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Short Communication

Analgesic Effect of Intravenous Pamidronate on Chronic Back Pain due to Osteoporotic Vertebral Fractures

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Abstracts: Pamidronate, a bisphosphonate analogue has been evaluated in a retrospective study for its analgesic effect on chronic back pain due to vertebral fractures in 26 patients suffering from senile osteoporosis or glucocorticoid-induced osteoporosis. Sixty milligrams of pamidronate was administered intravenously every 3 months for one year. After three months of treatment, the pain score fell from 3.2 $\pm$ 0.1 to 1.2 $\pm$ 0.2 in both groups. In conclusion, intravenous pamidronate seems to be a valuable treatment for chronic back pain due to osteoporotic vertebral fractures.

Keywords: Bisphosphonate; Low back pain; Osteoporosis

Introduction

Osteoporosis is a major public health problem. In the USA, osteoporosis predisposes to more than 1.3 million fractures annually, including 500 000 spine fractures [1]. Vertebral fractures occur in the natural history of osteoporosis and are associated with pain, immobility, disability and deterioration of the quality of life. Fortunately, in several patients the complaints disappear within a few weeks with the help of some rest, analgesics, back supports and physiotherapy. However, for patients with refractory chronic back pain due to osteoporotic vertebral fractures, there are not many efficient therapeutic interventions available.

Bisphosphonates have shown their efficacy in the treatment of postmenopausal [2], senile and glucocorticoid-induced osteoporosis [3] by reducing the incidence of fracture and increasing bone mass. However, in cancer with lytic bone metastases and in Paget's disease of bone, bisphosphonates are now widely used for their effect on pain. Pamidronate, a second generation bisphosphonate, reduces skeletal pain and biochemical markers of bone resorption in pain with skeletal metastases. It has been shown that half of the patients suffering from breast cancer metastases treated with intravenous pamidronate had relief of pain [4,5]. Moreover, risedronate has been shown to decrease bone pain in 56% of patients with Paget's disease of bone [6]. Therefore, the objective of the study was to evaluate the effect of intravenous pamidronate on chronic back pain and mobility due to osteoporotic vertebral fractures.

Patients and Methods

In a retrospective study, we included 26 patients (mean age 75 $\pm$ 0.8 years; 10 males and 16 females) suffering from refractory back pain due to one or more vertebral fractures present for at least 2 months (mean 3.2 $\pm$ 1.1 months). Fifteen patients suffered from senile osteoporosis (four males and 11 females) and 11 patients from glucocorticoid-induced osteoporosis (six males and five females). All patients were receiving 3 g paracetamol and 50 mg tilidine chlorhydrate daily without sufficient benefit. The patients were hospitalised for 48 h. The treatment consisted of an infusion of 30 mg pamidronate in 250 ml 0.9% NaCl solution administered over a 3-h period, which was then repeated the day after. This treatment was carried out every 3 months for 1 year. All patients were receiving concomitantly 1000 mg calcium and 600 IU vitamin D_3 daily. Before the treatment and

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after 48 h, 1 month, 3 months and 1 year, the patients were evaluated for pain and mobility. All results are expressed as the mean ± SE of the mean. Data were compared using analysis of variance and paired or unpaired Student's *t*-test. Statistical significance was assigned as $p < 0.05$. To assess pain, patients were asked how severe was their pain (0, no pain; 1, mild pain; 2, moderate pain; 3, severe pain; 4, unbearable pain). Mobility was assessed by asking the patients if they could get up from a chair (0, without difficulty; 1,with a little difficulty; 2, with moderate difficulty; 3, with great difficulty; 4, only with help) [7].

Results

After the first treatment, the pain score fell from 3.2 ± 0.1 to 1.7 ± 0.1 ($p < 0.005$) within 48 h. After 1 month and 3 months the mean pain score decreased, respectively, to 1.2 ± 0.2 and 0.8 ± 0.1 ($p < 0.025$). After 1 year, there was no change in the pain complaints compared with the pain scores at 3 months. Analgesic therapy could be discontinued in all the patients. After the treatment the mobility score fell from 2.6 ± 0.2 to 1.9 ± 0.4 ($p < 0.005$) within 48 h. After 1 month and 3 months, the mobility score decreased, respectively, to 1.1 ± 0.2 and 0.8 ± 0.1 ($p < 0.025$). After 1 year, there was no change in mobility compared with the mobility score at 3 months. There were no statistical differences in pain score or in mobility score between the two groups of osteoporosis patients. The following biological bone markers were within normal limits before the treatment: blood calcium, phosphate, alkaline phosphatases, total protein, and fasting 2 h urinary calcium excretion and hydroxyproline/creatinine ratio. After 3 months, the alkaline phosphatase levels (60–310 IU/l) decreased from 175 ± 12 IU/l to 126 ± 7 IU/l ($p < 0.005$) in the senile osteoporosis group and from 165 ± 8 IU/l to 124 ± 12 IU/l ($p < 0.005$) in the glucocorticoid-induced osteoporosis group. This effect was sustained for 1 year. Similarly, the fasting 2 h urinary hydroxyproline/creatinine ratio significantly decreased in both groups from 20 ± 1.2 to 15.2 ± 0.7 ($p < 0.025$) in the senile osteoporosis group and from 22 ± 4.3 to 12 ± 0.8 ($p < 0.025$) in the glucocorticoid-induced osteoporosis group. Serum calcium, phosphate and fasting 2 h urinary calcium excretion remained unchanged. Bone mineral density, evaluated before the treatment and after 1 year using dual-energy X-ray absorptiometry, showed an increase from 0.85 ± 0.06 g/cm^2 to 0.90 ± 0.08 g/cm^2 in the senile osteoporosis group and no significant increase in the glucocorticoid-induced osteoporosis group. No new vertebral fractures occurred during the 1-year follow-up. Pamidronate was well tolerated because only one patient reported fever and myalgia during the first course of pamidronate therapy.

Discussion

Besides bed rest, analgesic drugs and physiotherapy, there is no alternative treatment for chronic back pain due to osteoporotic vertebral fractures. From this study, infusions of pamidronate seemed to decrease significantly bone pain and improve mobility after 48 h. This effect was sustained at 1 month, 3 months and 1 year. The very early effect at 48 h can probably be explained by a placebo effect. However, the rapid and strong reduction in pain and improvement in mobility remained for at least 1 year and seemed to be related to pamidronate infusions in patients suffering from severe chronic and refractory back pain. Moreover, the same effect has been observed for painful metastases treated with pamidronate. Pamidronate seems to have a moderate effect on bone mass, which might be due to the variability of dual-energy X-ray absorptiometry or to insufficient dosage of pamidronate.

In conclusion, intravenous pamidronate seems to be a valuable treatment for pain as well as for rehabilitating the elderly suffering from chronic and refractory back pain due to osteoporotic vertebral fractures. However, our study is preliminary and needs to be extended and conducted under controlled conditions.

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