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Original Article

THE COST-EFFECTIVENESS OF IBANDRONATE AND ALENDRONATE FOR THE TREATMENT OF OSTEOPOROSIS IN A SPECIALIZED CLINIC IN TIRANA

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ABSTRACT

Objective: Biphosphonates are well known drugs for their efficacy in reducing fracture incidence, increasing bone density and improving bone micro architecture. The aim of this study is to evaluate the effectiveness of ibandronate and alendronate used in the treatment of osteoporosis in post-menopausal women over the age of 50 y at a specialized clinic in Tirana and to calculate the annual cost of osteoporosis treatment and perform a cost-effectiveness analysis.

Methods: Study design: Retrospective study The patients included were all female, in menopause or post-menopause with T-score-1 to-6, treated with alendronate or ibandronate. The effectiveness of the treatment was calculated as the average percentage of change in bone mineral density (av. % of change in BMD) between 2011 and 2010 (baseline). The annual cost of the osteoporosis treatment according to the protocols and the cost of the DXA (dual x-ray absorptiometry) scan were calculated and the comparison of cost-effectiveness was performed.

Results: Patients with osteoporosis treated with ibandronate (n=24) had a statistically significant higher average change from baseline compared to patients treated with alendronate (n=46) (Mann Whitney U = 66.0, $p<0.01$). The annual cost of treatment with ibandronate was 1.3 times higher than that of alendronate.

The cost/efficacy ratio was 13.434 units for ibandronate and 31.677 units for alendronate type A1.

Conclusion: Ibandronate is more effective and cost-effective than alendronate in the treatment of osteoporosis.

Keywords: Biphosphonates, Osteoporosis, Alendronate, Tirana.

INTRODUCTION

Osteoporosis is "a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fractures" [1]. The World Health Organization defines osteoporosis as "bone density 2.5 standard deviations (SDs) below the mean for young white adult women at lumbar spine, femoral neck or forearm" [2].

Osteoporosis leads to nearly 9 million fractures each year worldwide and over 300,000 patients with fragility fractures are registered in UK hospitals each year according to the British Orthopedic Association [3]. In Albania, there is a high prevalence of osteoporosis as well (7.28 % prevalence in the overall population and 9.6% prevalence in the female population). This prevalence is comparable to that of cardiac diseases and asthma [4].

Direct medical costs due to fragility fractures in the United Kingdom healthcare economy were estimated at £1.8 billion in 2000, with the potential to increase to £2.2 billion by 2025 and the major part of these costs were related to hip fracture care [5].

The annual cost of osteoporosis and fractures in the United States of America's elderly population was estimated at $16 billion [6]. Osteoporosis is diagnosed by a *T*-score, that is the number of standard deviation (SD) that the patient's bone mineral density (BMD) (measured using dual X-ray absorptiometry) differs from the mean BMD of 30-years old premenopausal women. Patients presenting *T*-score between-1 and-2.5 SD are considered to have osteoporosis [7-11].

Biphosphonates are well known drugs for their efficacy in reducing fracture incidence, increasing bone density and improving bone micro-architecture [9-17].

The aim of this study is (1) to evaluate the effectiveness of ibandronate and alendronate used in the treatment of osteoporosis in post-menopausal women over the age of 50 y at a specialized clinic in Tirana; (2) to calculate the annual cost of osteoporosis treatment and perform a cost-effectiveness analysis [18]. This cost-effectiveness analyse will be a novel solution for osteoporosis treatments here in Albania.

MATERIALS AND METHODS

This is a retrospective study. Patients included in the study were all female, in menopause or post menopause, 50 y old or older, with T-score-1 to-6, diagnosed for the 1st time in 2010 (the 1rst BMD measurement). All included patients were treated according to the protocols for 12 mo with alendronate or ibandronate and in 2011 performed a 2nd BMD measurement.

The effectiveness of the treatment was calculated as the average percentage of change in BMD (av.% of change in BMD) between 2011 and 2010 (baseline). The annual cost of the osteoporosis treatment was calculated as well for once monthly 150 mg oral ibandronate plus supplements (calcium, vitamine D) and once weekly 70 mg alendronate (4 times per month) plus supplements (calcium, vitamine D). Other direct costs such as the examination with DXA scan (dual x-ray absorptiometry) to determine the diagnosis and the medical visits were included. Finally, a comparison of the cost-effectiveness was performed. Having all the annual costs and the efficacy for each drug, we can compare the cost (C)/efficacy (E) ratios as below:

C1/E1 vs C2/E2

Statistical analysis

Data were analyzed with SPSS 20 statistical package. The non-parametric Mann-Whitney U test was used to compare the continuous variables; the Fisher Exact test was used to compare proportions between variables and the odds ratio (OR) to assess the association between variables. Point estimations are accompanied with interval estimation by 95 % confidence interval (CI). Continuous variables are presented as average, standard deviation

and the minimum and maximum values. The level of statistical significance is defined at α ≤ 005Two sided statistical tests are used.

