



Switching from one generic alendronate to another — a common procedure in Poland in the years 2001–2005

Częste zmiany leku z jednego alendronianu na drugi
w Polsce w latach 2001–2005

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Abstract

Introduction: In clinical ambulatory practice, patients often, rather than discontinuing treatment, change to another one. This study aims to assess the reasons why patients with osteoporosis switch from one alendronate to another with a different brand name.

Material and methods: A retrospective analysis of 747 bisphosphonate-treated patients was performed (651 female, average age 67.3 ± 8.9 years, BMI 26.5 ± 4.0 kg/m²). The frequency and reasons for drug switching during the 19.4 ± 13.4 months of observation were analysed.

Results: In 387 (51.8%) patients, treatment was not changed during the observation period, whereas in 360 (48.2%) patients, at least one drug switch occurred. Almost 40% of patients from that group (138 patients) switched from one alendronate to another alendronate with a different brand name. The most frequent reasons were: adverse event (36.9%), high price of the drug (23.2%) and request of patient (16.7%).

Conclusions: A substantial proportion of persistent bisphosphonate-treated patients switch treatment from one alendronate to another. The most frequent reasons for that kind of switching are the occurrence of an adverse event and the high cost of treatment.

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Key words: osteoporosis, alendronate, adherence, persistence, compliance, switching

Streszczenie

Wstęp: W praktyce lekarskiej pacjenci ambulatoryjni raczej zmieniają leczenie, niż zaprzestają go w ogóle. Niniejsze badanie miało na celu ocenę powodów, z jakich pacjenci chorzy na osteoporozę zmieniają jeden preparat alendronianu na drugi o innej nazwie.

Materiał i metody: Przeprowadzono retrospektywną analizę 747 chorych leczonych bisfosfonianami (651 kobiet, średni wiek $67,3 \pm 8,9$ lat, BMI $26,5 \pm 4,0$ kg/m²). Analizowano częstość i powody zmian leków w trakcie obserwacji przez $19,4 \pm 13,4$ miesięcy.

Wyniki: U 387 (51,8%) chorych leczenie nie było zmieniane w trakcie obserwacji, podczas gdy u pozostałych 360 (48,2%) leki zmieniano przynajmniej raz. Prawie 40% chorych z tej grupy (138) zmieniło leczenie z jednego alendronianu na drugi, o innej nazwie. Najczęstszymi powodami takiej zmiany były: działania niepożądane (36,9%), wysoka cena leku (23,2%) i prośba chorego (16,7% zmian).

Wnioski: Znaczny odsetek leczonych bisfosfonianami chorych zmienia leczenie z jednego alendronianu na drugi. Najczęstszymi przyczynami takich zmian było wystąpienie objawów niepożądanych i wysoki koszt leku. (Endokrynol Pol 2011; 62 (1): 14–17)

Słowa kluczowe: osteoporoza, alendronian, stosowanie się do zaleceń lekarskich, zmiana leku

Introduction

To achieve the main aim of osteoporotic treatment, i.e. a reduction of incident fractures, long-term pharmacological treatment is necessary. However, even during short treatment periods it is not easy to achieve proper adherence to the therapy. Many patients are either non-

compliant, or non-persistent, or both [1]. In such patients, treatment is suboptimal and the risk of bone fracture is increased [2]. Therefore, another consequence of poor adherence is an increase in healthcare costs [3].

There is a great deal of published data relating to non-adherence, most of which comes from prospective, pre-designed clinical trials. For example, it has been



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Table I. Basal characteristics of patients

