Original Article

Proton pump inhibitors – over-prescribed in a rural community?

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ABSTRACT

Objectives: There are specific licensed indications for the use of Proton Pump Inhibitors (PPIs). However it is over-prescribed globally. We performed a study to find out the uses and misuses of this expensive drug in our rural and financially poor population.

Methodology: Prospective survey of patients successively admitted in medical and surgical wards of a teaching hospital in rural setting.

Results: Two hundred fifty successively admitted patients over a month were interviewed. Of them 144 (58%) were females. Mean age was 42 years (range = 10 - 100 years). Ninety (36%) were using PPIs for which there was a licensed clinical indication in 44 (49%), whereas 46 (51%) had no definite indications. Fifty three patients (59%) who were taking PPIs were either self prescribing or were prescribed by an unqualified medical practitioner. Of these, 34 (64%) did not appear to have a valid indication. Of the remaining, 15 patients were prescribed PPI by a specialist, and 22 by a qualified general practitioner.

Conclusions: Over half of patients (51%) in our setting are using PPIs with no definite indication. Over 2/3 (64%) of those were prescribed either by unqualified practitioner or bought over-the-counter, had no licensed indication.

KEY WORDS: Proton Pump Inhibitors, Dyspepsia, Indications.

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INTRODUCTION

Dyspepsia and Heartburn are common presenting complaints to general practitioners, and there is continuing debate about their management. Chronic disorders and their treatment, such as rheumatic disorders, are associated with increased frequency of gastrointestinal (GI) symptoms.[1] Dyspepsia itself is not a diagnosis but stands for a constellation of symptoms referable to the upper gastrointestinal tract. It consists of a variable combination of symptoms including abdominal pain or discomfort, postprandial fullness, abdominal bloating, early satiety, nausea, vomiting, heartburn and acid regurgitation.[2] Acid suppressant drugs, the most potent of which are proton pump inhibitors (PPIs), are often prescribed for variable duration. It has been suggested that PPIs are probably too widely prescribed for minor symptoms with obvious cost implications.[3]

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The first PPI, omeprazole, was introduced in 1989, and the first generic PPI (again omeprazole) was introduced in 2002.[3] Other drugs in this class are also being marketed, including lansoprazole, rabeprazole, pantoprazole and esomeprazole. There has been a substantial, continuing, and unexplained rise in prescribing of PPIs. Along with the financial aspect, potential side effects should also be considered. Nevertheless, there are reports from many countries in the world that PPIs may sometimes be overused and even misused.[3] Although there is little published work available in Pakistan on this topic, anecdotally, situation is not much different. We undertook a study to determine the licensed uses and abuses of PPIs in our community, resident in a rural and financially poor area of Pakistan.

METHODOLOGY

Two hundred and fifty patients successively admitted in medical & surgical wards of our teaching hospital were prospectively interviewed on admission. If they were on a PPI, attempt was made to find out the indication by interviewing patients and reviewing their prescriptions when they were first prescribed PPI (where they were available). The indications were accepted valid if they were listed in a recent edition of British National Formulary (BNF) as licensed indication (Table-I).[4] We divided the patients into two groups - those who are using PPIs for some indication and those who are using them without any sound explanations.

Approval was taken to conduct this study from hospital's Research Ethics Committee. Verbal consent of participating patients was taken.

RESULTS

Two hundred and fifty patients (144 [58%] males) were interviewed on admission. Ninety (36%) were taking a PPI. Of them, 43 (48%) were females. Mean Age was 41 years (range = 15 - 100 years). Forty four (49%) were using PPIs because of a total of 55 valid indications (11 of these patients had 2 indications each). The indications included epigastric pain / dyspepsia (n = 34 [38%]), gastro-oesophageal reflux symptoms (n = 18 [20%]), upper GI bleed (n = 2) and prevention of NSAID-induced ulcer (n = 1). Table-II shows the characteristics of the two groups.

