Section: Orthopedics

Original Research Article

A STUDY OF EFFICACY AND ROLE OF TERIPARATIDE(rh-PTH) THERAPY IN SURGICALLY CORRECTED COMMINUTED FRACTURES AT A TERTIARY CARE CENTER

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ABSTRACT

Background: To study the efficacy of teriparatide therapy in surgically corrected comminuted fractures.

Materials and Methods: Prospective observational study was conducted in 50 patients of either gender who are skeletally mature presenting with comminuted fracture or nonunion after surgical correction, without comorbidities who are medically fit for taking the teriparatide are included in study.

Results: One third of the patients belonged to the age group of 30-39 years and 40-49 years. 82% of the study population were males, 18% of them were females. 70% of the study population were injured on the right side, 30% of them were injured on the left side. 76% of the study population lower limbs were injured, 30% of them had injury on the upper limbs. 74% of the study population had Road Traffic Accident. 36% of the study population had fracture of femur. 6% of them had fracture of both tibia and fibula. 2% of them had fracture of both radius and ulna. Only one patient had fracture neck of humerus. 42% of the study population showed signs of radiological union after 3-4 months of drug administration, followed by within 3 months (30%), 5-6 months (20%). 92% of the study population had achieved complete radiological union at the end of one year follow up. 44% of the study population showed complete radiological union after 7-9 months of drug administration. Complete range of movements was achieved in 52% of the study population. The range of movements was increased in 40% of the study population. 8% of the study population had restricted movements at the end of the study period. 56% of the study population had experienced side effects. 52% of the study population had nausea, 28% of them had dizziness and 18% had hypercalcemia.

Conclusion: The present study concluded that the efficacy of teriparatide in surgically treated comminuted fracture healing cases is 92%. The drug was tolerated well with minor side effects like nausea and dizziness.

Keywords: Teriparatide, comminuted fracture, Radiological union.

INTRODUCTION

Fracture healing is a process which requires the involvement of multiple tissue mechanisms for a successful outcome. Bony tissue is highly efficacious in its ability to regenerate completely under normal conditions. Delayed union or non-union remains a devastating complication of fracture in around about 10-15% of the patients.[1] Nonunion of bone is the body's inability to heal a fracture. The most agreed-upon standard definition of nonunion made by the FDA is a fracture that persists for a minimum of nine months without signs of healing for three months.[2] Nonunion is a complex orthopedic problem that is multi-factorial, and clinicians need to entertain multiple modalities as therapeutic interventions.

Currently there is a plethora of various treatment strategies available for delayed or non-union fractures to augment the bone regeneration. These include autologous bone graft, distraction osteogenesis, allograft implantation, gene therapy, of which autologous bone graft is the gold standard. Autologous bone graft besides a successful treatment outcome has its own limitations: Major limitation is the high cost as second surgery is required for harvesting the bone material and material is highly limited.[3]

An improved understanding of the patho-physiology of bone repair and remodeling has led to the development of various pharmacological therapies which include ortho-biologics such as stem cells, growth factors such as BMPs (Bone morphogenetic proteins), VEGF (Vascular endothelial growth factor), osteo-progenitor cells, osteoinductive growth factors and anabolic agents (parathormone and analogues). These newer therapies have the potential to accelerate fracture repair in case of delayed or non-union of fractures.[4]

Teriparatide (rhPTH [1-34]) is a peptide representing the amino-terminal portion of human parathyroid hormone. It is an osteo-anabolic agent approved in various countries for postmenopausal women and men with osteoporosis for prevention of fractures. Teriparatide is manufactured by using a genetically modified strain of E. coli and is given as a solution for subcutaneous injection.

