

Community Pharmacists' Knowledge towards the Proper Dosing Instructions and Interactions of Alendronate Therapy

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ABSTRACT

Alendronate is one of the most commonly prescribed drugs for the treatment of osteoporosis and other diseases characterized by increased bone resorption. Poor compliance increases the fracture risks, and ultimately treatment failure. This study aims to evaluate Palestinian pharmacist's knowledge of the proper administration instructions, interactions and side effects of Alendronate as this significantly affect the medical effectiveness and the development of adverse effects. Self-administered questionnaires were completed by 230 pharmacists working in community pharmacies in the northern area of the West Bank. Data were collected using a validated questionnaire consisting of 4 sections and analyzed by descriptive statistics. A scoring scheme was developed to estimate the knowledge scores of participants for the various parameters. The obtained knowledge scores were correlated with the socio-demographics characteristics of the pharmacist's. The median knowledge score of the pharmacists regarding the proper use of Alendronate was moderate i.e., 6 out of a possible maximum score of 9. The knowledge score of Alendronate interactions with food and other medications was 10.5 out of a possible maximum of 14 which is considered as a moderate score, whereas, that for side effects was 4 (0-8). Factors affecting the knowledge towards Alendronate dosing instructions, side effects, and interactions were gender, employment status, years of experience and work place. In conclusion, Palestinian pharmacists have intermediate knowledge about the proper use, drug-food interactions and side effects of Alendronate. Knowledge gaps were identified by this study. Therefore, improving pharmacist's knowledge is of great importance to achieve better efficacy and safety from the treatment.

Keywords: Osteoporosis, Alendronate, Dosing instructions, Knowledge.

INTRODUCTION

Osteoporosis is a degenerative bone disease characterized by low bone mass and an increased susceptibility to fractures that is common in postmenopausal women. Bisphosphonates are commonly prescribed for the treatment of osteoporosis. They exert their effects by increasing bone mineral density and inhibiting the osteoclast-mediated bone resorption, thus, reducing the incidence of major osteoporotic fractures (1, 2). The adherence to oral bisphosphonates therapy among patients was shown to be inadequate (3, 4). Such poor adherence was associated with a lower rate of bone turnover and greater risk of fractures (5, 6, 7). About 75% of postmenopausal women who took oral bisphosphonates were non adherent to the treatment within one year and half of patients

stop their therapy by this time (8). Similar findings were reported by Weycker *et.al*, 2006. The overall compliance rate of patients was approximately 40% one year after the initial dose (9). The compliance and persistence in patients using bisphosphonates weekly was better than those using them daily, but in both cases persistence rate was suboptimal (10,11). The most common barriers for optimal adherence included: the experienced adverse effects (GI intolerance) and the complex dosing requirements (9, 12, 13, 14).

The oral bioavailability of Alendronate is low (0.75% in the fasting state). Co-administration of the drug with food, black coffee, orange juice, mineral water and dairy products was shown to further decrease the oral absorption of Alendronate. Moreover,

medications containing calcium salts, iron, magnesium salts, antacids and multivitamins can further reduce the absorption of Alendronate (15, 16). The concomitant intake of aspirin and non-steroidal anti-inflammatory agents (NSAIDs) may increase the incidence of upper gastrointestinal side effects of Alendronate and the risk of nephrotoxicity. Food and drug interactions with Alendronate may lead to treatment failure, as the oral bioavailability may decline to negligible levels. For this reason, dosing instructions require that bisphosphonates should be administered in the early morning at least 30 minutes before breakfast or other medications with 6 to 8 ounces of plain water and to remain in upright either sitting or standing for at least 30 minutes after dose administration (17).

Poor understanding of dosing instructions by patients could increase the risk of adverse effects and reduce the therapeutic effectiveness of the drug or may result in poor adherence. Adherence to the dosing instructions will reduce the risk of the side effects.

The pharmacist is responsible for educating the patient about the proper dosing information to minimize adverse effects severity and incorrect use of the drug. Pharmacists should provide patient counseling about Alendronate adverse effects, dose instructions, drug-drug interactions and drug food interactions. Therefore, improving the outcomes of the therapeutic process will depend to a great extent on the knowledge of pharmacists about the proper dosing information. A wide variability in pharmacists' knowledge toward the correct administration instructions of Alendronate can lead to poor compliance. Thus identifying the knowledge deficit is important (18, 19).

