

## Irrational use of alendronate sodium by the elderly

Uso irracional de alendronato de sódio por idosos

*Uso irracional de alendronato de sodio en los ancianos*

Camila Pereira Alvim<sup>1</sup>, Roberta Carvalho Figueiredo<sup>1</sup>, Camila Tavares Sousa<sup>1</sup>, Ricardo Augusto dos Santos Silva<sup>1</sup>, Samira Moreira Ferreira<sup>1</sup>, Camilo Molino Guidoni<sup>2</sup>, Paulo Roque Obreli-Neto<sup>1</sup>, André Oliveira Baldoni<sup>1</sup>

<sup>1</sup> Universidade Federal de São João del-Rei (UFSJ)

<sup>2</sup> Universidade Estadual de Londrina (UEL)

<sup>3</sup> Faculdades Integradas de Ourinhos (FIO)

### Abstract

**Introduction:** The effectiveness and safety of alendronate sodium are dependent on patient adherence to very specific guidelines regarding use. This study aims to estimate the rational use of alendronate sodium in the elderly. **Methods:** This is a cross-sectional study carried out with a structured questionnaire containing form of use and occurrence of adverse events related to alendronate sodium. The patients were recruited in their own homes. Rational use was considered as being the participants who: a) took the tablet in the morning; b) were fasting; c) waited at least 30 minutes before eating; d) ingested with a full glass of water; e) ingested the whole tablet; f) and remained in the orthostatic position for at least 30 minutes after use. Additionally, the odds ratio (OR) was used to analyze the association between the irrational use of alendronate sodium and the independent variables. **Results and Discussion:** Of the 248 participants in the study, most of the participants administered the medication in the morning (95.2%), with fasting (89.1%), waited at least 30 minutes to eat the first meal of the day (87.9%), and were in the orthostatic position until the time of the first meal (78.6%), but less than half ingested the tablet with a full glass of water (43.6%). Rational use of the medication was observed in only 30.7% of the participants. Regarding possible adverse events, 13.3% of the participants reported some event. Among the most prevalent were dry cough (6.5%), stomach pain (5.2%) and some throat discomfort (4.8%). The irrational use of this medication is associated with age and education level. **Conclusion:** The prevalence of irrational use of alendronate sodium in the elderly is high, and this use is associated with patients' sociodemographic factors.

**Keywords:** Alendronate; Aged; Osteoporosis; Pharmacoepidemiology.

#### Autor correspondente:

André Oliveira Baldoni  
E-mail: andrebaldoni@ufsj.edu.br

#### Fonte de financiamento:

Declararam não haver.

#### Parecer CEP:

579.793

#### Procedência:

não encomendado.  
Recebido em: 04/12/2019.  
Aprovado em: 13/08/2020.

**Como citar:** Alvim CP, Figueiredo RC, Sousa CT, Silva RAS, Ferreira SM, Guidoni CM, Obreli-Neto PR, Baldoni AO. Irrational use of alendronate sodium by the elderly. Rev Bras Med Fam Comunidade. 2020;15(42):2310. [https://doi.org/10.5712/rbmfc15\(42\)2310](https://doi.org/10.5712/rbmfc15(42)2310)



## Resumo

**Introdução:** A efetividade e segurança do alendronato de sódio são dependentes da adesão dos pacientes em relação às orientações específicas sobre o uso. Assim, este trabalho, tem como objetivo estimar a racionalidade de uso do alendronato de sódio em idosos. **Metodologia:** Trata-se de um estudo transversal realizado através de um questionário estruturado contendo a forma de utilização e a ocorrência de eventos adversos relacionados ao uso do medicamento. Os pacientes foram recrutados em suas próprias casas. Considerou-se uso racional os participantes que: a) tomaram o comprimido pela manhã; b) em jejum; c) esperaram pelo menos 30 minutos para se alimentar; d) ingeriu com um copo cheio de água; e) ingeriu o comprimido inteiro; f) e permaneceu na posição ortostática por pelo menos 30 minutos após o uso. Adicionalmente, o odds ratio (OR) foi utilizado para analisar associação entre o uso irracional do alendronato de sódio e as variáveis independentes. **Resultados e Discussão:** Dos 248 participantes do estudo a maioria administravam o medicamento pela manhã (95,2%), em jejum (89,1%), aguardavam pelo menos 30 minutos para realizar a primeira refeição do dia (87,9%), ficavam em posição ortostática até o horário da primeira refeição (78,6%), porém menos da metade ingeria o comprimido com um copo cheio de água (43,6%). O uso racional do medicamento foi observado em apenas 30,7% dos participantes. Em relação aos possíveis eventos adversos, 13,3% dos participantes relataram algum evento. Dentre os mais prevalentes, destacaram-se a tosse seca (6,5%), dor de estômago (5,2%) e algum desconforto na garganta (4,8%). O uso irracional deste medicamento está associado à idade e ao nível de escolaridade. **Conclusão:** É elevada a prevalência de uso irracional do alendronato de sódio em idosos e este uso está associado a fatores sociodemográficos dos pacientes.

