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Efficacy of Zoledronic Acid Treatment in Paget Disease of Bone

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Abstract

Purpose: Paget disease is a disease of bone of unknown etiology with increased bone turnover that results in defective bone microarchitecture and bone deformity. Bisphosphonates are used in symptomatic Paget disease of bone. Clinical trials have shown that zoledronic acid was more effective than other bisphosphonates in treatment of Paget disease.

Methods: In this study, we retrospectively reviewed the remission and relapse statuses of 12 patients with Paget disease of bone, who were seen as outpatients between October 2011 and October 2013. We evaluated alkaline phosphates, osteocalcin, deoxypyridinoline levels measured before and at 6th, 12th, 18th months of treatment.

Results: Pretreatment values for alkaline phosphates, deoxypyridinoline, osteocalcin were as follows; 473 ± 256 U/L, 14.99 ± 7.63 mmol/L, 21.09 ± 3.18 ng/ml and post-treatmen valus for alkaline phosphates, deoxypyridinoline, osteocalcin were as follows; 82 ± 13 U/L, 5.14 ± 1.11 mmol/L, 8.57 ± 4.31 ng/ml. Remission was achieved in all patients after treatment. The levels indicated remission continued at 12th and 18th months of treatment. There was statistically significant difference between pretreatment and post-treatment values. No statistically significant difference between the levels measured at 6th, 12th and 18th months of treatment was detected.

Conclusion: We recommend zoledronic acid in the first line treatment of Paget disease of bone in achieving and maintaining remission.

Keywords: Zoledronic acid; Bisphosphonates; Bone turnover; Paget disease

Introduction

Paget disease is a disorder of bone of unknown etiology with increased bone turnover that results in defective bone microarchitecture. Defective microarchitecture results in deformity in skull and long bones, arthritis, deafness and pathologic fractures. Therefore, quality of life in patients with Paget disease is worse than normal population [1].

While formerly calcitonin was used in treatment of symptomatic Paget disease, bisphosphonates are used currently for the same indication. In clinical use, zoledronic acid provided a better clinical response with 96% normalization in ALP level with one dose, whereas 89% normalization was obtained after six months of treatment with other bisphosphonates. A significant improvement in quality of life was reported with zoledronic acid treatment [2]. Normalization in bone turnover, restoration in structure of bone, and regression in bone lesions were observed with bisphosphonate treatment [3]. Remission was shorter with other bisphosphonates and retreatment was required in every 1-3 years [4]. Zoledronic acid shows high affinity to bone [5]. Quite low recurrence rates were reported in patients with Paget disease treated with zoledronic acid [6].

We retrospectively reviewed relapse and remission rates with single dose zoledronic acid in patients with Paget disease.

Patients and Methods

Alkaline Phosphates (ALP), Osteocalcin (OC), and Deoxypyridinoline (DPD) levels measured before and at 6th, 12th, 18th months of treatment were retrospectively reviewed in twelve patients diagnosed with Paget disease (having typical symptoms, high ALP, OC, and DPD levels, bone lesions relevant with Paget disease on direct radiographs or bone scintigraphy) treated with zoledronic acid between October 2011 and October 2013. Vitamin D (400-1000 IU/day) and calcium (1 gr/day) supplementations were given to all patients before and after treatment with zoledronic acid. Neither hypocalcemia nor hypocalcemic symptoms were observed during zoledronic acid treatment. Subfebrile fever and myalgias were observed in three patients and were controlled with paracetamol.

Patients whose ALP levels reduced by 75% of the basal levels or within normal range according to the reference values were regarded as remission and 20% increase in the basal levels was regarded as relapse.

Total serum ALP was measured with Roche Hitachi 797 and normal reference range was 40–129 U/L. Serum OC and urine DPD were measured with Immulife 1000 and normal reference range was; 2–15 ng/ml, and 2.3–5.4 mmol/L, respectively.

Statistical analysis

Statistical analysis was conducted by using SPSS version 16. Student t test was used in comparison between two groups. A p value<0.05 was regarded as statistically significant

Results

Records of twelve patients with Paget disease were retrospectively analysed. Mean age of the patients was 58.37 ± 10. 92 and there were 9 males and 3 females. Nine of these 12 patients were newly diagnosed and received no therapy before the study. Remaining three patients were previously diagnosed patients in whom remission could not be provided with risedronate (2 patients) or pamidronate (1 patient).

