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Original Research Article

Effectiveness of teriparatide in enhancing bone formation and reducing aseptic loosening risks post-hip arthroplasty in patients with avascular necrosis

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ABSTRACT

Background: The hip joint's critical role in weight-bearing and mobility is often compromised by avascular necrosis (AVN), leading to osteoarthritis (OA). This study evaluates the impact of teriparatide, a synthetic parathyroid hormone analog, on bone formation and the risk of aseptic loosening in post-hip arthroplasty patients affected by AVN.
Methods: In this retrospective, single-centre study, 26 patients who underwent hip replacement surgery due to AVN between November 2021 and November 2023 were included. Participants were selected based on specific inclusion and exclusion criteria and received daily subcutaneous injections of teriparatide (20 µg) for six months. The study focused on assessing the efficacy of Teriparatide in mitigating prosthetic loosening and enhancing bone formation post-hip arthroplasty, alongside monitoring for adverse events.
Results: The cohort had a mean age of 37.63 years, predominantly male (77%). The median time for post-surgical pain onset was 31 days. After 3 months of teriparatide therapy, all patients showed a significant reduction in joint pain and swelling, with improved mobility. Radiographic evaluations demonstrated a decrease in previously observed radiolucent lines, indicating successful prosthesis integration. At the 6-month mark, tomosynthesis revealed no space between either the femoral head or hip components and the osteotomy load surfaces. No adverse events were reported during the therapy period.
Conclusions: Teriparatide is a promising therapeutic agent for enhancing surgical outcomes in post-hip arthroplasty in patients with AVN. Its role in promoting bone formation and reducing aseptic loosening risks is significant, suggesting its potential in improving patient recovery and pre-empting postoperative complications.

Keywords: Teriparatide, Hip arthroplasty, AVN, Bone formation, Aseptic loosening, OA

INTRODUCTION

In the daily biomechanical demands placed on the human body, the hip joint is pivotal for weight-bearing and mobility. It is, however, prone to AVN, particularly in young adults, which leads to progressive femoral head degradation and subsequent osteoarthritic changes.[1] OA is a substantial contributor to global disability; however, it is frequently misdiagnosed and inadequately managed. According to the 2019 global burden of disease study, OA was responsible for 114.5% more disability-adjusted life years (days) in 2019 compared to 1990. Despite having a lower prevalence in India, cases have more than doubled in 2019, reaching 62.35 million.[2]

The primary objective of joint management includes symptom alleviation, functional enhancement, and further joint injury prevention.[3] Non-surgical interventions, based on symptom severity and patient preferences, are preferred. However, arthroplasty may be necessitated

when conservative treatments are insufficient or unsuitable.[4-6]

Arthroplasty, especially for knee and hip joints, is determined by patient demographics, with a higher incidence in elderly females. In India, the expectation for an increase in arthroplasty procedures by 2026 underscores the need for advancements in surgical outcomes. Although arthroplasty can improve life quality and mitigate pain, it also involves risks like periprosthetic fractures and implant failure.[7] Osteoporosis is a significant periprosthetic fracture risk factor, affecting global bone health and straining healthcare resources. Current osteoporosis treatments predominantly focus on bone resorption inhibition, with inadequate promotion of bone formation or strength enhancement, presenting a gap in therapeutic strategies.

Teriparatide, a recombinant human parathyroid hormone composed of a 1-34 N-terminal amino acid extracted from the intact parathyroid hormone molecule that has been approved for the treatment of osteoporosis, is one such therapy. Teriparatide acts as an anabolic agent through two mechanisms: it enhances the quantity and functionality of osteoblasts, which are accountable for bone formation; and it regulates the activity of osteoclasts, which are responsible for bone resorption.[8] In contrast to traditional anti-resorptive medications like bisphosphonates, raloxifene, and calcitonin, this therapeutic approach promotes both bone formation and resorption while ultimately yielding a beneficial impact on bone mass.[9] It has been demonstrated that Teriparatide enhances bone quality and strength in patients with osteoporosis and decreases the risk of fracture.[10]

Teriparatide may offer therapeutic advantages in joint replacement surgeries, particularly for patients with OA or trauma-induced joint damage.[11] Osseointegration, the critical process of implant integration with bone tissue, is essential for the success of such surgeries.[12] However, patients with osteoporosis face challenges due to reduced bone density and quality, increasing the risk of periprosthetic fractures and implant failure.[13] Teriparatide's role in enhancing bone strength and stimulating bone formation at the implant site could improve osseointegration, thus bolstering implant stability and reducing post-operative complications.[14,15] This study primarily focused on evaluating teriparatide's effectiveness in enhancing surgical outcomes and reducing postoperative complications, specifically assessing its impact on bone formation and aseptic loosening in patients undergoing hip replacement due to AVN.

