Original Article

Does Proton Pump Inhibitors Therapy Impair Bone? Study in Young Patients of Hyderabad, Sindh Pakistan

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ABSTRACT

Objectives: To assess the negative impact of proton pump inhibitors on calcium and vitamin d on adults of Hyderabad sindh Pakistan

Study Design: Observational / descriptive study.

Place and Duration of Study: This study was conducted at Clive nics of sadder Hyderabad Sindh, June to December 2016

Materials and Methods: 50 patients were selected as inclusion criteria . all were young subjects age was 22.4±5.4 years. Mean duration of PPI was 3.4±2.1 months. None of subject was having complicated peptic ulcer disease. Sampling technique was non probability convenience. statical soft ware was SPSS 16 . Student paired t test was used to calculate p value before and after PPI use. P value was considered <0.05 significant.

Results: There was no significant impact noted. P value was <0.08 for serum calcium and <0.09 for serum vitamin D

Conclusion: There is no negative impact of long term PPI over calcium and vitamin d on young individuals

Key Words: PPI, Young, calcium , Hyderabad.

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INTRODUCTION

Most guidelines are supporting proton pump inhibitor (PPI) use as the sole option for treatment of nonerosive gastroesophageal reflux disease (GERD), erosive esophagitis, dyspepsia and peptic ulcer disease.

Omeprazole was first introduced in 1988, to become largest prescribed salt till 1996. Lansprazole was second to be marketed in 1991, Pantoprazole in 1994, Rabeprazole in 1999, Esomeprazole in 2001, and Dexlansprazole in 2009.

Rationale or irrational use uses of PPIs are still on the rise. In a London, only 8% of inpatients were receiving PPI therapy in 1997.[1] while Vliel et in 2008 showed that 43% of patients were taking PPIs during hospitalization even in chest wards.[2]

Sadaf Shafi et al in 2011 reported 51% of patients on Proton pump inhibitors without a definite indication.[3] A Karachi-based study demonstrated 47.2% patients were prescribed PPIs on their discharge card.[4]

Haroon et al showed in 2013, 79% patients were taking PPIs.[5] clearly indicating an upward trends for PPI prescription.

The practice of PPI overutilization is considered a direct result of the lack of determination of need for continuous therapy in many outdoor patients . chronic use of PPI increases financial burden, various minerals and vitamin deficiencies [6]

Regarding mechanism of action of PPI on inhibition of the H+/K+ ATPase enzyme in gastric mucosal parietal cells, which is responsible for hydrogen ion secretion in exchange for potassium ions in the gastric lumen[7]

Proton pump inhibitors (PPIs) were identified recently as an independent risk factor for osteoporotic fracture.[8] The possible mechanism is effect of high pH due to PPI use, which reduces absorption of calcium and vitamin B12, resulting in decreased bone mineral density.[9]

While there is conflicting evidence with regard to the role of intragastric hydrochloric acid in calcium absorption, and PPIs are known to inhibit this mechanism, one study found that gastric acid secretion and gastric acidity do not normally play a role in the absorption of dietary calcium[10]

Newer research offers conflicting data, implying that study subjects who had been on PPI therapy may be at a higher risk of osteoporotic fracture compared with an individual at average risk, yet the researcher concluded that PPI use was not associated with a change in bone mineral density[11]

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Literature shown multiple observational, case–control and cohort studies have shown a remarkable increase in fractures with chronic PPI use but Other studies have, however, failed to substantiate this association.[12]
Many of these studies, however, had important limitations, including retrospective design, inability to control for important potential confounders, small sample size, heterogeneous population at risk (older than 18 years of age vs. post-menopausal females vs. males), retrospective outcome (fracture) ascertainment and limited information on PPI exposure[13]
Duration of use of PPI is controversial like in some studies ≥ 5 years can increase the risk of osteoporotic fractures by 1.62 or more than ≥ 7 years increases the risk of osteoporotic hip fractures by 4.55-fold . PPI use for 6-12 months has been reported to be associated with an increased risk of osteoporotic hip and spine fractures [14]
The rationale of this study is to see the negative impact of chronic use of PPI over serum calcium and vitamin d in young individuals in Hyderabad sindh.

