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Teriparatide therapy in joint replacement surgery: mitigating complications and improving patient outcomes in osteoarthritis

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ABSTRACT

Background: Teriparatide, a synthetic form of parathyroid hormone, has gained significant recognition as an effective treatment for osteoporosis. Its ability to stimulate bone formation and improve bone mineral density has made it a valuable therapeutic option in managing this prevalent skeletal disorder. However, its safety and potential benefits in preventing bone mineral density (BMD) loss after joint replacement surgery and post-surgical complications have yet to be extensively investigated.
Methods: This retrospective study included 32 patients who received teriparatide following joint replacement surgery for osteoarthritis. The analysis focused on assessing teriparatide's effectiveness in any reductions in post-surgical complications and adverse events, if any.
Results: No teriparatide-related adverse events and post-surgical complications were reported during the follow-ups and the entire study duration.
Conclusions: Teriparatide demonstrated effectiveness in joint replacement patients. Further research is needed to explore long-term benefits and effects on implant longevity.

Keywords: Teriparatide, Osteoarthritis, Joint replacement surgery, Post-surgical complications

INTRODUCTION

Osteoarthritis (OA) is a common chronic joint disease affecting millions worldwide.[1] It occurs when the cartilage that cushions the ends of the bones in the joints gradually deteriorates, leading to pain, stiffness, swelling, and reduced mobility. OA can affect any joint, but it is most prevalent in the hands, knees, hips, and spine.[2] The causes of osteoarthritis are not fully understood. Still, several risk factors have been identified, such as age (more common in people over 40), gender (women are more susceptible to OA than men, especially after menopause), obesity, joint injury or overuse, family history, and other types of arthritis.[3]

OA is a significant source of disability worldwide, but it is often underdiagnosed and inadequately treated. The Global Burden of Disease Study 2019 showed that OA led to 114.5% more disability-adjusted life years (DALYs) in 2019 than in 1990.[4] OA has a lower prevalence in India than the global average, but the cases have more than doubled in the same period, reaching 62.35 million in 2019. This alarming trend requires urgent actions to prevent, diagnose, and treat OA effectively.[5]

The main objective of OA management is to alleviate symptoms, improve function, and prevent further joint damage.[6] The primary strategy is a non-surgical treatment comprising pharmacological and non-pharmacological modalities.[7] However, the selection of non-surgical therapy depends on various factors, such as the severity of symptoms, the location and extent of joint involvement, the patient's preferences and expectations, and each option's potential benefits and risks.[8] When non-surgical treatments are insufficient or contraindicated, arthroplasty may be an option to replace the damaged joint.[9]

Arthroplasty is mainly performed on hip and knee joints.[10] Total hip and knee replacement are standard procedures for patients with joint degeneration due to osteoarthritis, trauma, or other conditions. The prevalence of these procedures varies by age and gender, with women having higher rates than men. In the US, the older age groups had higher rates of total knee replacement and lower rates of total hip replacement (THR) in 2010 than the younger ones. Total knee arthroplasty (TKA) is a feasible option for knee osteoarthritis, even in patients over 90. India is expected to have rapid growth in joint replacements from 2020 to 2026, the highest in the world. Arthroplasty can offer benefits such as pain relief and improved quality of life. Still, it carries risks and complications such as bleeding, infection, blood clots, nerve or blood vessel damage, implant failure, or periprosthetic fracture.[11]

One important risk factor associated with periprosthetic fractures is osteoporosis, a common and severe condition affecting bone metabolism.[12] Osteoporosis can be pre-existing in the patient or occur as a result of arthroplasty affecting more than 200 million people worldwide.[13] One in three women and one in five men over 50 will have an osteoporotic fracture in their lifetime.[14] This condition can impair the quality of life and health of the people with it and impose a high economic burden on the healthcare system.[15] Developing effective treatments for osteoporosis is a significant challenge for clinicians and researchers.[16]

