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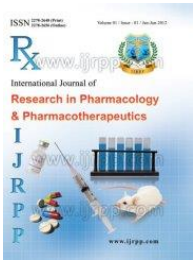

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A study to evaluate the effect of proton pump inhibitors (PPI'S) on vitamin d levels

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ABSTRACT

Background

Proton pump inhibitors (PPI's) remain the superior choice worldwide in antisecretory therapy in the evidence-based treatment of upper gastrointestinal disorders including gastroesophageal reflux disease, erosive esophagitis, dyspepsia and peptic ulcer disease. Nonjudicious use of PPIs creates both preventable financial as well as medical concerns. PPIs have been associated with an increased risk of vitamin and mineral deficiencies.

Objective

To study the effect of Proton Pump Inhibitors (PPI's) effect on vitamin D levels.

Design

A study To evaluate the effect of PPI's on vitamin D levels in patients who were treated for vitamin D deficiency.

Duration

February 2017 to July 2017.

Setting

Participants

One hundred patients treated for vitamin D deficiency at

Methods

100 patients were included in the study. 40 patients were taking PPI at the time and during the study. 60 patients were not on any medications. Results were assessed by improvement in repeat serum 25(OH) vitamin D levels obtained after replacement therapy. Demographics, vitamin D levels, medical history and medication lists were obtained. Percentage increase in 25-OH vitamin D levels from baseline was considered the end point. Results were compared between the two groups. Statistics include unpaired t-test done to compare two groups of subjects and p value less than 0.05 was considered statistically significant.

Results

The mean improvement in 25(OH) vitamin D levels for the "PPI" group was 40.9% with a mean raw difference of 9.1. "No PPI" group demonstrated a mean improvement of 59.1 % with a mean difference of 13.8. The improvement in 25(OH) vitamin D levels in the "no PPI" cohort was 64.2% greater than those taking a PPI.

Conclusion

PPIs are associated with an increased risk of vitamin D deficiency impacting vitamin D metabolism.

Keywords: Proton Pump Inhibitors (PPI's), Vitamin D, Metabloism.

INTRODUCTION

Proton pump inhibitors (PPIs) have been available since 1989, when the first drug of this class, omeprazole, was released. They are currently one of the most frequently prescribed drugs and are available for "over-the-counter" acquisition in several countries. They decrease acid production by irreversible blockage of H+/K+-adenosine triphosphatase that is present on gastric parietal cells and are currently the treatment of choice in several clinical conditions, such as symptomatic and complicated gastroesophageal reflux disease (GERD), Zollinger-Ellison syndrome, prevention of ulcers in nonsteroidal anti-inflammatory drug (NSAID) users, induction of peptic ulcer healing, and even in the eradication of Helicobacter pylori. They are generally considered safe and are associated with mild side effects; however, there is growing concern regarding their safety. Common adverse effects include headache, nausea, diarrhea, abdominal pain, fatigue, and dizziness. Infrequent adverse effects include rash, itch, flatulence, constipation, anxiety, and depression. Also infrequently, PPI use may be associated with occurrence of myopathies, including the serious reaction rhabdomyolysis. PPIs have also been associated with an increased risk of vitamin and mineral deficiencies. Vitamin D is a group of fat-soluble secosteroids responsible for increasing intestinal absorption of calcium, magnesium, and phosphate, and multiple other biological effects. In humans, the most important compounds in this group are vitamin D3 (also known as cholecalciferol) and vitamin D2 (ergocalciferol). Cholecalciferol and ergocalciferol can be ingested from the diet and from supplements. Only a few foods contain vitamin D. The major natural source of the vitamin is synthesis of cholecalciferol in the skin from cholesterol through a chemical reaction that is dependent on sun exposure (specifically UVB radiation). Dietary recommendations typically assume that all of a person's vitamin D is taken by mouth, as sun exposure in the population is variable and recommendations about the amount of sun exposure that is safe are uncertain in view of the skin cancer risk. Recent epidemiologic studies have observed relationships between low vitamin D levels and multiple disease states. Low vitamin D levels are associated with increased overall and cardiovascular mortality, cancer incidence and mortality, and autoimmune diseases such as multiple sclerosis. Although it is well known that the combination of vitamin D and calcium is necessary to maintain bone density as people age, vitamin D may also be an independent risk factor for falls among the elderly. New recommendations address the need for supplementation in breastfed newborns and many questions are raised regarding the role of maternal supplementation during lactation. Unfortunately, little evidence guides clinicians on when to screen for vitamin D deficiency or effective treatment options. This study aims to evaluate the effect of PPI's on vitamin D levels in patients who were treated for vitamin D deficiency.

