

# Adherence to Bisphosphonates among People Admitted to an Orthopaedic and Geriatric Ward at a University Hospital in Sweden

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**Abstract:** When it comes to treating osteoporotic fractures, oral bisphosphonates are the gold standard. Because of the limited oral bioavailability of these medications—which may be worsened by taking them with certain meals and other medications—it is critical to take them exactly as prescribed. People hospitalized to two wards at Umeå University hospital in Sweden were studied to determine their general and particular adherence to oral bisphosphonate and administration guidelines. Homebound seniors using oral bisphosphonates are the subject of this interview research. A total of twenty-seven patients hospitalized to either an orthopedic or geriatric ward between March 28, 2017, and December 5, 2017, were invited to participate. The adherence to oral bisphosphonate treatment was assessed in 21 individuals. Fifteen patients (62%) were deemed non-compliant out of twenty-one. Intake of calcium less than 2 hours after oral bisphosphonate therapy accounted for 54% of cases. The number of medications usually administered to patients who were found to be non-adherent to bisphosphonates was considerably greater than to those who were found to be adherent ( $p = 0.004$ ). Among home-dwelling seniors, adherence to bisphosphonate administration instructions was low. To validate these findings and learn more about non-adherence and how to enhance bisphosphonate adherence, more study is required.

**Keywords:** adherence; bisphosphonates; elderly

## 1. Introduction

Low bone mass and structural degradation of bone tissue define osteoporosis, a systemic illness that increases the risk of fractures without substantial damage. As the world's population ages, osteoporotic fractures are likely to become more common, adding to the enormous morbidity and death caused by osteoporosis [1]. Postmenopausal osteoporosis is one form of primary osteoporosis; secondary osteoporosis is another. Glucocorticoids and other drugs may induce secondary osteoporosis, which can be caused by a variety of illnesses [1].

Preventing osteoporosis and osteoporotic fractures requires a combination of medications. Sweden has a nationwide recommendation for oral bisphosphonates such as alendronic acid [2]. Bony surfaces, particularly those experiencing active resorption, have hydroxyapatite binding sites that bisphosphonates bind to. Bisphosphonates inhibit osteoclast activity and bone absorption. Enhanced osteoclast apoptosis and reduced osteoclast progenitor formation also suppress osteoclast activity [3]. Low oral bioavailability—roughly 1% to 7% of the amount given [3]—and the possibility of even lower absorption when combined with certain meals and drugs is a major issue with bisphosphonates. Because of this, patients have unique needs. Based on Janusmed interactions [5] and Swedish pharmaceutical specializations [4],

To get the best possible absorption, it is necessary to adhere to the given instructions. Take bisphosphonates first thing in the morning with a certain quantity of water on an empty stomach for the best absorption. For 30–60 minutes after treatment, the patient must remain upright and not drink, eat, or take any supplements [4]. Additionally, it is best to avoid taking iron supplements, magnesium, calcium, and other divalent cations for at least two hours after taking bisphosphonates since they may form complexes with bisphosphonates and further decrease their absorption [5].

Patients with osteoporosis should take bisphosphonates as prescribed since a decreased fracture incidence has been linked to good adherence [6]. The problem with osteoporosis medication adherence is that it is low. Some studies have shown poor rates of beginning, implementation, and adherence to these drugs; one such research was carried out in Estonia [7].

There is a lack of focus in medical literature about the need of following particular administration guidelines for bisphosphonates. This research set out to check how well older patients hospitalized to the orthopedic and geriatric wards at Umeå University Hospital in Sweden followed both the general and specialized instructions for taking oral bisphosphonates.

## 2. Materials and Methods

### *Material and Procedures*

The geriatric and orthopedic wards of Umeå University hospital in Sweden were the settings for this interview research. Patients who were hospitalized to the two wards between 5 June and 1 July 2017, as well as to the orthopaedic ward between 3 March and 5 December 2017, and who were sent home with an oral bisphosphonate prescription were invited to participate. The patients were enrolled later on in these time frames. The interviews took place in the hospital, right next to the patients' beds.

