Consumption of PPI Drugs in Primary Health Care in Albania During 2010-2020

Laerta Kakariqi

Department of Biomedical and Experimental, Section of Pharmacology, Faculty of Medicine, University of Medicine in Tirana, Tirana, Albania

Abstract

The aim of the study was to estimate the out-of hospital Proton-pump inhibitors use in Albania (national level) during 2010-2020. All data were collected from Health Insurance Institute (HII) and analyzed reflecting the ambulatory and outpatient use for the period 2010-2020. The data about the consumption of drugs were expressed as a number of Defined Daily Dose (DDDs) /1000 inhabitants/day. For all the period under study 2010-2020, there were collected and analyzed data of import and domestic production of drugs, which represent the real consumption of drugs in the country. These data were subsequently included in a comparative analysis with the utilization data according to the Health Insurance Institute. Furthermore, it becomes visible the poor coverage by the scheme of the necessary alternative cures of the ulcerous disease. The reimbursement scheme offers only omeprazole. However, the consumption of omeprazole under the scheme is in much lower levels compared to the real data of omeprazole consumption coming from import figures, which shows its excessive utilization without medical prescription.

Keywords: Drug utilization, DDD/1000 inhabitants/day, PPI drugs

Introduction

Proton pump inhibitors (PPIs) are essentially H^+-K^+-ATPase inhibitors suppressing gastric acid secretion. These drugs tend to be used for the management of acid-related diseases, such as peptic ulcer disease (PUD), gastro-esophageal reflux disease (GORD), gastrointestinal (GI) bleeding and *Helicobacter pylori* infection, or the prevention of gastric ulcers in patients who are taking non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids (GCs), antiplatelet and anticoagulants.(1)

PPIs are one of the most commonly prescribed drug class worldwide, and off-label use is widespread (2).

The currently marketed main PPIs include omeprazole, esomeprazole, lansoprazole, pantoprazole and rabeprazole. PPI usage has dramatically increased since the

introduction in the late 1980s. Nowadays, they have become one of the most commonly prescribed and used drugs in the world(3). For instance, in the UK, nearly 59 million PPIs were dispensed annually, and the total usage doubled since 2007.(4) In one of the largest teaching hospitals in the southwest of China, an appreciable increase in PPI utilization was observed rising about 10.4-fold between 2004 and 2013.(5) Meanwhile, urgent concern about the overutilization of PPIs has been growing. It has been estimated that between 25% and 70% of the PPI prescriptions in the USA have no appropriate indication (3 6)

These facts alert the increasing worries regarding the cost and also safety, especially for long-term use.

I. Materials and Methods

The data were obtained from the Health Insurance Institute (HII) (7). All data were collected and analyzed reflecting the ambulatory and outpatient use for the period 2010-2020. The analysis included the total number of prescriptions, and quantities of drugs. The data about the population were obtained from the Institute of Statistics (INSTAT)(8). The data about the consumption of drugs were expressed as a number of Defined Daily Dose (DDDs)/1000inhabitants/day. All drugs were classified by groups of Anatomic Therapeutic Chemical Classification (ATC).

Data on real consumption (import and domestic production)

For all the period under study 2010-2020 there were collected and analyzed data from the import and domestic production of the drugs,(9) which represent the real consumption of drugs in the country. It was noted that the increase in consumption from one year to another were small, e.g. the consumption from 2018 to 2020 (i.e. 3 years) was increased by only 2.58%. Consequently, in order to obtain an updated study, there were chosen the data of import and domestic consumption only for the last three years, 2018, 2019,2020, and those were involved in a comparative analysis with the equivalent consumption data according to HII. In order to minimize the effect of variations consumption-inventory balances from one year to another, it was calculated and put to analysis the annual average value of the three chosen years (on one hand that of the import and domestic consumption, and on the other hand that of HII).

II. Results

The only proton pomp inhibitor included in the reimbursement list during these years is omeprasol. The other PPI registered in our country are esomeprazole, lansoprazole, pantoprazole and rabeprazole. But their consumption flows out of the reimbursement system.

