

Using proton-pump inhibitors among haemodialysis patients-single academic dialysis centre preliminary experience

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A - Conception and study design; **B** - Collection of data; **C** - Data analysis; **D** - Writing the paper; **E** - Review article; **F** - Approval of the final version of the article

ABSTRACT

Introduction: Proton-pump inhibitors (PPIs) are a class of drugs which decrease gastric acid production, their overuse is becoming increasingly common.

Purpose: The aim of this study was to evaluate medical indications for PPIs in a cohort of prevalent haemodialysis (HD) patients and their awareness about the medical effects of these drugs.

Material and methods: The study was performed in 78 HD patients enrolled in chronic dialysis programme in single academic dialysis unit. The study was based on medical history obtained from patients (survey about drugs they take with intention of revealing PPIs, indications for the treatment, their awareness of mechanism of action of these drugs).

Results: 46 of patients (59%) took or have been taking PPIs. Almost half (49%; n=22) of them had no clear

medical indications for the drugs. Prescription of PPIs without medical indications was more common among nephrologists (27%), when compared to gastroenterologists (5%; p<0.05). Only 29% (n=13) of patients taking PPIs were aware of the mechanism of action of the drugs.

Conclusions: Results of this study reveal the problem of PPI overuse among HD patients. Gastroenterologists usually prescribed PPIs according to medical indications. The lack of patients' knowledge about the indications for PPIs therapy is overwhelming.

Key words: Proton-pump inhibitors, haemodialysis, overuse, side effects, nephrology

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INTRODUCTION

Proton pump inhibitors (PPIs) are among the most commonly used medications for the treatment of upper gastrointestinal disorders [1] and one of the most frequently prescribed classes of drugs in the world [2], because of their high effectiveness in decreasing gastric acid production and seemingly low toxicity. Their safety profile makes overuse of these drugs an increasingly common custom [3]. Many patients receive PPIs for unapproved or inappropriate indications. Those include: nonspecific abdominal symptoms without acid related disease features, prescription with low dose of NSAIDs in asymptomatic or low risk patients “just in case”, but the most common reason for a long term therapy is its continuation although the problem of disease had already been resolved [4].

With the advent of over-the-counter omeprazole, self-directed PPI therapy is now widely available, though this increases the potential for its inappropriate use. The risk of a minor symptomatic adverse effect from PPIs (nausea, diarrhoea or headache) is low, approximately 1-3%, with no significant differences noted between the PPIs [5]. Serious adverse events are rare, with case reports of interstitial nephritis induced by omeprazole [6] and hepatitis with omeprazole and lansoprazole [7,8]. Nevertheless, there have been emerging concerns with reports of potential long-term adverse effects associated with the use of PPIs. These include alteration of absorption of vitamin B12, especially in elderly patients [9], hypomagnesemia [10], increase of a risk of osteoporotic fractures [11] and influence on pharmacokinetics, pharmacodynamics and drug interactions [12].

The recently performed retrospective study, based on population of 99,269 patients showed that long-term use of PPIs is associated with increased risk of development of chronic kidney disease and death [13]. Overuse of PPIs is of concern also in haemodialysis (HD) patients. End stage kidney disease patients, being in HD programme, commonly suffer from many comorbid diseases like arterial hypertension, ischemic heart disease, chronic heart failure, and diabetes mellitus. This makes them medically prone for taking a lot of different, potentially interacting, drugs.

The aim of the present study was to evaluate the prevalence of PPIs use and medical indications for their prescription among a cohort of chronic HD patients. Secondly, the study was to assess patients' awareness about the medical effects of these drugs.

MATERIALS AND METHODS

The study was performed in 78 prevalent HD patients being treated in Ist Department of Nephrology

and Transplantation with Dialysis Unit in Medical University of Bialystok. All patients were fully informed about the aim of the study and afterwards gave their consent. Patients were on conventional maintenance HD programme (three times a week, 4-4.5 hour per HD session). The study was based on medical history taken individually from patients (survey about drugs they take with intention of revealing PPIs, medical indications for the treatment, their awareness of mechanism and effects of action of this class of medication). Information obtained by this way was verified and complemented by the review of medical documentation. Collected information included: clinical characteristic of patients (age, sex and etiology of chronic kidney disease), medications prescribed and their quantity. In case of treatment with PPIs: the type of drug prescribed, information who prescribed the therapy (gastroenterologist, nephrologist, or other specialist), medical indications for and the duration of therapy were retrieved. Finally patients' awareness of indications, mechanisms and effects of action of this class of medications were verified.

