Clinical science

MONITORING THE REDUCTION AND MAINTENANCE OF PERIPROSTHETIC BONE TISSUE IN CEMENTLESS PRIMARY HIP ENDOPROSTHESIS WITH ALENDRONATE THERAPY

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Abstract

Loss of periprosthetic bone tissue in primary hip endoprostheses is common in clinical practice. This loss can be progressive and in extreme conditions can jeopardize the longevity of the prosthesis. In order to monitor the function of Alendronate therapy for bone maintenance, the study included 50 patients with implanted total cement-free hip endoprosthesis (TPH). The first group of 25 patients received Alendronate, calcium and vitamin D3 orally postoperatively. The second group of 25 patients were examined postoperatively without therapy. Patients were followed by radiographic and dual-energy X-ray absorptiometry (DXA) at 6 and 12 months. The study showed that in patients with TPH there was a difference in the X-ray findings as well as occurrence of osteolysis in certain Gruen zones, which was confirmed by changes in the state of bone mineral density (BMD) and bone mineral content (BMC) in the interval between 6 and 12 months using the DXA method. Alendronate therapy after TPH implantation allows reduction of periprosthetic bone mass loss, maintenance of bone mineralization and implant hardening.

Клинички истражувања

СЛЕДЕЊЕ НА РЕДУКЦИЈА И ОДРЖУВАЊЕ НА ПЕРИПРОСТЕТИЧНО КОСКЕНО ТКИВО КАЈ БЕЗЦЕМЕНТНА ПРИМАРНА ЕНДОПРОТЕЗА НА КОЛК СО АЛЕНДРОНАТНА ТЕРАПИЈА

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Извадок

Губењето на перипростетичното коскено ткиво кај примарните ендопротези на колкот е честа појава во клиничката пракса. Ваквиот губиток може да биде прогресивен и во екстремни услови да ја загрозува долготрајноста на протезата. Заради наблудување на функцијата на алендронатната терапија за одржување на коскеното ткиво во студијата беа вклучени 50 пациенти со вградена тотална безцементна ендопротеза на колк (ТПК). Првата група од 25 пациенти постоперативно примаа орално алендронат, калциум и витамин Д3. Втората група од 25 пациентипостоперативно беа иследувани без примена на терапија. Пациентите беа следени со радиографски и двојно-енергетска рендгензрачна апсорптометрија (DXA) на 6 и 12 месеци. Студијата покажа дека кај пациентите со ТПК постои разлика во РТГ наодите како и појава на остеолиза во одредени Gruenovi зони, што се потврди со промени и во состојбата на вредностите на коскената минерална густина(BMD) и коскената минерална содржина (BMC) во интервалот помеѓу 6 и 12 месеци со помош на DXA методот. Алендронатната терапија по вградување на ТПК овозможува намалување на перипростетичната загуба на коскената маса, одржување на минерализацијата на коскеното ткиво и зацврстување на имплантот.

Introduction

Poor bone quality is a significant risk factor when implanting a total hip arthroplasty (TPH). The loss of bone mass affects the longevity and stability of the implant. With the reduction of bone mass, complications such as periprosthetic fractures of the femur or loosening of the prosthesis occur immediately [1,2].

Periprosthetic bone loss is present in both cement and non-cement hip prostheses. When an endoprosthesis is implanted, the proximal part of the femur is surrounded by a spongy bone. The distal end of the endoprosthesis is in contact with a predominantly cortical bone. This provides a variety of biological and biomechanical conditions for TPH implantation. During exercise, body weight changes from proximal to distal. This imbalance of load forces causes bone resorption mechanisms under Wolf's law. This bone loss is seen in the proximal femur [3-5].

Bobin *et al.* found that periprosthetic bone resorption was more pronounced in large femurs with a broad but porous sheath. To avoid resorption, the bending coefficient of the implant should be less than that of the surrounding bone. Postoperative weight gain and aseptic relaxation also play a role in the periprosthetic bone loss [6-8].

