

## THE APPLICATION OF BISPHOSPHONATES IN THE TREATMENT OF PATIENTS WITH DISTURBED RENAL FUNCTION—CASE REPORT

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**Abstract.** Renal osteodystrophy and osteoporosis are related to chronic renal disease. In the present research and clinical dilemmas, indications have been proposed concerning the possible application of bisphosphonates in patients suffering from renal insufficiency. The aim of the study is to present a patient with disturbed renal function who was treated with parenteral bisphosphonates. The patient is a 56-year old male who was receiving hemodialysis for 29 years. In order to estimate risk for further bone fractures and to evaluate possible indication for intravenous bisphosphonates a bone mineral densitometry was performed, as well as transiliac biopsy with histological examination of the bone. The etiology of bone fractures in renal patients is multifactorial and cannot be fully explained only with the aid of pathohistological examination. After the thorough diagnostics, it could be possible to apply bisphosphonates in the treatment of patients with renal osteodystrophy on chronic hemodialysis or peritoneal dialysis.

**Key words:** Bisphosphonates, renal failure, dialysis

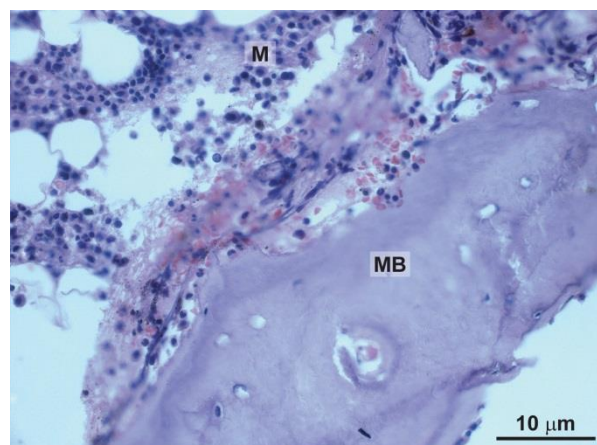
### Introduction

Bisphosphonates are inhibitors of osteoclastic bone resorption and are commonly used for the treatment of osteoporosis, bone resorption and hypercalcemia of different etiology [1]. Because of the adverse side-effects bisphosphonates are not used in the treatment of patients with terminal renal failure [2]. They are studied for possible use in the treatment of renal osteodystrophy and have not been approved for use yet in patients with renal failure [3]. Approximately 80% of the bisphosphonate is eliminated by the kidneys, with the remaining 20% taken up by the bone. Because of the risk of accumulation, elevated serum creatinine is listed in the manufacturers' literature as a contraindication to bisphosphonates use [4]. However, they have been safely used in dialysis patients and after renal transplantation for the treatment of high turnover bone disease, as well as vascular calcification and osteoporosis [5].

### Case Report

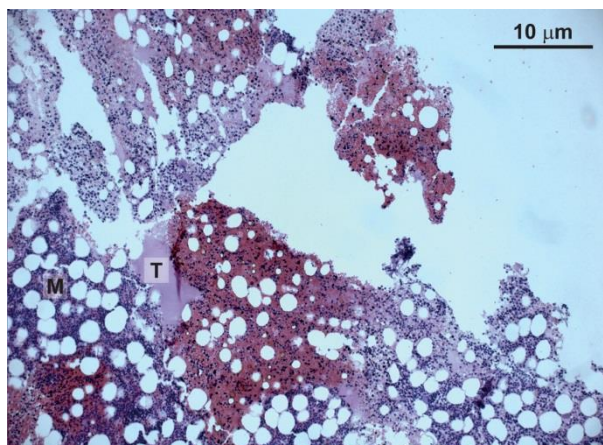
Among 120 peritoneal dialysis (PD) patients, the study describes a 56-year old male who had been on hemodialysis (HD) since 1977 and started peritoneal dialysis in 2001. In 2006 he had an episode of syncope when he fell down and got left femoral neck fractures with low mechanical impact. Dual energy x-ray absorptiometry of

the spine (L1–L4) was used to measure bone mineral density (BMD) in range of osteoporosis: 0,878 g/cm<sup>2</sup>, T score -2,5. Furthermore, BMD was also measured in left femur in a range osteoporosis: total left femur BMD 0,631 g/cm<sup>2</sup>, T score -3,1. We have been using cyclically one intravenous infusion of clodronate 300 mg/weekly during 6 months. After 6 months of therapy bone densitometry was repeated and it revealed deterioration in BMD of the spine (L1–L4) 0,847g/cm<sup>2</sup> with T score -2.78; on left femur BMD (total femur was 0,592 g/cm<sup>2</sup>, T score -3,4). The therapy was terminated although the desired effect of the inhibition of osteoclast activity was not achieved due to the inability to determine the cumulative