METHODS

Study design and participants

The present study is a retrospective, single-centre study conducted from November 2021 to November 2023. This study aimed to investigate the effects of teriparatide on bone formation and its potential in diminishing aseptic loosening of periprosthetic implants in patients who underwent hip replacement surgery for AVN. Given the study's retrospective design, the ethical committee granted a waiver for its conduct.

Inclusion and exclusion criteria

Inclusion criteria encompassed individuals who, after 3-8 weeks post-hip replacement surgery for AVN, reported joint pain and were radiologically confirmed to have prosthesis loosening. Exclusion criteria included high C-reactive protein (CRP) levels, any history of prior infection or fracture, patients with mechanical or septic joint loosening, and known contraindications to Teriparatide therapy.

Procedure

From November 2021, patients undergoing hip replacement surgery for AVN and presenting with pain and mobility issues within 3-8 weeks post-operatively were considered for inclusion. Initial evaluations included blood tests to rule out infections. Following this, patients showing radiolucent lines on X-ray examinations were further investigated using CT scans to confirm prosthesis loosening. Patients with confirmed loosening were offered teriparatide (Inj. Bonmax PTH) as an adjunct therapy (20 µg/day) under an empirical, off-label approach, contingent on their informed consent. The regimen involved a daily 20 µg Teriparatide injection for six months, with discontinuation in cases of patient refusal, intolerable side effects, or financial constraints.

Follow-up and assessment

Patients were monitored at three months and six months from the initiation of therapy to evaluate symptomatic relief, adverse reactions, progression of prosthetic fixation, and the potential need for ongoing teriparatide therapy. Post-therapy, annual clinical visits were scheduled for each patient. The assessment of prosthesis fixation was determined through radiographic evaluations during each visit.

Outcome measures

The study focused on the efficacy of teriparatide in mitigating prosthetic loosening and enhancing bone formation in patients post-hip arthroplasty. The incidence of adverse events and any complications were meticulously recorded.

Data analysis

Data compilation and management were conducted using Microsoft excel. Basic statistical analyses, including calculation of means and percentages, were performed to further interpret the outcomes related to prosthesis fixation and bone formation.

RESULTS

This study involved 26 patients undergoing hip replacement due to AVN, with a noteworthy mean age of 37.63±6 years. Furthermore, the gender distribution was predominantly male (75%), pointing to potential gender-specific susceptibility or risk factor exposure. Significantly, the median time for post-surgical pain onset was 31 days (interquartile range: 20-43 days), indicating a critical period for monitoring and early intervention for complications like prosthesis loosening (Table 1).

Table 1: Baseline characteristics of the patient in the study

Parameters	Value
Total number of patients	26
Gender	
Male	20 (76.92%)
Female	6 (23.07%)
Mean age (in years)	37.63±6
Median days of post-surgical pain development	31 (20-43)
Median WBC count at treatment start (cells/µl)	8100 (5600-8800)
Median CRP count (mg/dl)	24 (18-32)

WBC-White blood cells, CRP-C-reactive protein.

In the study, 56% of patients received a 10-day antibiotic regimen post-surgery, presumably to pre-empt or address postoperative infections. Initiation of teriparatide therapy at 6 weeks post-surgery was strategically timed, allowing initial healing and the resolution of acute postoperative issues, such as infection/inflammation, before introducing anabolic agent. This delay is beneficial for teriparatide's efficacy in bone remodelling and osseointegration enhancement during critical bone healing phase.