With dual energy X-ray absorption (DXA), even small changes in bone mass near the metal implant can be accurately tracked. Recently, DXA has been accepted as an accurate method for monitoring periprosthetic bone mineral density (BMD). Periprosthetic BMD decreases more rapidly during the first 6 months after TPH. After the initial period of rapid loss, the plateau phase is reached during the first year after surgery, and changes in BMD in the periprosthetic bone are minimal over the next few years [9-18].

DXA studies have also shown that patients with low BMD preoperatively have the highest BMD loss after TPH implantation [19].

The positive effect of bisphosphonates on bones has been scientifically proven. These osteoactive drugs reduce the loss of bone density and increase bone mass in postmenopausal women with or without osteoporosis [20-25]. Devogelaer *et al.* gave 5,10 and 20 mg of Alendronate daily to 516 postmenopausal women with osteoporosis in their multicenter study. A daily dose of 10mg significantly and gradually increased the bone mass of the lumbar spine, hip and overall skeleton during a 3-year-follow-up. The increase in BMD was 5.5% in the femoral neck and 7.2% in the trochanter. This continuous daily dose was well tolerated, and no improvement was found in the results with increasing dose [26].

Black *et al.*, in their randomized study showed that postmenopausal women with low bone mass, receiving 5 and 10 mg of Alendronate daily, had a lower incidence of several types of fractures, including hip fractures [27].

To our knowledge, there are not enough studies published on the effects of bisphosphonates on periprosthetic bone loss after primary TPH implantation.

The aim of this scientific study was to evaluate the value of Alendronate application in reducing periprosthetic bone loss after implantation of a total cement-free hip endoprosthesis.

Material and methods

The clinical material consisted of 50 patients treated at the University Clinic for Orthopedic Diseases with implantation of a total hip endoprosthesis in the period from 2018 to 2020 due to degenerative hip diseases.

The age distribution of patients was between 35-65 years, of whom 35 female and 15 male patients. All patients in the study were clinically and osteodensitometrically without visible signs of osteoporosis. All patients underwent spinal anesthesia with anterolateral hip approach, with standard verticalization 3 days after operative treatment and standard postoperative rehabilitation. The first group of patients (25) were permanently treated with Alendronate bisphosphonate therapy as well as with standard vitamin therapy and calcium substitution. The second group of patients (25) were without therapy and were only examined.

Methodology: This study was based on a clinical trial using two diagnostic methods: native hip radiography and dual energy with X-ray absorption (DXA). Densitometric analysis refers to 7 Gruen zones of thefemur, through which periprosthetic osteolysis formed in the femur after implantation of a total hip endoprosthesis (TPH) is implanted.