**Palavras-chave:** Alendronato; Idoso; Osteoporose; Farmacoepidemiologia.

## Resumen

**Introducción:** La eficacia y seguridad del alendronato sódico dependen de la adherencia de los pacientes en relación con directrices específicas sobre el uso. Por lo tanto, este trabajo tiene como objetivo estimar la racionalidad del uso del alendronato sódico en los ancianos. **Metodos:** Este es un estudio transversal realizado a través de un cuestionario estructurado que contiene la forma de uso y la ocurrencia de eventos adversos relacionados con el uso de la droga. Los pacientes fueron reclutados en sus propias habitación. Se consideró el uso racional como los participantes que: a) tomaron la tableta por la mañana, b) en ayuno, c) esperaron al menos 30 minutos antes de comer; d) Ingerido con un vaso lleno de agua; e) ingirió toda la tableta, f) y permaneció en la posición ortostática durante al menos 30 minutos después de su uso. Además, el odds ratio (OR) se utilizó para analizar la asociación entre el uso irracional de alendronato de sodio y las variables independientes. **Resultados y Discusión:** De los 248 participantes en el estudio, la mayoría administró el medicamento por la mañana (95,2%), em ayuno (89,1%), esperó al menos 30 minutos para realizar la primera comida del día (87,9%), estaban en posición ortostática hasta el momento de La primera comida (78,6%), pero menos de la mitad ingeriría el comprimido con un vaso lleno de agua (43,6%). El uso racional de la droga se observó en sólo 30.7% de los participantes. En cuanto a los posibles acontecimientos adversos, el 13,3% de los participantes informaron de algún evento. Entre los más frecuentes, tos seca (6,5%), dolor de estómago (5,2%) Y algunas molestias en la garganta (4,8%). El uso irracional del medicamento está asociado a la ida y al nivel de escolaridad. **Conclusión:** La prevalencia del uso irracional del alendronato de sodio en los ancianos es alta, y este uso está asociado a factores sociodemográficos de los pacientes.

**Palabras clave:** Alendronato; Anciano; Osteoporosis; Farmacoepidemiologia.

## INTRODUCTION

The rational use of medications (RUM) is a complex process that comprises from the availability of affordable, effective, safe, and quality medicines, to their appropriate prescription, dispensation and use.<sup>1</sup> The WHO estimates that more than 50% of medications are prescribed, dispensed or sold incorrectly, and more than half of the patients also use the medications incorrectly. In addition, more than 50% of all countries do not implement basic policies to promote RUM.<sup>2</sup> In this sense, RUM has been considered a public health problem with compromised patient quality of life and a substantial burden to the public health service.<sup>3,4</sup> In this context of rational use, alendronate sodium stands out, as it is a medication that requires special conditions of use.

Alendronate sodium comprises one of the most widely used medications for the prevention and treatment of osteoporosis, and in Brazil it is the only oral medication for the treatment of osteoporosis dispensed free by the Unified Health System (SUS).<sup>5,6</sup> Its effectiveness and safety are dependent on patient adherence to very specific guidelines regarding use.<sup>6</sup> Inappropriate use of the medication can reduce bioavailability by up to 99%, reducing effectiveness, favoring an increase in the risk of bone fractures and hospitalizations, and consequently, a significant increase in sanitary and economic costs.<sup>7</sup> For safe use, it is necessary that the patient uses the medication with a full glass of water and remains in the orthostatic

position for 30 minutes after use, thus avoiding serious adverse events such as esophageal perforation, ulcers, and irritation in the gastrointestinal tract.<sup>7,8</sup>

Osteoporosis is an osteometabolic disease that affects the elderly more often. It is associated with an increased risk of bone fracture, physical disability, and disease-related mortality. Furthermore, it is considered one of the greatest challenges for global public health, since it represents high expenses for its prevention and treatment.<sup>9-11</sup> It is estimated that in Brazil the prevalence of osteoporosis in women is between 15% and 36% of the population, regardless of age.<sup>12</sup> In addition, during the triennium 2008-2010, 3,252,756 procedures were performed related to the treatment of osteoporosis in the elderly, which totaled an expense of R\$288,986,335.15 to the health system.<sup>13</sup> Therefore, in view of these costs, the prevalence of osteoporosis, the rapid process of Brazilian population aging, and the absence of studies that analyze the rationality in the use of alendronate sodium, this study is essential in the scope of osteoporosis treatment in primary health care. Thus, the objective of this study is to estimate the prevalence of rational use of alendronate sodium in the elderly. Additionally, we had a particular interest in to investigate the association between irrational use of alendronate sodium and age, education, number of drugs used and receive advices from health professional about correct use of drugs, once these characteristics seems to determine, at least partially, the behaviors related to drug use.<sup>14,15</sup>

## METHODS

### Design and study population

This cross-sectional study was conducted with the elderly, 60 years or older, using alendronate sodium and attended by the public health system, the SUS, in the city of Divinópolis, in the Brazilian state of Minas Gerais, a municipality with an estimated population of 238,230 inhabitants in 2019.<sup>16</sup> The city has 44 primary health care units located in 12 health regions, and has 43.9% coverage of the family health strategy. In relation to the five pharmacies in the municipalities, they dispense medicines only for SUS users, from all levels of health care.

The participants were identified by the electronic medication dispensing system used by the five public pharmacies. All patients who withdrew alendronate sodium in one of the five pharmacies in the past 12 months were considered potential participants in the study. The use of data of this system was authorized by the municipal administration, and used to perform the sampling, and obtain the addresses for recruitment of the participants. For sample calculation, purposes the following parameters were considered: a) elderly people living in the urban area; b) prevalence of 50% in the rational use of this medication, given the lack of scientific evidence; c) margin of error (confidence interval) of  $\pm 5\%$ ; d) confidence level of 95%; and e) 20% of losses. According to the municipality's electronic medication dispensing registration system, Divinópolis had during the study period, 959 elderly patients using alendronate sodium. Considering this scenario, 275 participants were estimated to be interviewed.

