

Case Report

Teriparatide treatment in non-uniting fracture: a case report

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ABSTRACT

Impaired healing of fractures delays the rehabilitation process, which in turn impacts quality of life. The associated costs cause an economic burden to both the society and the patients. Till date, no systemic treatment is approved for fracture healing. Teriparatide is a synthetic polypeptide hormone consisting of the 1–34 fragment of human parathyroid hormone. Apart from its recognized indication of osteoporosis, there is a growing body of evidence suggesting its ability to accelerate fracture healing and heal non-unions. The purpose of this case report is to elucidate the Indian experience of 5 cases of use of Teriparatide for fracture healing - delayed unions and non-unions and in the setting of osteoporotic fracture. The primary observation of our case report depicts that teriparatide is a viable therapy not only to treat osteoporosis but also to accelerate fracture healing. Teriparatide therapy accelerates healing, which allows patients to return to normal life and work faster, optimizes medical resource utilization, reduces chances for future second surgery, requirement of bone graft and overall chronic morbidity associated with long-term treatment. The advantages of teriparatide therapy are that it can be prescribed in any types of fractures, including those that will be treated non-surgically; it can be commenced at any time, and can be applied through the entire healing period. Our observations are in line with other studies showing the effects of Teriparatide on delayed union and non-unions in human subjects.

Keywords: Teriparatide, Fracture healing, Non union, Anabolic therapy

INTRODUCTION

Teriparatide is a synthetic polypeptide hormone consisting of the 1–34 fragment of human parathyroid hormone. It retains most of the biological activities of PTH. Intermittent administration of teriparatide has anabolic effects that stimulate bone formation and activate bone remodeling, improve the micro-architecture of trabecular bone and cortical bone and increase bone mineral density.¹⁻³ Teriparatide is the only anabolic drug for osteoporosis licensed for use by the FDA in 2002. The recommended dose is 20 µg once daily and treatment is not recommended for a duration exceeding 2 years.

Apart from this recognized indication, there is a growing body of evidence suggesting its ability to accelerate

fracture healing and heal non-unions. The purpose of this case report is to elucidate the Indian experience of 5 cases of use of Teriparatide for fracture healing - delayed unions and non-unions and in the setting of osteoporotic fracture.

CASE REPORT

Case 1

A 50 year old male presented with fall on right arm. The patient had a fracture of middle one-third part of humerus of the oblique pattern. The patient's medical history was free of cardiovascular problems, malignancies or unexplained weight loss. He gave history that two years back he had a fracture of humerus. X-ray revealed a

healed fracture of lower one-third of humerus with a fixed LC-LCP instrument in-situ. The fracture was fixed with interfrag screw and then long Lc-Lcp. This peri-prosthetic fracture was kept in sling and calcium and vitamin D supplements were given.

At 2 months, X-ray revealed no union. The authors decided to initiate Injection Teriparatide. Patient continued to take calcium and vitamin D supplements.

X-ray at 6 months showed complete union of fracture and at 1 year showed complete union of fracture.

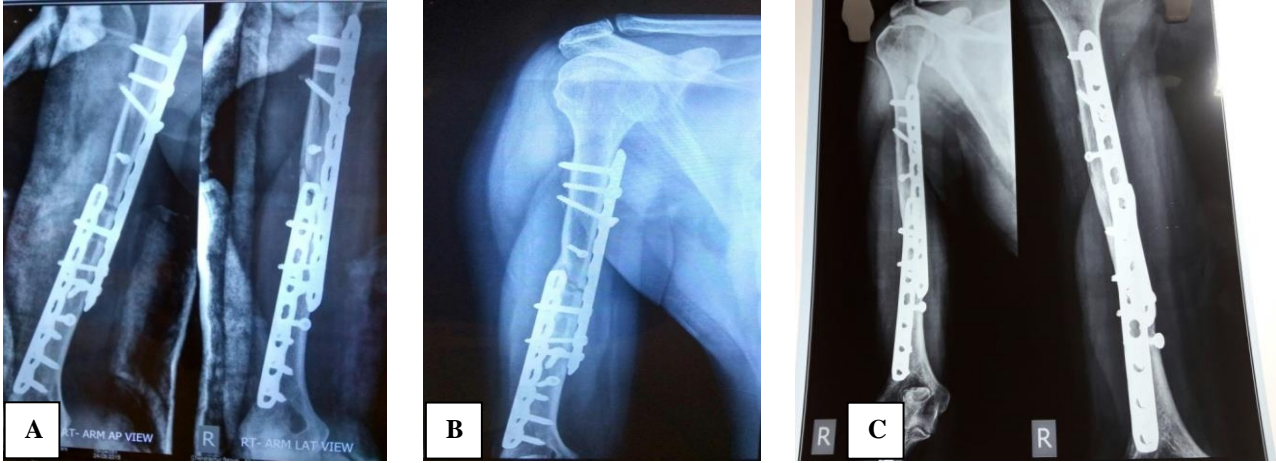


Figure 1: X-ray right shoulder antero-posterior view of case 1 at 2, 6 and 12 months (A: 2nd month; B: 6th month; C: 1 year)

Case 2

A 55 year old female presented with history of fall over right shoulder. X-ray revealed a Neer three part fracture (fracture lines involved 3-4 parts, two part were displaced). No signs of union were seen and author suspected chances of avascular necrosis (AVN) of head

of humerus. Although no AVN was observed on 2 month Xray. Injection Teriparatide was initiated along with calcium and vitamin D supplements.

