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Efficacy of Alendronate in Preventing Periprosthetic Bone Loss after Implantation of a Primary Hip Endoprosthesis

Ilir Shabani*, Milan Samardziski, Viktor Kamnar, Nenad Atanasov, Milena Bogojevska-Doksevska, Danica Popovska, Anila Belchishta

Department of Orthopedic Surgery, University Clinic "Mother Theresa", Faculty of Medicine, Ss. Cyril and Methodius University, Skopje, Republic of Macedonia

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***Correspondence:** Ilir Shabani, Department of Orthopedic Surgery, University Clinic "Mother Theresa", Faculty of Medicine, Ss. Cyril and Methodius University, Skopje, Macedonia. E-mail: dr_ilir_shabani@yahoo.com
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Abstract

BACKGROUND: Total hip arthroplasty (THA) is now the gold standard for the surgical treatment of coxarthrosis. The appearance of bone loss after implantation of the hip endoprosthesis over time reduces the primary stability of the implant and leads to progressive loosening of the implant or periprosthetic fracture, which are considered to be the most common causes of hip revision.

AIM: The aim of this study is to evaluate the value of alendronate application in reducing periprosthetic osteolysis reduction after implantation of total cementless hip endoprosthesis.

METHODS: The study analyzed 50 patients operated on with implantation of a cementless THA. The first group of 25 patients received oral alendronate, calcium, and Vitamin D3 postoperatively. The second group of 25 patients was examined and followed postoperatively without any therapy. Patients were examined by RTG and dual energy X-ray absorption (DXA) methods at 6, 12, and 18 months.

RESULTS: The study showed a difference in the values of bone mineral density and bone mineral content in the interval of 6,12, and 18 months, using the DXA method.

CONCLUSION: Alendronate therapy after total hip implantation reduces periprosthetic bone loss, maintains bone mineralization, and strengthens the implant.

Introduction

Total hip arthroplasty (THA) is now the golden standard for surgical treatment of coxarthrosis [1], [2], [3]. The implantation of total hip endoprosthesis solves the following problems: Elimination of pain, correction of deformity, preservation of motility, equalization of the limb, etc. It is estimated that approximately 30% more patients will require primary THA worldwide by 2030 [4].

Periprosthetic bone resorption after THA is a well-known phenomenon [5]. The appearance of bone loss after implantation of the hip endoprosthesis over time reduces the primary stability of the implant and leads to progressive loosening of the implant or periprosthetic fracture, which are considered to be the most common causes of hip revision [6], [7], [8]. Compared to primary hip endoprosthetics, revision surgeries are more complex and have more complications locally and generally for the body, with less benefit to the patient [9]. Therefore, research to inhibit periprosthetic bone resorption and maintain bone marrow is necessary. Alendronate from the bisphosphonate family of drugs with potent antiosteoclast activity has been widely used as a first line treatment for periprosthetic bone loss after total hip implantation [10]. Mass data have shown that alendronate inhibits bone resorption, increases their mineral density, and reduces the risk of periprosthetic fractures [11].

Treatment with alendronate at a therapeutic dose of 10mg per day plus 1000 mg of calcium and Vitamin D3 fpr 18 months provides opportunities for prevention of periprosthetic osteolysis, which is expected to make significant progress in post-implant stabilization of implanted endoprosthetic implants and the risk of all cobsequences [12], [13], [14], [15]. However, there was still controversy about the impact and mechanism of action of bisphosphonates on the inhibition of periprosthetic bone loss by THA. Some studies have shown that bisphosphonates do not have a significant effect on suppressing bone loss after THA [12], [13]. In contrast, the previous meta-analyses have suggested that BP may inhibit early bone resorption around the implant [14], [15], [16], [17].

In 2001, Wenesma *et al*. find that alendronate therapy results in a significant reduction in periprosthetic bone loss after primary hip implantation compared with the group of patients without therapy [18].

The aim of this study is to evaluate the value of alendronate application in reducing periprosthetic

osteolysis after implantation of total cementless hip endoprosthesis.

Materials and Methods

The clinical material consists of 50 patients treated at the clinic for orthopedix diseases with implantation of a total hip endoprosthesis due to degenerative diseases of the hip.

The age distribution of patients was 35–65 years, of which 35 were females and 15 were males. The first group of 25 patients was permanently treated with alendronate therapy, vitamin therapy, and calcium. The second group of 25 patients was without therapy in the role of a control group (CG).

Methodology

This study is based on a clinical trial using two diagnostic methods: Native hip radiography and dual energy X-ray absorption. Densitometric analysis refers to 7 Gruen zones of the femur, through which periprosthetic osteolysis formed in the femur after implantation of a total cementless hip prosthesis is assessed.