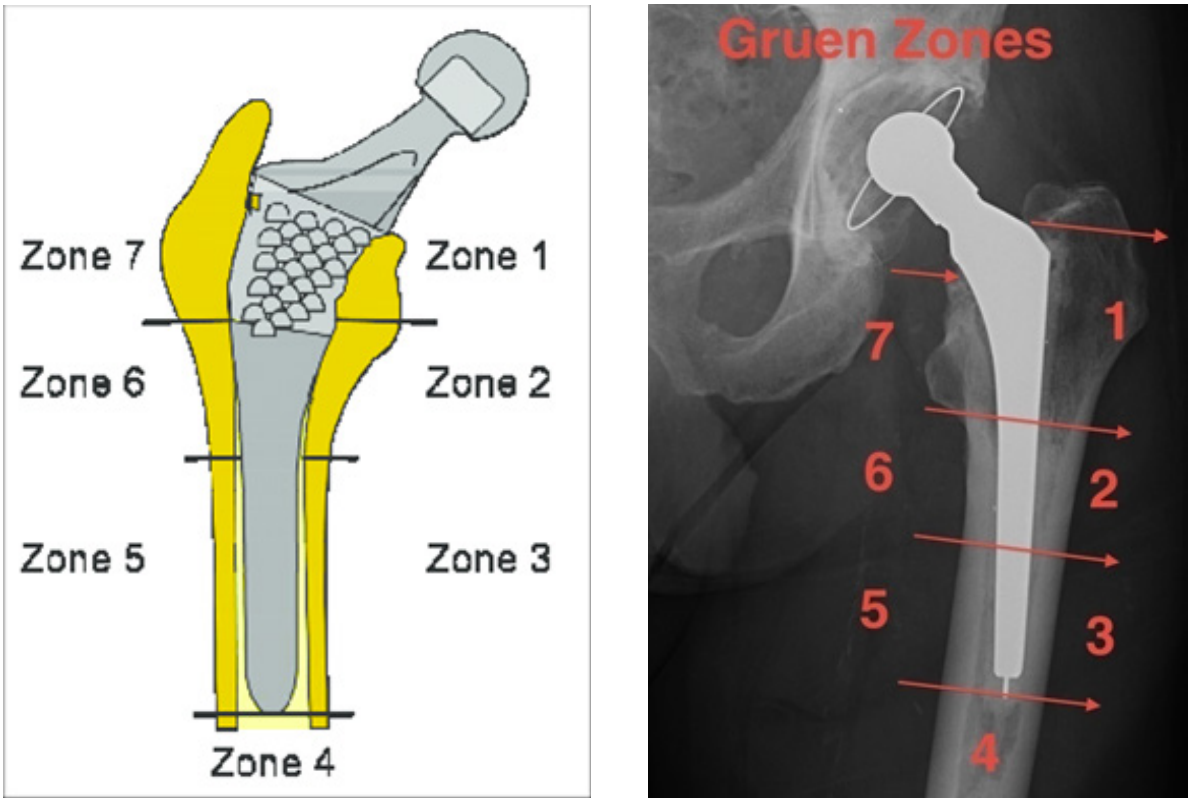

Figure 1. Schematic and X ray representation of the Gruen Zones

The results of both examinations were obtained and analyzed at time points, 6 and 12 months from the day of surgery.

The analysis consisted of comparing the results for BMD (bone mineral density) and BMC (bone mineral content) obtained at different time points in both groups.

Results

Patients in the study group, treated with medication, and patients in the control group, without medication treatment protocol were homogeneous in terms of gender structure (p=0.76). Female patients were the majority of examinees in both groups -68% (17) and 72% (18), respectively.

Table 1. Gender distribution

Gender	Group			p-level
	N	SG n (%)	CG n (%)	
Female	35	17 (68)	18 (72)	χ^2=0.095
Male	15	8(32)	7 (28)	p=0.76 ns

χ^2 (Pearson Chi-square)

No statistically significant difference was found in the age of patients in both groups (p=0.09). SG subjects were insignificantly younger than CG subjects (52.3 ± 9.7 vs 56.8 ± 8.6).

Tables 2,3,4 show the average and mean values of the BMC parameter in subjects from both groups, measured in the 7 Gruen zones of the femoral stem, at two time points (6 and 12 months after implantation of a total hip endoprosthesis).

According to the results shown in Table 2, six months after implantation of the total hip endoprosthesis, patients receiving bisphosphonate therapy with Alendronate and patients without drug therapy had significantly different bone mineral composition in the 4th Gruen zone (p=0.034). The BMC parameter had a significantly lower mean value in this zone in the group of patients with drug therapy (median 1.87 vs 3.58).

In the other zones, with the exception of Zone 2, lower values for the BMC parameter were measured in SG patients compared to CG patients in this time control points, but the differences were not sufficient to be confirmed as statistically significant.

At one year of surgery, Table 3, bone mineral composition was significantly different between the two groups in zone 2 (p=0.008), and this significance is due to a significantly higher BMC value in Alendronate therapy patients (median 2.92 vs 1.53).

BMC presented slightly higher values in patients on Alendronate therapy compared to patients without this type of therapy in the other 6 Gruen's zones of the femoral stem.

Six months after surgery (Table 4), no significant difference in bone mineral density (BMD parameter) was found between patients treated with Alendronate and those without medication. The differences between the two groups in all 7 Gruen zones of the femoral stem were insignificant.

