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REVIEW - ON DO CHRONIC USE OF PROTON PUMP INHIBITORS EFFECT YOUR BONE HEALTH?

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Abstract:
Many medications can cause nutritional deficiencies, and proton pump inhibitors (PPIs) are no different, First is magnesium deficiency. Magnesium (Mg (2+)) is that the second most copious element within human cells and also the fourth most plentiful charged particle within the human body. It is of central importance for a broad form of physiological processes, as well as intracellular signal, neural excitability, muscular contraction, bone formation and protein activation. Several reports have linked long-term PPI use with an increased risk of hypomagnesemia, especially over a year. Results of studies suggest that PPIs inhibit active transport of magnesium in the intestine. Severe hypomagnesemia can potentially lead to serious adverse effects including arrhythmias, hypocalcemia, hypokalemia, hypoparathyroidism, muscle spasms, and seizures. Its overall balance is tightly regulated by the combined actions of the internal organ, bones and kidneys. Disturbance of this balance can have serious consequences. In distinction to prescription PPIs, over-the-counter PPIs are marketed at low doses and are solely meant for a fourteen-day course of treatment up to 3 times each year. FDA believes that there's little risk of hypomagnesemia once over-the-counter PPIs are used in step with the directions on the over-the-counter label. Healthcare professionals need to take into consideration getting humor Mg levels before initiation of prescription PPI treatment in patients expected to induce on these medications for long periods of time, as well as patients who take PPIs with medications such as digoxin, diuretics or drugs which will cause hypomagnesemia. Healthcare professionals should consider obtaining magnesium levels periodically in these patients and the Suggested dose supplementation of magnesium is 250 to 400 mg/day for hypomagnesemia.
Keywords: -hypomagnesemia,bone fracture,proton pump inhibitors

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INTRODUCTION:

First introduced in the late 1980s PPIs are the most potent inhibitors of gastric secretion available, with efficacy superior to histamine-2 receptor antagonists [1]. Proton-pump inhibitor drugs (e.g. omeprazole, esomeprazole, lansoprazole, pantoprazole and rabeprazole) are potent inhibitors of gastric acid secretion, and act by blocking the hydrogen–potassium adenosine triphosphatase enzyme system (the 'proton pump') of the gastric parietal cell. These medication generate over $13.5 billion in sales (3rd largest marketing drug class) and in 2009 over 119 million PPI prescriptions were written within the US, thus they're terribly wide used, and plenty of patients still take them for extended periods of time [7,8,9]. They are widely used for the treatment and prevention of dyspeptic symptoms associated with peptic ulcer disease, gastritis and esophagitis. Proton-pump inhibitors have become one of the most commonly prescribed class of drugs in primary and specialty care. Long-term, sometimes lifetime use is becoming increasingly common, even in the absence of appropriate indications, and there is growing concern for potential adverse effects from such long-term therapy. Furthermore, since PPIs are available over-the-counter, many patients use them without prior medical advice. Each year, an calculable 1.5 million individuals within the united states suffer an osteoporosis-related fracture, an event which will result in minimized quality of life and augmented risk of death. [14,15] Medications within the PPI category are widely offered with or while not a prescription. Currently, the U.S. market contains six PPIs, 2 of that are offered as over-the-counter product. [Table1]

Table1:Commercially available proton pump inhibitors

Drug	Dosages, mg	IV	Liquid or suspension	Generic	Over-the-counter
Omeprazole	10, 20, 40	Yes	No	Yes	Yes
Esomeprazole	20, 40	Yes	Yes	Yes	Yes
Lansoprazole	15, 30	Yes	Yes	Yes	Yes
Dexlansoprazole	30, 60	No	No	No	No
Pantoprazole	20, 40	Yes	Yes	Yes	No
Rabeprazole	20	No	No	Yes	No

Table2:Pharmacokinetic Properties of Commercially available Proton pump inhibitors.

