

## Sociodemographic and clinical profile of elderly people chronic users of omeprazole attending the basic health network

Perfil sociodemográfico e clínico de idosos usuários crônicos de omeprazol na rede básica de saúde

Perfil sociodemográfico y clínico de los ancianos usuarios crônicos de omeprazol em la red básica de salud

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### ABSTRACT

**Objective:** The study's purpose has been to describe the sociodemographic and clinical profile of elderly chronic omeprazole users. **Methods:** This is a cross-sectional study. The participants were patients within the age group over 60 years old, who used omeprazole from the Public Pharmacy located in *Panambi city, Rio Grande do Sul State*. **Results:** A total of 60 elderly chronic omeprazole users participated in the study with an average of  $67.90 \pm 5.6$  years old. Two serious drug interactions were identified involving citalopram and clopidogrel. It was found in some prescriptions the presence of drugs that have their absorption altered by concomitant use of omeprazole, such as captopril (25%) and enalapril (16.7%). **Conclusion:** Based on the findings, it is possible to highlight that this particular population is susceptible to risks that needs pharmaceutical follow-up.

**Descriptors:** Antiulcer, elderly, omeprazole.

### RESUMO

**Objetivo:** Descrever o perfil sociodemográfico e clínico de idosos usuários crônicos de omeprazol. **Método:** Trata-se de um estudo transversal com usuários com idade superior a 60 anos, que retiraram o omeprazol na Farmácia Pública de Panambi/RS. **Resultados:** Participaram da pesquisa sessenta idosos, com idade média de  $67,90 \pm 5,6$  anos. Duas interações graves foram identificadas envolvendo citalopram e clopidogrel. Observou-se a presença nas prescrições de medicamentos que tem a sua absorção alterada pelo uso concomitante com o omeprazol como captopril (25%) e enalapril (16,7%). **Conclusão:** Dessa forma, evidenciou-se uma população suscetível a riscos que necessita de acompanhamento farmacêutico.

**Descritores:** Antiulcerosos, Idosos, Omeprazol

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## RESUMÉN

**Objetivo:** Describir el perfil sociodemográfico y clínico de los ancianos usuarios crónicos de omeprazol. **Método:** Es un estudio transversal descriptivo cuantitativo. Participaron en el estudio pacientes con edad igual o mayor de 60 años, usuarios crónicos de omeprazol, y que acudieron al medicamento en la Farmacia Pública de la ciudad de Panambi/RS.

**Resultados:** Participaron de la investigación 60 ancianos 51,7% del sexo femenino, con edad media de 67,90 ±5,6 años, 81,7% relataron alguna comorbilidad, siendo la más prevalente la hipertensión arterial sistémica (61,7%). Los medicamentos que actúan en el tracto alimentar y metabólico fueron los más frecuentes. Se identificaron dos graves interacciones relacionado al citalopram (8,4%) y clopidogrel (1,7%). Se observó en las prescripciones la presencia de medicamentos cuya absorción es alterada por el uso concomitante con el omeprazol, como el captopril (25%) y enalapril (16,7%). **Conclusión:** De esta forma, se ha evidenciado una población susceptible a los riesgos y que necesita de acompañamiento farmacéutico.

**Descriptor:** Antiulceroso, Anciano, Omeprazol.

## INTRODUCTION

The increase in the elderly population in Brazil is bringing increasing challenges to health services and professionals,<sup>1</sup> evidencing the need for changes in the model of health care in the country.<sup>2</sup> Population aging causes a greater demand for health services and, consequently, by drug therapy, increasing the occurrence of polypharmacy, which may be associated with the indiscriminate use of medications, and contribute to drug interactions, compromising treatment efficacy and patient safety.<sup>3</sup>