Table 2. Evaluation of BMC at 6 months

BMC 6 months				
zone	GROUP	mean ± SD	median (IQR)	p-level
Z1	SG CG	4.19 ± 3.7 4.51 ± 3.6	2.85(1.23 – 7.11) 3.25 (2.02 – 7.13)	Z=0.43 p=0.67 ns
Z2	SG CG	3.51 ± 2.8 3.09 ± 2.7	2.35 (1.12 – 5.31) 1.85 (1.02 – 5.14)	Z=-0.66 p=0.51ns
Z3	SG CG	3.05 ± 1.9 3.94 ± 2.3	2.75 (1.63 – 3.42) 3.65 (1.73 – 5.56)	Z=1.19 p=0.23ns
Z4	SG CG	2.45 ± 1.5 3.36 ± 1.7	1.87 (1.23 – 3.54) 3.58 (1.98 – 4.72)	Z=2.11 p=0.034sig
Z5	SG CG	2.67 ± 1.4 3.67 ± 1.9	2.63 (1.45 – 3.36) 3.06 (2.31 – 4.6)	Z=1.9 p=0.057ns
Z6	SG CG	3.72 ± 3.2 4.41 ± 3.3	2.36 (1.35 – 3.97) 3.12 (1.98 – 6.32)	Z=0.85 p=0.39ns
Z7	SG CG	3.41 ± 3.1 3.83 ± 2.9	1.95 (1.23 – 6.02) 2.76 (1.03 – 6.37)	Z=0.56 p=0.57 ns

p (Mann-Whitney U Test)

At the control examination one year after the surgical intervention (Table 6), significantly higher values for the BMD parameter were measured in patients with Alendronate therapy in all 7 Gruen Zones (p=0.0001,p=0.0002,p=0.000004,p=0.000003,p=0.000002, p=0.000007, and p<0.0001, respectively).

The mean value of bone mineral density in the examined and control group in the 1st Gruen zone was 1.43

Table 3. Evaluation of BMC at 12 months

BMC 6 months				
zone	GROUP	mean ± SD	median (IQR)	p-level
Z1	SG CG	4.75 ± 3.7 3.54 ± 2.4	3.64 (1.98 – 7.47) 2.63 (2.0 – 5.45)	Z=0.95 p=0.34ns
Z2	SG CG	4.08 ± 2.7 2.33 ± 2.2	2.92 (1.83 – 5.83) 1.53 (0.95 – 3.12)	Z=2.67 p=0.008sig
Z3	SG CG	3.58 ± 1.8 3.21 ± 2.3	3.21 (2.35 – 3.98) 2.45 (1.25 – 4.11)	Z=1.03 p=0.3ns
Z4	SG CG	3.07 ± 1.5 2.57 ± 1.6	2.65 (1.98 – 4.11) 2.25 (1.32 – 3.03)	Z=1.31 p=0.19ns
Z5	SG CG	3.29 ± 1.4 2.73 ± 1.4	3.11 (1.98 – 3.93) 2.34 (1.63 – 3.85)	Z=1.31 p=0.19ns
Z6	SG CG	4.32 ± 3.1 4.32 ± 3.1	3.12 (2.12 – 5.12) 2.75 (1.9 – 5.11)	Z=1.37 p=0.17ns
Z7	SG CG	4.14 ± 2.9 3.04 ± 2.3	2.94 (1.87 – 6.3) 2.11 (0.92 – 5.37)	Z=1.44 p=0.15ns

p (Mann-Whitney U Test)

and 0.68, respectively; in the 2nd Gruen zone 1.63 and 1.01, respectively; in the 3rd Gruen zone 1.88 and 1.12, respectively; in the 4th Gruen zone 1.98 and 1.13, respectively; in the 5th Gruen zone 2.12 and 1,12, respectively; in the 6th Gruen zone 2.32 and 1.12, respectively; and, in the 7th Gruen zone, the mean BMD values of 2.1 in SG and 1.12 in CG were measured.

