

Osteoporosis, Fracture Healing and Teriparatide

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Abstract

The major concern about osteoporosis is the high risk of fracture that is often associated with decreased of the quality of life. Few drugs available for osteoporosis treatment may affect the bone repair, which can increase and accelerate fracture healing. Randomized studies and case reports show that Teriparatide, an anabolic agent, may have a positive impact on fracture healing, in both osteoporotic fractures and atypical femoral fractures. Other agents, such as strontium ranelate and anti-sclerostin also showed a benefit in bone repair. In spite of promising results with osteoporotic drugs in fracture healing, especially osteoanabolic agents, more randomized trials are required to whether approve or not the use of these drugs as a conservative and non conservative therapy for osteoporotic fractures.

Keywords: Osteoporosis; Fracture healing; Bone repair; Teriparatide

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Introduction

Osteoporosis is characterized by reducing bone mineral density (BMD) and the gradual but increased the risk of fragility fracture [1]. Osteoporotic fractures are often associated with decreased of the quality of life due to pain, bone deformities and loss of independence. Moreover, osteoporotic fractures are associated with high health-care costs, once they can generate hospitalization and rehabilitation [2].

To diminish the risk of osteoporotic fractures and its complications, some drugs available that reduce the rate of bone loss. Bisphosphonates, Strontium ranelate, Teriparatide, Calcitonin, and Denosumab are some of the options approved for treatment of osteoporosis [3].

Teriparatide is an analog of human parathyroid hormone used as an anabolic agent for patients with osteoporosis and high risk of fracture. It stimulates the net of bone connection through osteoblasts and osteoclasts cells activity, which increases bone formation [1] Because of its anabolic effect, there has been an interest for its role in improving bone repair. There are studies demonstrating that Teriparatide can also enhance and accelerate the rate of fracture healing. These findings could have an impact on decreasing the osteoporotic fracture morbidity, particularly in individuals with a high risk for impaired fracture healing [4].

Discussion

The bone repair occurs in three particular stages: inflammatory, reparative, and remodeling. The reparative stage is, perhaps, the phase in which Teriparatide have its most important anabolic role [5]. Studies using small and large animal models demonstrated that Teriparatide could significantly improve callus mineralization, quality, and rate of an effective union at the fracture site [6].

Manabe et al. in 2006, used cynomolgus monkeys because their remodeling phase is similar to humans, and observed that Teriparatide accelerates fracture healing process by decreasing callus measure and increasing its mineralization [7].

A randomized, double-blind study involving 102 post-menopausal women with distal radial fractures was performed by Aspenberg et al. The study showed that there was an abbreviated time of fracture healing in the group who received 20 mcg of Teriparatide compared with placebo [8].

A case series performed in India with 22 postmenopausal women with osteoporosis and fractures showed radiographic signs consistent with fracture healing during four weeks into therapy with Teriparatide [4].

Borges et al. reported a case involving an 84-year old woman with a fall-related trochanteric fracture who was submitted to surgical treatment. Radiographic image of the fracture site was performed a month after the surgery and showed no evidence of fracture

healing. She received 20 mcg of Teriparatide daily and after only one month of treatment, X-ray revealed dense callus formation. The case report strengthens the evidence that Teriparatide can accelerate fracture healing [5].

Chiang et al. developed a prospective study with 14 patients presenting with two years with the atypical femoral fracture. It was offered 20 mcg of Teriparatide daily for six months. In 5 treated patients, 2 to 3 fold increment in bone remodeling markers and fracture healing. The results suggested that Teriparatide could assist in healing atypical fractures [9].

Atypical femoral fracture (AFF) can be a long-term bisphosphonate use. Teriparatide treatment appears to significantly shorten the postoperative time to fracture healing and reduce rates of delayed healing or non-union after bisphosphonate-associated AFF [10].

An Asian systematic review provides support for the clinical effectiveness of Teriparatide for treatment of postmenopausal women with osteoporosis who are at high risk of fracture in terms of improvement in BMD and tolerability. However, additional studies are needed in Asian populations to confirm the reduction in fracture risk with Teriparatide [11].

Strontium ranelate is an anti-osteoporotic agent, which stimulates bone formation by increasing bone cell replication. Ozturan et al.

developed a study to evaluate the effect of Strontium ranelate on fracture healing in the osteoporotic rat model. They employed both ovariectomy and subsequent heparin injection to induce osteoporosis. The group that received treatment with 450 mg/kg/day of Strontium ranelate had more developed woven bone and also a higher fracture stiffness and mechanical strength contrasted with the control group [12].

A new therapeutic option for patients with osteoporosis is to block sclerostin with an antibody to increase bone formation. Sclerostin is delivered by osteocytes and is an inhibitor of bone formation. Anti-sclerostin antibody was also associated with fracture repair improvement. Li et al. demonstrated that exposure of the anti-sclerostin antibody in a rat model increased bone formation and screw fixation both in loaded and unloaded bone [13].

In summary, widespread evidence acquired from studies with animals show that Teriparatide improves and may accelerate fracture healing. Nevertheless, results from human studies suggest that it may be effective in accelerating and increasing the rate of fracture healing. However, more randomized controlled trials are needed to evaluate with certainty the impacts of Teriparatide osteoanabolic role in fracture healing to decide on incorporate this drug as a standard option for conservative management of osteoporotic fracture.

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