Interpretation of proper indications for PPI administration were limited to cases of:

- Barrett's oesophagus
- oesophageal peptic stricture
- GERD / oesophagitis / dyspepsia
- ulcer healing and/or *Helicobacter pylori* eradication
- upper GI bleed (including varices)
- Zollinger-Ellison syndrome
- short bowel syndromes
- peptic ulcer disease prophylaxis for patients taking NSAID / aspirin / steroid/ clopidogrel; according to bleeding risk assessment.

Descriptive statistics of variables are expressed as mean \pm SD and numbers (%). Chi² test was used to compare variables as appropriate. Differences were regarded as statistically significant when $p < 0.05$. Statistical analysis was performed with the use of Statistica 9.0 (StatSoft, Inc. Tulsa, Okla., USA).

RESULTS

Seventy eight patients participated in the study. The mean age of patients was 65 ± 15 years and 53% of them were males ($n=41$). Etiology of kidney disease was as follows: diabetic nephropathy 19% ($n=15$), autosomal dominant polycystic kidney disease 18% ($n=14$), glomerulonephritis 17% ($n=13$), hypertensive nephropathy 9% ($n=7$) and others or unknown ($n=22$).

Forty six of examined patients (59%) were treated with PPIs. Most of PPI users were administered omeprazole ($n=30$; 65%), pantoprazole was selected in eleven (24%) patients (Table 1).

Table 1 Frequency and type of PPI administration in the studied group.

| Proton pump inhibitor | N | % |
|-----------------------|----|-----|
| Omeprazole | 30 | 65 |
| Pantoprazole | 11 | 24 |
| Others | 5 | 11 |
| Total | 46 | 100 |

Almost half (n=22; 48%) of patients taking PPIs had no medical indications for this therapy. Prescription of PPIs without accepted medical indications is more common among nephrologists and

other physicians, when compared to gastroenterologists (p<0.05). Generally gastroenterologists prescribed PPIs according to accepted medical guidelines (Table 2).

Table 2 Prescribing PPIs in accordance with medical guidelines

| Specialist | Accordance with medical guidelines | |
|---------------------|------------------------------------|--------|
| | Yes (n) | No (n) |
| Nephrologists | 4 | 6 |
| Other physicians | 6 | 15 |
| Gastroenterologists | 13 | 1 |

Results of the study revealed that 28% (n=13) of patients taking PPIs were familiar with the mechanism of action of the drugs. 47% (n=21) of PPIs taking patients were on chronic therapy (regular schedule), while 27% (n=12) of them administered the drug as a rescue therapy (“as needed”), related to presence of symptoms. Patients on chronic treatment were more often the ones treated according to medical

guidelines (p<0.05) when compared to others. The study showed that 15% (n=7) of patients take PPIs at inappropriate time.

Figure 1 depicts daily pill burden for HD patients. It ranges from 1 to 15 different drugs per day with an average of 6, as shown in the study. However, there is no relation between taking PPIs and daily pill burden among HD patients.

