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This is the author's manuscript

Original Citation:

Availability:

This version is available <http://hdl.handle.net/2318/155134> since 2018-10-16T12:07:15Z

Published version:

DOI:10.1111/jgs.13212

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This is the author's final version of the contribution published as:

Pastorino A; Greppi F; Bergamo D; Versino E; Bo M; Pezzilli MS; Furno E; Rrodhe S; Isaia G. Proton pump inhibitors and hypomagnesemia in polymorbid elderly adults. JOURNAL OF THE AMERICAN GERIATRICS SOCIETY. 63 (1) pp: 179-180.
DOI: 10.1111/jgs.13212

The publisher's version is available at:

<http://doi.wiley.com/10.1111/jgs.13212>

When citing, please refer to the published version.

Link to this full text:

<http://hdl.handle.net/2318/155134>

Proton Pump Inhibitors and Hypomagnesemia in Polymorbid Elderly Adults

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To the Editor: The use of proton pump inhibitors (PPIs) has risen in the last decade, but according to several studies, their prescription is inappropriate in 40% to 80% of individuals [1, 2]. Although PPIs are safe, they can cause adverse drug effects such as nausea, abdominal pain, constipation, and diarrhea. In March 2011, the Food and Drug Administration stated that PPIs may cause low serum magnesium levels if taken for prolonged periods of time and that healthcare professionals should consider obtaining serum magnesium levels before initiation of PPI treatment in individuals expected to be taking these drugs for long periods of time [3]. Nevertheless, no conclusive evidence has been found on the association between long-term therapy with PPIs and hypomagnesemia [4, 5]. The main aim of the current study was to assess the prevalence of hypomagnesemia in a hospitalized elderly population. Secondary aims were to find whether there is a relationship between hypomagnesemia and long-term PPI therapy.

Participants were individuals aged 65 and older consecutively admitted to a geriatric unit (N = 260). Exclusion criteria were diagnosis of acute pathology of the gastrointestinal tract and presence of severe dysphagia. Written informed consent was obtained from all participants. Information was gathered about socioeconomic status, clinical and drug history, comorbidities, functional assessment, cognitive status, and blood tests at baseline. Hypomagnesemia is defined as levels lower than 1.7 mg/dL (0.70 mmol/L).

The mean age of participants was 82.2 ± 69.8 , and 56.2% were women. Fifty-nine (22.7%) were dependent in all six activities of daily living. The Short Portable Mental Status Questionnaire indicated severe intellectual impairment in 32.3% (n = 84) of participants. The mean Cumulative Illness Rating Scale (CIRS) severity index was 1.69 ± 0.29 , and the mean CIRS comorbidity index was 3.07 ± 1.51 . The most-frequent comorbidities detected were diabetes mellitus (27.7%, n = 72) and heart failure (23.1%, n = 60).

The prevalence of hypomagnesemia in this study was 16.5% (95% confidence interval = 12.2–21.6%, n = 43). In participants who had been using PPIs for at least 6 months (n = 146), the prevalence of hypomagnesemia was slightly higher (19.9%, n = 29), but this difference was not statistically significant ($P = .10$). Serum magnesium levels were not correlated with long-term therapy with PPIs ($P = .25$) or with age, sex, comorbidities (CIRS-s), potassium and magnesium supplementation, serum potassium, serum creatinine, or use of diuretics. Conversely, magnesemia was associated with serum albumin ($P = .001$). PPI users had greater CIRS-c (3.34, vs 2.72 in PPI nonusers; $P < .001$) and CIRS-s (1.75, vs 1.61 in PPI nonusers; $P < .001$). No difference was detected between the two groups in serum magnesium level ($P = .20$). The majority of participants with hypomagnesemia (n = 43) were women (67.4%, vs 32.6% of men; $P = .10$). The prevalence of PPI use was higher (67.4%, n = 29) in these patients than in the total population, although the difference was not statistically significant. Use of diuretics did not have any effect on the association between long-term therapy with PPI and hypomagnesemia ($P = .39$). No association was found between serum magnesium levels and diabetes mellitus ($P = .13$) or heart failure ($P = .82$).

Study participants had severe functional impairment, which is not surprising because participants were hospitalized elderly adults, who are at risk of functional decline before [6] and during hospitalization [7]. Among other factors, low albumin level and large number of drugs prescribed are associated with functional decline [7]. The observed prevalence of hypomagnesemia in hospitalized elderly adults was similar to what has been found in previous studies [8, 9]. This study suggests that many factors affect serum magnesium levels, although only serum albumin levels were significantly associated with hypomagnesemia.

Long-term PPI users had serum magnesium levels (1.95 mg/dL) similar to those of PPI nonusers (2.00 mg/dL; $P = .20$). A large percentage of elderly adults have been prescribed PPIs [10]. Because PPIs, even though generally considered to be safe, have some adverse effects, their prescription must always be motivated by and based on scientific evidence. A large prevalence of hypomagnesemia in hospitalized older adults was found, and there is not a statistically significant relationship between PPI and hypomagnesemia. Future randomized prospective studies performed on a larger number of individuals analyzing serum magnesium levels before and after PPI therapy could add more knowledge to this topic. Hypomagnesemia cannot be considered a contraindication to the initiation of long-term PPI therapy.

Author Contributions: Pastorino, Greppi, Bergamo: preparation of manuscript, acquisition of subjects and data. Versino: analysis and interpretation of data. Bo: study concept and design. Pezzilli, Furno, Rrodhe: acquisition of subjects and data. Isaia: study concept and design, preparation of manuscript.

Sponsor's Role: None.

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