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	BASAL	6th month	12th month	18th month
	(n:12)	(n:12)	(n:12)	(n:12)
ALP				
(40–129 U/L)	473 ± 256	82 ± 67	67 ± 15*^	74 ± 12.5 * ^ +
DPD				
(2.3–5.4 mmol/L)	14,99 ± 7,63	5,14 ± 1,11*	4,90 ± 1,18*^	5.09 ± 1,31 * ^+
OC				
(2–15 ng/ml)	21,09 ± 3,18	8,57 ± 4,31*	4,34 ± 1,82*^	5,45 ± 1,35 * ^+
* p < 0.001; ALP, DPD, OC values at 6th, 12th, 18th months were significantly lower than basal values.				
^ + p>0.05; Difference between values of 6th, 12th, and 18th months were not statistically significant				

Table 1: Pretreatment and posttreatment results.

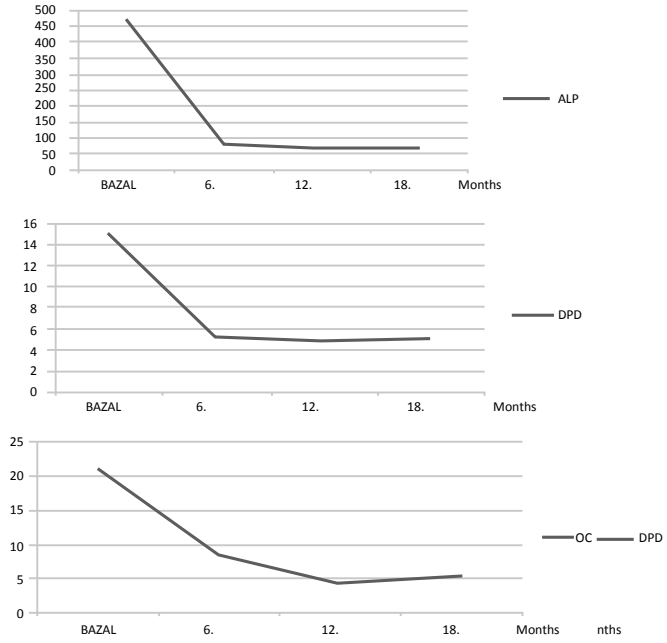

Figure 1: Remission after treatment.

Pretreatment results were: ALP: 473 ± 256 U/L; DPD: 14.99 ± 7.63 mmol/L; OC: 21.09 ± 3.18 ng/ml. The results at the 6th month of therapy were: ALP: 82 ± 13 U/L; DPD: 5.14 ± 1.11 mmol/L; OC: 8.57 ± 4.31 ng/ml. Remission was provided in all patients (Table 1). Comparison of the results of 12th and 18th months revealed that remission was persistent (Figure 1). There was statistically significant difference between pretreatment values and values at 6th, 12th and 18th months of treatment ($p<0.05$). No statistically significant difference between the levels measured at 6th, 12th and 18th months of treatment was detected ($p>0.05$).

Discussion

In a study by Ried et al. [2], single dose of zoledronic acid (5 mg) was given to 176 patiets and 60 days of treament with risedronate (30mg/day) was given to 171 patients. Remission was provided at the 6th month of treatment in 74.3% of patients treated with risedronate and 96% of patients treated with zoledronic acid [2]. In a study by Merlotti et al. [7], pamidronate was given to 60 patients at a dose of 30 mg/day in sequential two days/per three months and single dose of 4 mg zoledronic acid was given to 30 patients. Remission rate was 45% in the pamidronate group and 97% in the zoledronic acid group at the 6th month of treatment [7]. In our study, remission was obtained in all patients with a single dose of 5 mg zoledronic acid at the 6th month of treatment. Two of these patients treated with risedronate and one treated with pamidronate previously did not have remission. All of these three patients remitted with a single dose of zoledronic acid.

In a study by Ried et al. [8], zoledronic acid was given to 152 patients; risedronate to 112 patients and followed-up for a period of 6.5 years. Relapse rate was 20% in risedronate group and 0.7% (1/152) in zoledronic acid group. No relapse was observed in our study in the follow-up duration of 18 months.

Conclusion

This study showed that, remission can be achieved in all 12 patients at the 6th month and can be maintained at the 18th month of zoledronic acid treatment. No relapse was observed during the study period.

Limitations of the study; Case series observations. Only the results of patients treated with zoledronic acid were evaluated. Comparison with other bisphosphonates cannot be made. Long term results cannot be given as the follow-up duration was short.

In conclusion zoledronic acid can be recommended a good therapeutic option treatment of Paget disease.

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