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## ORIGINAL RESEARCH

# Assessment of the Effect of Proton Pump Inhibitors on Renal Profile

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**ABSTRACT**
**Background: To assess the effect of Proton Pump Inhibitors on renal profile.**
**Materials & methods: A total of 100 subjects were enrolled. The age of subjects included was between 18 to 70 years. Values of blood urea and serum creatinine were taken twice, first before start of therapy and then after at least one week of therapy.**
**Results: The subjects with AKI present were 11 out of the total. The age wise distribution of the incidence of AKI was more in the population over 50 years, with the maximal incidence in the group above 51 years.**
**Conclusion: Prescription of PPIs in AKI should be monitored.**
**Keywords: urea, pantoprazole, renal profile**.

## INTRODUCTION

Proton Pump Inhibitors (PPIs) are a group of drugs commonly prescribed in the management and prophylaxis of acid peptic disorders. They act by inhibiting the H+-K+-ATPase enzyme (proton pump) present in the parietal cells of the gastric mucosa. These drugs are the most potent blockers of gastric acid secretion, as they block the secretion irreversibly. Their efficacy has been estimated to be better than that of histamine-2 receptor blockers.[1,2] PPIs are also recommended for prophylaxis of peptic ulcer in NSAID users, eradication of Helicobacter pylori-related ulcers and also for the management of Gastroesophageal Reflux Disease (GERD). Pantoprazole is arguably the most commonly prescribed PPI. Rabeprazole, omeprazole and lansoprazole are few of the other PPIs that are routinely prescribed around the world. [3-5]

Enzyme H+/K+-ATPase (proton pump), found in the canaliculi of the parietal cells of the stomach, plays a key role in the secretion of hydrochloric acid in the gastric lumen. The enzyme is activated by three distinct stimuli: histamine, gastrin, and acetylcholine. The production of acid occurs with the exchange of K+ (potassium) for H+ (hydrogen) in an ATP-consuming process. [6,7]PPIs were designed to block acid secretion in the stomach and increase the pH of the gastric juice. They inhibit the action of enzyme H+/K+-ATPase and prevent the exchange of K+ for H+, while differentiating themselves from other drugs used to treat gastric diseases for also inhibiting the last step in the production of hydrochloric acid. This process enhances the potency of inhibition, making PPIs the current drug of choice. [7,8]PPIs inhibit the enzyme by merging with its receptor and covalently binding to cysteine

residues known as irreversible inhibitors. After the reaction, the proton pump cannot regenerate and acid production occurs only after the synthesis of new enzymes. Irreversible inhibition ensures the medication is active for 24 to 48 hours. [8,9]

With the widespread use of PPIs, more and more studies concerned for the safety of PPIs treatment.[10,11] Among which, kidney injury including acute kidney injury (AKI) and chronic kidney disease (CKD) following PPI therapy was a hot issue. However, original studies concerning PPIs-associated kidney injury were almost cohort or retrospective studies and systematic reviews based on them,[12,13] the only randomized controlled trial evaluated only pantoprazole and found no significant relationship between pantoprazole and CKD. [14] Hence, this study was conducted to assess the effect of Proton Pump Inhibitors on renal profile.

## MATERIALS & METHODS

A total of 100 subjects were enrolled. The age of subjects included was between 18 to 70 years. Values of blood urea and serum creatinine were taken twice, first before start of therapy and then after at least one week of therapy.The laboratory based biochemical criteria (urea and creatinine levels) were used. The data was collected and analysed using SPSS software.

## RESULTS

A total of 100 subjects were analysed. The subjects with AKI present were 11 out of the total. The age wise distribution of the incidence of AKI was more in the population over 50 years, with the maximal incidence in the group above 51 years.

**Table 1: Age-wise distribution of the incidence of acute kidney injury**

| Age groups | % of subjects |
|---|---|
| 18-30 years | 10 |
| 31-40 years | 13 |
| 41-50 years | 8 |
| Above 51 years | 69 |

The normal values in laboratory are as follows: blood urea; 10 to 40 mg/dl; serum creatinine; 0.4 to 1.2 mg/dl.No relationship was found to be present between the duration of PPI therapy and the onset of AKI.