Antiulcer medications are often used among elderly people, and a Saatkamp<sup>4</sup> study highlighted the omeprazole use. This substance is a Proton-Pump Inhibitor (PPI) that suppresses gastric acid secretion by specific inhibition of the H<sup>+</sup>/K<sup>+</sup>-ATPase enzyme on the secretory surface of the gastric parietal cell and its metabolism mainly occurs via the CYP2C19 isoform of the hepatic P450. This drug is indicated for the treatment of peptic ulcer, reflux esophagitis and as a component of therapy in *Helicobacter pylori* infection.<sup>5</sup>

Omeprazole was the fourth medication most used by elderly people attending the public health network in Santa Rosa city, Rio Grande do Sul (RS) State, over 2006.<sup>6</sup> Another study found that the drug was among the five most marketed in the popular pharmacy located in Ijuí city/RS.<sup>7</sup>

The use of omeprazole is safe when according to the medical recommendation, however, prolonged treatment may lead to loss of gastric acidity, which may decrease the absorption of vitamin B<sub>12</sub>, as well as affect the bioavailability of some drugs. This medicinal product, when administered, decreases up to 95% the production of acid in the stomach, increasing the pH of the medium<sup>5</sup> and the decrease in acidity may impair the absorption of other medicinal products in concomitant use.

According to the National Therapeutic Form (NTF), omeprazole interacts with benzodiazepine medications, carbamazepine, digoxin, methotrexate increasing the risk of toxicity; and also with *Hypericum perforatum* and

*Ginkgo biloba* decreasing the efficacy of omeprazole, and with warfarin increasing the drug anticoagulant effect.<sup>8</sup> Furthermore, one study found that omeprazole, when administered, is able to significantly decrease bone mineral density once that some salts, such as calcium, are insoluble at basic pH and therefore less absorbable.<sup>9</sup> Another study suggests that the use of omeprazole tends to decrease bone resorption and prevent progression to osteopenia, so prolonged use of this drug may be related to bone demineralization and the risk of fractures.<sup>10</sup>

As a result, the American Society of Geriatrics updated Beers' criteria, which identified potentially inappropriate medications for elderly use. In the new list of drugs, PPIs are included as potentially inappropriate for elderly people due to the risk of bone loss, fractures, and infection by *Clostridium difficile*.<sup>11</sup> Up to now, no studies have been conducted addressing the Beers issue regarding the use of omeprazole by elderly people.

Given the aforementioned, the study's goal was to describe the sociodemographic and clinical profile of elderly chronic omeprazole users.

## METHODS

It is a cross-sectional and descriptive study with a quantitative approach. The participants were patients within the age group over 60 years old, who used omeprazole from the Public Pharmacy located in Panambi city, Rio Grande do Sul State, and over the period from June to August 2016. The sample was of the intentional type, and omeprazole users were identified through the prescriptions containing the study drug at the time it was dispensed at the Public Pharmacy. The interviewees were invited to spontaneously participate in the research and to sign the Free and Informed Consent Term.

The study inclusion criteria were as follows: being aged over 60 years old; continued use of omeprazole for at least six months; being able to understand, verbalize and respond to questions; and agree to participate in the survey.

The data were evaluated through simple descriptive analysis with mean and standard deviation, with the aid of Statistical Package for Social Science (SPSS) software version 20.0. The pharmacological classification of the drugs was performed according to the Anatomical Therapeutic Chemical (ATC)<sup>12</sup> from the WHO Collaborating Center for Drug Statistics Methodology. Specific drug interactions were analyzed in the *Micromedex* database.<sup>13</sup> Moreover, the pKa value search was performed through the Drug Information System,<sup>14</sup> Drugbank.<sup>15</sup>

This study was approved by the Research Ethics Committee from the Universidade Regional do Noroeste do Estado do Rio Grande do Sul (UNIJUI), under the Legal Opinion No. 1.587.720, and Certificado de Apresentação para Apreciação Ética (CAAE) [Certificate of Presentation for Ethical Appreciation] No. 55931116.2.0000.5350.