RESULTS

150 clinical records were evaluated. Seventy patients who fulfilled the inclusion criteria were included in this study. 24 patients were treated once monthly with 150 mg oral ibandronate tablets and 46 patients were treated once weekly with 70 mg alendronate tablets. There was no case of fracture among the patients.

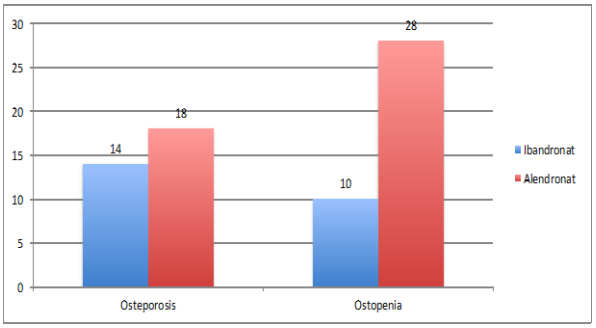

Fig. 1: Comparison between the numbers of patients included in the study according to the pathology treated

As shown in fig. 1, the number of patients treated with alendronate is 1.3 times higher than the number of patients treated with ibandronate in the case of osteoporosis. (OR = 1.3, 95% CI 0.5-4.2, p = 0.4).

The efficacy of treatment with alendronate and ibandronate

The 2 groups with different treatments were analyzed separately. Table 2 presents the data from the group treated with alendronate (N=46).

There were 46 patients treated with alendronate Eighteen (39.1 %) (95% CI 29.7-52.1) of them had osteoporosis and 28 (60.9 %) (95 % CI 47.8-74.2) osteopenia without a statistically significant difference (p = 0.9).

The age group 60-69 y had 1.6 times more probability to have osteoporosis compared to the 50-59 age group, but this was not statistically significant (OR=1.6; 95%CI 0.4–6.7; p=0.4).

The patients over 70 y old had 2.8 times more probability to have osteoporosis compared to those 50-59 y old, but without a statistically significant difference in between them (OR=2.8; 95%CI 0.4–25.2; p=0.3).

Patients with osteopenia had higher weight compared to those with osteoporosis (Mann-Whitney U=376.5, p=0.01). Patients with osteoporosis had similar mean height compared to those with (Mann-Whitney U=304.5, p=0.3).

Table 1: It shows the frequency of osteopenia and osteoporosis in the patients treated with ibandronate and alendronate

	Osteoporosis	Osteopenia
Ibandronate	14	10
Alendronate	18	28

Table 2: Summary of data from the group of patients treated with alendronate

	Osteoporosis n=18	Osteopenia n= 28		
	M (SD) min-max	M (SD) min-max	Mann-Whitney U	p
T Score 2010	-3.2 (0.7) -4.6--2.5	-1.9 (0.4) -2.4--1.1	507.0	**<0.001**
T Score 2011	-3.1 (0.8) -4.7--2.2	-1.8 (0.6) -2.4--1.1	515.5	**<0.001**
Age (years)	61.2 (8.0) 51.0–79.0	59.1 (7.8) 51.0–81.0	223.5	0.3
Height (metres)	1.5 (0.05) 1.4–1.6	1.5 (0.07) 1.4–1.7	304.5	0.3
Weight (kilograms)	58.8 (8.3) 46.0–73.0	68.6 (11.1) 51.0–95.0	376.5	0.01
**Age-Group, yrs*	n (%)	n (%)	OR (95% CI)	
50-59 y	8 (17)	19 (41)	-	
60-69 y	7 (15.2)	6 (13.0)	1.6 0.4–6.7	0.4
>70 y	3 (7)	3 (7)	2.8 0.4–25.2	0.3

*Fisher exact test p=0.3

Table 3: Change from baseline for the group of patients treated with alendronate

	Osteoporosis n=18	Osteopenia n= 28		
	M (SD) min-max	M (SD) min-max	Mann-Whitney U	p
The change from baseline	2.1 (4.5) -7.6–13.9	1.7 (6.2) -23–11.1	316.0	0.2

Patients with osteopenia had higher average change from baseline compared to those with osteoporosis, but this was not a statistically significant difference (Mann-Whitney U = 316.0, p = 0.2).