Teriparatide (rhPTH [1-34]) is a peptide representing the amino-terminal portion of human parathyroid hormone. It is an osteo-anabolic agent approved in various countries for postmenopausal women and men with osteoporosis for prevention of fractures.[5] It has the ability to accelerate fracture healing and also heals non-unions. It allows patients to return to normal life and work faster by early union of fracture improving bone mineralization, cortical strength, corrects osteopenia, osteoporosis effectively, optimizes medical resource utilization, reduces chances of second surgery in form of bone grafting and reduces overall chronic morbidity associated with long term treatment. There are various case reports and case series of fracture healing with teriparatide. At present there are only limited studies that have proved the role of teriparatide in fracture healing. Hence this study was taken up to assess the role of teraparatide in surgically corrected cases of communited fractures.

MATERIAL AND METHODS

Prospective observational study was conducted in the Department of Orthopaedics, Prathima Institute of Medical Sciences. 50 patients presenting with surgically corrected comminuted fractures who were admitted for treatment in the department of Orthopaedics, Pratima Institute of Medical Sciences.

Inclusion Criteria

Patients of either gender who are skeletally mature presenting with comminuted fracture or nonunion after surgical correction, without comorbidities who are medically fit for taking the teriparatide.

Exclusion Criteria

Children and young adults with open epiphysis, patients presenting with fracture or non-union with Hypercalcemia, Severe renal impairment with low GFR, Pregnant and Breastfeeding mothers, Prior history of bone metastasis and Prior radiotherapy of skeletal system.

After taking a detailed history, complete clinical examination was done. All the findings were recorded in a pre-tested semi structured proforma. The parameters were taken are age, gender, religion, occupation, history of fall, time and place of fall, time interval between injury and treatment, medical history of the patient and details of surgical correction.

Systemic examination, Local examination, swelling and deformity, restriction of movements of the nearest joint and Condition of the skin. Teriparatide was administered on post-operative day 3 or 11 or as soon as the signs of non-union were evident on radiological examination for three months. Follow up was continued for three months to a year after the administration of teriparatide.

Outcome was measured based on clinical improvement and radiological assessment of the fracture site at regular intervals by one single examiner. X-rays were used for radiological assessment. X-rays were taken at immediate post-operative period and during follow up visits. Radiological assessment was done in terms of callus formation and complete union. Time required for union, range of motion of surrounding joints and complications occurred (if any) were studied in detail.

RESULTS

The study was conducted in the Department of Orthopaedics, Pratima Institute of Medical Sciences. One third of the patients belonged to the age group of 30-39 years and 40-49 years. 12% of the patients belonged to age group of 50-59 year and 10% of the patients belonged to 20-29 years and >60 years each. 82% of the study population were males, 18% of them were females.

70% of the study population were injured on the right side, 30% of them were injured on the left side. 76% of the study population lower limbs were injured, 30% of them had injury on the upper limbs. 74% of the study population had Road Traffic Accident, 26% of them had suffered fall. [Tabel 1]

36% of the study population had fracture of femur, followed by tibia (24%), radius (16%). 10% of them had fracture of both femur and tibia. 6% of them had fracture of both tibia and fibula. 2% of them had fracture of both radius, ulna and humerus. [Table 2]

The most common surgical technique was DHS for femur (34%), followed by Bone grafting (15%) for fibula and ulnar fractures, IMIL nailing for tibia (14%), Ellies plate for distal radius (10%), Plating with K wire for distal radius(8%). DCP for distal humerus and PHILOS for proximal humerus constituted to 2% each. [Table 3]

42% of the study population showed signs of radiological union after 3-4 months of drug administration, followed by within 3 months (30%), 5-6 months (20%). Only in 8%the signs of radiological union appeared within 6-9 months. [Table 4]

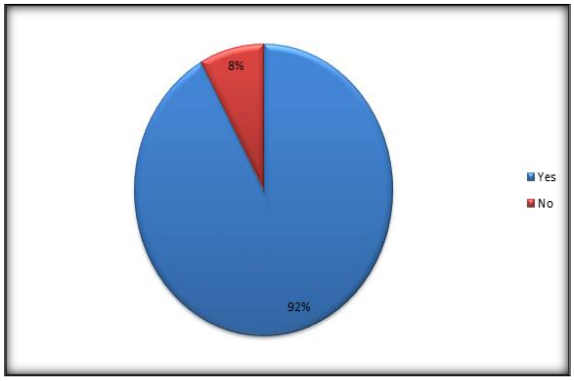

Figure 1: showing achievement of complete radiological union of study population

92% of the study population had achieved complete radiological union at the end of one year follow up.