. During the interviews, participants were asked a series of questions regarding their bisphosphonate intake. These included when the medication is taken, how it is compared to other medications and food they eat, whether they swallow the bisphosphonates with water or another beverage, how frequently they forget to take them, and whether they receive assistance from family or friends with their medication. The Meaning of Bisphosphonate Adherence

This research did not account for patients following these recommendations for administration since it is difficult for them to estimate the quantity of water to use and because being upright is primarily advised to prevent injury to the oesophagus and not to boost bioavailability. However, the research also added an extra criteria for measuring bisphosphonate intake adherence, which is being reminded to take the bisphosphonates either infrequently or never. Statistically, the Pearson chi-square test and the independent sample t-test were used to study various aspects pertaining to adherence and non-adherence, respectively. It was deemed statistically significant if the p-value was less than 0.05. We used SPSS Statistics to do all of our statistical computations. The research was authorized by the regional Ethics Review Board in Umeå (nr 2017/216-31 and 2017/319-32).

## 3. Results

Between 28 March 2017, and 5 December 2017, 27 patients admitted to the orthopaedic and the geriatric ward and treated with oral bisphosphonates, were invited to participate in the study. Six patients declined participation. The remaining 21 patients were interviewed during their hospital stay. The average mean age of the patients was 75.2 years, the average mean number of medicines was 10.0 and the average mean numbers of years patients had bisphosphonate was 3.4 years (see Table 1).

**Table 1.** Characteristics of study population and comparison between people adherent and non-adherent to bisphosphonates.

	Non-Adherent (n = 13)	Adherent (n = 8)	Total (n = 21)	p-Value
Women; n (%)	13	8	21 (100.0)	
Mean age ± SD	74.8 ± 15.6	75.9 ± 8.5	75.2 ± 13.1	0.857
Ward				0.421
Orthopaedic ward; n (%)	12 (92.3)	8 (100.0)	20 (95.2)	
Geriatric ward; n (%)	1 (7.7)	0 (0.0)	1 (4.8)	
Cause of admission *				0.604
Fractures; n (%)	5 (38.5)	4 (50.0)	9 (42.9)	
Other; n (%)	8 (61.5)	4 (50.0)	12 (57.1)	
Cognitive impairment ** n (%)	3 (14.3)	0 (0.0)	3 (14.3)	0.142
Number of regular medications mean ± SD	12.5 ± 5.3	5.9 ± 2.7	10.0 ± 5.5 (3-23)	0.004
Dose-dispensed drugs n (%)	3 (14.3)	0 (0.0)	3 (14.3)	0.142
Help with medications n (%)	4 (30.8)	1 (12.5)	5 (23.8)	0.340
Indications for bisphosphonates				
Confirmed osteoporosis; n (%)	9 (69.2)	7 (87.5)	16 (76.2)	0.340
Glucocorticoid use; n (%)	4 (30.8)	1 (12.5)	5 (23.8)	
Numbers of years with bisphosphonates mean ± SD	3.1 ± 2.6	4.0 ± 4.8	3.4 ± 3.5 (1-15)	0.619
Calcium intake; n (%)	13 (100.0)	7 (87.5)	20 (95.2)	0.191

\* The most common fractures were femure fractures. Other causes of hospitalisation were for example pain, infections, and post-operative care. \*\* A patient was defined with cognitive impairment if this was stated in the medical record when the patient was admitted to the hospital.

According to the definition used in this study, 13 of the 21 interviewed patients (61.9%) were classified as non-adherent. The most common cause of non-adherence was calcium administration within 2 h of oral bisphosphonate intake ( $n = 7/13$ , 54%) (see Table 2). Two of these patients had dose-dispensed drugs (the drugs are dispensed into one unit for each dose occasion) and, in addition, assistance in drug administration by health care professionals. Intake of bisphosphonates together with food/other beverages than water and always/often/sometimes forget to take their bisphosphonates, were other causes for non-adherence. Moreover, two persons did not remember how they took their bisphosphonates and were therefore judged as non-adherent.

**Table 2.** Reasons for non-adherence to bisphosphonates.

Patients non-adherent	<i>n</i> = 13
Calcium administrated within two hours; <i>n</i> (%)	7 (54.0)
Intake of bisphosphonates together with food/other beverages than water; <i>n</i> (%)	2 (15.4)
Always/often/sometimes forget to take their bisphosphonates; <i>n</i> (%)	2 (15.4)
Did not remember how they took their bisphosphonates; <i>n</i> (%)	2 (15.4)

When comparing patients judged as non-adherent with patients considered adherent to bisphosphonates on a group base, there was no statistically significant difference between the groups except for the number of regularly prescribed drugs, which was significantly higher among patients judged non-adherent to bisphosphonates ( $p = 0.004$ ) (see Table 1).