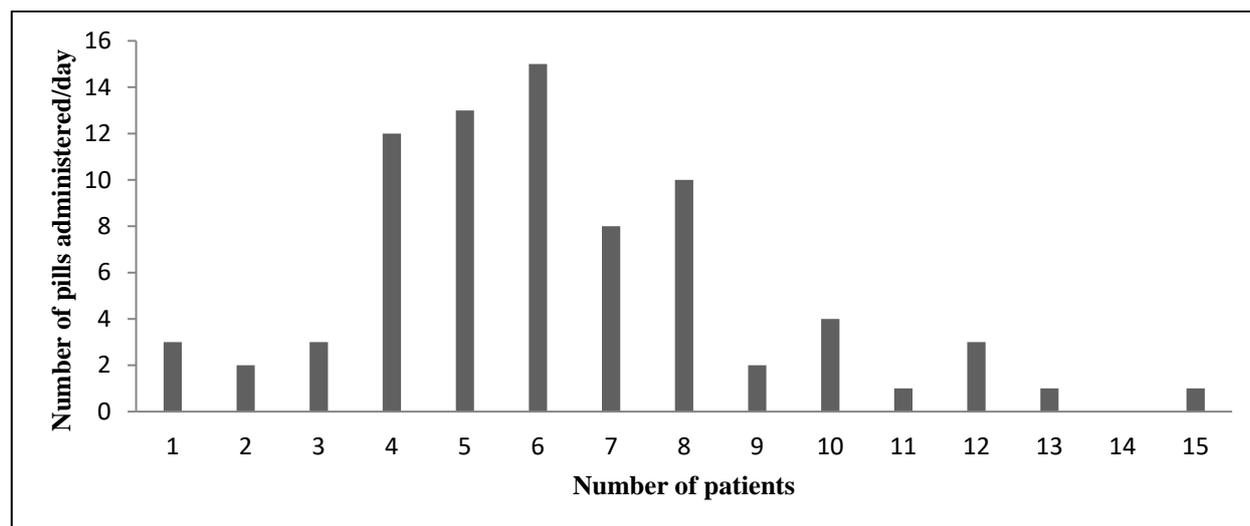


Figure 1 Daily pill burden among HD patients

DISCUSSION

Present study shows, that majority (59%) of examined HD patients currently take or have been taking PPIs, which is a common phenomenon [3,4] both in general and chronic kidney disease population [14]. Noteworthy is the fact, that long term PPI therapy increases the risk for enteric infections - Clostridium

difficile [15], Campylobacter, Salmonella [16]. There is also evidence of an increased risk of osteoporosis and bone fractures, nutritional deficiencies of vitamin B12, iron [17], impaired calcium and magnesium absorption [18,19] related to PPI therapy. Recent studies have suggested that avoidance of PPIs may prevent the development of dementia [20].

Although omeprazole is the most popular PPI among examined patients, pantoprazole seems to be safer, because of reported lower risk of drug interactions [21,22]. Furthermore, pantoprazole has no influence on pharmacodynamics or pharmacokinetics of drugs like: carbamazepine, diazepam, diclofenac, digoxin, ethanol, gliben-clamide, metoprolol, nifedipine, phenpro-coumon, phenytoin, theophylline or warfarin [21].

According to our study, the main indication for prescribing PPIs was prophylaxis or treatment of peptic ulcer disease. Gastroenterologists were the physicians most commonly prescribing PPIs according to medical guidelines.

As the study shows, almost half of HD patients taking PPIs had no medical indication for it. Similar studies consistently present, that PPIs are being overprescribed in both primary and secondary medical care [23]. 40% of examined patients admitted lack of awareness of the mechanism of action of PPIs, they described them mostly as “protective”. Our findings are consistent with studies reporting the lack of knowledge concerning this group of drugs among patients in general practice [24]. This phenomenon might be caused by poor patient-doctor communication. We should also consider patient’s personality and age [24], which make physician’s efforts even harder.

Results of present study indicate, that a substantial number of patients administer the drug in a wrong time or manner - occasional use. Some patients took PPIs at night, in contrast to recommendation of a once-daily morning dosage [25] prior to a meal [26]. Furthermore, many of them were not aware of this importance. PPI failure is a frequent problem in gastroenterology clinics and at the primary care level as well [27]. Patients knowledge about the treated disorder and prescribed drug is crucial to successful treatment [24]. One quarter of examined patients admitted taking drugs “as needed”, however occasional use of PPI does not provide appropriate acid inhibition and clinical response as well [28,29].

High daily pill burden increases the problem of lack of compliance. The more pills are prescribed, the more possible it is to skip portions of drugs by patients [30]. HD patients are a specific group suffering from comorbidities in many ways. Not only do they take a lot of drugs, but also they are being cared for by a few specialists. It could make an issue of adhering to medical recommendations by patient. Better communication might also prevent drug interactions, caused by insufficient awareness about the medications prescribed by other specialists. All of these arguments clearly point out, that information about treatment should be more transparent and abundant, which leads to the fact that doctors should dedicate more time and patience to it.

The study has potential limitations, such as relatively small number of examined patients and lacks in their medical documentation. We are aware that a larger trial is needed in order to draw a final conclusion.

CONCLUSIONS

Results of this study reveal the problem of overuse of PPIs among HD patients. They often do not know, when to take the drug or how the drug works. Among medical specialties, only gastroenterologists prescribe PPIs according to accepted guidelines whereas other doctors mostly prescribe PPIs without clear medical indications. The most popular PPI used in HD population is omeprazole. There is a necessity to develop communication skills among doctors to improve patients adherence to their recommendations and improve effectiveness of treatment.

Conflicts of Interest

The authors declare no conflict of interest.

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