Physiological signs of union seen on 6 months X-ray. Injection Teriparatide was continued for 3 more months. Complete union of X-ray was observed at 1 year. No AVN was observed.



Figure 2. X ray right shoulder antero-posterior view of case 2 at pre-operative, post-operative and 12 months (A: day 0 pre-operative; B: day 0 post-operative; C: 1 year)

Case 3

A 70 year old osteoporotic female patient presented to the clinic with history of fall on left arm. X-ray revealed spiral oblique fracture of the humerus.

At 2 months, X-ray revealed no union. The author decided to initiate Injection Teriparatide for 3 months along with calcium and vitamin D supplements.

X-ray at 6 months showed complete union of fracture.



Figure 3: X-ray left shoulder antero-posterior view of case 3 at day 0, 1 month and 2 months (A: day 0; B: 1st month, C: 2nd month).

Case 4

A 20 year old patient fell on right arm while playing cricket. The patient got fracture humerus. Operation was

done on 5th Feb. 2015. After 4th month, the X-ray showed hypertrophic nonunion. Injection teriperatide was started for 3 months. The fracture was united on 7th month.

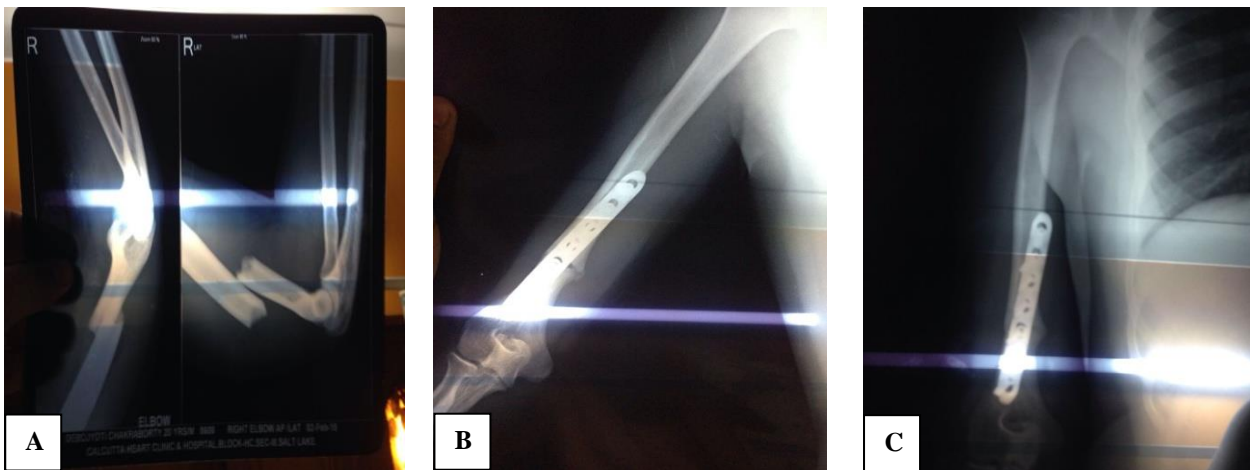


Figure 4: X-ray right arm antero-posterior view of case 4 at day 0, 4 month and 7 months (A: day 0; B: 4th month, C: 7th month).