MATERIALS AND METHODS

100 patients were included in the study. 40 patients were taking PPI at the time and during the study. 60 patients were not on any medications.

Inclusion criteria

1. Men and women were included.
2. Age ≥18.
3. Vitamin D levels ≥10 and <30ng/ml.

Exclusion criteria

1. Vitamin D levels below 10 ng/dl.
2. Malabsorption syndrome.
3. Intestinal bypass.

4. Chronic liver or kidney disease.
5. Sever SLE.
6. Sever Scleroderma.
7. History of cancer within the last 5 years.

Results were assessed by improvement in repeat serum 25(OH) vitamin D levels obtained after replacement therapy. Demographics, vitamin D levels, medical history and medication lists were obtained. Percentage increase in 25-OH vitamin D levels from baseline was considered to be the end point. Results were compared between the two groups. Statistics include unpaired t-test done to compare two groups of subjects and p value less than 0.05 was considered statistically significant.

OBSERVATIONS AND RESULTS

Demographics

Table 1. Demographics

	PPI	No PPI
Subjects	40	60
Gender		
Male	16	21
Female	24	39
Age	59±9	55±11
BMI	31±3	30±8

100 patients were included in the study. 40 patients were taking PPI at the time and during the study. 60 patients were not on any medications. Female gender was more in both the cohorts. Mean age in PPI group was 59±9 while in no PPI group was 55±11.

Mean vitamin d dosage

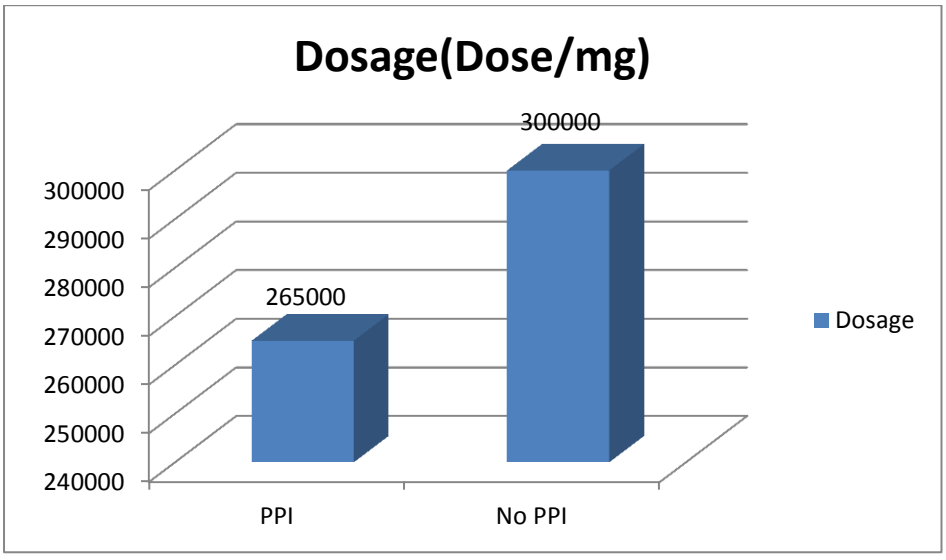

Figure 1. Mean Vitamin D Dosage

The mean vitamin D dosage in case of subjects on PPI's was less than that of subjects not taking any medications.