The change from baseline for the group of patients treated with alendronate

The change from baseline was calculated according to the formula:

$$\frac{BMD20011 - BMD2010}{BMD2010} \times 100$$

Twenty-four patients were treated with ibandronate. Fourteen (58.3%, 95% CI 33.2-76.5) of them had osteoporosis and 10 (43.7%, 95% CI 23.4-61.7) had osteopenia without a statistically significant difference between them (p = 0.9). Patients with osteoporosis had a higher mean age compared to patients with osteopenia, but this was not a statistically significant difference (Mann-Whitney U=39.5, p=0.07).

Patients with osteoporosis had the same mean height as patients with osteopenia (Mann-Whitney U=71.0, p=0.9).

Patients who were 60-69 y old had 3.7 times more probability to have osteoporosis compared to those 50-59 y old, but this was not statistically significant (OR=3.7; 95%CI 0.6–27.8; p=0.2).

The patients over 70 y old had 13 times more probability to suffer from osteoporosis compared to those 50-59 y old (OR=13; 95% CI 0.5–33.0; p=0.03).

Patients with osteopenia had higher weight compared to those with osteoporosis, but without a statistically significant difference between them (Mann-Whitney U=90.5, p=0.2).

The change from baseline for the group of patients treated with ibandronate

The same formula was applied for the patients treated with ibandronate.

The comparison of change from baseline for patients with osteoporosis treated with ibandronate or alendronate is presented in table 6 and fig. 2.

Patients with osteoporosis treated with ibandronate had a higher mean change from baseline compared to patients treated with alendronate (Mann-Whitney U=66.0, p<0.01).

Table 4: It presents the data from the group of patients treated with ibandronate.

	Osteoporosis n=14	**Osteopenia n= 10**		
	M (SD) min-max	**M (SD) min-max**	**Mann-Whitney U**	**p**
T Score 2010	-3.7 (0.7) -5.0--2.7	-1.8 (0.3) -2.2--1.4	140.0	**<0.001**
T Score 2011	-3.2 (0.8) -4.4--1.7	-1.5 (0.4) -2.1--1.0	134.5	**<0.001**
Age (years)	64.3 (7.3) 53.0-77.0	59.1 (5.0) 53.0–68.0	39.5	0.07
Height (metres)	1.5 (0.05) 1.4–1.6	1.5 (0.06) 1.4–1.6	71.0	0.9
Weight (kilograms)	66.2 (10.9) 47.0–84.0	70.7 (7.1) 65.0–82.0	90.5	0.2
**Age-group, yrs*	n (%)	n (%)	OR (95% CI)	
50-59 y	3 (12.5)	6 (25.0)	-	
60-69 y	8 (33.3)	4 (16.7)	3.7 0.6–27.8	0.2
>70 y	3 (12.5)	0	13 0.5–33.0	**0.03**

*Fisher exact test p<0.05

Table 5: Change from baseline for the group of patients treated with ibandronate

	Osteoporosis n=14	**Osteopenia n= 10**		
	Mean (SD) min-max	**Mean (SD) min–max**	**Mann-Whitney U**	**p**
The change from baseline	7.3 (6.1) -0.5–17.3	3.3 (2.2) -1.3–6.3	43.0	0.1

Patients with osteoporosis had a higher change from baseline compared to the patients with osteopenia, but this difference was not statistically significant (Mann-Whitney U = 43.0, p = 0.1).

Table 6: It shows the comparison of change from baseline for patients with osteoporosis treated with ibandronate or alendronate

	Alendronate n=18	**Ibandronate n= 14**		
	Mean (SD) min-max	**Mean (SD) min–max**	**Mann-Whitney U**	**p**
The change from baseline	2.1 (4.5) -7.6–13.9	7.3 (6.1) -0.5–17.3	66.0	**<0.01**

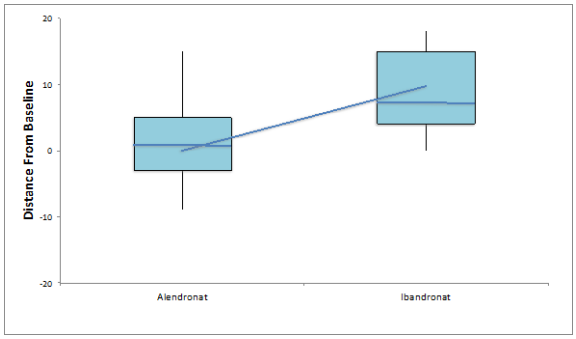

Fig. 2: The change from baseline for patients with osteoporosis treated with alendronate or ibandronate