Column1	Omeprazole	Esomeprazole	Lansoprazole	Dexlansoprazole	Pantoprazole	Rabeprazole
Bioavailability, %	30–40	64–90	80–85	-	77	52
Time to peak plasma level (tmax, hr)	0.5–3.5	1.5	1.7	1–2, 4–5	2–3	2–5
Protein binding, %	95	97	97	96	98	96.3
Half-life, hr	0.5–1	1–1.5	1.6	1–2	1–1.9	1–2
Primary excretion	Hepatic	Hepatic	Hepatic	Hepatic	Hepatic	Hepatic
Liver metabolism	CYP2C19	CYP2C19	CYP2C19	CYP2C19	CYP2C19	CYP2C19

Long-Term Use of PPIs: Effects on Magnesium Absorption/metabolism and bone fractures:

Hypomagnesemia has been reported with PPI use in fewer than 25 cases [2-5,6,7-9] . In a recent review of 10 cases [6] , the patients had been taking PPIs a mean of 8.3 years; they presented with severe symptomatic hypomagnesemia (≤ 0.54 mmol/L); and morbidity was significant (fatigue, unsteadiness, paresthesia, tetany, seizures, cardiac arrhythmias, hospitalizations). The hypomagnesemia resolved when PPI therapy was stopped and recurred if PPI therapy was re-introduced [2,3,6]. In some cases, hypomagnesemia was accompanied by hypokalemia and/or hypercalcemia. At present, the mechanism of PPI-induced hypomagnesemia is not clear. One study tested the hypothesis that it occurs in poor metabolizers of PPIs, but that was not the case. Long-term PPI use has been related to an augmented risk of osteoporosis and reduced bone mineral density (BMD), with a 35th increased risk of fractures. the most physiological modification induced by PPI medical care is profound suppression of gastric acid secretion. gastric acid suppression results in hypergastrinemia, and may cause malabsorption of metal. The hypothesis for the mechanism of PPI-induced bone fractures is that dietary magnesium absorption relies upon acidic surroundings within the gastrointestinal (GI) tract. The study investigators concluded that hypomagnesemia is not specific to a given PPI, but is a generic problem with the PPI class of drugs, because it recurs even when PPIs are changed from one to the other [7] . It was proposed that PPI-induced hypomagnesemia is likely caused by gastrointestinal magnesium loss, although this is unproven at present [3,6,7]. The large, case-control studies by Yang et al. [10] and Vestergaard et al. [15] led to considerable interest in the possibility that chronic PPI use could lead to an increase in bone fractures, and resulted in speculation about the possible mechanisms. These studies and others reviewed below aroused sufficient attention that in May 2010, the US Food and Drug Administration (FDA) issued a warning of the "possible increased risk of fractures of the hip, wrist, and spine with high doses or long use of a category of medicines known as proton pump inhibitors. The product labeling are going to be modified to explain this potential enhanced risk" (US FDA News unleash, May 25, 2010).

CONCLUSION:

The data reviewed here support the importance of long-term investigations of the possible effects of chronic PPI treatment on absorption of magnesium. In general, the studies in this area have led to differing conclusions, but when examined systematically, several studies show consistent results supporting the conclusion that long-term adverse effects on these processes can have important clinical implications. In addition to studies of bone fractures, more prospective studies are urgently needed for magnesium. Furthermore, whereas the clinical implications in many cases are much better defined, in almost all cases, the mechanisms of the observed clinical effects are unclear. Therefore, detailed, careful studies of the long-term effects of PPIs on the absorption of magnesium and studies of PPI mechanism for inducing clinical problems potentially related to these processes (fractures, cardiac abnormalities, hypomagnesemia) are critically needed.

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Justification

Various studies stated that there is a link between bone health and long-term usage of proton pump inhibitors but there is no perspicuity. So, the study was done to review the revealed evidence relating to these potential links and discuss their clinical implications.

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