Body mass index

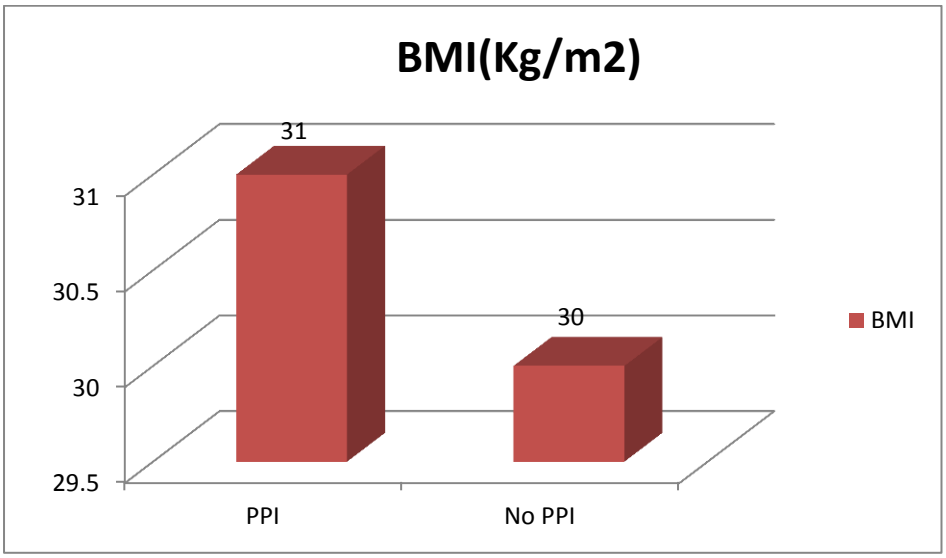

Figure 2. Body Mass Index

The mean BMI for the PPI group was 31±3 and that for the no PPI group was 30±8.

