

## Sodium alendronate: proposal and reliability of indicators

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The present study proposes and evaluates the test-retest reliability of indicators of the correct use of sodium alendronate in elderly patients. This is a test-retest reliability study for use of sodium alendronate. Six questions to evaluate the correct use of this medicine were elaborated after analysis of information in the literature. Data collection was performed through questionnaires in face-to-face in-home interviews by previously trained interviewers. The participants were initially interviewed (test) when they agreed to participate in the study, and secondly (retest), after a period of 7 to 14 days from the first interview. The reliability of the questions was evaluated by means of the agreement percentage and the Kappa coefficient. Fifty-seven pairs (test-retest) were obtained. The mean age was 69.3 (SD = 6.9) years, the majority (92.5%) completed elementary education, and declared themselves white (50.9%). All the questions presented high concordance ranging from 79.0% to 98.3%. The Kappa values ranged from 0.1 (low) to 0.83 (very good). The agreement percentage and the Kappa values suggest adequate reliability of the proposed questions. We suggest that they can be used as a simple and quick way to evaluate the quality of sodium alendronate use among the elderly.

**Keywords:** Drug utilization. Alendronate. Osteoporosis. Postmenopausal.

### INTRODUCTION

Rational use of medicines (RUM) comprises all stages of medicine development until their use, and must ensure that the patient receives the medicine according to their clinical needs, in the appropriate dose, duration, and cost (WHO, 2002). In this sense, RUM seeks to ensure that the medicine is effective and safe (Escher, Coutinho, 2017). Correct use of medicine, i.e. following the recommendations of how to take, use, and store, are essential for RUM (Mahamood *et al.*, 2016). However, according to the World Health Organization, 50.0%

of medicine prescriptions and dispensations are made incorrectly, and the same problem extends to use, which also approaches 50.0% (WHO, 2002).

Sodium alendronate is one of most recommended medicines for treating and preventing osteoporosis (Radominski *et al.*, 2017), a silent disease which has required special attention for public health since it represents high expenses for its prevention and treatment, and is associated with increased risk of falls, disability, decreased quality of life, as well as increased risk of mortality (Mata *et al.*, 2012).

Sodium alendronate is an example of a medicine which has several particularities in its use and can significantly interfere with its effectiveness and safety. For example, its ingestion should be taken with a full glass of water after fasting, and the patient should not sit

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or lie down within 30 minutes of taking the medicine (Radominski *et al.*, 2017). Non-adherence to these recommendations compromises the therapeutic effect, and increases the risk of adverse reactions such as dyspepsia, nausea/vomiting, abdominal pain, esophagitis and esophageal stenosis (Mackay *et al.*, 1998).

Studies on adherence to guidance by users of sodium alendronate are still scarce. However, a study conducted by Camargo, Minosso and Lopes, showed that numerous guidelines for the correct use of sodium alendronate were not provided to patients by medical professionals. Only 28.0% of physicians said they advised their patients that the medicine should be taken with a full glass of water (Camargo, Minosso, Lopes, 2007).

Knowing the profile of medicine use in populations is one of the objectives of drug utilization studies. In this sense, they allow the identification of possible pharmacotherapeutic problems and generate information that is fundamental for the promotion of RUM (Griep *et al.*, 2003). The quality of epidemiological studies, including drug utilization studies, is dependent on valid and reliable measuring instruments. Reliability is the ability of an instrument to faithfully measure a phenomenon. One of the ways to assess reliability is test-retest, in which the same questionnaire is applied to the same individual at different times (Griep *et al.*, 2003). As far as we know, there is still no instrument to measure the correct use of sodium alendronate in populations. Therefore, the present study proposes indicators to evaluate the correct use of sodium alendronate, as well as to evaluate the reliability of these indicators.

## MATERIAL AND METHODS

### Study design and setting

This is a test-retest reliability study. This study is part of a survey conducted with elderly patients (60+ years old) using sodium alendronate, being users of the Brazilian public health service in the municipality of Divinópolis, Minas Gerais state, Brazil, between October 2014 and May 2016.