## RESULTS

The sample consisted of 60 chronic omeprazole users, of whom 51.7% were female. The age ranged from 60 to 82 years old, with an average of  $67.90 \pm 5.6$  years old (Table 1).

**Table 1** - Sociodemographic data of the elderly patients under chronic use of omeprazole from the public system in Panambi city, Rio Grande do Sul State. n=60. 2016.

Description	n	%
<b>Gender</b>		
Female	31	51.7
Male	29	48.3
<b>Age</b>		
60 to 70 years old	43	71.7
71 to 80 years old	14	23.3
More than 80 years old	3	5
<b>Ethnicity</b>		
White	57	95
Brown/Black	3	5
<b>Schooling</b>		
Elementary school	57	95
High school	3	5
<b>Marital status</b>		
Married/companion	45	75
Divorced	8	13.3
Widowed	5	8.3
Single	2	3.3
<b>Profession</b>		
Retired	42	70
Housekeeper	11	18.3
Farmer	6	10
Driver	1	1.7
<b>With whom do you live</b>		
Companion/family members	50	83.3
Alone	10	16.7

Considering the interviewees, the majority were white (95%) and with elementary school education (95%). The most frequent marital situation was married/companion (75%), followed by divorced (13.3%). The majority of respondents reported being retired (70%) and living with relatives (83.3%) according to Table 1.

Pondering about the chronic omeprazole users interviewed, 81.7% reported some comorbidities, the most prevalent being Systemic Arterial Hypertension (SAH) (61.7%), followed by dyslipidemia according to Table 2.

**Table 2** - Clinical data of the elderly patients under chronic use of omeprazole from the public system in Panambi city, Rio Grande do Sul State. n=60. 2016.

Description	n	%
<b>Do you have any comorbidity?</b>		
Yes	49	81.7
No	11	18.3
<b>Concomitant diseases</b>		
Systemic Arterial Hypertension	37	61.7
Dyslipidemia	24	40

Description	n	%
Type 2 Diabetes Mellitus	19	31.7
Cardiopathy	12	20
Hepatopathy	2	3.3
<b>Using purpose (self-reported)</b>		
Gastritis	22	36.6
Heartburn	21	35
Reflux esophagitis	16	26.7
Stomach ulcer	1	1.7
<b>Do you have dyspeptic symptoms?</b>		
Yes	32	53.3
No	26	43.3
Did not answer	2	3.4
<b>Omeprazole daily dose</b>		
20 mg	51	85
40 mg	9	15
<b>For how long have you been taking omeprazole?</b>		
1 to 5 years	30	50
6 to 10 years	22	36.7
More than 10 years	5	8.3
Less than 1 year	3	5
<b>When do you take omeprazole?</b>		
Morning	52	86.7
Night	2	3.3
Did not answer	6	10
<b>Did you feel any side effect during the omeprazole use?</b>		
No	58	96.7
Yes	2	3.3

For all the interviewees of this study, the physician indicated the use of omeprazole and the most commonly reported purposes were gastritis (36.6%), heartburn (35%) and reflux oesophagitis (26.7%), and a large part of omeprazole users reported dyspeptic symptoms (53.3%) and none reported *Helicobacter pylori* infection.

The daily dose of 20 mg was the most evidenced among the respondents, corresponding to 85% of these. Half of the interviewees used omeprazole for less than five years, and five patients have been using it for more than 10 years, as seen in Table 2. Considering those interviewed, nine (15%) use calcium concurrently with omeprazole. Furthermore, the most cited interviewee was the morning, corresponding to 86.7% (Table 2).

When asked about the side effects related to omeprazole, 96.7% answered that they did not feel any alteration with the use of this medication, only two (3.3%) interviewed reported headaches, 18.3% of patients used other medications for the stomach, and of these, 11.7% reported using *Olina*<sup>\*</sup> and 6.6% *Leite de Magnésia*<sup>\*</sup>.