Pharmacist's knowledge of Alendronate dosing information has not been widely studied. A previous study was conducted to assess the knowledge of pharmacists toward the proper dosing instructions of three bisphosphonates (Alendronate, Risedronate and Etidronate) in British Columbia, Canada. A wide range of knowledge basis regarding the proper use of bisphosphonates was shown. The study, which involved 163 community pharmacy practitioners, showed higher

knowledge scores for the questions related to Alendronate than Etidronate and Residronate. The pharmacists demonstrated less awareness of some general dosing principles such as the need to remain in upright position after drug intake, drug spacing from other medications, food and drinks. Pharmacists who were employed in higher volume pharmacies and those who had higher number of years in practice had higher knowledge scores (20).

Palestinian pharmacists' knowledge toward the dosing instructions and interactions of Alendronate has not been studied before. The main objectives of this study were to assess community pharmacists' knowledge of the proper administration instructions of Alendronate and the potential Alendronate - drug and Alendronate -food interactions as this significantly correlates with the medical effectiveness and development of adverse effects. Part of the aim of this study is to highlight the therapeutic role of community pharmacists on improving medication adherence and maximizing the therapeutic efficacy of Alendronate therapy.

MATERIALS AND METHODS

Study design

This is a cross sectional study using a self-administered questionnaire that was conducted in the time period between July 2015 and December 2015. The population of the study was 230 pharmacists working in community pharmacies in the Northern area of the West Bank, which consist of 4 governorates: Nablus, Qalqiliah, Jenin and Tulkarem.

The tools of the study

The questionnaire used in the tool consisted of four parts: the first section consisted of general demographic data of the pharmacist, which included: gender, age, workplace, education level and years of experience. The second section was measuring pharmacist's knowledge of the proper use instructions, and contained 9 questions. These were multiple-choice questions and were designed to test pharmacist's information about the proper dosing instruction of Alendronate. A knowledge score was defined as the number of correct answers to the 9 questions that evaluated the participants' knowledge of

Alendronate use. The respondent had a good knowledge when the total score ranged from 7 to 9 points; intermediate knowledge if the total score ranged from 4 to 6 points and the respondent had a poor knowledge if the total score ranged from 0 to 3 points. The third section was designed to measure the knowledge of pharmacists about Alendronate food and drugs interactions; it contained 15 questions. This section offered the following answers: yes, no, I don't know. The respondent had a good level of knowledge if the total knowledge score ranged from 11 to 15 points; intermediate knowledge if the total score ranged from 6 to 10 points and the respondents had a poor knowledge if the total score ranged from 0 to 5 points. The fourth section was to assess pharmacist's knowledge about the common adverse effects of Alendronate; it contained 8 questions.

This section consisted of the following answers: yes, no, I don't know. The respondent had a good level of knowledge when the total knowledge score ranged from 6 to 8 points, whereas, the respondent had intermediate knowledge if the total score ranged from 3 to 5 points and poor knowledge if the total score ranged from 0 to 2 points.

Ethical Considerations

The study protocol was approved by the Institutional Review Board (IRB) committee at An-Najah National University, Palestine. The authors obtained verbal consent from the community pharmacists who participated in the study.

Statistical analysis

Data were analyzed using Statistical package for social sciences program version (6) (SPSS). Continuous variables were expressed as mean \pm SD, while categorical variable were expressed frequency. Mann-witney test used for gender, work place, work type and employment status, whereas, kruksalwallis H test used for work locality, educational level, and expert years.

RESULTS

Socio-demographic of the pharmacists

The total number of surveys distributed was 264, of which 230 were returned back (response rate 87.12%). Nearly half of the

surveys were answered by male (50.4%). The ages of the pharmacists were divided into five categories, with the category (20-29 year) being the highest in frequency 43.8% (n=101). About 61.7% (n=142) pharmacists were primarily from pharmacies located in urban areas, whereas, 34.3% (n=79) were from rural area. The majority of the pharmacists 86.1% (n=198) had a bachelor of pharmacy level of education. About 61.3% (n=141) were employees in the pharmacies and not pharmacy owners.

