp.[9,10]

Distal gastrectomy frequently causes postgastrectomy syndrome. Reflux gastritis is almost inevitable in cases with postgastrectomy syndrome, and this is defined as a risk factor in the development of carcinoma in the residual mucosa. Hyperemia, edema, and tendency for bleeding are encountered in the remaining mucosa, particularly at the site of anastomosis following distal gastrectomy. The reflux of bile and duodenal contents is the main pathogenic factor in reflux gastritis. Recently, it has been possible to decrease gastroduodenal regurgitation by reconstruction methods such as Roux-en-Y and jejunal interposition (J-I). Additionally; following the isolation of Hp from the gastric mucosa; this bacteria has been found to be associated with many gastroduodenal diseases such as atrophic gastritis, gastroduodenal ulcer and MALT lymphoma. Furthermore, Hp has been found to be related with gastric carcinoma.[5-8] Atrophic gastritis is qualified as a precancerous lesion as well and the treatment of gastritis is thought to be effective in the prevention of gastric cancer.[9]

Smoking, alcohol, ulcer disease, nutritional factors play a role in the development of gastric cancer. But since the discovery of Hp in 1983, Hp has been the main focus. The reason that most of the studies on this subject have been performed in Japan is that gastric cancer and Hp positivity is a frequent finding in the Japanese population, especially in the middle and old age population. In 1988, in a typical Japanese village representing the general population, Hajime Yamagata et al have followed selectively chosen 2602 cases above 40 years of age with no history of gastrectomy or gastric cancer age for 9 years. As a result, they found that Hp infection was more frequent in men (was found in 71.5% of the men in the study group, and in 62.5% of the women) and gastric cancer frequency was higher in Hp positive men compared to Hp negative men; there was no difference in women. In this Japanese male population, an important relationship was established between Hp positivity and gastric cancer; but, this did not apply for the female population.[6]

In our study of 35 patients where the mean duration of time since the operation was 24 years, we did not detect cancer in any of the patients.

In its natural course, Hp infection does not heal by itself. '**The European HP Working Group'**, with the hope of decreasing the risk of cancer, recommends strongly the eradication of Hp in the residue stomach. In 2005, Keisuke et al have presented a new protocol for the eradication of Hp and compared it with the two protocols in current use (every group consisted of 55 Hp positive patients). The success rates of the protocols are out of the scope of this paper, but there are some topics of interest. Histologically, the inflammation of the gastric mucosa had decreased substantially after the eradication of Hp and this indicates a decrease in ulcer and cancer; visually, the gastritis state had faded totally and there was an apparent decrease in hyperplastic polyps.[18]

In our study group, there was stomatitis in the Hp positive patient group as well. In our opinion, the reason of inflammation is not only the presence of Hp and we think alcaline reflux gastritis is also partially responsible. Nevertheless, when identified, Hp should be eradicated.

For a long time, the bile acid reflux has been postulated to be the one and only cause of gastritis in residue stomach. However, as Hp has been better understood, it has been defined as the primary reason. In some studies, it is stated that Hp is not that frequent in residue stomachs. Can the reason for this be the eradication of Hp by bile reflux? Depending on the surgical technique used, Hp positivity is found at different ratios in the residue stomach. Can the amount of bile reflux, depending on the surgical procedure performed, affect the presence of Hp? In order to clarify all these questions, Tomtitchong et al have conducted a study between 1992-1997 and published it in 1998. A total of 109 patients were included in the study. They have found that Hp positivity is significantly lower in patients with B II anastomosis compared to the ones with B I. Some Hp positive patients even became Hp negative spontanously following B II operation. This phenomenon was not found in B I patients. This can be explained by the fact that bile reflux is much more frequent and abundant in B II patients.[7]

We did not establish a difference in the frequency of alcaline reflux seen in stomachs with B I and B II reconstruction. But, in the first endoscopy group, Hp positivity decreased significantly as alkaline reflux increased.

In patients with partial gastrectomy; dyspeptic complaints are readily attributed to alcaline reflux but here we point that Hp can be responsible as well. Therefore, biopsies for Hp are mandatory in the follow-up of this subgroup of patients. We should keep in mind that partial gastrectomy does not destroy the Hp population, just reducing in size so Hp related complications can still be expected.

CONCLUSION

There is no statistically significant difference between Hp positivity or negativity and atrophy, inflammation and stomatitis.

No statistically significant relationship was found between Hp positivity and the duration of time since the operation.

In the previous endoscopies; Hp positivity drops significantly as alcaline reflux gastritis incidence increases.

In the initial endoscopies, alkaline reflux gastritis frequency decreased significantly as the duration of time since the operation increased.

There was no statistically significant relationship between reconstruction methods (B I, B II), Hp positivity and alkaline reflux gastritis frequency.

As dysplasia or cancer was not observed in any of the patients, no relationship could be established between Hp and gastric resection.

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