44% of the study population showed complete radiological union after 7-9 months of drug administration, followed by 3-6 months (24%), <3 months (16%). 8% showed complete radiological union within 10-12 months. [Table 5]

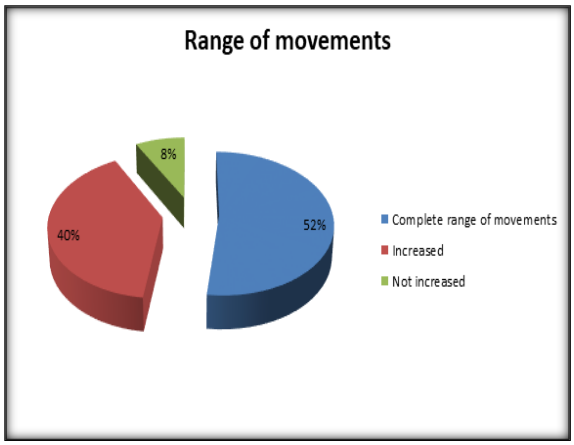

Figure 2: showing the functional outcome

Complete range of movements was achieved in 52% of the study population. The range of movements was increased in 40% of the study population. 8% of the study population had restricted movements at the end of the study period.

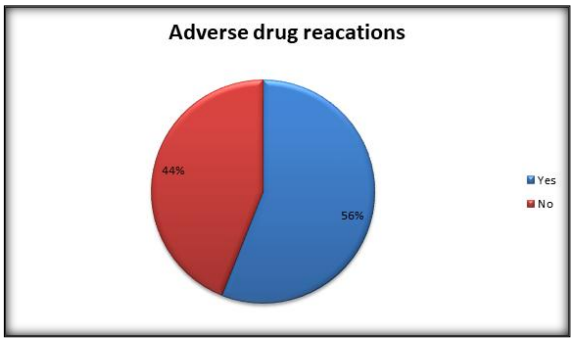

Figure 3: showing adverse drug reactions of study population

56% of the study population had experienced side effects.

52% of the study population had nausea, 28% of them had dizziness and 18% had hypercalcemia. [Table 6]

Figure 4: Images in present study


Pre Operative X-ray
Immediate Post-Operative
3 Months Post operative
6 Months Post-Operative
12 Months Post Operative


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PRATHIMA HOSPTIAL KARIMNAGAR

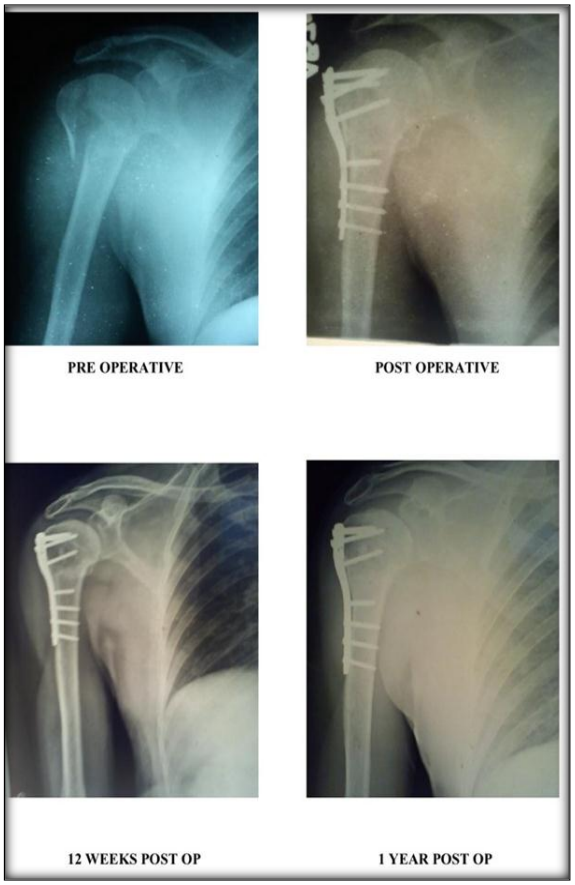
PRE OPERATIVE
POST OPERATIVE
12 WEEKS POST OP
1 YEAR POST OP