Knowledge of the pharmacist's about the proper alendronate administration instructions

In this section, the pharmacists were asked about the proper administration instructions for Alendronate as a medicine for the treatment of osteoporosis (Table 1). All of participants were able to recognize Alendronate and 88.3% (n=203) of them believed that they have sufficient knowledge about this drug. The sources of this knowledge were reported to be from the university studies (40%, n=92), the practice experience (37%, n=85), drug leaflets (16.1%, n=37) and media (4.3%, n=10), whereas 2.6% (n=6) could not remember their information source.

The weekly dose of Alendronate (70mg) was recognized by the pharmacists to be the most commonly dispensed dose in their pharmacies (87%, n=200). Regarding the daily dose (10 mg) inquires, the pharmacists were asked about their recommendations if the patients missed their daily dose: 31.3% (n=72) of the pharmacists recommended taking the missed dose as soon as they remembered, 48.7% (n=112) of the pharmacists advised skipping the missed dose, while 20% (n=46) of pharmacists recommended taking the missed dose and the following dose together.

On the other hand, if the patients missed their weekly dose, 78.3% (n=180) of the pharmacists answered correctly: to take the tablet the next day of the same week and return to taking the dose once a week as originally scheduled.

Table (1): The knowledge about the proper administration instructions of Alendronate.

| Variable | Frequency for correct answer |
|---|------------------------------|
| Forgotten daily dose | |
| Take it as soon as you remember | 72 (31.3%) |
| Forgotten weekly dose | |
| Take the tablet on the morning once remembered and return to taking one tablet once a week as originally scheduled. | 180 (78.3%) |
| It's important to take the dose in the same time weekly or daily | |
| Yes | 217 (94.3%) |
| What is the usual time for taking it | |
| Morning | 170 (73.9%) |
| Timing of Alendronate intake regarding to meal | |
| Thirty mint before meal intake | 137 (59.6%) |
| Amount of water normally taken with it | |
| Large cup | 196 (85.2%) |
| It's important to take a special position while dose intake | |
| Yes | 206 (89.6%) |
| Pharmacist advice patient for up-right position while dose intake | |
| Yes | 172 (74.8%) |
| What to do if the patient take an over dose | |
| Taking a glass of milk | 167 (72.6%) |
| The time that patients can continue taking Alendronate | |
| It does not matter; It can continue as it wants | 66 (28.7%) |
| Patients counseling | |
| Yes | 219 (95.2%) |
| Advising patient for leaflet reading | |
| Yes | 164 (71.3%) |
| No | 66 (28.7%) |
| It's important for patient to notice their dentist about Alendronate | |
| Yes | 97 (42.2%) |
| No | 133 (57.8%) |
| Timing between alendronate and other medication | |
| Take Alendronate 30 minutes before other drugs | 163(70.9%) |

While 8.3% (n=19) of pharmacists recommended taking two tablets in the next week at the same time, and 13.5% (n=31) pharmacists advised to ignore the missed dose and take the same usual dose in the next week. The majority of the pharmacists (94.3%, n=217) emphasized the importance of taking Alendronate dose at the same time either daily or weekly with the favoring time for intake of Alendronate the morning 73.9% (n=170). When the pharmacists were asked about the timing of the drug with regards to food. The results indicated that 59.6% (n=137) of the pharmacists recommended taking the drug 30 minutes before the meal, 20% (n=46) recommended to take the drug

one hour before the meal, 9.6% (n=22) recommend taking the drug immediately before the meal. While small percentage of pharmacists recommended to take the drug one hour after the meal, or didn't know the answer. Regarding the amount of water to be taken with the drug, the majority of the pharmacists (85.2%, n=196) advised to take a large cup of water, whereas, only 12.6% (n=29) with small cup of water, While 2.2% (n=5) of pharmacists didn't know the answer. The majority of pharmacists recognized the importance of the body position with Alendronate dose intake (89.6 %, n=206) and was able to identify the up-right position as the most appropriate position (74.8%, n=172). About 72.6% (n=167) of the pharmacists

recommended drinking a glass of milk in case of overdose of Alendronate. Regarding the duration of Alendronate therapy, 41.7% (n=96) of the pharmacists thought that the duration must not exceed 1 to 2 year, 29.6% (n=68) the duration must not exceed 3 to 5 year. While 28.7% (n=66) of the pharmacists answered the patients can continue their therapy as long as they can.