The majority (51.7%) reported using the drug every day and 48.3% reported forgetting a few times during the week. When questioned about what they do when they forget to administer the medicine, 33.3% say they no longer use that day and 15% administer at the time they remember. When the drug is missing in the public network, 40% of respondents reported purchasing at commercial pharmacies (Table 2).

Of the chronic users of omeprazole, 30% use 5 or more medications concomitantly. And only one claimed to use this drug for the purpose of protecting the gastric tract.

According to **Table 3**, most elderly chronic users of omeprazole take drugs that act on the gastrointestinal tract and metabolism, followed by the cardiovascular system. Simvastatin (40%) and captopril (25%) were the most commonly used drugs in the study participants.

**Table 3** - Medications sorted according to the Anatomical Therapeutic Chemical (ATC) in first level and being taken by patients under chronic use of omeprazole from the public system in *Panambi city, Rio Grande do Sul State*. n=60. 2016.

Medicines	n	%
<b>Gastrointestinal tract and metabolism (A)</b>	<b>101</b>	<b>45.09</b>
Omeprazole	60	100
Metformin	14	23.3
Acetylsalicylic acid	9	15
Calcium carbonate	9	15
Glibenclamide	5	8.3
Others	4	6.7
<b>Blood and hematopoietic organs (B)</b>	<b>1</b>	<b>0.44</b>
Clopidogrel	1	1.6
<b>Cardiovascular system (C)</b>	<b>99</b>	<b>44.2</b>
Simvastatin	24	40
Captopril	15	25
Hydrochlorothiazide	12	20
Enalapril	10	16.6
Metoprolol	9	15
Doxazosin	8	13.3
Others	21	35
<b>Systemic hormones (H)</b>	<b>3</b>	<b>1.34</b>
Levothyroxine	3	5
<b>Musculoskeletal system (M)</b>	<b>2</b>	<b>0.9</b>
Nimesulide	1	1.6
Piroxicam	1	1.6
<b>Central Nervous System (N)</b>	<b>18</b>	<b>8.03</b>
Citalopram	5	8.3
Bromazepam	3	5
Paracetamol	2	3.3
Alprazolam	1	1.6
Others	7	11.67

Considering the **Table 4**, there were two serious drug interactions and five moderate interactions involving omeprazole. Of the drugs most involved in interactions, we can highlight citalopram (8.4%), *Ginkgo biloba* (6.7%) and levothyroxine (5%).

**Table 4** - Medications interacting with omeprazole, measure of severity and outcome of the drug interaction in elderly people under chronic use of omeprazole from the public system in *Panambi city, Rio Grande do Sul State*. n=60. 2016.

Medicines that interact with omeprazole	Interaction severity	Interaction outcome	n	%
Citalopram	Serious	Increased exposure of citalopram and risk of QT prolongation	5	8.4
<i>Ginkgo biloba</i>	Moderate	The effectiveness of omeprazole is reduced	4	6.7
Levothyroxine	Moderate	Increased TSH levels	3	5
Clopidogrel	Serious	Reduced efficacy of clopidogrel and increased risk of thrombosis	1	1.7
Carbamazepine	Moderate	Increased risk of toxicity of the carbamazepine	1	1.7
Propranolol	Moderate	Increased exposure of propranolol	1	1.7
Alprazolam	Moderate	Toxicity, CNS depression, ataxia, lethargy	1	1.7

Bearing in mind the drugs that have their absorption altered by the concomitant intake of omeprazole due to the gastric alteration, we can mention those present in the cardiovascular system, with predominance of captopril (25%), enalapril (16.7%) and acetylsalicylic acid (15%), as can be seen in **Table 5**.

**Table 5** - Medications with the description of their pKa and physiological changes occasioned by the drug associated use in patients under chronic use of omeprazole from the public system in *Panambi city, Rio Grande do Sul State*. n=60. 2016.