**Fig. 1.** Bone biopsy; hematoxylin and eosin, original magnification  $\times 200$ . H & E staining of a biopsy sample for general histology (MB, mineralized bone; M, marrow). Scale bar = 10  $\mu\text{m}$

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**Fig. 2.** Bone marrow medulla; hematoxylin and eosin, original magnification  $\times 200$ . H & E staining of a biopsy sample the ratio of cells to fat about 50% (T, trabeculae; M, marrow). Scale bar = 10  $\mu\text{m}$

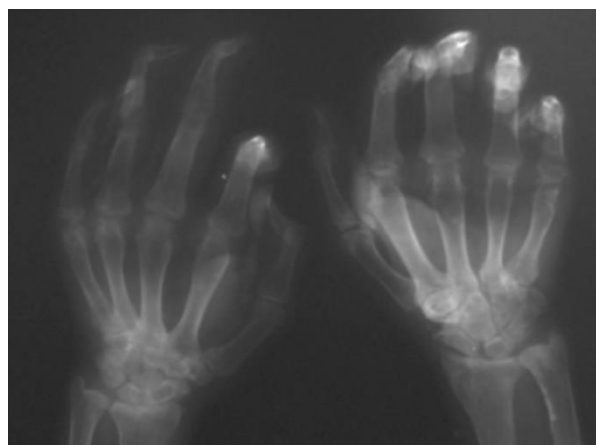
dose and because of the concern of possible side effects of the medication [6]. In order to exclude low bone turnover iliac biopsy was performed which excluded other mechanisms except osteoporosis.

## Discussion

In the present research, indications have been proposed concerning the possible application of bisphosphonates in patients suffering from renal insufficiency. The national guidelines have no recommendations on the treatment of renal rapid turnover osteodystrophy and osteoporosis using bisphosphonates in renal patients [7]. Previous clinical

## References

1. Hawley C, Elder G; Caring for Australasians with Renal Impairment (CARI). The CARI guidelines. *Biochemical targets. Nephrology (Carlton)* 2006; 11:S198–216.
2. Saadi H, Boobes Y, Bernieh B, Abouchacra S. Osteoporosis in renal failure: how accurate is the diagnosis and is there any role for bisphosphonates? *Int J Diabetes & Metab* 2005; 13:99–102.
3. Body JJ, Pfister T, Bauss F. Preclinical perspectives on bisphosphonate renal safety. *Oncologist* 2005; 10:3–7.
4. Jackson HG. Renal safety of ibandronate. *Oncologist* 2005; 10:14–18.
5. Tasić D. Mogući korisni aspekti bisfosfonata u lečenju bolesnika sa bubrežnom insuficijencijom. I Internacionalni kongres Lečenje osteoporoze sa međunarodnim učesćem: Niška Banja, 2006. (Serbian)



**Fig. 3.** X-ray; anteroposterior radiograph of the hands. Subperiosteal bone resorption is visible.

studies have shown that bisphosphonates can be safely used in preventing complications and preserving bone mass in a population of renal patients. Bisphosphonates can be used with caution and in especially treatment of malignant hypercalcemia [8]. The dose of drug, the length of treatment (delayed complications) should be adapted to dialysis modality and residual renal function [9].

## Conclusion

There is no clear beneficial effect of bisphosphonate treatment that outweighs possible side-effects in patients with renal failure at the moment. Positive result can be expected, but we need more clinical data regarding efficacy and safety of bisphosphonates in dialysis patients.

6. Tasić D, Avramović M, Veličković R, Veličković Lj. The application of bisphosphonates in the treatment of patients with disturbed renal function. 8th BANTAO Congress: Belgrade, 2007. (Serbian).
7. Cunningham J. Bisphosphonates in the renal patient. *Nephrol Dial Transplant* 2007; 22:1505–1507.
8. Toussaint ND, Elder JG, Kerr PG. Bisphosphonates in chronic kidney disease: balancing potential benefits and adverse effects on bone and soft tissue. *Clin J Am Soc Nephrol* 2009; 4:221–233.
9. Courtney AE, Maxwell AP. Chronic kidney disease and bisphosphonate treatment: are prescribing guidelines unnecessarily restrictive? *Postgrad Med J* 2009; 85:327–330.