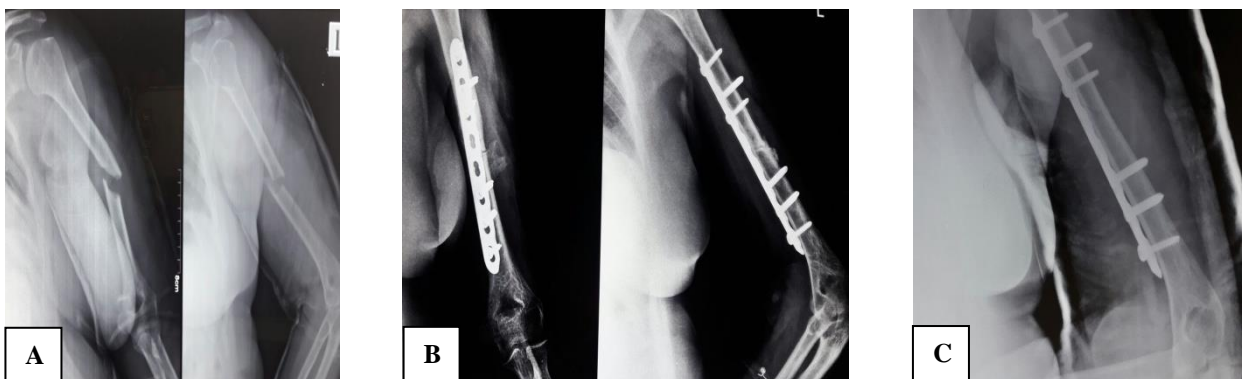


Figure 5: X-ray left humerus antero-posterior view of case 5 at day 10, 1 month and 3 months (A: day 10; B: 1st month; C: 3rd month).

Case 5

57 year old osteoporotic and diabetic female presented to the clinic with 10 days old fracture left humerus. Operation was done on day 10. On 2nd month X-ray revealed signs of no union. The author decided to initiate Injection teriparatide from 2nd month along with calcium and vitamin D supplements. Patient has completed 2 injections of teriparatide and fracture has almost united (Figure 5).

DISCUSSION

Our observations are in line with other studies showing the effects of Teriparatide on delayed union and non-unions in human subjects. Peichl et al evaluated the effect of PTH 1-84 on pelvic fracture healing and functional outcome in 65 postmenopausal women.⁴ The treatment arm received once daily 100 µg of PTH 1-84 starting within two days after admission to hospital. The median time from fracture to the first sign of complete cortical bridging of the pelvic fracture (verified with CT scanning) was 7.8 week for the treatment group compared with 12.6 week for controls.

Bukata et al reported 145 patients with fractures of the spine or other extremities that were treated with 20 µg of Teriparatide.⁵ Regardless of fracture site, 141 people reported resolution of pain at the fracture site within 12 wk of starting Teriparatide and the fracture united in 93%. Indicators of healing i.e. pain resolution and bridging of the fracture site by radiograph or CT scan were noted to occur earlier in fractures that were predominantly trabecular bone (vertebrae, sacral ala, metadiaphyseal long bones) compared with fractures of diaphyseal bone or fusion sites.

Aspenberg et al examined the effect of placebo compared to Teriparatide administered in doses 20 and 40 µg given daily to a population of female patients with distal radius fractures.⁶ Median time to the first radiographic evidence of healing was 9.1 week in the placebo group compared to 7.4 and 8.8 week in the groups treated with 20 µg and 40 µg of Teriparatide respectively. This was not statistically significant (p=0.15). Similarly, cases have been reported of almost normal fracture healing in elderly patients with established osteoporosis after starting treatment with Teriparatide.⁷

Chintamaneni et al reported on a 67-year-old male who sustained a fracture of the body of the sternum as a result of a road traffic accident.⁸ This subsequently failed to heal resulting in a painful atrophic non-union. A trial of 20 µg per day of Teriparatide was initiated and showed significant healing of the non-union within 3 months and complete healing and symptomatic resolution after 9 months.

Rubery and Bukata have also report 3 cases of painful delayed unions of type III odontoid fractures which

united and led to resolution of pain after treatment with Teriparatide.⁹

Clinical applications

The primary observation of our case report depicts that teriparatide is a viable therapy not only to treat osteoporosis but also to accelerate fracture healing. Till date, no systemic treatment is approved for fracture healing. Impaired healing of fractures delays the rehabilitation process, which in turn impacts quality of life. Elderly patients tend to deteriorate in general health during a long healing time. Also, the associated costs cause an economic burden to both the society and the patients. Teriparatide therapy accelerates healing, which allows patients to return to normal life and work faster, optimizes medical resource utilization, reduces chances for future second surgery, requirement of bone graft and overall chronic morbidity associated with long-term treatment.

The advantages of teriparatide therapy are that it can be prescribed in any types of fractures, including those that will be treated non-surgically; it can be commenced at any time, and can be applied through the entire healing period. Interestingly, Lou S et al discovered that there are different effects between fractures of upper limbs and lower limbs and the lower limb group has a better result than the upper limb group.¹⁰

CONCLUSION

Teriparatide is approved and marketed for the treatment of Osteoporosis. Emerging research in the last decade has shown a potential application in fracture management. Preclinical animal studies have shown improvements in callus volume, callus mineralization, bone mineral content, strength and rate of successful union at the fracture site in both normal and delayed healing models has been demonstrated. Role of teriparatide is promising for the management of fractures and non-unions. Some preclinical studies have shown dose-dependent increased risk of osteosarcoma, osteoblastoma and osteoma in rats with use of teriparatide, hence caution is warranted. Well-designed randomized placebo-controlled trials are required to comprehensively analyze the efficacy and safety of teriparatide as a standard therapy for conservative management of fractures and non-unions.

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