Patients were encouraged to engage in daily activities like supported walking and housework during the treatment. Notably, after three months of teriparatide therapy, all patients exhibited a complete resolution of joint pain and swelling, with significant improvements in mobility. Radiographic findings corroborated these clinical outcomes, showing a reduction in radiolucent lines indicative of improved prosthesis integration (Figure 1).

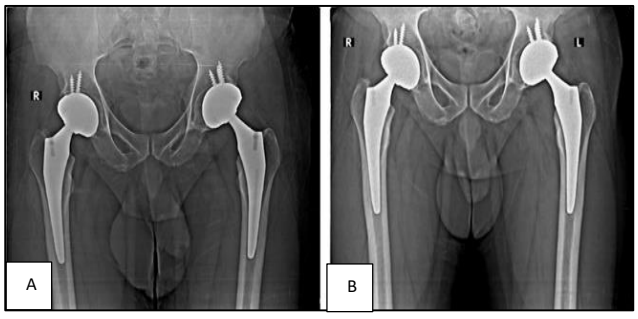

Figure 1 (A and B): Radiological images AP view after 4 and 12 weeks of teriparatide treatment started.

At the six-month mark, tomosynthesis confirmed successful osseointegration, with no gaps detected between the femoral head, hip components, and osteotomy load surfaces. Throughout the treatment period, no adverse events related to the therapy were reported.

DISCUSSION

This study provides valuable insights into managing post-arthroplasty complications in AVN patients, particularly males, who represent a significant portion (76.92%) of the cohort. The effectiveness of Teriparatide therapy, initiated 6 weeks post-surgery following antibiotic treatment, was pivotal in enhancing bone remodelling and osseointegration during critical healing phases. Remarkably, all patients experienced substantial relief from joint pain and swelling within three months, with radiographic evidence supporting improved prosthesis integration. The absence of adverse events and the successful osseointegration observed at the six-month mark underscore the safety and efficacy of teriparatide in improving outcomes for hip arthroplasty in this demographic, particularly in addressing early post-surgical complications and promoting long-term implant success.

Teriparatide is a well-established treatment for osteoporosis that has been proven to effectively improve bone mass and microstructure, thereby reducing the risk of fractures, both vertebral and nonvertebral, in patients with osteoporosis.[16,17] The mechanism of action for Teriparatide involves stimulating bone formation, particularly in the femoral neck, affecting the cancellous and endocortical envelopes, which provides a mechanistic basis for its efficacy in improving hip bone mass.

Teriparatide has been demonstrated to increase trabecular bone volume and connectivity, as well as cortical thickness, particularly in the femoral neck.[18] In a study comparing different treatments, Teriparatide was found to increase trabecular volumetric BMD and FEA-estimated strength at the distal radius and tibia, while progressively decreasing cortical volumetric BMD.[19] The combination of Teriparatide and the RANK-ligand inhibitor, denosumab, has been shown to increase bone density and estimated strength more than monotherapy and more than any currently available regimen.[18] These findings suggest that Teriparatide can play a significant role in managing post-arthroplasty complications in patients with AVN, potentially reducing the risk of aseptic loosening and improving long-term implant success.

The study, however, does have limitations. Its smaller sample size is typical for research in specialized medical fields but indicates the need for more extensive studies involving larger patient groups for broader insights. The retrospective design, while informative, underscores the value of prospective studies for a more comprehensive data collection and analysis. The lack of a control group in this initial study also points towards the necessity of future controlled trials to ascertain the treatment's efficacy more

definitively. These elements highlight key areas for ongoing and more detailed research within this domain.

CONCLUSION

The findings of this study highlight the promising role of teriparatide in enhancing the outcomes of hip arthroplasty in patients with AVN. The administration of teriparatide post-surgery not only facilitated an improvement in bone formation around the implant but also significantly reduced the incidence of aseptic loosening, a common complication in such procedures. This was evidenced by the decrease in radiolucent lines and the successful integration of the prosthesis as observed in radiographic evaluations. The absence of adverse events associated with the treatment further underscores its safety and potential as a valuable adjunct therapy in post-hip arthroplasty management. These findings suggest that Teriparatide could play a crucial role in improving the long-term success of hip replacement surgeries, particularly in patients prone to AVN, thereby enhancing their quality of life and reducing the burden on healthcare systems.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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