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Review Article

A review on decreased calcium and vitamin b_{12} absorption with long term proton pump inhibitor therapy

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Abstract

Proton pump inhibitors (PPI) are now one of the most widely used classes of drugs. PPIs have proven to have a very favorable safety profile and it is unusual for a patient to stop these drugs because of side effects. However, increasing numbers of patients are chronically taking PPIs for gastro esophageal reflux disease and a number of other common persistent conditions, therefore the long-term potential adverse effects are receiving increasing attention. Nowadays as PPI are the main drugs used for peptic ulcer disease and GERD ,a part from this they are also preferred in drug induced gastric irritation .In this article these studies are systematically examined, as well as the studies of the effects of chronic PPI usage on VB_{12} calcium , absorption which leads to neurologic disorders and osteoporosis. In general the studies in each of three areas have led to differing conclusions, but when examined systematically, a number of the studies are showing consistent results that support the conclusion that long-term adverse effects on these processes can have important clinical implications.

Introduction

The stomach is the main organ that secretes acidic liquid as low as pH 2. Such gastric emission is significant not just forsterilization of microorganisms contained in ingested nourishments, yet in addition for processing and adjustment of different healthy factors, for example, protein, iron, calcium, and nutrient B12. However, since secreted acid may harm the gastrointestinal tract, different kinds of defensive components, including mucosal mucous/bicarbonate discharge and sphincter contraction of the gastro oesophageal junction, are available to anticipate gastric secretion-induced gastro oesophageal damage. At the point when those defensive systems are overwhelmed by acid secretion, gastrointestinal mucosa can get damaged and irritated, resulting in side effects or even infection. Such conditions are referred to as acid related illnesses and include gastro esophageal reflux sickness (GERD), gastro duodenal ulcers, utilitarian dyspepsia, and Barrett's throat1.

For the treatment of GERD, Peptic ulcer, dyspepsia various acid secretion inhibitors and neutralizing agents are has been developed nowadays. PPI are most widely prescribed class of drugs throughout the world. Prescription of PPIs, along with OTC accounts for 13 billon dollars in global sales. As they are more effective acid suppressing agents, they are indicated for numerous conditions include short-term management of GERD, erosive esophagitis , H.pylori and duodenal and gastric ulcers2.

Some observational studies recently making questions about long term use of PPIs and they potential to cause variety of severe adverse reactions some of the ADRs are already noted in FDA approved information, now in this we are discussing about VIT-B12 and calcium deficiencywhich increased risk of neurological disorders,

anemia, osteoporosis related fractures of hip , wrist or spine [3].

Long term use of PPIs effects on vit-b12 absorption

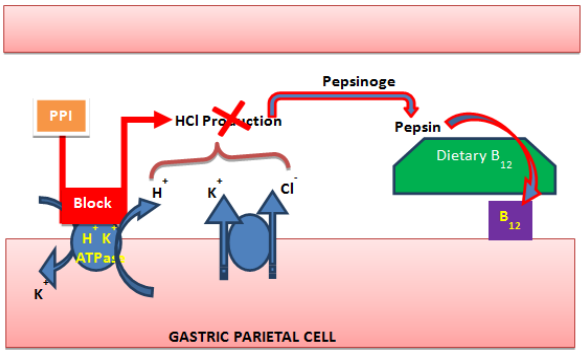

Fig 1: MOA of PPI and effect on Vit-B12 absorption

The possible mechanism behind increased risk of vitamin B12 deficiency in long term PPI users is vit B12 malabsorption [4].It is well known that gastric acid secretion is needed for absorption of vit B12 which we are taking through food is dietary 5 as shown in figure 1.

Vit B12 is essential nutrient that is present in foods is bound to proteins and it was clear that presence of gastric acid is important for pancreatic proteases to cleave vit B12 from protein,allowing its reassociation with intrinsic factor and eventual absorption in terminal ileum6. From many studies it is evident that various acid suppressants (H2 receptor antagonist, PPI) Can decrease the absorption of vit B12 from foods, but cannot decrease absorption of vitB12 from foods which is not protein bound [7].