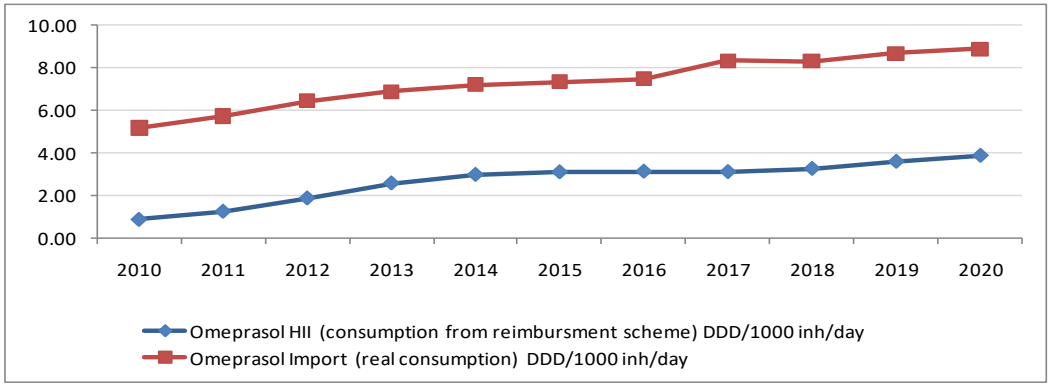

Figure 1 Annual average value of consumption of Omeprazole: consumption based on import (real consumption) [*] versus consumption based on HII.

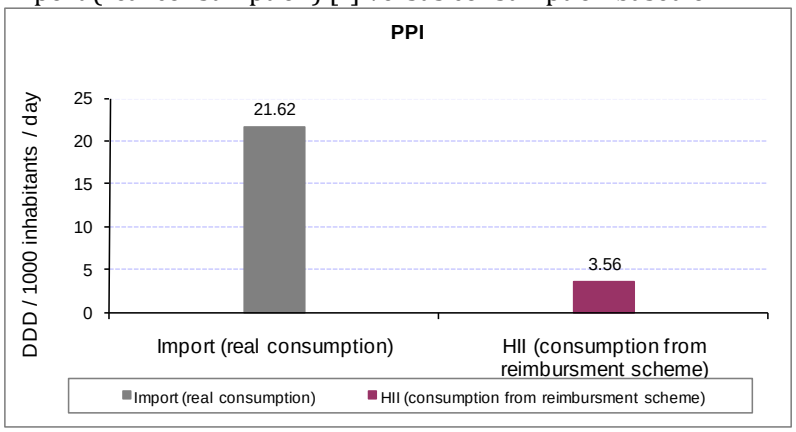

Figure 2 Annual average value of consumption of Proton-pump inhibitors class: consumption based on import (real consumption) [*] versus consumption based on HII.

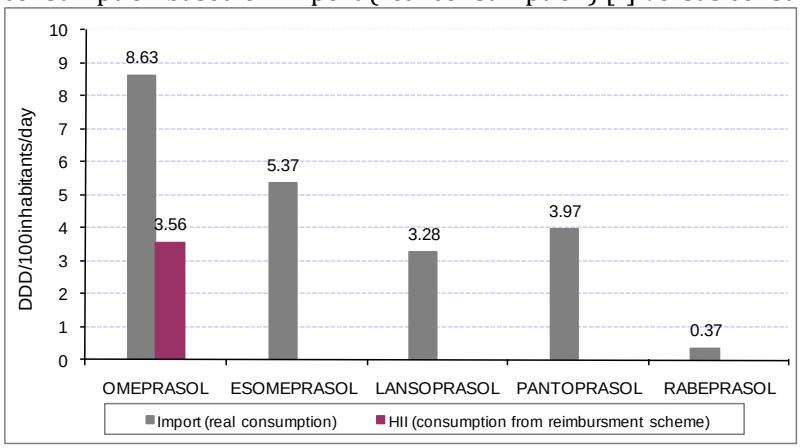

Figure 3 Annual average value of consumption of each Proton-pump inhibitor: consumption based on import (real consumption) [*] versus consumption based on HII.

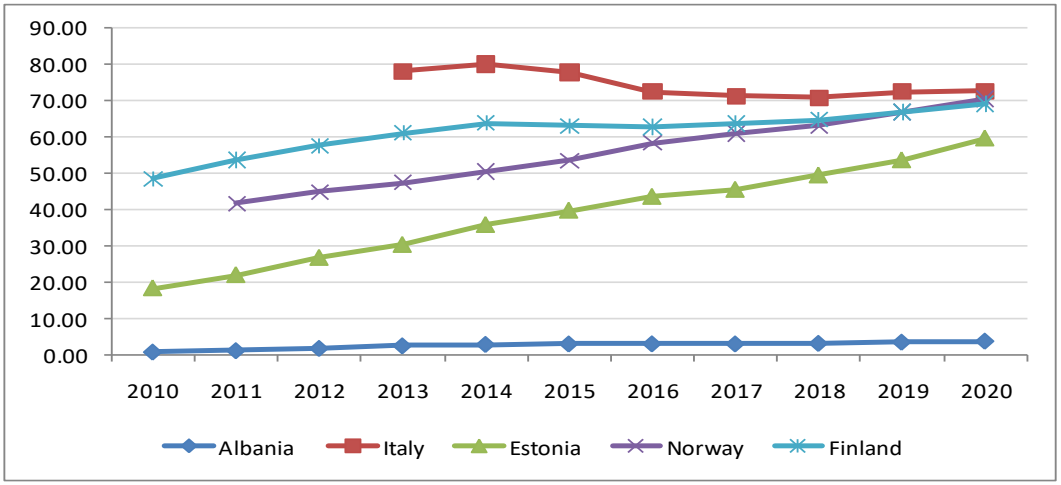

Figure 4 International comparison in the consumption of Proton-pump inhibitors drugs class (DDD/1000 inhabitants/day): Albania, Italy [10], Estonia [11], Norway [12-15], Finland [16-19]