Table 1: Showing the demographic distribution of patients

Age in years	Frequency	Percentage
20-29	5	10
30-39	17	34
40-49	17	34
50-59	6	12
>60	5	10
Total	50	100
Gender		
Male	41	82
Female	9	18
Side of injury		
Left	15	30
Right	35	70
Limb injured		
Upper	12	24
Lower	38	76
Mechanism of Injury		
Road Traffic Accident	37	74
Fall	13	26

Table 2: Showing bone involved in fracture

Bone involved	Frequency	Percentage
Femur	18	36
Tibia	12	24
Femur and Tibia	5	10
Tibia and Fibula	3	6
Radius	8	16
Radius and Ulnas	2	4
Humerus	2	4
Total	50	100

Table 3: Showing the surgical technique

Operative technique	Frequency	Percentage
DHS for femur	17	34
Bone grafting	15	30
IMIL nailing for tibia	7	14
Ellies plate for distal radius	5	10
Plating with K wire for distal radius	4	8
DCP for distal humerus	1	2
PHILOS for proximal humerus	1	2
Total	50	100

Table 4: Showing the duration for appearance of signs of union after teriparatide administration

Time duration in months for appearance of signs of union after teriparatide administration	Frequency	Percentage
<3 months	15	30
3-4 months	21	42
5-6 months	10	20
6-9 months	4	8
Total	50	100

Table 5: Showing the complete union after teriparatide administration

Time duration in months for complete union after teriparatide administration	Frequency	Percentage
Within 3 months	8	16
3-6 months	12	24
7-9 months	22	44
10-12months	4	8
Not achieved	4	8
Total	50	100

Table 6: showing the type of adverse drug reactions (side effects) of study population

Type of adverse drug reactions	Frequency	Percentage
Nausea	26	52
Dizziness	14	28
Hypercalcemia	9	18

DISCUSSION

In the present study, one third of the patients belonged to the age group of 30-39 years and 40-49 years. 12% of the patients belonged to age group of 50-59 year and 10% of the patients belonged to 20-29 years and >60 years each.

In the present study, 82% of the study population were males, 18% of them were females.

In the present study, 36% of the study population had fracture of femur, followed by tibia (24%), radius (16%). 10% of them had fracture of both femur and tibia. 6% of them had fracture of both tibia and fibula. 2% of them had fracture of both radius and ulna. Only one patient had fracture neck of humerus. [Table 7]

In the present study, Teriparatide was administered daily for 3 months. [Table 8]

In the present study, 42% of the study population showed signs of radiological union after 3-4months of drug administration, followed by within 3 months (30%), 5-6 months (20%). Only in 8%the signs of radiological union appeared within 6-9 months. [Table 9]

In the present study, 92% of the study population had achieved complete radiological union at the end of one year follow up. 44% of the study population showed complete radiological union after 7-9 months of drug administration, followed by 3-6 months (24%), <3 months (16%). 8% showed complete radiological union within 10-12 months.

