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Effects of Proton Pump Inhibitors on Renal Functions in Coronary Artery Disease Patients

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Abstract

Introduction: Proton Pump Inhibitors (PPI) are the most commonly used drug groups in the world. Although they are relatively safe medicines, there are data in the literature that they may cause dementia, myocardial infarction, infection, micro nutrient deficiency, kidney disease. Because of the use of antiaggregant and anticoagulant therapy in patients with coronary artery disease, PPI treatment is often given to this group of patients to prevent adverse effects on gastrointestinal system. In this study, creatinine and Glomerular Filtration Rate (GFR) values in patients of cardiovascular disease were evaluated after 1 year of use of PPI treatment.

Methods: This study evaluated coronary artery disease patients who applied to cardiology clinic between February 1, 2018 and May 31, 2018 and who had used PPIs for the last 1 year. Patients with a history of acute renal failure and chronic renal failure and patients under 18 years of age were excluded from the study.

Results: A total of 100 patients were included for this study.The mean age of the study group was 66, 6 ± 10, 7 and 69% were male. Creatinine level was 0.93 ± 0.20 at the beginning of the treatment and 0.98 ± 0.26 at the 12th month. When all study population was evaluated creatinine levels were significantly higher after the comparison of the beginning of the treatment and 12th month of the treatment (p=0.031). GFR was 85.89 ± 27.90 at 0th month and 86.25 ± 28.50 at 12th month. GFR showed no significant difference between 0th and 12th month comparison (p=0.878). When pantoprazole, lansoprazole, esomeprazole and rabeprazole were evaluated one by one GFR and creatinine levels were statistically similar.

Conclusion: The results of the study showed that even though creatinine levels increase, GFR levels do not change after a year of follow up. In conclusion PPIs seem safe in coronary artery disease patients for chronic renal outcomes. The major limitations of this study are the number of patients and the inadequacy of the follow-up period.

Keywords:

Proton pump inhibitors; Glomerular filtration rate; Creatinine

Introduction

Proton Pump Inhibitors (PPI) are the most commonly used drug groups in the world [1]. These drugs act on H^+-K^+-ATPase enzyme on the gastric mucosa and prescribed for prophylaxis and management of peptic acid disorders [2,3]. Although they are relatively safe medicines, there are data in the literature that they may cause dementia, myocardial infarction, infection, micro nutrient deficiency, kidney disease [4,5]. Examples of kidney diseases caused by the PPI group include acute interstitial nephritis, acute kidney damage, and chronic kidney disease [6-12]. PPIs are often used for coronary artery disease patients in order to prevent gastrointestinal adverse effects caused by antiaggregant and anticoagulant therapy in patients with coronary artery disease. Guidelines suggest acetylsalicylic acid or clopidogrel for all patients with stable coronary artery disease [13]. If the patient has a recent acute coronary syndrome history, prasugrel/ticagrelor/clopidogrel and acetylsalicylic acid may be used as dual therapy [14]. If the patient has atrial fibrillation or thrombus, anticoagulant therapy may be added to the treatment [15,16]. Because of the increased bleeding risk due to anticoagulant and antiaggregant therapies, physicians tend to prescribe PPIs to the patients with cardiovascular diseases. With this study we evaluated the renal functions of coronary artery disease patients under PPI treatment to see if there is a change in creatinine and glomerular filtration rate levels after 1 year use of PPI.

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	Number	%
Age, years	66, 6 ± 10, 7	
Gender, male	69	69%
Diabetes mellitus	22	
Ejection fraction, %	57, 3 ± 7, 9	
Drug use		
Acetylsalicylic acid	59	59%
Clopidogrel	44	44%
Prasugrel/Ticagrelor	7	7%
ACE inhibitor	36	36%
ARB	30	30%
Diuretics	52	52%
Beta blocker	73	73%
Nitrate	9	9%
Trimetazidine	23	23%
Ranolazine	14	14%
Calcium channel blocker	32	32%
Statin	58	58%
OAC	13	13%
Digoxin	2	2%
Ivabradine	4	4%

ACE: Angiotensin Converting Enzyme; ARB: Angiotensin Receptor Blocker; OAC: Oral Anticoagulant

Table1: Basic characteristics and drug use of the study population

Methods

This study evaluated coronary artery disease patients who applied to cardiology clinic between February 1, 2018 and May 31, 2018 and who had used PPIs for the last 1 year. Patients with a history of acute renal failure and chronic renal failure and patients under 18 years of age were excluded from the study. Biochemical records and patient histories were retrieved from the patient records. Glomerular Filtration Rate (GFR) was obtained by using Cockcroft-Gault formula.

Data are presented as mean ± standard deviation (SD) and as proportions for categorical variables. The t-test or Chi-square test was used for comparisons of continuous and categorical variables, respectively. Distribution of the data for normality was tested by the Shapiro-Wilk test and homogeneity of group variances were tested by the Levene te st. For the parameters which are not normally distributed, Mann Whithey U test is used. The data were analyzed using SPSS 20.0 (IBM SPSS Ver. 20.0, IBM Corp, Armonk NY, USA). The study was approved by the local ethics committee.