In a recent prospective study which was conducted in year 2010 on 34 patients (17 long term PPI using and 19 patients mot using PPI) 60-80 years aged long term care patients showed lower vit B12 levels in long term PPI users at base line and a greater percentage were vitB12 deficient (75%) and effect of vitB12 nasal spray on vitB12 status [8]. In a cross sectional study it was conducted in 2008 it was evident that vitB12 levels are lowered in patient's using proton pump inhibitors (long term) when compared to H2receptor antagonist [9]. After 8weeks of vit-B12nasal spray (500mcg/once pee week) as a pre treatment, there was significant increase in serum vit-B12 levels and significant decrease of vit-B12 deficiency in the chronic PPI users 8. from some studies it was evident that oral vit-B12 supplements cannot raise vit-B12 levels [9].

VitB12 deficiency can cause neurological disorders including neuropathy, spinal cord degeneration, gait disorders leading to falls, depression and dementia. If there are diagnosed in time they can be reversible [10]. And from these first cross sectional study it was also clear that VIT-B12deficiency occurs only in pts who are aged9.

In a prospective study which was conducted on 200 adult subjects with 50 members in each group. Each group receiving different type of proton pump inhibitor .Out of 4 drugs when compared to Pantoprazole and Lansoprazole, Omeprazole and Esomeprazole are more liable to cause delay in vitamin B12 absorption [11].

Long term use of PPIs effects on calcium absorption

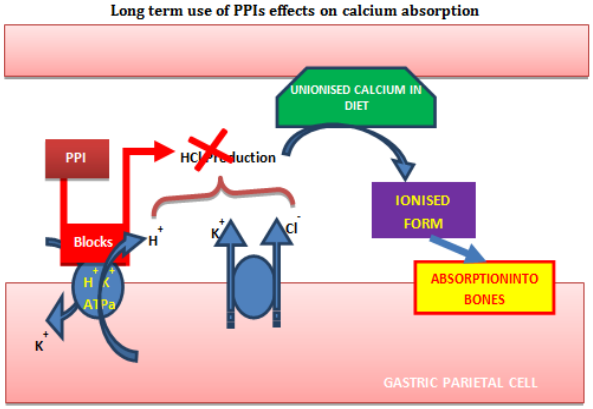

Fig 2: MOA of PPI and effect on calcium absorption

Calcium is one of the most important components that help in bone formation. About 99% of total calcium in human body is stored in bones [12]. Primary source of calcium to human body is through diet and oral supplements. Absorption of calcium from stomach into blood depends on stomach pH . If the pH of stomach is basic (too high) calcium cannot be absorbed into blood and remains in gastrointestinal tract for renal excretion i.e. through fecal matter [13]. If the pH of stomach is acidic the calcium absorption can be facilitated by release of ionized calcium from insoluble calcium salts (calcium binds with proteins) as shown in **figure2**.

As PPI increases the stomach pH, calcium cannot be absorbed into blood from stomach [14]. A study conducted by yang et.al, in 2006 reported that long-term PPI therapy at high doses is associated with increased risk of hip fractures14. A study conducted by Khalili and colleague's on 80,000 post menopausal women revealed that there was 35% increase in risk of hip fractures among women who are using PPIs regularly for a time period of two years .By this study it was evident that use of PPI therapy for longer time in women increases the risk of hip fractures [15].

Conclusion

In present days the use of PPI's was increased to a large extent. There are so many studies published on long term use of PPI's may delay in absorption of vitamin B_{12} leading to its deficiency. Due to vitamin B_{12} deficiency there is risk for development of anemias and neurological disorders. Even though, there are some studies stating the long term use of PPI's may lead to inhibition of calcium absorption, some studies does not approve this. But so far, there is no exact proof for long term use of PPI's can also cause inhibition of calcium absorption. When compared in PPI's Omeprazole and Esomeprazole are having more risk for delaying the vitaminB_{12} absorption. Due to inhibition of calcium absorption there are more chances for development of osteoarthritis. Hence, long term use of PPI's should be reduced to avoid these adverse effects.

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