Data collection was performed through questionnaires in face-to-face in-home interviews by

previously trained interviewers. For the training, material for study and instructions of a theoretical nature were available, and face-to-face interview simulations were made. The theoretical material consisted of a detailed manual to guide the accomplishment of the interview and completion of the questionnaire, based on pre-tests and a pilot study, carried out before the beginning of data collection. All participants read and signed the Informed Consent Form before the interview. After data collection, all questionnaires were typed (double-typing) into Epi Info software, version 7.2.

After completion of the first interview (test), all participants were asked to respond again to questions regarding the correct use of sodium alendronate (retest). The retest occurred between 7 and 14 days after the test. It is worth noting that there are no standardized periods for applying the retest, but in order to avoid memory effect or changes in the behavior of the participant that have an impact on their responses, this period is recommended and used by most of the studies of reliability (Martins, 2006). The participants were not informed about what issues they would respond to in the retest, so that they would not be able to remember any response.

### Study variables

#### *Correct use of sodium alendronate*

The questions to evaluate the correct use of sodium alendronate were proposed from a literature review and analyzed by a committee of three judges with expertise in the subject of interest, with making adjustments regarding the technical content and format of the questions being possible. The judges are PhDs in Pharmaceutical Sciences, knowledgeable about osteoporosis, and active in clinical pharmacy. The questions were pre-tested and a pilot study was carried out through the application of the questionnaire to 10 users, men and women, in order to test the comprehension of the questions asked.

Ultimately, six questions on the correct use of sodium alendronate were used and inserted into a questionnaire (questionnaire for correct use of sodium alendronate):

1. "What time of the day do you take this medicine?"  
Answer options: morning; evening; night.
2. "How do you take this medicine?" Answer options:  
with any food (liquid or solid); fasting; as soon as  
I wake up.
3. "With what liquid do you take this medicine?"  
Answer options: with a full glass of water (American  
glass); with less than one glass of water (less than  
one American glass); with milk; with juice; with tea;  
with coffee; I do not use any liquid to take the tablet.
4. "How do you ingest sodium alendronate?" Answer  
options: swallow whole; dissolve in the mouth before  
swallowing; chew the tablet and then swallow;  
dissolve the tablet in a glass of water, for example,  
before swallowing; other.
5. "After taking sodium alendronate, what do you do?"  
Answer options: lie down; sit down; stand or walk  
until the time of the first meal of the day.
6. "After you use sodium alendronate, how long will  
you wait to eat the first meal of the day?" Response  
options: eat immediately after use of the tablet; wait  
at least 30 minutes for the first meal.

#### *Socio-demographic and economic characteristics*

These characteristics were evaluated by means of self-reporting, and the participants were classified according to age group (60-69/70-79/80+ years); schooling (never attended school/completed elementary school/completed high school); self-reported race/color (white/black/brown/Asian descent or indigenous); and private healthcare plan (yes/no).

#### *Statistical analysis*

Initially, the study population was distributed according to socio-demographic and economic characteristics by means of frequencies. The test-retest reliability was evaluated by percentage of concordance and the Kappa statistic. The 95% confidence intervals (95% CI) for the Kappa values were estimated. The Altman criteria were used for the interpretation of the

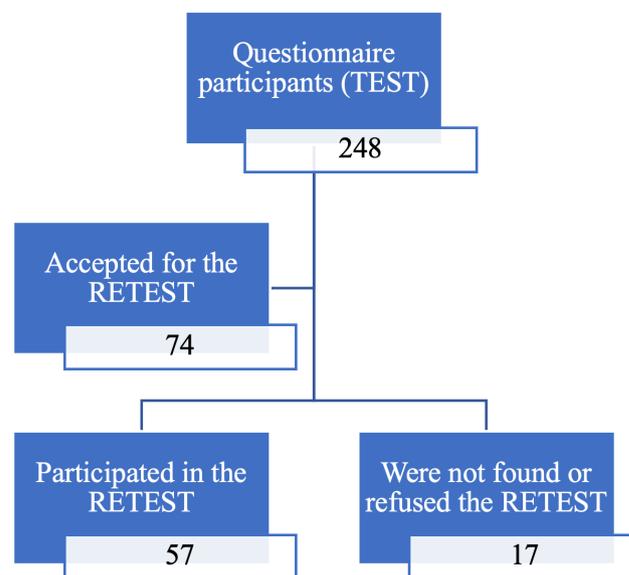
Kappa statistic: poor agreement: -1 to 0.2; weak: 0.2 to 0.4; moderate: 0.4 to 0.6; good: 0.6 to 0.8; very good: 0.8 to 1.0 (Altman, 1991). All analysis were performed with Stata 14 software.