### Data collection

Face-to-face interviews were conducted by two trained interviewers, between October 2014 and May 2016 at the participants' residences. The interviews were conducted in the morning and afternoon,

including weekends, to meet potential participants who were only available outside business hours. When the potential participant was not found at the residence, another attempt was made at a different time.

For data collection, a structured questionnaire was used. Prior to application to the participants, the questionnaire was analyzed by a committee of three experts through which it was possible to make adjustments regarding the technical content and format of the questions. The experts had knowledge of osteoporosis and the application of instruments for data collection. Subsequently, a pilot study was carried out through the application of the questionnaire to 10 patients, in order to test comprehension of the questions. These pilot study participants were contacted in the same way as the other study participants.

The variables of interest of the study were: demographic and socioeconomic variables (gender, age, education, and access to private health insurance), clinical (form of use, duration of treatment, and occurrence of adverse events related to alendronate sodium). The duration of treatment was collected because of the recommendation to limit the treatment time to three years, and with this it was possible to analyze the rationality of prescription of this medication and number of drugs used; in the last two weeks, other than alendronate sodium and been guided by a health professional on the correct use of drugs, by self-report.

To evaluate the rationality of use, six questions were used, classified according to effectiveness and safety:<sup>8,17</sup> effectiveness (a - took the tablet in the morning, b - fasting, c - waited at least 30 minutes before eating; d - ingested with a full glass of water; e - ingested the whole tablet,); and safety (f - remained in the orthostatic position for at least 30 minutes after use). If the participant did not meet one of these conditions, irrational use of this medication was considered. In addition, an analysis of the number of items considered irrational was performed regarding the use of alendronate sodium. The data were presented as a percentage and 95% confidence interval (CI) in four subgroups: none, one, two, and three or more items that that were not fulfilled (a to f). It is worth mentioning that the test-retest reliability of these six questions was investigated in a sub-sample of 57 (23.0%) participants and results showed adequate reliability, with an average kappa of 0.80.

To identify the possible adverse events associated with the use of alendronate sodium, a checklist containing all events described in the scientific literature was prepared.<sup>7,8,17</sup> At the time of the interview this instrument was used to question the participant in relation to the presence of each of these adverse events.

The structured questionnaire and guidance booklet regarding correct and rational use of alendronate sodium are available on the Open Science Framework (OSF) virtual platform.<sup>18</sup> As decided by the researchers, the complete database is not available.

The study was approved by the Research Ethics Committee of the Federal University of São João Del-Rei, CAAE: 27582214.9.0000.5545. All study participants signed an informed consent form. At the end of the study, all participants received verbal and written information about rational use of alendronate.<sup>18</sup> And none elderly participated in the planning and conduct of the research.

The funding source did not interfere with the study planning, execution and publication of results.

## Analysis of data

For the continuous variable, the distribution of median and its range were performed, and for the categorical variables, frequency distribution was performed. We also estimated 95% confidence intervals (95% CI) of our estimates of rational use of alendronate sodium as well of adverse events. Additionally, crude and

adjusted odds ratios (OR) of the association between irrational use of alendronate sodium and age, education, number of drugs used other than alendronate sodium and been guided by a health professional on the correct use of drugs were estimated by logistic regression. The level of significance was set at  $p < 0.05$ . Data were entered in duplicate into Epi Info™ version 7 and analyzed by Stata® statistical software, version 14.

## RESULTS

A total of 959 elderly participants were identified, of which 678 were visited, and 248 were met in their homes and accepted the invitation to participate in the study (Figure 1).

Of the total participants, 95.6% were female and 45.2% were between 60 and 69 years of age. Most of the participants had low level of education, those who had never attended school or had incomplete elementary education represent almost 80% of the sample and 50.0% of them had access to a private health insurance. The median of the drug use in the last two weeks was 1.0, varying from 1.0 to 18.0. The majority of the participants (80.4%) reported to receive none advice from health professional regarding the correct use of drugs (Table 1).

Regarding the use of alendronate sodium, the majority of the participants administered the medication in the morning (95.2%), fasted (89.1%), waited at least 30 minutes to take the first meal of the day (87.9%), and were in the orthostatic position until the first meal of the day (78.6%), but less than half ingested the tablet with a full glass of water (43.6%) (Table 2). Rational use of the medication was observed in only 30.7% of the participants (Table 2).

In the analysis of the duration of alendronate sodium treatment by the interviewees, a mean time of use of 5.7 years, with standard deviation of 5.5 years (minimum: 1 month, maximum: 48 years) was observed (Table 2).