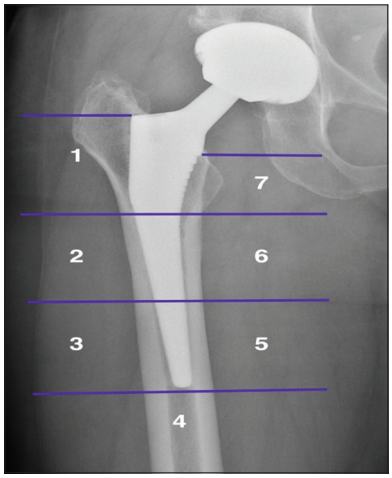

Figure 1: Seven Gruen zones of the femur

The analysis consists of a comparing the results for bone mineral density (BMD) and bone mineral content (BMC) obtained at different time points, 6,12, and 18 months from the day of implant placement in both groups.

Results

The results obtained by processing and analyzing 50 patients, all operatively treated with implantation of a cementless total hip prosthesis are presented. The subjects were divided into two groups:

Table 1: BMC 6 months

Zone	Group	Mean ± SD	Median (IQR)	p-level
Z1	SG	4.19 ± 3.7	2.85 (1.23 – 7.11)	Z = 0.43 p = 0.67 ns
	CG	4.51 ± 3.6	3.25 (2.02 – 7.13)	
Z2	SG	3.51 ± 2.8	2.35 (1.12 – 5.31)	Z = 0.66 p = 0.51 ns
	CG	3.09 ± 2.7	1.85 (1.02 – 5.14)	
Z3	SG	3.05 ± 1.9	2.75 (1.63 – 3.42)	Z = 1.19 p = 0.23 ns
	CG	3.94 ± 2.3	3.65 (1.73 – 5.56)	
Z4	SG	2.45 ± 1.5	1.87 (1.23 – 3.54)	Z = 2.11 p = 0.034 sig
	CG	3.36 ± 1.7	3.58 (1.98 – 4.72)	
Z5	SG	2.67 ± 1.4	2.63 (1.45 – 3.36)	Z = 1.9 p = 0.057 ns
	CG	3.67 ± 1.9	3.06 (2.31 – 4.6)	
Z6	SG	3.72 ± 3.2	2.36 (1.35 – 3.97)	Z = 0.85 p = 0.39 ns
	CG	4.41 ± 3.3	3.12 (1.98 – 6.32)	
Z7	SG	3.41 ± 3.1	1.95 (1.23 – 6.02)	Z = 0.56 p = 0.57 ns
	CG	3.83 ± 2.9	2.76 (1.03 – 6.37)	

p(Mann–Whitney U Test), SG: Study group, CG: Control group

A group of 25 patients treated with 10 mg alendronate and 1000 mg calcium and Vitamin D3 and constituted the study group (SG), and 25 patients who constituted the CG and were not treated after this medication protocol. In terms of gender, structure was homogeneous (p = 0.76).

Six months after total hip prosthesis implantation, patients receiving alendronate and patients without any therapy have significantly different BMC the 4th Gruen zone (p = 0.034) (Table 1). The BMC parameter had a significantly lower mean age in this and the zone in the group of patients with drug therapy (median 1.87 vs. 3.58).

Six months after surgery (Table 2), no significant difference in BMD was found between the two groups in all seven Gruen zones of the femoral stem.

Table 2: BMD 6 months

Zone	Group	Mean ± SD	Median (IQR)	p-level
Z1	SG	0.97 ± 0.3	0.97 (0.76 – 0.99)	Z = 0.02 p = 0.98 ns
	CG	1.11 ± 0.7	0.89 (0.64 – 1.45)	
Z2	SG	1.27 ± 0.6	1.12 (0.91 – 1.35)	Z = 0.04 p = 0.97 ns
	CG	1.39 ± 0.7	1.23 (0.87 – 1.87)	
Z3	SG	1.49 ± 0.6	1.24 (1.12 – 1.63)	Z = 0.05 p = 0.96 ns
	CG	1.56 ± 0.7	1.45 (1.02 – 1.98)	
Z4	SG	1.41 ± 0.8	1.21 (0.98 – 1.32)	Z = 1.29 p = 0.19 ns
	CG	1.54 ± 0.7	1.28 (1.09 – 2.12)	
Z5	SG	1.65 ± 0.8	1.42 (1.11 – 1.82)	Z = 0.44 p = 0.65 ns
	CG	1.55 ± 0.7	1.23 (1.06 – 1.87)	
Z6	SG	1.93 ± 0.97	1.67 (1.24 – 2.09)	Z = 0.93 p = 0.35 ns
	CG	1.83 ± 1.1	1.43 (0.98 – 2.31)	
Z7	SG	2.01 ± 1.7	1.67 (1.25 – 1.83)	Z = 0.93 p = 0.35 ns
	CG	1.61 ± 0.8	1.4 (1.03 – 1.9)	

SG: Study group, CG: Control group

One year of surgical intervention (Table 3), the BMC was significantly different between the two groups in zone 2 (p = 0.008) in patients with alendronate therapy (median 2.92 vs. 1.53).