Medicines with altered absorption	Drug pKa	Alteration	n	%
<b>Cardiovascular</b>				
Captopril	3.7	Decreases antihypertensive effect	15	25
Enalapril	3.0 - 5.4	Decreases antihypertensive effect	10	16.7
Acetylsalicylic acid	3.5	Decreases platelet antiaggregant effect	9	15
Doxazosin	6.93	Increases urinary flow	8	13.4
Losartan	4.1	Decreases antihypertensive effect	8	13.3
Ciprofibrate	4.6	Increases cholesterol	2	3.4
<b>Gastrointestinal tract/metabolic</b>				
Glibenclamide	6.5	Increases blood glucose	5	8.4
Calcium carbonate	A	A	9	15
<b>Hormonal</b>				
Levothyroxine	2.2 - 6.5 - 10.1	Decreases thyroid hormone replacement	3	5
Others	-		8	13.3

Note: A- does not have pKa.

## DISCUSSION

Herein, slightly more than half of the chronic users of omeprazole are women with an average age above 65 years old. Similar data were found in another study<sup>16</sup> with 349 adult omeprazole patients, the majority of whom were female, elderly and with an average age of 64.4 years old. Other studies with PPIs found similar results to this study with regards to both age and gender.<sup>6,17,18,19</sup> Most of the interviewees reside with relatives and one study identified that the elderly living alone are three times more likely to fail to adhere to pharmacological treatment and lack of companionship is associated with memory loss, which favors the forgetting of medication administration, which is a factor for irrational use and culminating in serious adverse events.<sup>20</sup>

The most prevalent comorbidity among the interviewees was SAH. This is the most frequent chronic disease in clinical practice among the elderly, and is characterized as a multifactorial and late detection problem due to its asymptomatic course and is considered the main risk factor for cardiovascular morbidity and mortality, and this risk increases with age.<sup>21</sup> Dyslipidemia was also cited by the interviewees, and the elderly have a high prevalence of this comorbidity, and their control is necessary since approximately 75% of this population presents subclinical atherosclerotic disorders.<sup>22</sup>

Concerning the most self-reported purposes of use by the elderly people, it was found that most used omeprazole for gastritis, followed by heartburn and reflux esophagitis. And yet, a large part claimed to have dyspeptic symptoms. According to the NTF, omeprazole is indicated for symptomatic gastroesophageal reflux disease, reflux esophagitis, hypersecretory conditions, peptic ulcers of multiple etiologies, and as an adjuvant in the treatment of *Helicobacter pylori* infections.<sup>8</sup> In one study, high use of omeprazole in omeprazole patients hospitalized with gastritis.<sup>23</sup> This drug is used to control gastric acidity and treat peptic ulcers and esophageal reflux disease.<sup>5</sup> As for dyspeptic symptoms, one study found that omeprazole was the most prescribed drug for the treatment of dyspepsia.<sup>24</sup> And another study adds that PPIs are promising in the treatment of dyspeptic symptoms and dyspepsia.<sup>25</sup>

No patient reported having *Helicobacter pylori*. Nonetheless, this bacterium is considered to be the main cause of chronic gastritis and its identification is performed through biopsy examination by digestive endoscopy, and the standard treatment for this infection is the combination of the use of two antibiotics, amoxicillin and clarithromycin, with an PPI such as omeprazole.<sup>5</sup> In one study, of the 150 patients followed up with complaints compatible with peptic diseases, 98 patients presented a positive result for *Helicobacter pylori*.<sup>26</sup> A systematic review published in Cochrane has assessed the combination of empirical therapy and research procedures initial in patients with heartburn and epigastric pain and it was found that PPIs were significantly more effective than H<sub>2</sub> antagonists and antacids in reducing the recurrence of symptoms. The

same author points out that the initial endoscopy and the test for *Helicobacter pylori* lead to the reduction of the risk of recurrence of problems related to gastric acidity in comparison to the treatment without proving, thus, the strategy of testing *Helicobacter pylori* and treating it exceeds the suppression acidity.<sup>27</sup>