#### *Ethical aspects*

This study was approved by the Research Ethics Committee of the Federal University of São João del Rei (number: 27582214.9.00005545).

## RESULTS AND DISCUSSION

Of the 779 elderly women eligible to participate in the study, 248 responded to the test. Of these, 74 (29.9%) initially accepted to participate in the retest, but 17 were not located or gave up at the time of the interview, thus totaling 57 (23.0%) elderly women who completed the research protocol (Figure 1). The mean time between the test and the retest was 9.3 days (SD =2.5 days).



**FIGURE 1** - Study participant input flow:

The mean age was 69.3 years (SD = 6.9 years), the majority had low education (92.5%), were self-declared white (50.9%), and approximately half (49.1%) had a private health care plan (Table I).

**TABLE I** - Socio-demographic and economic characteristics of users of sodium alendronate participating in the study. N = 57, Divinópolis, Minas Gerais State, Brazil (2014-2016)

Characteristics	N*	%
Age range (years)		
60 to 69	24	42.1
70 to 79	19	33.3
80 or more	14	24.6
Education		
Never attended school	5	13.2
Completed elementary school	42	79.3
Completed high school	4	7.5
Color/Race (self-reported)		
White	28	50.9
Black/Brown	20	36.4
Asian descent/Indigenous	7	12.7
Private health plan		
Yes	27	49.1
No	28	50.9

\*Different values are explained by missing information

In general, the questions presented high concordance, ranging from 79.0% to 98.3% and Kappa values ranged from 0.1 (poor) to 0.83 (very good) (Table II).

**TABLE II** - Concordance percentage and Kappa coefficient of the questions that evaluated correct use of sodium alendronate N = 57, Divinópolis, Minas Gerais State, Brazil (2014-2016)

Indicators	Test N (%)	Retest N (%)	Concordance (%)	Kappa (CI 95%)
What time of the day do you take this medicine?				
Morning	56 (98.2)	56 (98.2)	94.5	0.1 (0.008 - 0.398)
Afternoon	—	1 (1.8)		
Night	1 (1.8)	—		
How do you take this medicine?				
With any food	9 (15.8)	6 (10.5)	87.7	0.47 (0.134 - 0.798)
Fasting, as soon as I wake up	48 (84.2)	51 (89.5)		
With what liquid do you take this medicine?				
With a full glass of water	19 (33.3)	19 (33.3)	79.0	0.55 (0.473 - 0.651)
With less than one glass of water	36 (63.1)	38 (66.7)		
With milk	1 (1.8)	—		
I do not use any liquid	1 (1.8)	—		
How do you ingest sodium alendronate?				
Swallow whole	54 (94.7)	55 (96.5)	98.3	0.80 (0.491 - 1.000)
Dissolve in the mouth before swallowing	1 (1.8)	—		
Chew the tablet and then swallow	2 (3.5)	2 (3.5)		

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Indicators	Test N (%)	Retest N (%)	Concordance (%)	Kappa (CI 95%)
After taking sodium alendronate, what do you do?				
Lie down	8 (14.0)	8 (14.0)	93.0	0.83 (0.641 - 0.856)
Stay seated	7 (12.3)	7 (12.3)		
Stand or walk	42 (73.7)	42 (73.7)		
After you use sodium alendronate, how long will you wait to eat the first meal of the day?				
Eat immediately after use of the tablet	4 (7.0)	4 (7.0)	93.0	0.46 (0.006 - 0.908)
Wait at least 30 minutes for the first meal	53 (93.0)	53 (93.0)		

CI 95%: 95% confidence interval.