III. Discussion

Due to their efficacy and tolerability, utilization of proton pump inhibitors (PPI) has significantly increased worldwide. Parallel to the clinical benefits, potential long-term side effects have been observed.

Figures 2 and 3 put emphasis on the poor coverage by the scheme of the necessary alternatives in the cure of peptic morbidity. The reimbursements scheme offers only omeprazole. Another issue which can be raised by analyzing these graphics is why the consumption of omeprazole under the scheme is such in lower values compared to the real consumption of omeprazole. This indicates that even this alternative, although covered by the scheme, is actually taken in large scale without prescription.

According to HII, omeprazole is reimbursed only for ulcerous disease and gastroesophageal reflux disease certified through endoscopic examination and the duration of the treatment is 4-6 weeks. After 4-6 weeks, the patient should reperform the endoscopy in order for the family doctor to have the right to repeat the prescription. It is comprehensible that in a similar situation, the patient is almost conditioned to obtain the drug directly in the pharmacy by avoiding the consultation with the family doctor.

In previous studies performed some years earlier (20), a common finding was that there is consumed a lot more ranitidine rather than omeprazole, while from the pharmacological perspective, PPI are superior compared to antiH2 in the cure of ulcerous morbidity (21). Beginning from 2008 and onwarts, there can be noted a shift in consumption, with decrease antiH2 receptors drugs and an increase of PPI, which

is reasonable considering that PPI have the highest efficacy in the reduction of gastric hyperacidity.

Omeprazole was the most widely used, at around 75%, although the rate should approach 100% as it is the first choice agent based on specific recommendations (22). In spite of this, pantoprazole is reported as the most widely used PPI in other countries such as the US (23). The most frequent indication for PPI use was GERD followed by NSAID ulcer prophylaxis which is in contrast to other studies in which the predominant indication for PPI use was NSAID ulcer prophylaxis (24-26).

PPIs are, in most cases, safe and well tolerated (a factor that explains their widespread usage) but they are not harmless. Mild reactions such as headaches, nausea or abdominal pain have been reported, as well as some other less frequent but more serious events such as an increase in infections (pneumonia, C. difficile diarrhea), acid reflux, increased bone fracture risk, hypomagnesemia and acute interstitial nephritis.

Measures should be taken in order to achieve a better PPI use, such as improving the distribution of therapeutic recommendation guidelines. Studies have demonstrated its association with an improvement in the appropriateness of PPI prescription, paired with a decrease in interactions and adverse effects and a reduction in pharmaceutical spending (27, 28).

International Comparison of Consumption

As shown in Figure 4, the consumption of PPI drugs in Albania, as compared to other countries, is very low (consumption values presented for all countries, including Albania, are the official values as referred by the respective reimbursement systems).

In France, studies performed (29) suggest PPI overuse, not always in line with the French guidelines. In particular, inappropriate co-prescription with NSAID was frequent.(29)

The same results outcome from another similar study conducted in China (30)

In Hungary the prevalence of proton pump inhibitor use was between from 41.9 to 50.4 DDD per 1,000 inhabitants and per day between 2014 and 2018. Pantoprazole was the most frequently used active ingredient, both in the nationwide data and in the patient-level surveys.(31)

In Hungary (as in Denmark), pantoprazole was the most frequently prescribed and dispensed PPI, while in Iceland, omeprazole and esomeprazole were the most frequently used PPIs (32;33). The dominance of pantoprazole in Hungary can be explained by the high number of generic products and their consequent lower price compared to other PPI agents.

In another study conducted in Spain, in a district of Basque health service, PPI prescription increased by 23.75% (from 78.14 DHD in 2009 to 96.70 DHD in 2014). Their use was much higher than that of other European countries. In the same period,

omeprazole relative prescription compared to other PPIs decreased by 4.56% (omeprazole % Defined daily dose (DDD) went from 74.67% in 2009 to 70.11% in 2014).(34**)**

IV. Conclusions

The consumption values of PPI drugs in Albania are comparatively low. An important part of the PPI drugs flows out from the reimbursement scheme. A comparative analysis in the consumption of PPI between Albania and other countries suggested also important differences in the overall consumption values. We need to perform further studies in the future to get deeper information about this topic.

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