#### 4. Discussion

The data can only provide an idea of patients' degree of adherence to bisphosphonates since this is a tiny trial. Nevertheless, it is crucial to pay attention to these outcomes since bisphosphonate administration instructions adherence has been understudied. Eight out of twenty-one patients were considered to have adhered to bisphosphonate treatment based on the standards set forth in this research. In particular, most patients did not follow the advice to wait at least two hours after taking bisphosphonate before taking any medications, including calcium, that might interfere with bisphosphonate absorption.

A recent thorough assessment predicted that 6–55% of home-dwelling elderly adults with polypharmacy would not adhere to their medication regimens [8]. In this research, a somewhat greater frequency of non-adherence to bisphosphonates was found (62%). The main issue with adherence in this content is incorrect drug ingestion, not medication persistence. It is also difficult to compare prevalence figures across research due to the fact that many publications utilize different definitions of adherence [9–18]. According to a prior Swedish registry research, half of all osteoporosis patients stopped taking their medication after a year, indicating that treatment adherence is low. On the other hand, adherence was strong among those patients who kept taking their osteoporosis medication [6]. With the exception of two patients who were interviewed, all patients in this research had begun bisphosphonate therapy and were consistently taking their medicine as prescribed. Treatment start and maintenance seem to be minimal issues with this material. In this research, non-compliance with the detailed instructions for administration was the leading cause of nonadherence. Intake of bisphosphonate and calcium at the same time or failing to observe the prescribed intervals between doses was the leading cause of non-adherence. Bisphosphonates should be administered with vitamin D and calcium supplements; however, the patient should be aware and follow the directions not to take calcium within two hours after taking bisphosphonates orally in order to ensure bioavailability.

While participating in this research, two patients had trouble comprehending certain interview questions and forgot to take their medicine as prescribed. Given that they were often living at home and managing their prescription regimen alone, this brings up concerns about their overall capacity for effective drug administration. Pharmacists have shown that even mild cognitive impairments reduce drug adherence [19]. The correct administration of bisphosphonates is complicated and calls for a great deal of patient knowledge and detailed instructions from healthcare providers [20]. Those who have trouble taking alendronic acid as prescribed should be given zoledronic acid (intravenous bisphosphonate) instead, according to the guidelines [5]. This alternative could be used more frequently to guarantee that osteoporosis prophylaxis is effective [20].

The current research found that compared to patients who were not deemed non-adherent to bisphosphonates, those who were treated with a higher number of drugs were also not considered adherent. More substantial correlations between adherence and other variables may have been discovered in a bigger research. However, the finding is consistent with a previous analysis that found a negative correlation between medication adherence and the quantity of medicines used by those living at home [8]. In particular, the elderly may be more susceptible to the negative effects of polypharmacy on drug adherence [21]. It stands to reason that patients who have access to dose-dispensing devices are more likely to stick to their prescription regimens and to seek out external assistance when needed [22]. Unfortunately, our data did not show any good impacts of dosage distribution devices or assistance with drug administration since prescribers likely did not provide correct administration instructions when they administered calcium and alendronate together. The small sample size might be a contributing factor here. On the other hand, a major Swiss research on diabetic medication adherence found no effect of dosage delivery methods on medication adherence [23]. Proper information on the administration of oral bisphosphonates should be more heavily emphasised, according to the results and observations of the current research. This is true not only for patients but also for prescribers, home care workers, and relatives of patients.

We must take into account the fact that this research has certain limitations. During the research period, a small number of patients were admitted to the hospital for various causes; the majority of these patients were admitted to an orthopedic ward, while just one patient was admitted to a geriatric ward. This study's results should be treated with caution due to the low level of population representation and the potential for bias and chance findings. Furthermore, the findings should be taken with care since the possibility of finding statistically significant associations is quite low owing to the minimal number of data. In conclusion, the degree to which patients adhere to bisphosphonates while living at home can only be approximated by this research. Patients' memory functions may be impaired due to the stress that comes with being admitted to the hospital [24]. Although there is a lack of adherence among this group of patients administered bisphosphonates, our findings are generally consistent with previous research. Improving adherence to bisphosphonates requires more investigation.

## 5. Conclusions

This small study found that adherence to bisphosphonates among elderly people living at home was poor and mostly related to improper administration. More research is needed to confirm these results and to investigate the reasons for non-adherence and how adherence to bisphosphonates can be improved.

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