The question “*After taking sodium alendronate, what do you do?*” presented very good agreement, and the question “*How do you ingest sodium alendronate?*” presented good agreement. These results suggest that these questions may not present much subjectivity and therefore have been better understood by participants, in addition to the interviewees having prior knowledge about the guidelines.

The questions “*How do you take this medicine?*”; “*With what liquid do you take this medicine?*”; and “*After you use sodium alendronate, how long will you wait to eat the first meal of the day?*” showed moderate agreement. Some hypotheses may be used to explain this result: the question “*How do you take this medicine?*” may have been influenced by the subjectivity of the response options, since the term fasting may have different interpretations and generated confusion in answering the question. The question “*With what liquid do you take this medicine?*” may have been influenced by the amount of response options, which can knowingly influence the quality of the question, make it difficult for the respondent to answer, and as a consequence, reduce reliability (Terwee *et al.*, 2012). The question “*After you use sodium alendronate, how long will you wait to eat the first meal of the day?*” may have been influenced by the size and difficulty of interpreting the question.

Only the question “*What time of the day do you take this medicine?*” presented poor reliability ( $\geq 0.1$ ) and a high agreement percentage (94.5%), since only one of the respondents presented different answers between the test and the retest. It is known that one of the limitations of the Kappa statistic is that the result can be influenced

by the marginal totals being symmetrically unbalanced, which leads to a high concordance percentage and a low Kappa value (Feinstein, Cicchetti, 1990). However, even with the low Kappa value, we do not believe that the question cannot be used in epidemiological studies and clinical practice, since it is not difficult to understand.

It is necessary to present some limitations of the present study. It is suggested that samples of reliability studies have at least 100 participants (Terwee *et al.*, 2012). Thus, our sample of 57 participants limited the ability to evaluate the results stratified by characteristics that may influence reliability, for example, schooling and age. It is worth mentioning that studies show that individuals with more advanced age and a lower level of education tend to have greater difficulty answering some questionnaires (Pilger, Menon, Mathias, 2011), which may have compromised the understanding of some questions and generated confusion in choosing the answer, reducing the agreement of some questions of the questionnaire. Generally, a good part of the population of sodium alendronate users are public health system users and have, on average, high age and low schooling. In addition, our study population is composed of only women, which was expected, since the prevalence of osteoporosis is much higher among women (17.0%) than men (7.0%) (Fontes, Araujo, Soares, 2012). Therefore, it is expected that the number of female users of sodium alendronate will be much higher than that of males. Women are also the main users of health services and preventive treatments (Pinheiro *et al.*, 2002), as well as tend to participate more frequently in health surveys than men (Aquino *et al.*, 2013). Thus, we believe that our results support the use

of these questions for this population, which in general are women, with a high age and low educational level.

Finally, questions to assess the correct use of sodium alendronate were included in a larger survey in the first interview (test), which had an average duration of 30 minutes. Thus, time may have generated fatigue and wear on the participants, leading to different responses at the two different times, impacting differently on reliability. Two interviewers participated in the survey, which may have led to inter-interviewer interference, which sought to be reduced by prior training and standardization of the interviews.

On the other hand, we emphasize that as far as we know there are no instruments that are able to evaluate the use of sodium alendronate. The use of questionnaires in data collection in epidemiological studies, as well as in clinical practice, is quite frequent since they are non-invasive, and in general easy to apply (Pilatti, Pedroso, Gutierrez, 2010). The development of instruments such as those evaluated in this study is an interesting strategy to evaluate how sodium alendronate is being used. This is because it is a quick and easy to apply questionnaire that can also be easily applied during medicine dispensing. This study therefore innovates since it proposes quick and simple questions to evaluate the quality of the use of sodium alendronate and that the questions presented adequate reliability.

The concordance and Kappa percentage values found suggest adequate reliability of the six proposed questions as indicators of the correct use of sodium alendronate. In this sense, we suggest that the proposed questions can be used as a simple and quick way to evaluate the quality of use of sodium alendronate among the elderly, and thus contribute to strategies to promote the correct use of this medicine.

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