The majority of the pharmacists (95.2%) reported providing adequate counseling about the proper way for administration of Alendronate while dispensing the alendronate drug and (71.3%) advised their patients to read drug leaflet. Whereas 42.2% of pharmacists thought that it is important to notify the dentist that the patient is taking Alendronate drug.

Pharmacists Knowledge about alendronate interactions

In the section of food - Alendronate interactions: As can be seen in Table (2), 81.3% (n=187) of the respondents believed that Alendronate could be taken with tap water, when 37.8% (n=87) reported that it could be administered with mineral water. On the

other hand, 13.0% (n=30) responded that Alendronate can be administered with coffee, whereas, 13.5% (n=31) answered yes to the question whether Alendronate can be administered with tea or not. Among all participants, a small number believed that it could be taken with milk 25.2% (n=58). Furthermore, 35.2% (n=81) and 20.9% (n=48) believed that Alendronate could be taken with fruit juices and dairy products, respectively.

Regarding pharmacists' knowledge about Alendronate drug-drug interactions (Table 2). When the respondents were asked about the specific Alendronate -drug interactions (59.6%) reported that Alendronate could be taken concomitantly with calcium supplements, (73%) with vitamin D without affecting Alendronate absorption and (34.3%) reported that it can be taken concomitantly with antacids. While, (30%) reported that Alendronate can be administered with cortisone, and (58.7%) believed that it can be taken with NSAIDS. Whereas, (56.5%) reported that it can be taken with Antibiotic.

Table (2): About Alendronate food-drug interactions.

| Is it possible to administer it with the following | | | |
|---|-------------|-------------|---------------------|
| Food or beverages | Yes | No | I don't know |
| Tap water | 187 (81.3%) | 37 (16.1%) | 6 (2.6%) |
| Mineral water | 87 (37.8%) | 123 (53.5%) | 20 (8.7%) |
| Milk | 58 (25.2%) | 146 (63.5%) | 26 (11.3%) |
| Coffee | 30 (13.0%) | 168 (73.0%) | 32 (13.9%) |
| Tea | 28 (12.2%) | 171 (74.3%) | 31 (13.5%) |
| Dairy products | 48 (20.9%) | 150 (65.2%) | 32 (13.9%) |
| Leafy vegetables | 83 (36.1%) | 91 (39.6%) | 56 (24.3%) |
| Fruit juices | 81 (35.2%) | 97 (42.2%) | 52 (22.6%) |
| Medications | | | |
| Ca supplements | 137 (59.6%) | 88 (38.3%) | 5 (2.2%) |
| Vitamin D | 168 (73%) | 54 (23.5%) | 8(3.5%) |
| Antacids | 79 (34.3%) | 129 (56.1%) | 22 (9.6%) |
| Cortisone | 69 (30%) | 131 (57%) | 30 (13%) |
| NSAIDS | 135 (58.7%) | 72 (31.3%) | 23 (10%) |
| Antibiotic | 130 (56.5%) | 57 (24.8%) | 43 (18.7%) |

Pharmacists' knowledge about Alendronate side effects

As we proceeded to the side effects section, the prevalence of side effects among patients on alendronate therapy was reported to be (Table 3): gastritis 86.5% (n=199), pep-

tic ulcer 51.3% (n=118) indigestion problems 58.7% (n=135), and difficulty swallowing 56.1% (n=129). Others reported side effects were bleeding, periorbital and joint and muscle pains.