**Table 2: Biochemical laboratory values of the patients who developed AKI**

| S no. | PPI used | Duration in PPI therapy (in days) | Baseline values | | Values at the end of PPI therapy | |
|---|---|---|---|---|---|---|
| | | | Blood urea | Serum creatinine | Blood urea | Serum creatinine |
| 1 | Pantoprazole | 14 | 22 | 1.0 | 40 | 1.6 |
| 2 | Pantoprazole | 11 | 12 | 1.1 | 32 | 1.2 |
| 3 | Pantoprazole | 8 | 20 | 0.6 | 40 | 1.4 |
| 4 | Pantoprazole | 9 | 16 | 1.1 | 36 | 2.0 |
| 5 | Pantoprazole | 14 | 11 | 0.8 | 98 | 3.2 |
| 6 | Omeprazole | 22 | 28 | 0.3 | 52 | 1.2 |
| 7 | Pantoprazole | 7 | 23 | 1.0 | 69 | 1.7 |
| 8 | Pantoprazole | 16 | 22 | 1.1 | 58 | 2.1 |
| 9 | Omeprazole | 8 | 18 | 1.1 | 44 | 3.0 |
| 10 | Pantoprazole | 21 | 11 | 0.9 | 46 | 1.8 |
| 11 | Pantoprazole | 14 | 13 | 0.6 | 77 | 2.6 |

## DISCUSSION

Kidney injury associated with PPIs has gained limelight in recent times. Both acute and chronic varieties have been listed to be adverse effects of long term PPI usage. Acute Kidney Injury (AKI) is said to have set in, when the glomerular filtration rate declines rapidly, which causes the nitrogen based waste products to get accumulated in the body. This is evidenced by an increase in the levels of blood urea nitrogen and serum creatinine. Although these biomarkers are not very specific, they are commonly used to determine whether a patient has developed AKI or not, in the Indian setup, irrespective of the cause of AKI. [15]Hence, this study was conducted to assess the effect of Proton Pump Inhibitors on renal profile.

In the present study, a total of 100 subjects were analysed. The subjects with AKI present were 11 out of the total. The age wise distribution of the incidence of AKI was more in the population over 50 years, with the maximal incidence in the group above 51 years. A study by Avinash A et al, assess the effect of PPIs on blood urea and serum creatinine, when administered for at least seven consecutive days. A total of 175 subjects were selected. When their case files were analysed, acute kidney injury was identified in 19 (10.86%) of them. Pantoprazole was the most common drug involved (84.21%). Renal injury was more common in the age group of over 50 years of age.[16]

In the present study, the normal values in laboratory are as follows: blood urea; 10 to 40 mg/dl; serum creatinine; 0.4 to 1.2 mg/dl.No relationship was found to be present between the duration of PPI therapy and the onset of AKI. Another study by Flothow DJG et al, studied proton pump inhibitor (PPI) intake has been linked to acute kidney injury and chronic kidney disease. The objective was to assess the effect of PPIs on renal function and rejection rate in kidney transplant patients. PPI prescription was assessed in half-year intervals. Primary outcome parameters were the estimated glomerular filtration rate (eGFR), change in the eGFR, and >30% and >50% eGFR decline for different time periods (up to four years post-transplantation). Except for >30% eGFR decline from half a year to two years post-transplantation ($p = 0.044$) and change in the eGFR, >30% and >50% eGFR decline showed no association with PPI intake in our patient cohort ($p > 0.05$). Similarly, by analyzing 158 rejection episodes, BPAR showed no correspondence with mean daily PPI intake. They concluded that prolonged PPI intake has no relevant adverse effect on kidney transplant function or rejection rates. Polypharmacy, however, remains a problem in renal transplant recipients and it is thus advisable to question the necessity of PPI prescriptions when clear indications are missing.[17]Omeprazole was the first to be synthesized and is still the most often used drug of this class of medications. [18] PPIs are prescribed to treat gastric diseases such as gastric and duodenal ulcers, gastroesophageal reflux disease, and erosive esophagitis.[19]However, as the years went by PPIs began to be prescribed injudiciously to patients outside the scope of indication, for periods longer than recommended, and taken by self-medicating individuals. [20,21] In addition, the drug is often used to treat digestive manifestations or to prevent symptoms derived from the use of other medications. All such factors have included PPIs in the list of the most used medications in the world.[22]

## CONCLUSION

Prescription of PPIs in AKI should be monitored.

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