Change in vitamin d levels

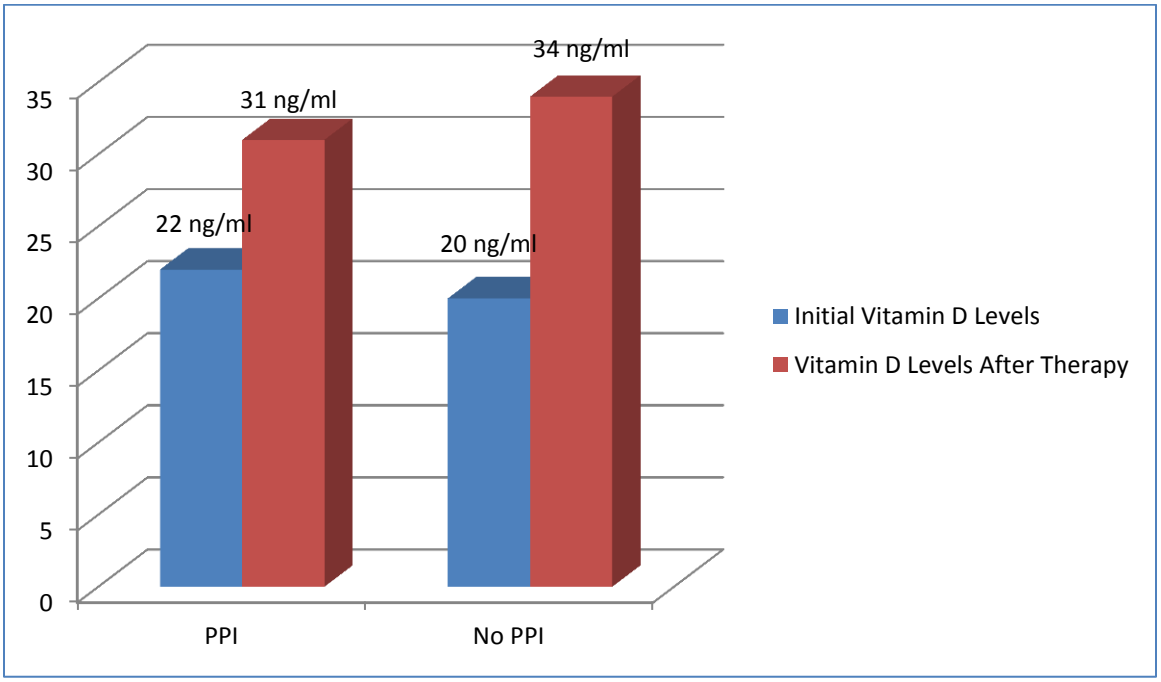

Figure 3. Change In Vitamin D Levels

The mean improvement in 25(OH) vitamin D levels for the "PPI" group was 40.9% with a mean raw difference of 9.1. "No PPI" group demonstrated a mean improvement of 59.1 % with a mean difference of 13.8.

Percentage increase in vitamin d levels

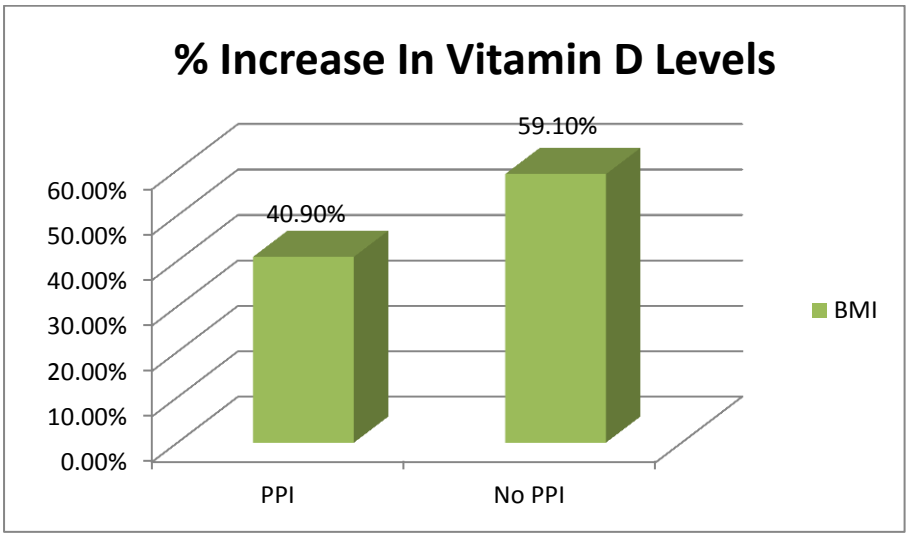

Figure 4. Percentage Increase In Vitamin D Levels

The mean improvement in 25(OH) vitamin D levels for the "PPI" group was 40.9%. "No PPI" group demonstrated a mean improvement of 59.1 %.