In the present study, complete range of movements was achieved in 52% of the study population. The range of movements was increased in 40% of the study population. 8% of the study population had restricted movements at the end of the study period. Simple exercises were taught to these patients. The patients were advised to use the affected limb freely. On an average period of physiotherapy by which the patient recovered the full range moments after the removal of plaster cast was not considered. [Table 10]

In the present study, 56% of the study population had experienced side effects. 52% of the study population had nausea, 28% of them had dizziness and 18% had hypercalcemia. Though follow up was difficult not only in terms of assesement of patients but also compliance with the medicine for 3 months. In order to determine the presence of any undesirable conditions by operative methods or due to administration of teriparatide the follow of study of 50 cases was under taken bearing in mind the following points. These patients complained of pain in the region around the fracture. Surgical treatment was reconsidered or any other underlying medical condition revaluated. Anatomical appearance was normal in most cases. Even in cases where there was five degree of deviation of, the external appearance was normal. Radiological appearance in all the studied cases good union at the site of fracture was seen. There has been no evidence of synostosis. The cases with still no evidence of union had alternate surgeries planned with revaluation of any underlying medical cause for non-union. The average duration for union to take place was 12 to 24 weeks. The average period of hospital stay was 8 to 10 days. Return to active use of effected limb average period between operation and return to active use of the affected limb was 3 months.

Good with Radiological union, return to full use of limb, regaining full range of movements and absence of any major complication. Fair with Radiological union, return to occupation, restricted range of movements.

Table 7: The findings of the study in regard to age and gender with comparision of other studies

Age distribution	Findings
Present study	One third of the patients belonged to the age group of 30-39 years and 40-49 years. 12% of the patients belonged to age group of 50-59 year and 10% of the patients belonged to 20-29 years and >60 years each. Age range:30-75 years
Tsai and Hu 2019[6]	60 years
Dr. Sujoy Kundu 2018[7],	39 years
Garg B et al. 2017[8]	67 years
Biro Izolda et al. 2017[9]	57 years
Yonezu hiroshi et al. 2017[10]	57 years
Yu and Guo 2017[11],	47 years
Emanuele C et al.2017[12]	64 years
Xiofeng LI et al. 2017[13]	44 years
Mancilla et al 2015[14],	19-64 years
Mitani 2013[15],	88 years
Ochi et al 2013[16],	73 years
Giannot et al 2013[17],	88 years
Lee et al 2013[18],	29-64 years
Chintamaneni S et al. 2010[19]	67 years
Gender	
Present study	82% of the study population were males, 18% of them were females.
Tsai and Hu 2019 [6]	Male
Dr. Sujoy Kundu 2018 [7],	Male
Garg B et al. 2017 [8]	Female
Biro Izolda et al. 2017[9]	Male
Yonezu hiroshi et al. 2017[10]	Female
Emanuele C et al.2017[12]	Female
Xiofeng LI et al. 2017[13]	Female

Ochi et al 2013[16],	Male
Giannot et al 2013[17],	Male
Chintamaneni S et al. 2010[19]	Male

Table 8: The findings of the study Fractures associated with comparision of other studies.

Fractures associated	Findings
Present study	36% of the study population had fracture of femur, followed by tibia (24%), radius (16%). 10% of them had fracture of both femur and tibia. 6% of them had fracture of both tibia and fibula. 2% of them had fracture of both radius and ulna. Only one patient had fracture neck of humerus.
Tsai and Hu 2019[6]	Shaft of femur
Dr. Sujoy Kundu 2018[7],	Intra capsular neck of femur
Garg B et al. 2017[8]	Neck of radius
Biro Izolda et al. 2017[9]	Vertebra C5 and T2
Yonezu hiroshi et al. 2017[10]	Distal humerus
Yu and Guo 2017[11],	Shaft of femur
Emanuele C et al.2017[12]	Distal humerus
Xiofeng LI et al. 2017[13]	Tibia and Femur
Mancilla et al 2015[14],	Tibia and Femur
Mitani 2013[15],	Femur neck
Ochi et al 2013[16],	Hip fracture
Giannot et al 2013[17],	Distal femur
Lee et al 2013[18],	Neck and shaft of femur
Chintamaneni S et al. 2010[19]	Sternal fracture