Table 4. Evaluation of BMD at 6 months

BMD 6 months				
zone	GROUP	mean ± SD	median (IQR)	p-level
Z1	SG CG	0.97 ± 0.3 1.11 ± 0.7	0.97 (0.76 – 0.99) 0.89 (0.64 – 1.45)	Z=0.02 p=0.98ns
Z2	SG CG	1.27 ± 0.6 1.39 ± 0.7	1.12 (0.91 – 1.35) 1.23 (0.87 – 1.87)	Z=0.04 p=0.97ns
Z3	SG CG	1.49 ± 0.6 1.56 ± 0.7	1.24 (1.12 – 1.63) 1.45 (1.02 – 1.98)	Z=0.05 p=0.96ns
Z4	SG CG	1.41 ± 0.8 1.54 ± 0.7	1.21 (0.98 – 1.32) 1.28 (1.09 – 2.12)	Z=1.29 p=0.19ns
Z5	SG CG	1.65 ± 0.8 1.55 ± 0.7	1.42 (1.11 – 1.82) 1.23 (1.06 – 1.87)	Z=0.44 p=0.65ns
Z6	SG CG	1.93 ± 0.97 1.83 ± 1.1	1.67 (1.24 – 2.09) 1.43 (0.98 – 2.31)	Z=0.93 p=0.35ns
Z7	SG CG	2.01 ± 1.7 1.61 ± 0.8	1.67 (1.25 – 1.83) 1.4 (1.03 – 1.9)	Z=0.93 p=0.35ns

p (Mann-Whitney U Test)

Discussion

Studies investigating periprosthetic BMD have shown that the most significant bone loss occurs in the first 3 to 6 months after endoprosthesis implantation, followed by a period of stabilization during the first postoperative year [9,27].

Few studies have investigated the effect of Alendronate on this periprosthetic bone loss. A prospective randomized trial examined 13 patients treated for coxarthrosis with a cement-free hip endoprosthesis. Patients were randomized to receive only calcium or calcium Alendronate. This study showed that in patients treated with Alendronate, bone loss was significantly lower than in the control group

Table 5. Evaluation of BMD at 12 months

BMD 6 months				
zone	GROUP	mean ± SD	median (IQR)	p-level
Z1	SG CG	1.71 ± 0.7 0.93 ± 0.6	1.43 (1.13 – 1.98) 0.68 (0.51 – 1.23)	Z=3.87 p=0.0001sig
Z2	SG CG	2.02 ± 0.9 1.15 ± 0.5	1.63 (1.35 – 2.34) 1.01 (0.73 – 1.53)	Z=3.74 p=0.0002sig

Z3	SG CG	2.38 ± 1.5 1.24 ± 0.4	1.88 (1.56 – 2.32) 1.12 (0.97 – 1.37)	Z=4.59 p=0.000004sig
Z4	SG CG	2.26 ± 1.1 1.18 ± 0.4	1.98 (1.63 – 2.43) 1.13 (0.94 – 1.23)	Z=4.65 p=0.000003sig
Z5	SG CG	2.48 ± 1.2 1.22 ± 0.5	2.12 (1.71 – 2.72) 1.12 (0.89 – 1.28)	Z=4.76 p=0.000002sig
Z6	SG CG	2.63 ± 1.2 1.32 ± 0.6	2.32 (1.87 – 3.13) 1.12 (0.83 – 1.87)	Z=4.5 p=0.000007sig
Z7	SG CG	2.43 ± 1.02 1.18 ± 0.5	2.10 (1.64 – 2.84) 1.12 (0.89 – 1.32)	Z=5.05 p=0.000000sig

p (Mann-Whitney U Test)

(0.9% vs. 17.1% for proximal Gruen zones and 2.6% vs. 9.9% for all Gruen- zones)[20,22].

In our group of patients, the results showed an increase in BMD in all Gruen zones for all patients individually over a period of 6 months (measured 6 and 12 months after surgery), indicating the benefit of Alendronate in reducing periprosthetic osteolysis.

Our results from examining the values of BMD, but also of BMC, support the potential benefit of Alendronate in improving denture implantation, as studies show that the mechanism of action of Alendronate is expressed through an increase in bone mass and of the cortical and trabecular bones, with the greatest growth being in the trabecular bone, which is necessary for the implantation of the cement-free stem.

Conclusion

Alendronate is a proven inhibitor of periprosthetic bone loss that occurs after primary implantation of a total cement-free hip endoprosthesis. Our preliminary study reaffirms the effect of bisphosphonate therapy as an inhibitor of periprosthetic bone loss and aseptic implant loosening.

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