Table (3): The prevalence of side effects experienced by patients on Alendronate.

| Side effects | Yes | No | I don't know |
|----------------------------|-------------|------------|--------------|
| Gastritis | 199 (86.5%) | 13 (5.7%) | 18 (7.8%) |
| Peptic ulcer | 118 (51.3%) | 47 (20.4%) | 65 (28.3%) |
| Bleeding | 59 (25.7%) | 84 (36.5%) | 87 (37.8%) |
| Indigestion | 135 (58.7%) | 54 (23.5%) | 41 (17.8%) |
| Difficulty in swallowing | 129 (56.1%) | 47 (20.4%) | 54 (23.5%) |
| Periorbital pain | 91 (39.6%) | 65 (28.3%) | 74 (32.2%) |
| Joint pain and muscle pain | 106 (46.1%) | 67 (29.1%) | 57 (24.8%) |

Relationship between the socio-demographic properties of the pharmacists and the Knowledge scores

Table (4) shows the association between the socio-demographic characteristics of the pharmacists and the various knowledge scores. The median knowledge score for Alendronate use was intermediate 6 (1-9). The median knowledge score use for Alen-

dronate interactions was 10.5 (2-14), which indicate good knowledge. Whereas, the median Alendronate side affects knowledge score was 4 (0-8). Knowledge scores for females were higher than for males. Pharmacists who had experience years more than 40 years had higher knowledge score values compared with less experienced pharmacists.

Table (4): The relationship between socio-demographic characteristics of the pharmacists and the various knowledge scores.

| Variable | Knowledge Score for proper use | | Knowledge Score for interactions | | Knowledge Score for Side effects | |
|--------------------------|--------------------------------|---------|----------------------------------|---------|----------------------------------|---------|
| | Inter quartiles Median | P-value | Inter quartiles Median | P-value | Inter quartiles Median | P-value |
| Gender | | | | | | |
| Male | 6 (5-7) | 0.027 | 9(6-11) | 0.072 | 4(2-6) | 0.521 |
| Female | 6 (5-7) | | 10(8-12) | | 4(3-6) | |
| Work locality | | | | | | |
| Urban | 6 (5-7) | 0.536 | 10(7-12) | 0.533 | 4(3-6) | 0.803 |
| Rural | 6(5-7) | | 10(8-12) | | 4(2-6) | |
| Camp | 7(4.5-8) | | 8(5-10) | | 4(2.5-5) | |
| Educational level | | | | | | |
| Bachelor pharmacy | 6 (5-7) | 0.992 | 10(7-11) | 0.111 | 4(2-6) | 0.248 |
| Doctor of pharmacy | 6 (5-7) | | 10(9-13) | | 5(4-6) | |
| Post graduated | 6 (5-7) | | 10(9-14) | | 5(4-5) | |
| Employment status | | | | | | |
| Pharmacy owner | 6 (5-7) | 0.904 | 10(6-12) | 0.729 | 4(2-6) | 0.793 |
| Employee of pharmacy | 6(5-7) | | 10(8-11) | | 4(3-6) | |
| Expert years | | | | | | |
| 0-9 | 6 (5-7) | 0.000 | 10(8-12) | 0.000 | 4(3-6) | 0.000 |
| 10-19 | 6 (5-7) | | 9.5 (7-11) | | 4(2-6) | |
| 20-29 | 5 (4-7) | | 9.5 (6-10) | | 3(1-5) | |
| 30-39 | 6 (5-7) | | 11 (7.5-12.5) | | 4(2.5-6) | |
| More than 40 | 6 (5.5-7) | | 6(4-8.5) | | 5(4-5.5) | |

DISCUSSION

Osteoporosis is a bone degenerative disease characterized by high risk of fractures. Patient's adherence to osteoporosis medications is suboptimal, which is considered a problem that increases their potential to fractures. The experienced side effects and the improper way of using oral bisphosphonate medications by patients are strongly associated with bisphosphonate non-adherence.

Community pharmacies are the most accessible health care facilities to the patients. Knowledge of pharmacists on the proper dosing information could greatly influence their patient compliance to their therapy. The pharmacist position is to deliver counseling on the proper dosing instructions and the interactions of the medication to improve patient's awareness about the disease and adherence. The present study is the first study of its kind in Palestine, which tried to assess the knowledge of community pharmacists to the proper dosing instructions and food-drug interactions of Alendronate.