DISCUSSION

Proton pump inhibitors (PPIs) are known as a class of pharmaceutical agents that target H+/K+-ATPase, which is located in gastric parietal cells. PPIs are widely used in the treatment of gastric acid-related diseases including peptic ulcer disease, erosive esophagitis and gastroesophageal reflux disease, and so on. These drugs present an excellent safety profile and have become one of the most commonly prescribed drugs in primary and specialty care. Except for gastric acid-related diseases, PPIs can also be used in the treatment of Helicobacter pylori infection, viral infections, respiratory system diseases, cancer and so on. Although PPIs are mainly used short term in patients with peptic ulcer disease, nowadays these drugs are increasingly used long term, and frequently for a lifetime, for instance in patients with typical or atypical symptoms of gastroesophageal reflux disease and in NSAID or aspirin users at risk of gastrotoxicity and related complications including hemorrhage, perforation and gastric outlet obstruction. Long-term use of PPIs may lead to potential adverse effects, such as osteoporotic fracture, renal damage, infection (pneumonia and clostridium difficile infection), rhabdomyolysis, nutritional deficiencies (vitamin), anemia and thrombocytopenia. The purpose of this study is to evaluate the effect of proton pump inhibitors on vitamin D levels in patients who are treated for vitamin D deficiency or insufficiency. 100 patients were included in the study. 40 patients were taking PPI at the time and during the study. 60 patients were not on any medications. Results were assessed by improvement in repeat serum 25(OH) vitamin D levels obtained after replacement therapy. Demographics, vitamin D levels, medical history and medication lists were obtained. Percentage increase in 25-OH vitamin D levels from baseline was considered the end point. Results were compared between the two groups. Statistics include unpaired t-test done to compare two groups of subjects and p value less than 0.05 was considered statistically significant. The mean vitamin D dosage in case of subjects on PPI's was less than that of subjects not taking any medications. The mean BMI for the PPI group was 31±3 and that for the no PPI group was 30±8. The mean improvement in 25(OH) vitamin D levels for the "PPI" group was 40.9% with a mean raw difference of 9.1. "No PPI" group demonstrated a mean improvement of 59.1 % with a mean difference of 13.8. The improvement in 25(OH) vitamin D levels in the "no PPI" cohort was 64.2% greater than those taking a PPI. Hence we conclude that PPIs are associated with an increased risk of vitamin D deficiency impacting vitamin D metabolism.

CONCLUSIONS

PPIs are associated with an increased risk of vitamin D deficiency impacting vitamin D metabolism. We recommend revaluating the need for PPI, regular vitamin D level measurements and further larger studies to be conducted.

REFERENCES

[1]. Long J, Wright E, Molesti E, Temperton N, Barclay W. Antiviral therapies against Ebola and other emerging viral diseases using existing medicines that block virus entry. F1000Research. 4, 2015, 30.

[2]. Sasaki T, Nakayama K, Yasuda H, Yoshida M, Asamura T, Ohrui T, et al. A randomized, single-blind study of lansoprazole for the prevention of exacerbations of chronic obstructive pulmonary disease in older patients. J Am Geriatr Soc. 57(8), 2009, 1453–1457.

[3]. Vanfleteren LE, Spruit MA, Wouters EF, Franssen FM. Management of chronic obstructive pulmonary disease beyond the lungs. Lancet Respir Med. 4(11), 2016, 911–924. doi: 10.1016/S2213-2600(16)00097-7.

[4]. Sasaki T, Nakayama K, Yasuda H, Yamaya M. A new strategy with proton pump inhibitors for the prevention of acute exacerbations in COPD. Ther Adv Respir Dis. 5(2), 2011, 91–103. doi: 10.1177/1753465810392264.

[5]. Becker JC, Grosser N, Waltke C, Schulz S, Erdmann K, Domschke W, et al. Beyond gastric acid reduction: proton pump inhibitors induce heme oxygenase-1 in gastric and endothelial cells. Biochem Biophys Res Commun. 2006;345(3):1014–1021. doi: 10.1016/j.bbrc. 04, 2006, 170.

[6]. Dimango E, Walker P, Keating C, Berdella M, Robinson N, Langfelderschwind E, et al. Effect of esomeprazole versus placebo on pulmonary exacerbations in cystic fibrosis. BMC Pulm Med. 14(1), 2014, 1–7. doi: 10.1186/1471-2466-14-21.

[7]. Kim YJ, Lee JS, Hong KS, Chung JW, Kim JH, Hahm KB. Novel application of proton pump inhibitor for the prevention of colitis-induced colorectal carcinogenesis beyond acid suppression. Cancer Prev Res (Philadelphia, Pa). 3(8), 2010, 963–974. doi: 10.1158/1940-6207.CAPR-10-0033.