It is believed that many patients are unaware that they present this bacterium, as well as its diagnosis and treatment. The same happens with the use of antimicrobials for *Helicobacter pylori*, as already described, that many patients use without the accomplishment of an antibiogram to identify the aggressor microorganism and its sensitivity. The need for a complete investigation of the problem concomitant to the initiation of pharmacological treatment is emphasized since the non-identification of the pathogen can mask the diagnosis, cause serious toxicity, and select resistant microorganisms.<sup>28</sup>

According to **Table 2**, most interviewees use doses of 20 mg a day. According to *Micromedex*<sup>13</sup> the daily dose of 20 mg is recommended for most indications of omeprazole use as active duodenal ulcer, gastroesophageal reflux disease, reflux esophagitis, treatment of NSAID-induced ulcers, gastric ulcer infection of the gastrointestinal tract by *Helicobacter pylori*, among others. Some interviewees use a dose higher than 20 mg/day and the most frequent justification for the use of this dose was gastritis, yet, in a data collection study, reflux disease was the most described justification for the use of the dose above of 20 mg/day.<sup>16</sup> Still according to *Micromedex*,<sup>13</sup> in cases of duodenal ulcer disease caused by *Helicobacter pylori*, hypersecretory gastritis, and active gastric ulcer, it is recommended to use 40 mg or more for a specific time. The appropriate one would be to evaluate the dose and to correlate with the therapeutic indication, but in this study the indication was self-reported, being a limitation of the same.

Observing the omeprazole treatment time, half of the participants have been using for less than 5 years according to **Table 2**. Few interviewees use calcium concurrently with omeprazole. The use of omeprazole for long periods can significantly reduce bone mineral density, since elevated gastric pH interferes with the absorption of calcium.<sup>9</sup> In the sources studied, no information was found on pKa for calcium carbonate.<sup>29,30</sup>

The association of prolonged use of omeprazole with the aging process, which decreases the rate of bone remodeling, allows the occurrence of microfractures that, when accumulating, compromise the bone,<sup>31</sup> influences the recurrence of problems related to falls in elderly people. The occurrence of falls in the elderly is related to the duration of use and the dose of PPI.<sup>32</sup> The PPIs can lead to an increase in the risk of spinal, wrist and total fractures in postmenopausal women.<sup>8</sup> Consequently, it is very important the correct indication for use of this medication with periods established by the prescribers,<sup>33</sup> as well as monitoring its use by the professionals.

The most frequently cited shift was in the morning. PPIs should be administered 30 to 60 minutes before breakfast or the first substantial meal of the day. This

schedule not only increases absorption but also allows a high level of drug to reach the parietal cells when the proton pumps are ready to be activated.<sup>34</sup> This data demonstrates that the participants in the present study are using properly, time of administration, omeprazole ensuring maximum absorption.

Few elderly have reported side effects with omeprazole, the most frequent complaint about headaches. In one study of 46 elderly omeprazole users, only one had diarrhea as an adverse reaction to the drug.<sup>35</sup> A literature review pointed to the low frequency of adverse effects in prolonged treatment with PPI.<sup>36</sup> It is noteworthy that adverse reactions are more frequent at baseline of the treatment and for this study, only the elderly who used omeprazole for six months or more were considered. Nevertheless, safety and lack of toxicity in the long term still require further studies.

Side effects may be more frequent with the use of associated medications. In the present research, some elderly people use other drugs for the stomach. According to NTE, PPIs, when administered alone, have a definite efficacy in reducing symptoms and accelerating the healing of ulcers, gastric or duodenal and being considered more effective than H<sub>2</sub> antagonists. Nonetheless, the same form advises that its use is not for the purpose of immediately relieving the epigastric burning, since the complete effect occurs after 1 to 4 days of treatment, therefore, antacids can be administered concomitantly to relieve stomach acid.<sup>8</sup>