Table 3: BMC 12 months

Zone	Group	Mean ± SD	Median (IQR)	p-level
Z1	SG	4.75 ± 3.7	3.64 (1.98 – 7.47)	Z = 0.95 p = 0.34 ns
	CG	3.54 ± 2.4	2.63 (2.0 – 5.45)	
Z2	SG	4.08 ± 2.7	2.92 (1.83 – 5.83)	Z = 2.67 p = 0.008 sig
	CG	2.33 ± 2.2	1.53 (0.95 – 3.12)	
Z3	SG	3.58 ± 1.8	3.21 (2.35 – 3.98)	Z = 1.03 p = 0.3 ns
	CG	3.21 ± 2.3	2.45 (1.25 – 4.11)	
Z4	SG	3.07 ± 1.5	2.65 (1.98 – 4.11)	Z = 1.31 p = 0.19 ns
	CG	2.57 ± 1.6	2.25 (1.32 – 3.03)	
Z5	SG	3.29 ± 1.4	3.11 (1.98 – 3.93)	Z = 1.31 p = 0.19 ns
	CG	2.73 ± 1.4	2.34 (1.63 – 3.85)	
Z6	SG	4.32 ± 3.1	3.12 (2.12 – 5.12)	Z = 1.37 p = 0.17 ns
	CG	3.53 ± 2.7	2.75 (1.9 – 5.11)	
Z7	SG	4.14 ± 2.9	2.94 (1.87 – 6.3)	Z = 1.44 p = 0.15 ns
	CG	3.04 ± 2.3	2.11 (0.92 – 5.37)	

SG: Study group, CG: Control group

The control examination after 1 year of surgical treatment (Table 4) in the patients of alendronate therapy,

Table 4: BMD 12 months

Zone	Group	Mean ± SD	Median (IQR)	p-level
Z1	SG	1.71 ± 0.7	1.43 (1.13 – 1.98)	Z = 3.87 p = 0.0001 sig
	CG	0.93 ± 0.6	0.68 (0.51 – 1.23)	
Z2	SG	2.02 ± 0.9	1.63 (1.35 – 2.34)	Z = 3.74 p = 0.0002 sig
	CG	1.15 ± 0.5	1.01 (0.73 – 1.53)	
Z3	SG	2.38 ± 1.5	1.88 (1.56 – 2.32)	Z = 4.59 p = 0.000004 sig
	CG	1.24 ± 0.4	1.12 (0.97 – 1.37)	
Z4	SG	2.26 ± 1.1	1.98 (1.63 – 2.43)	Z = 4.65 p = 0.000003 sig
	CG	1.18 ± 0.4	1.13 (0.94 – 1.23)	
Z5	SG	2.48 ± 1.2	2.12 (1.71 – 2.72)	Z = 4.76 p = 0.000002 sig
	CG	1.22 ± 0.5	1.12 (0.89 – 1.28)	
Z6	SG	2.63 ± 1.2	2.32 (1.87 – 3.13)	Z = 4.5 p = 0.000007 sig
	CG	1.32 ± 0.6	1.12 (0.83 – 1.87)	
Z7	SG	2.43 ± 1.02	2.10 (1.64 – 2.84)	Z = 5.05 p = 0.000000 sig

SG: Study group, CG: Control group

significantly higher values of the BMD parameter were measured in all seven Gruen zones.

At the end of the follow-up of the patients, after 18 months postoperatively, in all Gruen zones, a significantly different BMC is being registered between the patients from the examined and the CG. The results show that alendronate therapy after 12 months of implantation of a total cementless prosthesis on the hip had a significant effect on BMC in all Gruen zones (Table 5).

