Inappropriate proton pump inhibitor prescription in elderly adults: as usual as dangerous.

INAPPROPRIATE PPI PRESCRIPTION IN ELDERLY PATIENTS: AS USUAL AS DANGEROUS

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To the Editor: Physiological and physiopathological changes of elderly people lead to differences in the pharmacokinetics and pharmacodynamics of medications; given these alterations and since they often use many drugs at the same time, this results in higher risk of adverse drug effects and inappropriate prescriptions. The appropriateness of prescriptions is a considerable issue, both clinically and economically. The frequency of inappropriate medication prescription has been reported as higher than 30% in an in-hospital previous study[1]. In general the frequency varies between 14,7% and 56,1%[2,3].

In the last decade the use of Proton Pump Inhibitors (PPI) has risen-up, but according to several studies the prescription is inappropriate in 40-80% of patients[4].

Although PPIs are safe drugs, they can cause adverse drug effects[5,6].

Given all these assumptions, it is evident that the inappropriate prescription represents a relevant problem particularly in older patients.

The main aim of the present study was to assess the prevalence of hypomagnesemia, a controversial adverse effect of a long term PPI therapy, in a hospitalized elderly population (results reported in a previously published paper[7]). Secondary aim was to evaluate, during the first clinical evaluation at hospital admission, whether the home PPI prescription was appropriate or not among patients aged over 65. We considered a PPI appropriate prescription whether if the patient took PPI daily and had at least one indication according to the Italian drugs agency (AIFA) notes or if the patient didn't took any PPI not having any indication. AIFA notes, following the American College of Gastroenterology guidelines, consider a PPI therapy appropriate whether if the patient is on chronic NSAID treatment, or on antiplatelet treatment with low-dose aspirin having at least one of the following risk factors (advanced age, concomitant use of anticoagulants or corticosteroids, history of gastrointestinal bleeding or peptic ulcer not healed with eradication therapy), or if the patient suffer from H. pylori induced duodenal or gastric ulcer, duodenal or gastric ulcer not H. pylori induced, GERD

with or without esophagitis, Zollinger-Ellison syndrome, relapsing duodenal or gastric ulcer H. pylori not induced, or relapsing GERD with or without esophagitis, or if the patient is on H. pylori eradication therapy.

Exclusion criteria were the diagnosis of acute pathology of the gastrointestinal tract and the presence of severe dysphagia.

Two hundred sixty patients have been enrolled. Mean age was 82,2 years (± 6,98), and 56,2% of patients were women. Patients recruited were mildly compromised, both in terms of functional assessment and comorbidities (characteristics of the study population were already shown in a previously published letter to the editor[7]). More than half of the total enrolled population (56,2%; n=146) used a daily PPI therapy. Of them, 34,9% (n=51) were inappropriate prescription. According to the AIFA notes, 32,3% (n=84) of the total population (260 patients) had a wrong long-term PPI prescription: in 60,7% (n=51) PPIs were prescribed without indications while in 39,3% (n=33) PPIs were not prescribed even though patients had at least one indication. PPI users had greater CIRS-c (3,34 vs 2,72; P <.001) and CIRS-s (1,75 vs 1,6; P <.001) than PPI non users. No association was observed between the inappropriate PPI prescription and both the living condition and the CIRS comorbidity index.

Currently PPI prescription concerns a high percentage of elderly population. Since PPIs, even though generally considered safe drugs, have some adverse effects, their prescription must always be motivated and based on the major available scientific evidence. Nevertheless this study confirms that PPIs are frequently prescribed without an appropriate indication, but we observed a trend in overprescription instead of underprescription.

We tried to outline the characteristics of patients at higher risk of inappropriate PPI prescription. Age does not affect PPI appropriateness; indeed we observed similar percentage of PPI inappropriateness in different age groups. Similar results were shown by Jarchow-MacDonald et al[8].

Even CIRS comorbidity index was not associated in our study with inappropriate PPI prescription. This is in contrast with what observed by Jarchow-MacDonald[8], who found a statistically significant association between these two factors.

We instead observed an increasing trend in wrong PPI prescription as the number of daily taken drugs increases. No statistical significance was achieved, but we cannot exclude that a larger study could validate this[8].

In conclusion, the chronic use of PPIs seems to have a high margin of safety, but doubts have been raised about possible risks associated with their long-term use. The high prevalence of inappropriate PPI prescription must induce greater prescriptive attention, in order to protect patients from unnecessary adverse drug effects and to cut health-care costs.

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Conflict of Interest disclosure

Elements of Financial/Personal Conflicts	Daniele Bergamo		Alessandra Pastorino		Francesca Greppi		Elisabetta Versino		
	Yes	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	
Employment or Affiliation		X		X		X		X	
Grants/Funds		X		X		X		X	
Honoraria		X		X		X		X	
Speaker Forum		X		X		X		X	
Consultant		X		X		X		X	
Stocks		X		X		X		X	
Royalties		X		X		X		X	
Expert Testimony		X		X		X		X	
Board Member		X		X		X		X	
Patents		X		X		X		X	
Personal Relationship		X		X		X		X	

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	Yes	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**
Employment or Affiliation		X		X		X		X		X

Grants/Funds		X		X		X		X		X
Honoraria		X		X		X		X		X
Speaker Forum		X		X		X		X		X
Consultant		X		X		X		X		X
Stocks		X		X		X		X		X
Royalties		X		X		X		X		X
Expert Testimony		X		X		X		X		X
Board Member		X		X		X		X		X
Patents		X		X		X		X		X
Personal Relationship		X		X		X		X		X

Author Contributions:

Bergamo, Furno: preparation of manuscript, acquisition of subjects and data. Versino: analysis and interpretation of data. Bo, D'Amelio: study concept and design. Pezzilli, Pastorino, Greppi: acquisition of subjects and data. Isaia: study concept and design, preparation of manuscript.

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TABLES

Table 1. Characteristics of the Study Population

Variables	Appropriate PPI prescription - AIFA notes 1 and 48	Inappropriate PPI prescription - AIFA notes 1 and 48	P-value
Age			
65-74 years (n=38)	65,8% (n=25)	34,2% (n=13)	
75-84 years (n=123)	67,5% (n=83)	35,5% (n=40)	0,9464
85+ years (n=99)	68,7% (n=68)	31,3% (n=31)	
Living condition			
At home alone (n=61)	75,4% (n=46)	24,6% (n=15)	
At home with other people (n=176)	65,9% (n=116)	34,1% (n=60)	0,3002
Nursing home (n=23)	60,9% (n=14)	39,1% (n=9)	
CIRS (com)			
0 comorbidity (n=2)	100,0% (n=2)	0,0% (n=0)	
1-3 comorbidities (n=162)	69,1% (n=112)	30,9% (n=50)	0,6907
4-5 comorbidities (n=82)	63,4% (n=52)	36,6% (n=30)	
6-8 comorbidities (n=14)	71,4% (n=10)	28,6% (n=4)	

Number of daily taken drugs			
0-3 drugs (n=62)	77,4% (n=48)	22,6% (n=14)	
4-7 drugs (n=118)	67,8% (n=80)	32,2% (n=38)	0,1699
8-10 drugs (n=57)	61,4% (n=35)	38,6% (n=22)	
11+ drugs (n=23)	56,5% (n=13)	43,5% (n=10)	