Regarding the pharmacological compliance, the majority reported using omeprazole daily, the few who reported forgetting to administer the medications stated that when they forget they no longer use that day. In one study 81.4% of the elderly PPI users reported forgetting to administer antiulcer drugs frequently.<sup>17</sup> The lack of compliance to medical prescription affects unnecessary costs and impairs the patient's response to the proposed treatment.<sup>37</sup>

The compliance may also be related to access to the drug, although omeprazole is being made available by the public pharmacy of the municipality under scrutiny. In the municipality of *Serafina Correia/RS*, this medicine is also dispensed free of charge by the city's basic pharmacy and it was verified that omeprazole in 2014 was the most widely used drug.<sup>38</sup> When this drug is missing in the basic health network, most interviewees reported purchasing it from commercial pharmacies. It is worth noting that the lack of medication in public health units mainly affects the most vulnerable, the lower income individuals, who generally depend on the free acquisition of medication as the only treatment alternative.<sup>39</sup> In the present study, the majority of elderly users of omeprazole does not remain without the drug and this directly reflects on the therapeutic observance and consequently, on the improvement of the symptoms related to the purposes of use.

Some elderly chronic users of omeprazole also take 5 or more medications concomitantly. The use of five or more drugs in the therapy is considered polypharmacy and its use is frequent in the elderly due to chronic diseases and can generate the indiscriminate use of drugs, contributing to the drug interactions.<sup>40</sup> In a study with the elderly, it was

verified that 42% of these were polypharmacy,<sup>19</sup> and yet another study observed at the time of the hospitalization of the elderly in the *Santa Casa da Misericórdia Hospital in Vitória/ES* that 40.6% of them used more than 5 medicines.<sup>41</sup> The elderly population is more exposed to the related risks to drugs because they present physiological changes in the body that significantly affect both the pharmacokinetics and pharmacodynamics of most drugs, triggering either increased drug toxicity or adverse reactions.<sup>8</sup>

Most of the interviewees in this study use drugs that act on the gastrointestinal tract and metabolism, followed by the cardiovascular system, according to Anatomical Therapeutic Chemical (ATC) classification, first level. The results obtained in the present study differ from those found by Lucchett (2010)<sup>42</sup> in which 70.3% of the drugs used by elderly people act in the cardiovascular system, also in another study the drugs that act in this system were pointed out as being most used by this age group, corresponding to 35%,<sup>43</sup> also Guimarães and Silva (2016)<sup>44</sup> verified that the drugs most frequently prescribed in their study, involving potentially inappropriate drugs among the elderly, acted in the cardiovascular system (29%). This difference of the present study with the others mentioned is due to the inclusion criterion of this research that was to make continuous use of omeprazole, and this drug, according to ATC classification, acts on the gastrointestinal tract and metabolism.

Omeprazole was the most frequent drug in this study, however, it was an inclusion criterion to make continuous use of this drug. Following this, simvastatin and captopril, which act in the cardiovascular system, are more frequently used by the interviewees. Also in the study lead by Mascarenhas,<sup>19</sup> in which simvastatin was the second most commonly used by the elderly (38%) and also in the Vieira study,<sup>45</sup> it was verified that this drug is part of the drug therapy of 53.1% of the elderly studied. One study found that captopril was among the drugs most commonly used by elderly people living in a long-term institution, then totaling 31.7%.<sup>46</sup> Associated with the aging population, there is an increase in the prevalence of chronic-degenerative diseases associated with age, cardiovascular diseases.<sup>43</sup> The drugs most frequently used by elderly chronic users of omeprazole are related to the diseases most prevalent in this study, already mentioned.

Serious drug interactions with omeprazole have been identified in **Table 4**. The most frequent interaction was with citalopram, which when combined with omeprazole increases blood levels of the selective serotonin reuptake inhibitor (SSRI) antidepressant and may increase the risk of side effects, including changes in heart rhythm.