Tabela I. Podstawowe dane pacjentów

Parameter	Non-switchers n = 387	Switchers to alendronate n = 138	Switchers to another treatment n = 222	p*
Age	66.9 ± 8.9	67.9 ± 9.4	67.8 ± 8.6	0.21 (NS)
Gender	340 F/47 M	119 F/19 M	192 F/30 M	0.83 (NS)
BMI	26.6 ± 4.0	26.9 ± 4.4	25.9 ± 3.8 [^]	0.071
Fractures at baseline ^a	113/346 (32.7%)	43/109 (39.4%)	50/139 (36.0%)	0.40 (NS)
Time of observation	16.6 ± 8.5	20.1 ± 13.3 [#]	23.7 ± 18.4 [#]	< 0.0001
Time to the first switch	–	9.6 ± 9.7	10.8 ± 10.8	0.45 (NS)
Calcium/Vit. D supplementation ^a	345/354 (97.5%)	110/112 (98.2%)	146/148 (98.6%)	0.67 (NS)

*Statistical significance of differences among three groups; Kruskal-Wallis test was used for quantitative variables and χ^2 test for qualitative variables; [^]p < 0.05 for difference in comparison to switchers for alendronate group (Mann-Whitney test); [#]p < 0.05 for difference in comparison to non-switchers group (Mann-Whitney test); ^aData missing in some patients; percentage calculated for patients from data available

shown that in Poland more than 20% of post-menopausal women discontinue bisphosphonate treatment within 18 months of its initiation [4]. In clinical practice however, if patients are not compliant or persistent for any reason, they are usually encouraged by the treating physician to restart the drug or to start another drug in order to achieve the optimal adherence [5]. That means that many patients do not stop the treatment, but change it.

Our study aimed to re-analyse data from the previous trial [5], focusing on switching from one alendronate to another with a different brand, in order to assess the reasons for that switch, and the differences between switchers and non-switchers.

Material and methods

Seven hundred and forty seven alendronate-treated patients (from the 1,314 patients assessed retrospectively in four osteoporosis centres in Poland) were included in the analysis, the mean age of the group being 67.4 ± 8.9 years and the BMI 26.5 ± 4.0 kg/m².

Neither the presence of 'osteoporosis' according to the WHO definition (T-score < -2.5), nor the risk of fracture, were predefined as inclusion/exclusion criteria. Bone mineral density (BMD) results were therefore not recorded. Every change of medication and the reasons for it were recorded. The latter were classified as: adverse events, treatment failure, therapy cost being too high, patient request, the switch being made in another outpatient clinic or hospital, treatment success, or an overlong (in a physician's opinion) period of therapy. Treatment failure (as defined by the treating physician), was occurrence of osteoporotic fracture, a significant decrease of BMD, or an inadequate decrease of bone turnover markers. Treatment success was mostly defined as an increase of BMD. In participating centres,

BMD was assessed by dual-energy X-ray absorptiometry (DXA) and spine and proximal femur measurements. Bone markers used for monitoring varied from centre to centre.

During the study period, daily alendronate was the only bisphosphonate reimbursed in Poland. Therefore no switches from daily to weekly alendronate were recorded. In assessed patients, seven different alendronate generics were used.

Statistical analysis

Statistical significance of differences between groups was calculated using the Kruskal-Wallis test (for comparison of three groups) and the Mann-Whitney test (for comparison of two groups) for quantitative variables. For comparison of qualitative variables, the χ^2 test or Fisher's exact test was used. Data is presented as mean ± SD or number (percentage).

Results

Some 48.2% of all patients made at least one switch of their osteoporosis treatment during the observation period. Almost 40% of patients from the switching group (138 patients, 38.3%) changed treatment from one alendronate to another with a different brand name. Switches occurred from the original brand to a generic drug (32.1%), the reverse (16%), as well as from one generic drug to another (51.9%). 54.8% of switches were made from the original branded drug to a generic drug because of the high cost of treatment, but 45.2% of high cost switches included switching between generic drugs. A comparison of the basal data of switchers vs. non-switchers is shown in Table I. They differed significantly only in regard to the time of observation, which was slightly longer in both switchers' groups.