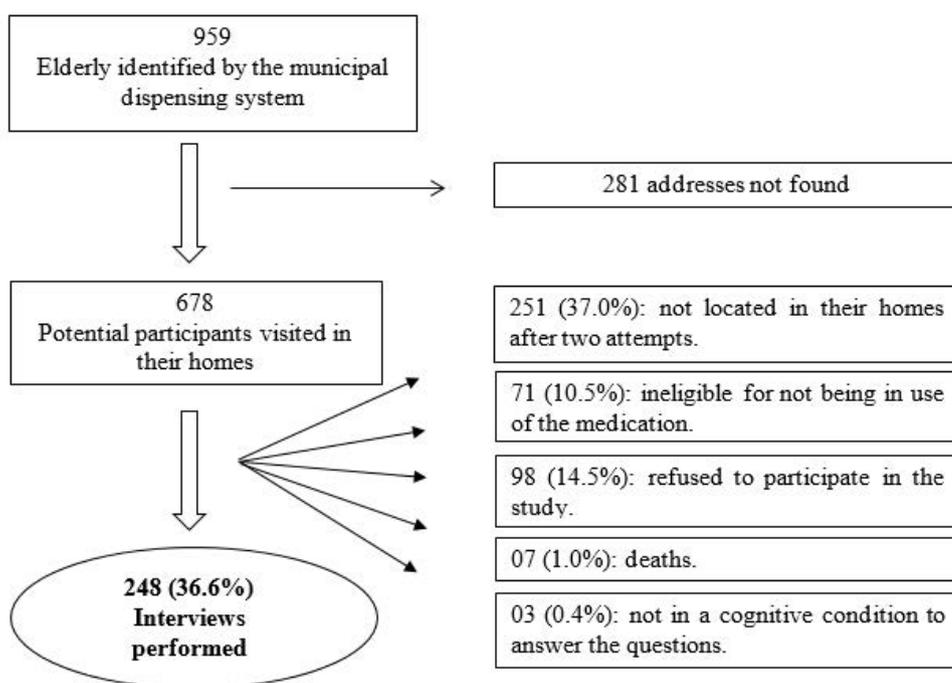


Figure 1. Inclusion flowchart among the elderly using alendronate sodium from Divinópolis, Brazil, 2014-2016 (n=248).

**Table 1.** Demographic and socioeconomic characteristics and drug use information of elderly patients using alendronate sodium from Divinópolis, Brazil, 2014-2016 (n=248).

Characteristics	n (%)
Gender	
Female	237 (95.6)
Male	11 (4.4)
Age (years)	
60 – 69	112 (45.2)
70 – 79	93 (37.5)
80 +	43 (17.3)
Level of education	
Never attended school or incomplete elementary education	187 (78.2)
Complete elementary education	33 (13.8)
Complete high school or higher	19 (8.0)
Private health insurance	
Yes	123 (50.0)
No	123 (50.0)
Number of drugs used other than alendronate sodium	1.0 (1.0 to 18.0)
Been guided by a health professional on the correct use of drugs	43 (20.0)

Differences in participants' totals are explained by missing data.

**Table 2.** Characterization of the use of alendronate sodium by elderly people of Divinópolis, Brazil, 2014-2016 (n=248).

Use of alendronate sodium	n (%) (95% CI)*
Participants observing each recommendation	
Taken in the morning	236 (95.2) (91.7-97.2)
Fasting	221 (89.1) (84.6-92.4)
Waited at least 30 minutes before eating	218 (87.9) (83.2-91.4)
Ingested with a full glass of water	108 (43.6) (37.5-49.8)
Ingested the whole tablet	234 (94.4) (90.7-96.6)
Remained in the orthostatic position until the time of the first meal	195 (78.6) (73.0-83.3)
<b>Correct use of alendronate sodium</b>	76 (30.7) (25.2-36.7)
<b>Number of unobserved recommendations</b>	
None	30.7 % (25.2-36.7)
One	40.7 % (34.7-46.9)
Two	19.4 % (14.9-24.8)
Three or more	9.2 % (6.2-13.6)
<b>Duration of alendronate use</b>	n (%)
Up to 3 years	95 (38.3 %)
From 3 to 5 years	58 (23.4 %)
More than 5 years	80 (32.3 %)
Duration of use not known	15 (6.0 %)

\*95% CI: 95% confidence interval.

In the univariate analysis, in comparing with those with age between 60 to 69 years old, the participants with 80 years old or more and those using more drugs in the last two weeks had higher chance to use sodium alendronate in irrational way. On the other hand, in comparing to those who had never attended school or had incomplete elementary education, the participants who had complete elementary education or higher had lower chance to use sodium alendronate in irrational way. After adjustments, the results about age and number of drugs did not change, however, regarding the education level, only complete high school or higher remained statistically associated with lower chance of irrational use of sodium alendronate. To been guided by a health professional on the correct use of drugs did not associated with irrational use of sodium alendronate neither in the univariate nor in the multivariate analysis (Table 3).

Regarding possible adverse events, 86.7% did not report any of the events described in the literature. However, 13.3% of the elderly reported some adverse events that may be associated with the use of alendronate sodium, with 8.9% reporting only one adverse event and 4.4% reporting two or more. Among the most prevalent were dry cough (6.5%), stomach pain (5.2%) and throat discomfort (4.8%), being observed (Table 4).

**Table 3.** Crude and adjusted odds ratios (OR) for the association between irrational use of sodium alendronate and age, education level, number of drugs used, and been guided by a health professional on the correct use among elderly patients using alendronate sodium from Divinópolis, Brazil, 2014-2016 (n=248).