Regarding the clopidogrel, the administration of omeprazole with this medicinal product decreases the cardioprotective effect of clopidogrel, since the route of metabolization of the two drugs occurs via Cytochrome P450 2C19. In a study of patients over 66 years old who began treatment with platelet antiaggregant after acute myocardial infarction and who were already using PPI, an increase in the risk of a new infarction in the short

term was found.<sup>47</sup> Another study verified that patients with coronary angioplasty using clopidogrel and PPI had a lower antiplatelet response compared to patients who did not use antiulcer drugs.<sup>48</sup>

Another potential drug interaction observed in this study was between omeprazole and *Ginkgo biloba*. Concomitant administration of these agents reduces the bioavailability of omeprazole and increases the plasma concentration of its active metabolite, termed 5-hydroxypyrazole. This data indicates that *Ginkgo biloba* can induce the CYP2C19 isoform and thereby reduce the plasma concentration of omeprazole,<sup>49</sup> then reducing its therapeutic effect.

An additional problem related to the use of omeprazole is the change in the absorption of some drugs, according to **Table 5**. The elderly chronic users of omeprazole who use medicinal products in association are likely to have their absorption compromised due to pH change caused by omeprazole in the gastric treatment. The drugs that undergo alteration of absorption by the decrease of acidity are those presenting pKa between 2,5 and 7,5, as the undissociated proportion varies considerably depending on the pH.<sup>50</sup>

Among the medications used by the interviewees, which have their absorption altered by concomitant use with omeprazole, the ones that work in the cardiovascular system stand out. The reduction of the antihypertensive effect may lead to complications such as stroke, acute myocardial infarction, and chronic kidney disease, as well as changes in systolic and diastolic blood pressures.<sup>51</sup> A study carried out with normotensive and hypertensive rats using omeprazole to verify the influence of gastric pH on the hypotensive effect of sodium nitrite. The results of this study suggest that omeprazole enhances the hypotensive effect of sodium nitrite.<sup>52</sup> Therefore, it is emphasized the need for pharmaceutical follow-up to identify drug-related problems and to ensure the efficacy and safety of pharmacological treatments.

Medications that act on the gastrointestinal tract and metabolism, like glibenclamide, also undergo changes of absorption due to gastric alterations caused by omeprazole. The change observed was an increase in blood glucose, as inadequate absorption of hypoglycemic drugs increases blood glucose levels. Thus, symptoms of hyperglycemia become more evident such as polyuria, polydipsia, weight loss, polyphagia and blurred vision or acute complications that can lead to diabetic ketoacidosis. Likewise, decreased control of hyperglycemia is associated with damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels.<sup>53</sup> The altered absorption of medications should be monitored by health professionals as they interfere directly efficacy and safety of the medicines used by patients taking omeprazole.

Considering the prolonged use of omeprazole, the drug interactions and the alterations of drug absorption caused by the continuous use of omeprazole, it is important to evaluate the practice of deprescription. This is based on a rigorous analysis of prescriptions to identify problems related to medicines used by the elderly, aiming to improve the quality of pharmacotherapy. Bearing in mind the aforesaid, health

professionals, especially physicians, pharmacists, and nurses, may suggest therapeutic approaches to prevent the occurrence of drug interactions and adverse reactions.<sup>54</sup> Hence, the Brazilian public health system needs to incorporate information about the process of deprescription aiming that this practice can become part of the therapeutic routine.

## CONCLUSIONS

Knowing the profile of omeprazole users is important to ensure safety and effectiveness in the treatment of elderly patients. It was observed that although the majority of chronic users of omeprazole take this drug correctly, they continue to take this PPI for prolonged periods, then being susceptible to drug interactions and altered absorption that might decrease the therapeutic effects and also increase adverse events.

The lack of knowledge of elderly people with regards to both diagnosis and treatment, which was verified in this study, reinforces the need for follow-up for these patients with an emphasis on the deprescription and rational use of medications to guarantee therapeutic efficacy. Moreover, it shows the need for implementation of care protocols and pharmacotherapeutic follow-up, which can help the elderly, by improving the medication use and their life quality as well.

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