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Impact of *CYP2C19* Gene Polymorphism on Gastroesophageal Reflux Disease

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Abstract

Background: The *CYP2C19**17 allele has been shown to be related to faster Pantoprazole metabolism, whereas the *2 and *3 alleles are related to poor metabolism. We aimed to investigate the effect of *CYP2C19* polymorphisms on treatment of gastro-esophageal reflux disease.

Materials and Methods: Patients admitted to the Endoscopy unit and diagnosed with grade A or B esophagitis were included in the study. Patients were enrolled in two groups: Group 1 (N: 50) consisted of patients taking 40 mg Pantoprazole, and Group 2 (N: 41) those taking 80 mg per day. After 8 weeks of treatment, a second endoscopic procedure was performed to evaluate healing of the esophagitis. In addition, CYP2C19 genotyping for *2, *3 and *17 was performed for all of the patients.

Results: The healing rates of esophagitis were 82% and 80.5% in Groups 1 and 2, respectively. All of the patients with the *2*2 polymorphism were cured, in contrast only 66.7% of those with the *17*17 polymorphism healed.

Conclusion: In this preliminary study, the healing rates of esophagitis were comparable to results of reported studies in the literature. Being slow metabolizer may be a favorable effect on GERD treatment outcome.

Keywords: Gastroesophageal reflux disease; *CYP2C19* polymorphism; Pantoprazole

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Introduction

Gastro-Esophageal Reflux Disease (GERD) is a serious health problem all around the world [1]. The healing rates of GERD are reported to be 80% to 85% after two months of therapy [2]. However, among obese GERD patients admitted with grade C or D esophagitis, doubling the dose of Proton Pump Inhibitors (PPI) has become necessary [3,4]. Activity of *CYP2C19* is crucial for the clinical efficiency of PPI's [5]. The genetic polymorphisms of *CYP2C19* encode poor (PM), homozygous (HomoEM), and heterozygous (HeteroEM) extensive metabolizer phenotypes. In Caucasians, the frequencies of CYP2C19*2 and *17 alleles are 11% to 16%, and 18% to 32.9%, respectively [6]. We, therefore, aimed to investigate the impact of *CYP2C19* polymorphism on GERD treatment outcome in our country.

Materials and Methods

Study population

A total of 91 patients over 18 years of age diagnosed with erosive esophagitis Grade A or B (according to the Los Angeles GERD classification) related to GERD between March 2010 and December 2010 were enrolled in the study [7]. Group 1 consisted of 50 patients (54.9%) who received 40 mg Pantoprazole once a day, and Group 2 consisted of 41 (45.1%) patients who received 40 mg Pantoprazole twice a day. After 8 weeks of medical therapy, to assess the effectiveness of the treatment, a second gastroscopic examination was performed. Endoscopists were all blinded to the treatment dose.

Table 1: Impact of *CYP2C19* polymorphism on healing rates of esophagitis regardless of dosage of the administered Pantoprazole.

CYP2C19	Healed	Not healed	Total
genotype	**N (%)**	**N (%)**	**N**
**1*1*	35 (83.3)	7 (16.7)	42
**1*17*	19 (82.6)	4 (17.4)	23
**1*2*	10 (71.4)	4 (28.6)	14
**1*3*	1 (100)	-	1
**2*17*	3 (75)	1 (25)	4
**2*2*	4 (100)	-	4
**17*17*	2 (66.7)	1 (33.3)	3
Total	74 (81.3)	17 (8.7)	**91**

Presence of gastro-intestinal system malignancies, any gastric outflow obstruction due to benign or malignant causes, having hiatus hernia, taking any immunosuppressive drug, presence of renal or liver impairment, being pregnant, and subjects who had drug or substance abuse or were taking PPI medication were excluded from the study.

Healing was accepted if LA grade B erosive esophagitis down to LA grade A or LA A or B erosive esophagitis was totally cured at the second gastroscopy. A peripheral blood sample was taken at the beginning of the study to perform *CYP2C19* genotyping performed as given elsewhere [7]. The local Ethics Committee of Diskapı Education and Research Hospital approved the study protocol, and written informed consent was obtained from all participants at the beginning of the study.

Analysis was done using the SPSS computer based program (SPSS 13.0, Chicago, IL). The demographic features of the patients are shown as mean ± standard deviation or median (minimum-maximum values). Comparisons of groups were done using Chi-square or Mann Whitney U tests. P value under 0.05 was accepted as statistically significant.

Results

The average age of the patients was 43.2 ± 15.1 years and 64.8% of them were male. Baseline demographic features of the patients, e.g. mean age, gender distribution, presence of smoking were similar in each group (not shown data). Sixty-six of the patients in Group 1, and 64% of Group 2 were have esophagitis grade B (p value, 0.52). Overall healing rate at the eight weeks of therapy was also similar in each group (82% in Group 1 and 80.5% in Group 2, p value, 0.58). In addition, mean age of the patients, gender distribution, smoking habit and dose of PPI were all similar in healed and non-healed groups. As expected, all of the patients with the *2*2genotype were healed at the end of the medical therapy, whereas the healing rate was 66.7% in patients having the *17*17 polymorphism (Table 1).

Conclusion

In conclusion, the efficacy of Pantoprazole in GERD treatment is very high. Given the low number of the assigned patients in each group, there was no statistical significance based on the healing rates between the groups. On the other hand, the highest success rate was seen in slow metabolizer patients, whereas the lowest rate was in extensive metabolizers.

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