Table 9: Duration of dose in the present study can be compared with other studies

Author	Dose	Duration
Present study	20 micrograms	3 months
Tsai and Hu 2019[6]	20 micrograms	6 months
Dr. Sujoy Kundu 201 [7],	2 doses	One month apart
Garg B et al. 2017[8]	----	3 months
Biro Izolda et al. 2017[9]	20 micrograms	6 months
Yonezu hiroshi et al. 2017[10]	20 micrograms	12 months {weekly}
Yu and Guo 2017[11],	20 micrograms	9 months
Emanuele C et al.2017[12]	---	3 months
Xiofeng LI et al. 2017[13]	20 micrograms	8 months
Mancilla et al 2015[14],	20 micrograms	3-9 months
Mitani 2013[15],	56.5 micrograms	Weekly
Ochi et al 2013[16],	20 micrograms	6 months
Giannot et al 2013[17],	20 micrograms	3 months
Lee et al 2013[18],	20 micrograms	3-9 months
Chintamaneni S et al. 2010[19]	20 micrograms	9 months

Table 10: Findings in present study with other studies

Signs of radiological union	Findings
Present study	42% of the study population showed signs of radiological union after 3-4 months of drug administration, followed by within 3 months (30%), 5-6 months (20%). Only in 8%the signs of radiological union appeared within 6-9 months.
Xiofeng LI et al. 2017[13]	4 months
Chintamaneni S et al. 2010[19]	3 months
Complete range of movements	
Present study	92% of the study population had achieved complete radiological union at the end of one year follow up. 44% of the study population showed complete radiological union after 7-9 months of drug administration, followed by 3-6 months (24%), <3 months (16%). 8% showed complete radiological union within 10-12 months.
Tsai and Hu 2019[6]	6 months after treatment
Dr. Sujoy Kundu 2018[7],	6 months after treatment
Garg B et al. 2017[8]	3 months after treatment
Biro Izolda et al. 2017[9]	6 months after treatment
Yonezu hiroshi et al. 2017[10]	3 months after treatment
Yu and Guo 2017[11],	6 months after treatment
Emanuele C et al.2017[12]	12 months after treatment
Xiofeng LI et al. 2017[13]	12 months after treatment
Mancilla et al 2015[14],	3-9 months after treatment
Mitani 2013[15],	6 months after treatment
Ochi et al 2013[16],	6 months after treatment
Giannot et al 2013[17],	3 months after treatment
Lee et al 2013[18],	3-9 months after treatment
Chintamaneni S et al. 2010[19]	9 months after treatment
Complete range of movements	

Present study	complete range of movements was achieved in 52% of the study population. The range of movements was increased in 40% of the study population. 8% of the study population had restricted movements at the end of the study period.
Yonezu hiroshi et al. 2017[10]	Improved range of movements
Experienced side effects	
Present study	56% of the study population had experienced side effects. 52% of the study population had nausea, 28% of them had dizziness and 18% had hypercalcemia.
Dr. Sujoy Kundu 2018[7],	No serious side effects were noted
Caggiari G et al.[20]	No serious side effects were noted
Yoshiki F et al. [21].	No serious side effects were noted
Nishikawa A, et al[22]	No serious side effects were noted

CONCLUSION

The study was conducted with the objective of studying the efficacy of teriparatide therapy in surgically corrected comminuted fractures in the Department of Orthopaedics, Pratima Institute of Medical Sciences. Teriparatide (PT 1-34) is a recombinant drug which is a biologically active component of parathormone. The drug is an osteoanabolic agent used in the treatment of osteoporosis and speeding of callus formation. The present study concluded that the efficacy of teriparatide in surgically treated comminuted fracture healing cases is 92%. The drug was tolerated well with minor side effects like nausea and dizziness.

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