Variables	Crude OR (95% CI)	Model 1 (95% CI)	Model 2 (95% CI)
<b>Age (years)</b>			
60-69	Reference	Reference	reference
70-79	1.32 (0.74;2.37)	1.22 (0.67;2.24)	1.12 (0.77;2.84)
80+	4.56* (1.66;12.49)	3.24* (1.15;9.14)	3.11* (1.06;9.17)
<b>Education level</b>			
Never attended school or Incomplete elementary education	Reference	Reference	reference
Complete elementary education	0.37* (0.10;0.98)	0.41 (0.13;1.29)	0.45 (0.17;2.29)
Complete high school or higher	0.23* (0.06;0.81)	0.28* (0.07;0.98)	0.26* (0.08;0.97)
<b>Number of drugs used other than alendronate sodium</b>			
(1.01;6.78)	1.10	—	—
(1.01;7.84)	—	1.05*	—
<b>Been guided by a health professional on the correct use of drugs</b>			
No	Reference	—	reference
Yes	0.97 (0.42;2.30)	—	0.88 (0.32;1.70)

\*p-value <0.05; Model 1: age + education level; Model 2: model 1 + number of drugs used other than alendronate sodium (continuous) + been guided by a health professional on the correct use of drugs.

**Table 4.** Profile of the adverse events of elderly patients using alendronate sodium from Divinópolis, Brazil, 2014-2016 (n=248).

Characteristics	N (%) (95% CI)*
Frequency of self-reported of adverse events	
None	215 (86,7) (81,8-94,4)
Only one	22 (8,9) (5,9-13,1)
Two or more	11 (4,4) (2,5-7,8)
<b>Most frequent adverse events</b>	
Dry cough	16 (6,5) (3,9-10,3)
Stomach pain	13 (5,2) (3,1-8,8)
Throat discomfort	12 (4,8) (2,8-8,6)
Hoarseness	9 (3,6) (1,9-6,9)

\*95% CI: 95% confidence interval.

## DISCUSSION

This study, developed with sodium alendronate users attended by Brazilian public health system, showed that approximately two-thirds of the elderly present irrational use of the medication, especially those older, less educated and using many drugs.

In our study, we had verified that 10.5% reported not using alendronate sodium at the time of the invitation to interview (even though registration of medication withdrawal at the pharmacy existed). This fact may indicate a situation of non-adherence or lack of knowledge of pharmacological treatment, since all the elderly who were invited to participate in the study received the medication free of charge in one of the five pharmacies in the municipality. In another study, it was observed that adherence to this medication is low, since 80% of patients discontinue treatment without medical guidance, especially for those with a longer time of use.<sup>19</sup> The results of the present study suggest that discontinuation of the treatment is a decision taken by the patient, since to have a registration of withdrawal of the medication in the pharmacy it is mandatory to present the prescription (and these patients have registration of withdrawal).

The sample of the present study is mostly composed by woman (95.6%). This profile is justified because bone loss is part of the aging process, being more pronounced in white women due to their ethnicity and hormonal changes, such as postmenopausal reduction of estrogen, which are responsible for the reduction of bone mineral density, leading to osteopenia or osteoporosis and consequently an increased risk of fractures.<sup>6,20</sup> Other factors that may explain the greater proportion of women is that they are more concerned with health and self-care, they use health services<sup>21,22</sup> and answer more health surveys more frequently compared to men.<sup>23</sup>

Many patients used alendronate sodium irrationally, either by not obeying the correct time of administration, absence of fasting, ingestion with chewing or dissolution of the tablet, insufficient amount of water, or lack of fasting after ingestion. Alendronate sodium, even when ingested correctly, is poorly absorbed by the intestine.<sup>23</sup> Thus, there is a need to carefully follow the recommendations for use, since its bioavailability can reach zero if not correctly administered, generating complications of the clinical state, hospitalizations, fractures, and expenditures for the health system.<sup>17,24,25</sup> Therefore, most of the participants of the present study (69.3%) do not use the medication rationally, compromising its effectiveness and

safety. Another Brazilian study shows a similar frequency of irrational use of alendronate sodium (68%),<sup>19</sup> but the present study differs when evaluating the use of the medication in the morning, a time that is more convenient and easy for fasting and to remain in an upright position until the next meal, thus avoiding the risk of gastroesophageal injury.<sup>17</sup>

Considering the rationality of prescription of this medication, it is important to highlight the high frequency of elderly patients (55.7%) receiving alendronate sodium for more than three consecutive years, since the use of bisphosphonates in general for more than three years is associated with bone complications, such as increased atypical femoral fractures.<sup>26</sup> However, there is a need to evaluate the benefit of individual patient use after this period, which was not possible in the present study, and this has been a matter of concern in the Brazilian SUS as the country is experiencing a high prevalence of osteoporosis,<sup>12</sup> and alendronate sodium is the only bisphosphonate regularly available, free of charge, to all Brazilians.<sup>27</sup>

Our results regarding the association between age and education with irrational use of sodium alendronate are corroborated by the economic and educational inequalities of the elderly, since older people who have better levels of schooling have a significant understanding of RUM.<sup>20,28</sup> On the other hand, it is important to emphasize that the adequacy of prescription and dispensing of medications are fundamental factors in rational use; the vast majority of the elderly do not receive orientation from the pharmacist regarding the use of the medication,<sup>29</sup> which corroborates with our results, as almost 80% of the participants had reported did not receive any advice from health professional about correct use of the medication. This result can explain, at least, partially, we did not find statistic association between irrational use of sodium alendronate and been guided by a health professional on the correct use of drugs. In addition, in Brazil, the pharmacist is not known as the practitioner who advises on use of medication<sup>30</sup> and they have unsatisfactory knowledge to adequately perform the dispensing of medication.<sup>31</sup> Brazil has made great strides in the last decade in relation to the clinical performance of the pharmacist, but in practice, this change is still discrete.<sup>32</sup>