Results

A total of 100 patients were included for this study. From 260 coronary artery disease patients 140 were excluded because they were not using PPI and 14 were excluded due to their history of chronic renal failure and 6 were excluded due to acute renal failure history. The mean age of the study group was 66, 6 ± 10, 7 and 69% were male. 22% of the patients were diabetic and mean ejection fraction was 57.3 ± 7.9 according to echocardiography results. In the study group, 59% acetylsalicylic acid, 44% clopidogrel, 7% prasugrel / ticagrelor, 36% angiotensin converting enzyme inhibitor, 30% aldosterone receptor blocker, 52% diuretic, 73% beta blocker, 9% nitrate, 23% trimetazidine, 14% ranolazine, 32% calcium channel blocker, 58% statin, 13% anticoagulant, 2% digoxin and 4% ivabradine use were seen in Table 1.

Majority of the patients were using pantoprazole (56%) as PPI. Value of creatinine level was 0.93 ± 0.20 at the beginning of the treatment and 0.98 ± 0.26 at the 12th month. When all study population was evaluated creatinine levels were significantly higher after the comparison of the beginning of the treatment and 12th month of the treatment (p=0.031). GFR was 85.89 ± 27.90 at 0th month and 86.25 ± 28.50 at 12th month. GFR showed no significant difference between 0th and 12th month comparison (p=0.878). When pantoprazole, lansoprazole, esomeprazole and rabeprazole were evaluated one by one GFR and creatinine levels were statistically similar. The comparison of creatinine and GFR values of the beginning and 12th month of PPI therapy can be seen in Table 2.

0th and 12th month values of creatinine and GFR levels of diabetic patients also showed no statistically significant difference (p=0.591 for creatinine and p=0.886 for GFR).

Discussion

In our study we found out that even though creatinine levels differ from the beginning of PPI use to 12th month of use in coronary artery disease patients GFR values did not significantly changed. Also in diabetic patients group, GFR and creatinine levels did not changed statistically. When pantoprazole, lansoprazole, esomeprazole and rabeprazole were evaluated within themselves, both creatinine and GFR levels were statistically similar.

Recent studies showed that PPI are associated with acute kidney injury but association of chronic kidney disease is less certain. There are controversial results in previous studies [12,17,18].

Antiaggregant therapy is recommended in patients with coronary artery disease [13], but the use of this class of drugs increases the risk of gastrointestinal bleeding. Therefore, PPI is frequently used in patients with coronary artery disease to reduce the risk of bleeding. So it is important to know if PPIs are safe drugs for these patients in terms of renal functions.

The aim of this study was to investigate the changes in creatinine and GFR values in 1 year follow-up of patients with coronary artery disease. Even though creatinine levels were higher after 1 year, GFR values were statistically similar. We also compared 0th and 12th month GFR and creatinine levels of pantoprazole, lansoprazole, esomeprazole and rabeprazole one by one and these comparisons showed no significant difference for both GFR and creatinine values. From all these results we thought that the value of p=0.031 we found comparing creatinine results for all study population could be a coincidence since GFR results does not differ after the comparison of the same study population. Since GFR is more reliable for the evaluation of renal functions, it would be better to use GFR for future studies. Also the number of study population should be higher for a

	Number of patients (%)	Creatinine (0th month)	Creatinine (12th month)	P*	GFR	(%)	(%)
All patients	100 (100%)	0.93 ± 0.20	0.98 ± 0.26	0.031	85.89 ± 27.90	86.25 ± 28.50	0.878
Pantoprazole	56 (56.0%)	0.91 ± 0.21	0.95 ± 0.27	0.276	86.92 ± 30.33	90.05 ± 28.09	0.396
Lansoprazole	19 (19.0%)	0.93 ± 0.18	1.00 ± 0.22	0.058	86.49 ± 25.37	80.94 ± 23.97	0.087
Esomeprazole	17 (17.0%)	1.04 ± 0.20	1.04 ± 0.28	0.968	80.72 ± 29.39	84.46 ± 36.73	0.414
Rabeprazole	8 (8.0%)	0.85 ± 0.15	1.00 ± 0.27	0.112	88.29 ± 15.51	78.56 ± 23.32	0.154

*Comparison of creatinine levels between beginning of the PPI therapy and 12th month of therapy

*Comparison of GFR levels between beginning of the PPI therapy and 12th month of therapy

GFR: Glomerular Filtration Rate

Table 2: Comparison of creatinine and GFR levels of the study population

better outcome and we think the major limitation of our study was inadequate number of patients.

A previous study showed no correlation of PPI, coronary artery disease and chronic kidney disease in diabetic patients [17]. In our study we also did not found worse outcomes in terms of creatinine and GFR in diabetic patients. This result is consistent with the previous study.

Conclusion

In this 1 year study PPIs seem safe in coronary artery disease patients for chronic renal outcomes. The major limitations of this study are the number of patients and the inadequacy of the follow-up period. It will be useful to repeat this study with a larger number of patients so that clearer results can be obtained.

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