Table 5: BMC 18 months

Zone	Group	Mean ± SD	Median (IQR)	p-level
Z1	SG	5.18 ± 3.8	3.67 (2.34 – 8.13)	Z = 2.4 p = 0.014 sig
	CG	2.65 ± 1.7	2.23 (1.12 – 4.12)	
Z2	SG	4.63 ± 2.9	3.12 (2.7 – 6.31)	Z = 4.8 p = 0.000002 sig
	CG	1.57 ± 1.4	0.98 (0.81 – 2.12)	
Z3	SG	4.08 ± 1.9	3.32 (3.11 – 4.73)	Z = 3.8 p = 0.00014 sig
	CG	2.31 ± 1.8	1.98 (1.0 – 2.95)	
Z4	SG	3.77 ± 1.6	3.33 (2.63 – 4.82)	Z = 4.6 p = 0.000004 sig
	CG	1.71 ± 1.3	1.05 (0.93 – 2.18)	
Z5	SG	3.91 ± 1.5	3.67 (2.73 – 4.63)	Z = 4.6 p = 0.000004 sig
	CG	1.94 ± 1.2	1.67 (1.02 – 2.23)	
Z6	SG	5.01 ± 3.1	3.97 (2.94 – 5.72)	Z = 3.6 p = 0.0003 sig
	CG	2.48 ± 1.99	1.76 (1.12 – 3.87)	
Z7	SG	5.04 ± 3.1	3.33 (2.81 – 6.45)	Z = 4.1 p = 0.00005 sig
	CG	1.92 ± 1.6	1.02 (0.7 – 3.12)	

SG: Study group, CG: Control group

The two groups of patients have significantly different BMD at the last control examination after 18 months postoperatively, in all seven Gruen zones ($p < 0.0001$). Significantly higher values for BMD parameter were measured in all seven Gruen zones (Table 6).

Table 6: BMD 18 months

Zone	Group	Mean ± SD	Median (IQR)	p-level
Z1	SG	2.59 ± 0.99	2.34 (2.13 – 2.93)	Z = 5.8 p = 0.0000 sig
	CG	0.71 ± 0.4	0.53 (0.41 – 1.01)	
Z2	SG	3.32 ± 1.8	2.64 (2.11 – 3.67)	Z = 6.1 p = 0.0000 sig
	CG	0.75 ± 0.3	0.71 (0.46 – 0.98)	
Z3	SG	3.42 ± 1.7	3.11 (2.35 – 3.53)	Z = 5.9 p = 0.0000 sig
	CG	0.88 ± 0.5	0.8 (0.63 – 0.98)	
Z4	SG	3.31 ± 1.3	3.12 (2.35 – 3.9)	Z = 5.9 p = 0.0000 sig
	CG	0.82 ± 0.4	0.86 (0.63 – 1.01)	
Z5	SG	3.61 ± 1.6	3.23 (2.54 – 4.01)	Z = 6.0 p = 0.0000 sig
	CG	0.81 ± 0.4	0.76 (0.52 – 1.01)	
Z6	SG	3.78 ± 2.2	3.01 (2.76 – 4.31)	Z = 5.9 p = 0.0000 sig
	CG	0.85 ± 0.3	0.89 (0.63 – 1.02)	
Z7	SG	3.53 ± 1.5	3.11 (2.63 – 3.64)	Z = 6.1 p = 0.0000 sig
	CG	0.73 ± 0.3	0.74 (0.54 – 0.97)	

Discussion

Lin *et al*. [17] in their meta-analysis of 14 patients comparing bisphosphonate treatment with placebo treatment in patients with THA found that bisphosphonates reduced periprosthetic bone loss after total hip implantation. The aim of this study was to evaluate the efficacy and safety of bisphosphonates (alendronalte, pamidronate, etidronate, zolendronate, risedronate, and clodronate) in patient with implanted hip implants.

Zhao *et al*. [14] examined similar meta-analysis for bisphosphonates for bone loss after implanted total hip endroprosthesis. In their study, the risendronate was compared with the placebo group. The duration of follow-up in the included studies ranges from 6 months to 4 years. Obviously, the relatively short use of bisphosphonate will reduce the effectiveness of the anti-resorption action.

Eberhardt *et al*. [19] report that post-operative continuous treatment and high doses of bisphosphonate are potent in accelerating osteointegration of the prosthesis and preventing migration and loosening of the implant.

Friedl *et al*. [20], however, doubt that the long-term efficacy of bisphosphonate may reduce bone loss after implantation of a total hip prosthesis and argue that risendronate treatment may increase Harris hip scores in comparison with the CG.

In our group of patients, the results show an increase in BMD and BMC in all Gruen zones in all patients individually over a period of 6 months (measured at 6, 12, and 18 months after surgery) indicating the benefit of alendronate in reducing periprosthetic osteolysis. Our BMD and BMC test results support the potential benefit of alendronate in improving prosthesis implantation [21].

Conclusion

Alendronate is a proven inhibitor of periprosthetic bone loss that occurs after primary implantation of a total cementless hip endoprosthesis.

Our study reaffirms the effect of bisphosphonate therapy as an inhibitor of periprosthetic bone loss and aseptic implant loosening.

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