Furthermore, increasing numbers of drugs were associated with higher chance to use sodium alendronate in an irrational way; this may be in line with findings in other studies,<sup>33-35</sup> where decreasing adherence of alendronate treatment was associated with increasing number of drugs prescribed. The results of this study show the need for the pharmacist and physician to contribute with their clinical skills in medication therapy management, especially in primary care, since there are many ways they contribute to the management of osteoporosis.<sup>36</sup>

In addition, to interfering with the effectiveness of the medication, it was observed that safety in use may also be compromised, since 21.4% of the interviewees were not in an orthostatic position after ingesting alendronate sodium, this might lead to serious adverse events, such as esophageal perforation, ulcers, and irritation in the gastrointestinal tract.<sup>17</sup> However, 86.7% of the elderly had no adverse events. Of those who presented, the symptoms might be associated with the incorrect form of medication use, since adverse events might be avoided and/or minimized by adequate water consumption and by remaining in the orthostatic position.<sup>17,37</sup> Indeed, the frequency of having reported at least one adverse event was 26.4% among participants who reported not remaining in the orthostatic position and 9.7% among those who reported following this recommendation (results not presented). It is important to highlight that although the adversities in the misuse of alendronate are considered well reported in the literature, these results need to be analyzed with caution, since the profile of other medications used by patients has not been investigated.

Regarding the limitations of the study, it is important to emphasize that the population studied is not representative of the elderly in the city where the study was conducted, since only the elderly users of the SUS were included. However, in relation to information regarding rational alendronate use, it is important to note that they are applicable in all health contexts, since they are universal. Additionally, we achieved 90.2% of our sample size goal; however, we do not believe that our evidence was compromised. Finally, it is important to highlight the potential of the study, which in addition to the novelty of evaluating the rational use of alendronate sodium in the elderly, the work followed methodological rigor that supports the robustness of the results, since in addition to the evaluation by experts and performing of the pre-test, the results have adequate reliability.

Regarding the implications for future research and professional practice, the originality of this article brings a neglected theme to direct new longitudinal studies that analyze the impact of the irrational use of this medication. Additionally for clinical practice, the results emphasize the need for the physician and the clinical pharmacist to advise all patients about particularities of the use of alendronate sodium.

## CONCLUSION

The use of alendronate sodium as well as the profile of adverse events found in the study evidences the need to implement health education strategies for the elderly, especially for the less educated ones, since the vast majority (69.3%) do not use the medication as recommended in clinical protocols, and more than 13% of the elderly report adverse events that may be associated with the use of this medication. In addition, 61.7% of the elderly have been using alendronate sodium for more than three years.

Finally, the alarming data resulting from this study must be considered by managers and clinicians, in order to direct concrete actions during the process of medical prescription and dispensation of medicines by the pharmacist.

## ACKNOWLEDGEMENTS

This study was financed in part by the Coordination for the Improvement of Higher Education Personnel - Brazil (CAPES) - Financial Code 001.

## CONTRIBUTIONS

All authors, CPA, RCF, CTS, RASS, SMF, CMG, PRON and AOB, participated equally in the following criteria: word conception and design of the work; acquisition, data analysis and interpretation; drafting the work and revising the work critically for important intellectual content. All authors approved the final version and agreed to report on all aspects of the work.

## REFERENCES

1. Ministério da Saúde (BR). Portaria nº 3.916, de 30 de outubro de 1998. Dispõe sobre a aprovação da Política Nacional de Medicamentos. Diário Oficial da União, Brasília (DF), 31 out 1998; [access in 2018 Jan 21]. Available from: [https://bvsms.saude.gov.br/bvs/saudelegis/gm/1998/prt3916\\_30\\_10\\_1998.html](https://bvsms.saude.gov.br/bvs/saudelegis/gm/1998/prt3916_30_10_1998.html)
2. World Health Organization (WHO). The pursuit of responsible use of medicines: sharing and learning from country experiences. Geneva: WHO; 2012; [access in 2018 Mar 28]. Available from: [http://www.who.int/medicines/areas/rational\\_use/en/](http://www.who.int/medicines/areas/rational_use/en/)