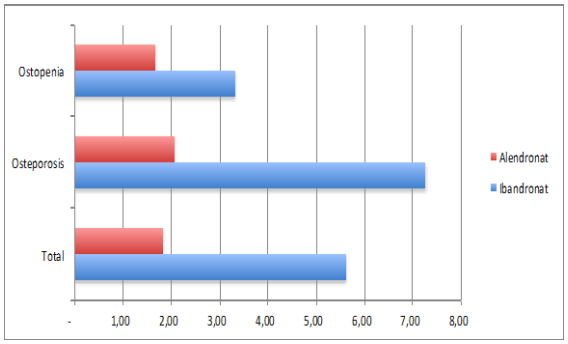

Fig. 3: Comparison between the percentages of the average change of BMD from baseline for the two treated groups

As shown in the fig. 3, the overall efficacy of ibandronate (5.6) is higher than that of alendronate (1.8). In patients treated for osteoporosis, the efficacy of ibandronate (7.3) is higher than that of alendronate (2.1). In patients with osteopenia, the efficacy of ibandronate (3.3) is also higher than that of alendronate (1.7).

Cost analysis

Only direct costs such as DXA scan examinations, medical visits and medications costs (drugs and the supplements) according to a well-defined treatment protocol were considered in the cost analysis.

In the Albanian pharmaceutical market, there is only one brand of ibandronate (150 mg tablets), while there are several brands of alendronate (70 mg tablets).

For ethical reasons these brands will be further reported as A1, A2, A3, A4 and A5. The costs included the price of the only available brand of ibandronate and the costs of five brands of alendronate, including that produced by a national pharmaceutical company which has the lowest price in the market. In both cases, treatment includes supplements such as calcium and vitamin D.

Table 7: It shows the annual cost of treatment and examination for all the studied drugs

S. No.		Quantity	Cost (in Lek)	Annual Costs
1	Diagnostics			
	DXA scan	1	4,000	4,000
	Medical examination	1	1,000	1,000
2	Alendronat 70 mg			
	A1	4	3,410	40,920
	A2	4	2,093	25,116
	A3	4	3,301	39,612
	A4	4	4,102	49,224
	A5 (Albanian product)	4	1,200	14,400
3	Ibandronat 150 mg			
		1	4,873	58,476
4	Calcium Carbonat 1000 mg+Colecalciferol 880 UI	30	1,019	12,228

Table 8: It summarizes the annual cost of illness for all types of medication applied

Type of Alendronat	1+2+4*	Annual costs (in Lek)
A1		58,148
A2		42,344
A3		56,840
A4		66,452
A5		31,628
Type of Ibandronat	1+3+4*	Annual costs
I1		75,704

*numbers according to description in table 7

The annual cost of the treatement with ibandronate is 2.4 times higher than that of alendronate (the alendronate produced by the national pharmaceutical company that has the lowest price in the market), respectively 75,704 Lek **(**540 euro) versus 31,628 Lek (226 euro) per patient.

Table 9: It shows the efficacy of both drugs in terms of percentage of change by baseline

Type of treatment	Change from baseline (%)
Alendronate	1.83565
Ibandronate	5.63536

Table10: It shows the cost/efficacy ratio (C/E)

Type of treatment	C/E (units)
Alendronate	
A1	31,677
A2	23,068
A3	30,965
A4	36,201
A5	17,230
Ibandronate	13,434

The cost/efficacy ratio was 13.434 units for ibandronate and 31.677 units for alendronate type A1.

DISCUSSION

Our results indicate that patients with osteoporosis treated with ibandronate in Tirana had a higher average change from baseline compared to patients treated with alendronate. According to data published in literature: once a month ibandronate was shown to be clinically comparable to weekly alendronate at increasing BMD after 12 mo in the lumbar spine and total hip [19]. Another similar study showed that the treatment effects of different bisphosphonates (ibandronate, alendronate and risedronate) did not differ significantly [20].

According to our data, the annual cost of treatment with ibandronate is 1.3 times higher than the annual cost of treatment with

alendronate (A1) and 2.4 times higher than the annual cost of treatment with the alendronate produced by a national pharmaceutical company which has the lowest price in the market.

The cost over effectiveness ratio is lower (about 2.3 times) for ibandronate compared to alendronate (A1) showing that ibandronate is more cost-effective. Ibandronate is more cost-effective than all the brands of alendronate available in Albania including the alendronate produced by a national pharmaceutical company which has the lowest price in the market.

Our findings are in concordance with similar studies showing that: Treating postmenopausal, osteoporotic women with monthly ibandronate is cost-effective. Even with small improvements in persistence, monthly ibandronate is more effective and less costly than weekly alendronate [21].