[8]. De Milito A, Iessi E, Logozzi M, Lozupone F, Spada M, Marino ML, et al. Proton pump inhibitors induce apoptosis of human B-cell tumors through a caspase-independent mechanism involving reactive oxygen species. Can Res. 67(11), 2007, 5408–5417. doi: 10.1158/0008-5472.CAN-06-4095.

[9]. Yeo M, Kim DK, Park HJ, Cho SW, Cheong JY, Lee KJ. Blockage of intracellular proton extrusion with proton extrusions with proton pump inhibitor induces apoptosis in gastric cancer. Cancer Sci. 99(1), 2008, 185.

[10]. Marino ML, Fais S, Djavaheri-Mergny M, Villa A, Meschini S, Lozupone F, et al. Proton pump inhibition induces autophagy as a survival mechanism following oxidative stress in human melanoma cells. Cell Death Dis. 1, 2010, e87. doi: 10.1038/cddis.2010.67.

[11]. Udelnow A, Kreyes A, Ellinger S, Landfester K, Walther P, Klapperstueck T, et al. Omeprazole inhibits proliferation and modulates autophagy in pancreatic cancer cells. PLoS One. 6(5), 2011, e20143. doi: 10.1371/journal.pone.0020143.

[12]. Canitano A, Iessi E, Spugnini EP, Federici C, Fais S. Proton pump inhibitors induce a caspase-independent antitumor effect against human multiple myeloma. Cancer Lett. 376(2), 2016, 278–283. doi: 10.1016/j.canlet.2016.04.015.

[13]. Lee YY, Jeon HK, Hong JE, Cho YJ, Ryu JY, Choi JJ, et al. Proton pump inhibitors enhance the effects of cytotoxic agents in chemoresistant epithelial ovarian carcinoma. Oncotarget. 6(33), 2015, 35040–35050.

[14]. Spugnini EP, Buglioni S, Carocci F, Francesco M, Vincenzi B, Fanciulli M, et al. High dose lansoprazole combined with metronomic chemotherapy: a phase I/II study in companion animals with spontaneously occurring tumors. J Transl Med. 12, 2014, 225. doi: 10.1186/s12967-014-0225-y.

[15]. Wang BY, Zhang J, Wang JL, Sun S, Wang ZH, Wang LP, et al. Intermittent high dose proton pump inhibitor enhances the antitumor effects of chemotherapy in metastatic breast cancer. J Experimen Clin Cancer Res. 34, 2015, 85. doi: 10.1186/s13046-015-0194-x.

[16]. Henry E., Carswell A., Wirz A., Fyffe V., McColl K. Proton pump inhibitors reduce the bioavailability of dietary Vitamin C. Aliment Pharmacol Ther 22, 2005, 539–545

[17]. Hirschowitz B., Worthington J., Mohnen J. Vitamin B12 deficiency in hypersecretors during long-term acid suppression with proton pump inhibitors. Aliment Pharmacol Ther 27, 2008, 1110–1121

[18]. Hoorn E., van der Hoek J., de Man R., Kuipers E., Bolwerk C., Zietse R. A case series of proton pump inhibitor-induced hypomagnesemia. Am J Kidney Dis 56, 2010, 112–116

[19]. Ho P., Maddox T., Wang L., Fihn S., Jesse R., Peterson E., et al. Risk of adverse outcomes associated with concomitant use of clopidogrel and proton pump inhibitors following acute coronary syndrome. JAMA 301, 2009, 937–944

[20]. Howden C. Vitamin B12 levels during prolonged treatment with proton pump inhibitors. J Clin Gastroenterol 30, 2000, 29–33.

[21]. Hutchinson C., Geissler C., Powell J., Bomford A Proton pump inhibitors suppress absorption of dietary non-haem iron in hereditary haemochromatosis. Gut 56, 2007, 1291–1295.

[22]. Inadomi J. On-demand and intermittent therapy for gastro-esophageal reflux disease. Pharmacoeconomics 20, 2002, 565–576.