3. World Health Organization (WHO). Promoción del uso racional de medicamentos : componentes centrales. Geneva: WHO; 2002. p. 1-6.
4. Agência Nacional de Vigilância Sanitária (ANVISA). Parcerias para diminuir o mau uso de medicamentos. *Rev Saúde Pública*. 2006;40(1):191-3. DOI: <https://doi.org/10.1590/S0034-89102006000100029>
5. Ministério da Saúde (BR). Portaria No. 96/2018, de 18 de maio de 2018. Regulamenta a organização e funcionamento do Registro Nacional do Testamento Vital (RENTEV) [Internet]. *Diário da República*, Lisboa (PT), 2018 mai 18; 2211-2; [access in 2019 Jun 10]. Available from: <https://data.dre.pt/eli/port/141/2018/05/18/p/dre/pt/htm>
6. Camacho PM, Petak SM, Binkley N, Clarke BL, Harris ST, Hurley DL, et al. American Association of Clinical Endocrinologists and American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis - 2016 - executive summary. *Endocr Pract*. 2016 Sep;22(9):1111-8. DOI: <https://doi.org/10.4158/EP161435.ESGL>
7. Meng J, Hu L. Positively-charged microemulsion for improving the oral bioavailability of alendronate: in-vitro and in-vivo assessment. *J Pharm Pharmacol*. 2011;63(3):400-8. PMID: 21749388 DOI: <https://doi.org/10.1111/j.2042-7158.2010.01229.x>
8. Reid IR. Efficacy, effectiveness and side effects of medications used to prevent fractures. *J Intern Med*. 2015 Jun;277(6):690-706. DOI: <https://doi.org/10.1111/joim.12339>
9. Yazbek MA, Marques Neto JF. Doenças osteometabólicas. Osteoporose e outras doenças osteometabólicas no idoso. *Eistein (São Paulo)*. 2008;6(Supl 1):S74-S8.
10. Fardellone P, Lello S, Cano A, Moreira ES, Oliveira RW, Julian GS, et al. Real-world adherence and persistence with bisphosphonate therapy in postmenopausal women: a systematic review. *Clin Ther [Internet]*. 2019 Aug;41(8):1576-88. DOI: <https://doi.org/10.1016/j.clinthera.2019.05.001> DOI: <https://doi.org/10.1016/j.clinthera.2019.05.001>
11. Sözen T, Özisik L, Basaran NC. An overview and management of osteoporosis. *Eur J Rheumatol*. 2017 Mar;4(1):46-56. PMID: 28293453 DOI: <https://doi.org/10.5152/eurjrheum.2016.048>
12. Baccaro LF, Conde DM, Costa-Paiva L, Pinto-Neto AM. The epidemiology and management of postmenopausal osteoporosis: a viewpoint from Brazil. *Clin Interv Aging [Internet]*. 2015 Mar; [cited 2018 Mar 28]; 10:583-91. Available from: <http://www.dovepress.com/the-epidemiology-and-management-of-postmenopausal-osteoporosis-a-viewp-peer-reviewed-article-CIA%5Cn> PMID: 25848234 DOI: <https://doi.org/10.2147/CIA.S54614>
13. Moraes LFS, Silva EN, Silva DAS, Paula AP. Gastos com o tratamento da osteoporose em idosos do Brasil (2008-2010): análise dos fatores associados. *Rev Bras Epidemiol*. 2014;17(3):719-34.
14. Horne R. Treatment perceptions and self-regulation. In: Cameron LD, Leventhal H, eds. *The self-regulation of health and illness behaviour*. London, UK: Routledge; 2003. p. 138-53.
15. Hansen C, Pedersen BD, Konradsen H, Abrahamsen B. Anti-osteoporotic therapy in Denmark--predictors and demographics of poor refill compliance and poor persistence. *Osteoporos Int*. 2013;24(7):2079-97. DOI: <https://doi.org/10.1007/s00198-012-2221-5> PMID: 23179576 DOI: <https://doi.org/10.1007/s00198-012-2221-5>
16. Instituto Brasileiro de Geografia e Estatística (IBGE). Panorama das cidades [Internet]. Brasília (DF): IBGE; 2019; [access in 2019 Jun 10]. Available from: <https://www.ibge.gov.br/cidades-e-estados/mg/divinopolis.html>
17. Micromedex Solutions. Drug interactions [Internet]. Ann Arbor, MI: Truven Health Analytics Inc.; 2013; [access in 2017 Jan 31]. Available from: [https://www.micromedexsolutions.com/micromedex2/4.14.0/WebHelp/Tools/Interactions/Drug\\_Interactions.htm](https://www.micromedexsolutions.com/micromedex2/4.14.0/WebHelp/Tools/Interactions/Drug_Interactions.htm)
18. Silva RAS. Questionário estruturado alendronato de sódio and orientações para uso de alendronato de sódio [Internet]. Charlottesville, VA: Open Science Framework (OSF); 2020. Available from: <https://osf.io/8a6fb>
19. Nobre C, Vieira VMSF, Nobre CA, Pamplona YAP. Caracterização do uso do alendronato para osteoporose na Atenção Primária à Saúde. *Rev Bras Med Fam Comunidade*. 2016 Apr;11(38):1-9. DOI: [http://doi.org/10.5712/rbmfc11\(38\)901](http://doi.org/10.5712/rbmfc11(38)901) DOI: [https://doi.org/10.5712/rbmfc11\(38\)901](https://doi.org/10.5712/rbmfc11(38)901)
20. Dewulf NLS, Santos V, Pereira LRL, Troncon LEA. The invisible pharmacist. *Am J Hosp Pharm Educ*. 2009 Jul;73(4):74.
21. Machin R, Couto MT, Silva GSN, Schraiber LB, Figueiredo WS, Valença OA, et al. Concepção de gênero, masculinidade e cuidados em saúde: estudo com profissionais de saúde da atenção primária. *Ciênc Saúde Coletiva*. 2011 Nov;16(11):4503-12. DOI: <https://doi.org/10.1590/s1413-81232011001200023> DOI: <https://doi.org/10.1590/S1413-81232011001200023>
22. Costa-Júnior FM, Maia ACB. Concepção de homens hospitalizados sobre a relação entre gênero e saúde. *Psicol Teor e Pesqui*. 2009 Mar;25(1):55-63. DOI: <https://doi.org/10.1590/S0102-37722009000100007> DOI: <https://doi.org/10.1590/S0102-37722009000100007>