We consider as a limitation of our study the small number of patients evaluated. It can seem that the study is limited only in one city, but the patients enrolled are representative of the whole country and not just of the Tirana city. This is because the center were our study was conducted, was the only one which could perform such analyze (DXA) in that time (2010-2011).

CONCLUSION

The findings of this study suggest the superiority of ibandronate compared to all alendronate brands in terms of efficacy and cost-effectiveness. Further investigation is needed to determine if the Albanian health authorities should consider the ibandronate treatment as first line treatment in osteoporosis.

CONFLICTS OF INTERESTS

All authors have none to declare

REFERENCES

1. Christiansen C. Diagnosis, prophylaxis and treatment of osteoporosis. Am J Med 1993;94:646–50.
2. Kanis JA, Johnell O. Requirements for DXA for the management of osteoporosis in europe. Osteoporosis Int 2005;16:229–38.
3. Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. Osteoporosis Int 2006;17:1726–33.
4. Dorina R. Osteoporosis in Tirana. PhD thesis; 2011. Available from: URL: http://www.bksh.al/adlib/scripts/ wwwopac. exe?DATABASE=catalo&OPAC_URL=/adlib/beginner/index_al. html&LANGUAGE=1&%250=700000678&LIMIT=0). [Last accessed on 20 May]
5. British Orthopaedic Association. The care of patients with fragility fracture; 2007. p. 37-8.
6. Burge RT, Worley D, Johansen A. The cost of osteoporotic fractures in the UK: projections for 2000–2020. J Med Econ 2008;4:51–2.
7. Blume SW, Curtis JR. Medical costs of osteoporosis in the elderly medicare population. Osteoporos Int 2011;22:1835-44.
8. BMJ Group. Annual zoledronic acid for osteoporosis. Drug Ther Bull 2008;46:93-6.
9. Cummings SR, Melton LJ. Epidemiology and outcomes of osteoporotic fractures. Lancet 2002;359:1761-7.
10. Srinivasa Rao Sirasanagandla, K Sreedhara Ranganath Pai, Kumar Mr Bhat. Preventive role of emblica offcinalis and cissus quadrangularis on bone loss in osteoporosis. Int J Pharm Pharm Sci 2013;5:465-70.
11. Anton Bahtiar, Aini Gusmira, Raymond Tjandrawinata. Functional analysis of 70% ethanolic extract of akar kelembak (Rheum Officinale Baill.) On 3t3 L1 preadipocyte cell lines in osteogenic medium. Int J Pharm Pharm Sci 2014;6:86-9.
12. Delmas PD. Treatment of postmenopausal osteoporosis. Lancet 2002;359:2018–26.
13. Hochberg MC, Ross PD, Black D. Larger increases in bone mineral density during alendronate therapy are associated with a lower risk of new vertebral fractures in women with postmenopausal osteoporosis. Fracture intervention trial research group. Arthritis Rheum 1999;42;1246-54.
14. Hochberg MC, Greenspan S, Wasnich RD. Changes in bone density and turnover explain the reductions in incidence of nonvertebral fractures that occur during treatment with antiresorptive agents. J Clin Endocrinol Metab 2002;87:1586-92.
15. Epstein S. The roles of bone mineral density, bone turnover, and other properties in reducing fracture risk during antiresorptive therapy. Mayo Clin Proc 2005;80:379-88.
16. McClung MR, Wasnich RD, Recker R. Oral daily ibandronate prevents bone loss in early postmenopausal women with osteoporosis. J Bone Miner Res 2004;19:11-8.
17. Rosen CJ. Postmenopausal osteoporosis. N Engl J Med 2005;353:595-603.
18. Surendra G Gattani, Abasaheb B Patil, Sachin S Kushare. Pharmacoeconomics: a review. Asian J Pharm Clin Res 2009;2:15-24.
19. Miller PD, Epstein S, Sedarati F, Reginster JY. Once-monthly oral ibandronate compared with weekly oral alendronate in postmenopausal osteoporosis: results from the head-to-head MOTION study. Available from: URL: http://www.ncbi.nlm.nih.gov/pubmed/18042311. [Last accessed on 20 May]
20. MA Paggiosi, N Peel, E McCloskey, JS Walsh, R Eastell. Comparison of the effects of three oral bisphosphonate therapies on the peripheral skeleton in postmenopausal osteoporosis: the TRIO study. Osteoporosis Int 2014;25:2729-41.
21. Earnshaw SR, Beard SM, Lynch NO, Cooper A, Cowell W, Middelhoven HA. Comparison of the cost-effectiveness of bisphosphonates using persistence data from a UK propsective RCT. 28th Annual Meeting of the American Society for Bone and Mineral Research; 2006.