In this study we analyzed pharmacists' knowledge in terms of Alendronate dosing instructions, interactions and side effects, which are described in this study as a knowledge score. Furthermore, we tried to find associations between pharmacist's socio-demographic characteristics, and their knowledge of Alendronate therapy.

It was clear that Palestinian pharmacists in general have an intermediate knowledge towards the general dosing principles of Alendronate (6/9). They have a good level of knowledge regarding the food and drug interactions of Alendronate (10.5/14). However, the pharmacists were least knowledgeable about adverse effects experienced by the patients (4/8). More than half of them have inadequate knowledge to the instructions regarding concomitant drinks, food and medications. The Pharmacists were less aware of the types of beverages that should not be administered with Alendronate.

Community pharmacists exhibit variable knowledge of Alendronate dosing, adverse effects, and interactions. These results are similar to a previous study in Canada that assessed pharmacist's knowledge of Alendronate dosing instructions and concluded that there is a wide range of knowledge of bisphosphonate dosing and delivery of pharmaceutical care amongst community pharmacists surveyed (20).

Moreover, higher scores were seen for pharmacists who have longer years of experience (p value less than 0.05). Older pharmacists might have more concern about medication use and interactions than younger pharmacists. However, these findings showed no association between the different knowledge scores and demographic factors such as age, work place, work status and Education Level (p value $>$ 0.05). Intuitively, it may be expected that pharmacist with higher educational level should have better knowledge about the Alendronate therapy.

However, there were no significant association between the higher level of education and knowledge score. "Higher level of education does not mean better knowledge". Pharmacy owners had lower knowledge score values than those who were employed in the pharmacies. Pharmacists working in camps had better knowledge score of proper use than those in urban and rural areas. Urban pharmacists had a good side effects knowledge score, whereas pharmacists in rural had a good food-drug interactions knowledge score.

Pharmacists have a significant role in improving medication adherence among patients. A previous study in Malaysia indicated that pharmacists have a role in improving medication adherence to Alendronate. Pharmacists have the responsibility of providing the patient with information about the drug, its potential side effects, the proper dosing instructions, when to take the medication in relation with food as well as types of beverages and medications to be avoided.

The quality of pharmacists-patient relationship is one of the most important factors to improve patients' adherence (18, 19). Poor pharmacists' communication concerning the benefits, instructions for use, and side effects of medications can contribute to patients' non-adherence. Pharmacists should assess patient's understanding of their illness and treatment, clearly communicate the benefits of the treatment and identify and discuss any barriers or obstacles to adherence, and formulate strategies for overcoming them with the patient.

Moreover, they should be aware that the crowded environment usually found in Palestinian community pharmacies may negatively affect patients' understanding of instructions and medications adherence. Furthermore, it is necessary for pharmacists to improve patients' understanding of Alendronate's leaflet contents.

Avoidance of drug interactions does not necessarily mean avoiding drugs or foods. In the case of Alendronate and dairy products and calcium supplement, these should simply be taken at different times; rather than eliminating one or the other from the diet. In addition, it is imperative for healthcare providers to keep up-to date on potential drug-food interactions of medications, in order to counsel properly to their patients.

This study emphasizes the importance of pharmacist's role in educating the patients about their drug therapy, and the benefits of compliance with dosing instructions, which in turn would help in improving future medical care in Palestine.

Efforts should be made to improve the pharmacists' knowledge about the proper use of Alendronate and food-drugs interactions as well as to identify the barriers that may interfere with the pharmacists' proper knowledge of instructions and implementing the strategies to overcome them.

The ministry of health should implement educational programs to educate health care providers about Alendronate therapy. Education programs are required as presentations,

conferences', workshops, study groups, home study courses, reading journals, accessing references' materials and online distance educating courses about Alendronate proper use, food-drug interactions and adverse effects.

CONCLUSIONS

In conclusion, the community pharmacists' knowledge towards the specific dosing instructions of Alendronate medication and its –food and-drug interactions was intermediate knowledge. There is a need to have training programs to improve the knowledge of pharmacists on the proper dosing instructions and interactions of Alendronate, which could greatly influence the impact on patient compliance to their medication.

CONFLICT OF INTERESTS

The authors report no conflicts of interest in this manuscript.

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