MATERIALS AND METHODS

The cross-sectional, observational study was conducted at the sadder Hyderabad sindh from June to December 2016
The sample size was based on convenience sampling, 50 patients were selected from different clinics of sadder Hyderabad, which was a biggest area of consultants of province and cover all patient seeking advise from whole province
Inclusion criteria; Young individuals 20-30 years
Taking proton pump inhibitors since 6 months
Exclusion criteria
Known endocrnopathies like hypo or hper parathryoidism
Co morbidities like cardiac, renal or inflammatory bowel diseases
Patients already had complicated peptic ulcer disease
Patents were young subjects mean age was 22.4±5.4 years and Mean duration of PPI was 3.4±2.1 months. All type s and all forms of proton pump inhibitors were included like omeprazole, lansoprazole and esomeprazole. The dose was 20-40 mg once or two times. BMI was 22.1±3.8 .
Patients base line characteristics were noted along with serum calcium and vitamin d were also done. Patients then advised to stop PPI for 1 month.
Serum levels of calcium and vitamin d were again noted after one month . Statical soft ware was SPSS 16 Student paired t test was used to calculate p value before and after PPI use. P value was considered <0.05 significant.

RESULTS

50 patients were enrolled in this study male to female ratio was 1:1.1. Base line characteristics noted shown in table 1.
After PPI abstinence the serum levels of calcium and vitamin d shown in table 2
P value was in significant for calcium <0.08 and vitamin d <0.09.

Table No.1: Base line characteristics at time of inclusion in study

Variables	Results	Percentage
Male	24	48
Female	26	52
Duration of PPI	3.5±1.7 months	
BMI	22.1±2.6	
Serum calcium	9.1±1.1	
Vitamin D	20±3.7	

Table No.2: Characteristics at stop on PPI 4 weeks

Variables	Results	P value
Male	24	
Female	26	
Serum calcium	8.9±1.2	0.08
vitamin d	20.3±2.8	0.09

DISCUSSION

This study was conducted in general population attending consultants clinics at sadder Hyderabad for different reasons . All included patients were young without any co morbidity. 50 subjects were selected , 48% were male and 52% were females. 75% were using PPI without any therapeutic indication .this is match able to Irish study reported that 32% (87 of 272 patients) were taking PPIs with only 37% having a valid indication and Vliel et al, reported that 40% of patients were taking PPIs for unregistered indications.[15]
In our study all subjects were selected young and there was no risk of fracture by reducing calcium air vitamin D , the risk of fractures increased in eder subjects with PPI use as shown by Elaine W. Yu,[16]of long term PPI use with modestly increased risk of non-spine fracture was found in elderly people with low calcium intake
Proton pump inhibitors did not impact on calcium and vitamin D as shown in our study where the p value was 0.08 calculated for calcium before and after PPI use and p value 0.09 calculated for serum vitamin d . Our results are supported to a study which showed that it remains uncertain whether PPI-associated hypochlorhydria truly decreases calcium absorption.[17]
One study shown PPI use for less than 6 years not associated with any risk of fracture.[18]
Wright Mj etal [19] done a study over serum calcium and urinary calcium excretion and did not show any difference in absorption or excretion with or without PPI use.
Sharara AI[1] et al[20] made two groups one on PPI and second without PPI of total of 58 participants. Mean age of participants was 33.2±7.5 years. Baseline characteristics and biomarkers were similar for both groups except for higher BMI (28.6 vs. 25.6 kg/m, in

the PPI group. There was no difference in parathormone (PTH), ionized calcium, vitamin D between the PPI and control subjects. Multiple linear regression modeling showed no effect of PPIs on any of the studied calcium or bone metabolism biomarkers. This study is matched with our study in which we didn't see any significant difference in single group with and without PPI on calcium and vitamin d.

According to a study on the impact of short-term (2-week) administration of omeprazole for the osteoclastic H+ -pump in children, none of the levels among urinary calcium excretion, serum total alkaline phosphatase activity, collagen type 1 cross-linked C-telopeptide, orosteocalcin were altered in any age or gender group [21]

CONCLUSION

Proton pump inhibitors are not impairing bone metabolism in chronic use in young individuals. PPI are quite safe if continue less than 6 years.

This conclusion is made as Canadian Association of Gastroenterology found no persuasive evidence that the association or change calcium in prescribing PPI therapy due to concerns about the risk of hip fractures[22].

Conflict of Interest: The study has no conflict of interest to declare by any author.

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