Table II. Reasons for the switch from one generic alendronate to another one to another treatment

Tabela II. Powody zamiany jednego preparatu alendronianu na inny preparat lub na inny lek

Reasons for the first switch	All switchers	Switchers to alendronate	Switchers to another treatment	p*
Adverse event	173 (48.0%)	51 (36.9%)	122 (54.9%)	0.0011
Treatment failure	41 (11.4%)	15 (10.9%)	26 (11.7%)	0.86 (NS)
High cost	36 (10.0%)	32 (23.2%)	4 (1.8%)	< 0.0001
Request of patient	37 (10.3%)	23 (16.7%)	14 (6.3%)	0.0022
Switch made in another centre	44 (12.2%)	13 (9.4%)	31 (14.0%)	0.25 (NS)
Treatment success	29 (8.1%)	4 (2.9%)	25 (11.3%)	0.0046
Total	360 (100%)	138 (100%)	222 (100%)	–

*Statistical significance of differences between switchers to alendronate and switchers to another treatment (Fisher's exact test)

Reasons why alendronate treated patients switch to another treatment (the 'first switch') are shown in Table II. Adverse events more often resulted in a switch to a treatment other than alendronate. However, they also caused a surprisingly frequent (in 36.9% of switchers) switch to another alendronate. High drug cost and the request of the patient were the most frequent reasons for alendronate-alendronate switching, whereas treatment failure and a switch made in another centre took place with similar frequency in both groups (Table II).

Discussion

The only data in the literature relating to the switching of bisphosphonates deals with switching from daily to weekly bisphosphonates [6]. There has been no study regarding switches to the same drug with a different brand. A possible reason for this is that most published data originates from countries in the west, where osteoporotic patients are rarely treated with generic drugs, although in the USA generic drugs now account for 63% of all prescriptions [7]. Generic antiosteoporotic drugs are frequently marketed in Eastern European countries and in the developing world. It is therefore possible that the published data does not reflect the situation in a large part of the world.

Most osteoporotic patients in Poland are treated with bisphosphonates. The most important reason for that is that alendronate is the only bisphosphonate and the only anti-fracture drug reimbursed in Poland. This is the main reason for replacing any initial therapy with alendronate in more than 50% of patients [5] who could not afford the former treatment.

It was expected that this would also be the main reason for switches from alendronate to the same alendronate, but one manufactured under a different commercial name. However, surprisingly, the commonest reason for that kind of switch was an adverse event.

Although a more common reaction if an adverse event occurred was a switch to another drug (Table II), in many cases (probably for financial reasons), the only possible action that did not leave the patient untreated was to undertake a purely psychological action, and to switch to another alendronate with a different brand. Such an action was probably made in the hope that if the adverse event was in fact not drug-related, the patient, who rarely looks at chemical names, will not expect the same adverse event, as he or she would do if restarting a drug with the same brand name.

The high cost of the drug was the second most frequent reason for switching to another alendronate (Table II). More than 50% of switches made because of the treatment cost were switches from the original brand to a generic drug. However, the remaining 45.2% of switches because of high cost occurred between different generic drugs, something which proves that there is also price competition between different generic brands.

A relatively high number of switchers from one alendronate to another changed their treatment at their own request (16.7% of all switches). Taking into account that only 23.2% changed their treatment because of the cost, it also seems possible that patients are unwilling to admit that they cannot afford the given treatment. Further research is required into the reasons behind a treatment switch at the request of the patient.

This study has some limitations. As in any study, patient selection may be specifically biased. Multi-centre design was employed to minimise this limitation.

Another limitation is that only the 10 mg daily alendronate treatment was analysed, whereas now 70 mg weekly alendronate is used in most patients. Taking into account, however, that frequency of adverse events after weekly alendronate treatment may be similar [8] and that four different brands of 70 mg alendronate with different prices are marketed in Poland, we believe that the described mechanisms remain the same.

A third limitation is that the retrospective study design may bias the results and make a precise answer to many questions impossible. In a prospective study, however, the assessed behaviour of patients and doctors and the results may also be biased by awareness of the study procedure.

Conclusions

In summary, our results suggest that if alendronate manufactured by different companies with different brands is available on the market, many persistent bisphosphonate-treated patients switch treatments from one alendronate to another. The most frequent reasons for that kind of switching are the occurrence of an adverse event and the high cost of the treatment.

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