Table-I: Licensed indications of proton pump inhibitors[4]

	Indications
1	Gastric Ulcer
2	Duodenal Ulcer
3	Eradication of *Helicobacter pylori* (in combination with antibacterials)
4	Severe peptic ulcer bleeding (following endoscopic treatment)
5	Dyspepsia
6	Gastro-oesophageal reflux disease
7	Prevention and treatment of NSAID-associated ulcers
8	Zollinger-Ellison syndrome

DISCUSSION

PPI is one of the most frequently prescribed and otherwise used classes of drugs in the world.[3] Their expenditure in 2006 as £425 million in England[6] and £7 billion globally.[3] The cost of using this class of drug for an individual person is also considerable, particularly if used for long-term. This is of obvious importance in a third world country like Pakistan, and even more so in a rural areas of Pakistan, where poverty is even a bigger problem, and where almost 2/3 (32.3%) of the population resides.[5] Despite this, studies consistently show that PPIs are being overprescribed worldwide in both primary and secondary care. Reports suggest between 25% and 70% of patients in western world with high literacy rate and better buying power than Pakistani population, take these medications with no appropriate indication. This means almost £2 billion worldwide is being spent unnecessarily on PPIs each year.[3] The financial implications of misuse of PPIs for a poor country like Pakistan are therefore obvious. It is therefore neither surprising nor encouraging that over half of our patients (51%) were found to have no appropriate indication for the use of PPI.

The first indication for which PPIs are used was reflux oesophagitis. Although one would need

Table-II: Characteristics of patients.

	On PPI n=90 (36%)	*Not on PPI n=160 (64%)*
Males	47 (52%)	70 (44%)
Females	43 (48%)	90 (56%)
Average Age in years (range)	41 (15-100)	41 (10 – 85)
Prescribed by a Doctor	37 (41%)	---
Suggested by a Quack/Over the counter	53(59%)	---

complicated diagnostic tests to prove this diagnosis, e.g. upper GI endoscopy and 24 hour esophageal pH monitoring, heartburn is a good symptom to give reasonable confidence in diagnosing gastro-esophageal reflux disease.[6] This might therefore reasonably be expected to be a major indication of its use as was found in this study (18 patients - 20%). Thirty four (38%) of patients in this study were prescribed PPIs for having epigastric pain or dyspepsia, all of which were uninvestigated at the time PPI was first prescribed. However, at least a proportion of them may represent peptic ulcer disease (PUD). These were counted as potentially valid indication in this study. A large number of our patients (58%) were taking PPI for "heartburn", epigastric pain and / or "dyspepsia" without these being investigated. However, given the fact that heartburn often suggests gastro-oesophageal reflux disease, and that 'Acid-related dyspepsia' without a definite and endoscopically or otherwise proven gastro duodenal pathology, is an acceptable indication for the use of PPI,[4] these two symptoms were accepted as valid indication for the use of PPI in one study.

There are a number of potential side effects of PPI.[4] Along with a long list of such side effects, recent reports of pneumonia,[7] *clostridium difficile*[8,9] and *campylobacter enteritis*[3] infections, acute interstitial nephritis[10] and osteoporosis-related fractures[11] are unusual but recognized consequences of treatment with PPIs. Although none of our patients is this study was admitted because of these problems, this aspect must also be considered while prescribing PPIs, particularly for long term.

Over-prescription of PPIs in developed world is not a new phenomenon.[3] Concerned physicians have been writing warnings on this for many years.[12] Despite this, PPI has been overprescribed in western countries as shown by a recent review.[3] Compounded with the problems of illiteracy, lack of awareness, lack of regulations and control on prescription, sale and use of drugs in a third world country like Pakistan, makes the task of containing the misuse of drugs like PPI even more challenging.

Reasons for prescribing outside licensed indications are manifold. Influences as diverse as poor training, unqualified medical practitioner, drug companies' marketing, and patient wishes, may all have their effects. Concerns about the long term safety of proton pump inhibitors and their overuse for minor symptoms have been expressed for long[12], but authoritative guidelines are available that may help general practitioners to prescribe proton pump inhibitors more appropriately.[4,13] Greater willingness to accept the recommendations and more emphasis on implementing them should constrain the future use of PPIs.

Limitations of study: We may have underestimated unlicensed use of proton pump inhibitors for several reasons. Consultant opinion or confirmation of diagnoses by investigation is more likely to result in the recording of a definitive and accurate diagnosis such as duodenal ulcer or oesophagitis, whereas this applies in only a minority of cases of gastrointestinal illness in primary care. It is possible, therefore, that unreal diagnoses are made and treated with PPIs.

CONCLUSIONS

A significant number of patients in our setting are using PPIs with no definite or licensed indication.

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