23. Aquino EML, Araujo MJ, Almeida MCC, Conceição P, Andrade CR, Cade NV, et al. Recrutamento de participantes no Estudo Longitudinal de Saúde do Adulto. *Rev Saúde Pública* [Internet]. 2013 Jun; [cited 2018 Mar 29]; 47(Suppl 2):10-8. Available from: [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S0034-89102013000800010&lng=en](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0034-89102013000800010&lng=en) DOI: <https://doi.org/10.1590/S0034-8910.2013047003953>
24. Leite MOR. Tratamento da osteoporose pós-menopausa. *Arq Bras Endocrinol Metab*. 1999;43(6):442-5. DOI: <https://doi.org/10.1590/S0004-27301999000600009>
25. Ribeiro AF, Volpato NM. Alendronato de sódio: metodologias para análise quantitativa. *Quím Nov*. 2005 Oct;28(5):852-8. DOI: <https://doi.org/10.1590/S0100-40422005000500024>
26. Diab DL, Watts NB. Biophosphonate drug holiday: who, when and how long. *Ther Adv Musculoskelet Dis*. 2013 May;5(3):107-11. DOI: <https://doi.org/10.1177/1759720X13477714> DOI: <https://doi.org/10.1177/1759720X13477714>
27. Caires ELP, Bezerra MC, Junqueira AFTA, Fontenele SMA, Andrade SCA, D'Alva CB. Tratamento da osteoporose pós-menopáusia: um algoritmo baseado na literatura para uso no sistema público de saúde. *Rev Bras Reumatol*. 2017 May/Jun;57(3):254-63. DOI: <https://doi.org/10.1016/j.rbre.2017.01.001> DOI: <https://doi.org/10.1016/j.rbre.2017.01.001>
28. Flores LM, Mengue SS. Drug use by the elderly in Southern Brazil. *Rev Saúde Pública*. 2005;39(6):924-9. PMID: 16341402
29. Baldoni AO, Dewulf NLS, Santos V, Reis TM, Ayres LR, Pereira LRL. Dificuldades de acesso aos serviços farmacêuticos pelos idosos. *Rev Ciênc Farm Básica Apl*. 2014;35(4):615-21.
30. Guénette L, Moisan J. Elderly people's knowledge of the purpose of their medicines. *Am J Geriatr Pharmacother*. 2011 Feb;9(1):49-57. DOI: <https://doi.org/10.1016/j.amjopharm.2011.02.007> DOI: <https://doi.org/10.1016/j.amjopharm.2011.02.007>
31. Reis TM, Guidoni CM, Giroto E, Rascado RR, Mastroianni PC, Cruciol JM, et al. Pharmaceutical care in Brazilian community pharmacies: knowledge and practice. *Afr J Pharm Pharmacol*. 2015;9(9):287-94. DOI: <https://doi.org/10.5897/AJPP2014.4239>
32. Melo AC, Galato D, Maniero HK, Frade JCQP, Palhano TJ, Silva WB, et al. Pharmacy in Brazil: progress and challenges on the road to expanding clinical practice. *Can J Hosp Pharm*. 2017;70(5):381-90. DOI: <https://doi.org/10.4212/cjhp.v70i5.1700> PMID: 29109582 DOI: <https://doi.org/10.4212/cjhp.v70i5.1700>
33. Landfeldt E, Ström O, Robbins S, Borgström F. Adherence to treatment of primary osteoporosis and its association to fractures--the Swedish Adherence Register Analysis (SARA). *Osteoporos Int*. 2012;23(2):433-43. DOI: <https://doi.org/10.1007/s00198-011-1549-6> PMID: 21286686 DOI: <https://doi.org/10.1007/s00198-011-1549-6>
34. Devold HM, Furu K, Skurtveit S, Tverdal A, Falch JA, Sogaard AJ. Influence of socioeconomic factors on the adherence of alendronate treatment in incident users in Norway. *Pharmacoepidemiol Drug Saf*. 2012 Jan;21(3):297-304. DOI: <https://doi.org/10.1002/pds.2344> DOI: <https://doi.org/10.1002/pds.2344>
35. Hansen C, Pedersen BD, Konradsen H, Abrahamsen B. Anti-osteoporotic therapy in Denmark--predictors and demographics of poor refill compliance and poor persistence. *Osteoporos Int*. 2013;24(7):2079-97. DOI: <https://doi.org/10.1007/s00198-012-2221-5> PMID: 23179576 DOI: <https://doi.org/10.1007/s00198-012-2221-5>
36. Laliberté MC, Perreault S, Damestoy N, Lalonde L. The role of community pharmacists in the prevention and management of osteoporosis and the risk of falls: results of a cross-sectional study and qualitative interviews. *Osteoporos Int*. 2013;24(6):1803-15. DOI: <https://doi.org/10.1007/s00198-012-2171-y> PMID: 23070479 DOI: <https://doi.org/10.1007/s00198-012-2171-y>
37. Recker RR, Lewiecki EM, Miller PD, Reiffel J. Safety of bisphosphonates in the treatment of osteoporosis. *Am J Med* [Internet]. 2009 Feb;122(2 Suppl):S22-S32. DOI: <http://doi.org/10.1016/j.amjmed.2008.12.004> PMID: 19187809 DOI: <https://doi.org/10.1016/j.amjmed.2008.12.004>