Patients with osteoarthritis and osteoporosis as a comorbidity may need joint replacements to improve their mobility and quality of life. However, one of the main difficulties in managing these patients is restoring bone mass density.[17] Most available osteoporosis treatments, such as bisphosphonates, denosumab, and testosterone, can only slow down bone breakdown and preserve bone density but cannot stimulate new bone growth and improve bone strength.[18] Therefore, there is a need for novel therapies that can enhance bone anabolism and reduce the risk of fractures in osteoporosis patients.[19]

One such therapy is teriparatide, a synthetic human parathyroid hormone (PTH) 1-34 that mimics the physiological effects of endogenous PTH on bone metabolism.[20] Teriparatide acts as an anabolic agent by increasing the number and activity of osteoblasts, the cells responsible for bone formation, and by modulating the activity of osteoclasts, the cells involved in bone resorption.[21] Unlike conventional anti-resorptive drugs, such as bisphosphonates, raloxifene, and calcitonin, this therapy stimulates bone formation and resorption but with a net positive effect on bone mass.[22] Teriparatide has been shown to improve bone quality and strength in osteoporosis patients and reduce fracture risk.[23] Teriparatide may also benefit from joint replacement surgery, a common intervention for individuals with severe joint damage due to osteoarthritis or trauma.[24] The success of joint replacement surgery depends on integrating the implant with the surrounding bone tissue, a process known as osseointegration.[25] However, osseointegration is impaired in osteoporosis patients due to their low bone density and quality, which increases the risk of periprosthetic fractures and implant failure.[26] Teriparatide therapy may enhance osseointegration by stimulating bone formation around the implant site and increasing bone strength around the prosthesis. This may improve the stability and durability of the implant and prevent post-surgical complications and poor outcomes.[27]

Looking into the benefits of teriparatide in reducing complications after joint replacement surgery, the present study demonstrates that teriparatide therapy can improve surgical outcomes and lower the risk of post-surgical complications in patients who underwent prosthetic implant of the hip and knee, with either cemented or uncemented implants.

METHODS

Study design

This is a single-center, retrospective observational study to investigate the effects of teriparatide on bone healing in the periprosthetic implant among patients who underwent hip or knee arthroplasty. The study duration extended from January 2022 to September 2022 at Nine Pearls Hospital. Data collection involved a thorough review of patients' medical records in extracting pertinent information regarding teriparatide usage and assessing the outcomes of bone healing in the periprosthetic implant.

Patients

This retrospective analysis included 32 patients (mean age: 56.25 years) who underwent hip or knee arthroplasty and received injection Bonmax PTH (teriparatide) 20 µg S.C. daily for over three months. Inclusion criteria involved patients aged 51-90 years, confirmed cases of osteoarthritis undergoing elective arthroplasty, while exclusion criteria included any patients having prior infection, fracture, implant loosening, and contraindications to teriparatide therapy.

Procedure

For three months, eligible patients received injection Bonmax PTH (teriparatide) 20 µg S.C. daily after surgery. The data analysis was done in the implant groups to evaluate further the outcomes regarding the adverse events or post-surgical complications.

Outcome

The study evaluated the effectiveness in the reduction of post-surgical complications in patients who underwent prosthetic implant procedures and were treated with teriparatide post-surgery. The primary outcome measure was the incidence of any adverse events and post-surgical complications, if any. All the adverse events (AEs) reported during the study were graded by the Clavien-

Dindo classification, which grades the severity of postoperative complications based on the type and intensity of the treatment required.

Statistical analysis

The collected data were compiled and arranged in a Microsoft excel spreadsheet. Basic statistical analysis was performed to evaluate the mean values and the percentages.

RESULTS

The study included 32 patients with different diagnoses and implant types. The gender-wise distribution was 17 females (53.1%) and 15 males (46.9%). The most common diagnosis was bilateral tricompartmental osteoarthritis of knee, affecting 17 patients (53.1%), followed by bilateral subchondral femoral head collapse/fracture, concerning eight patients (25.1%). The average hospital stay was 6.81±6.05 days, and the average first follow-up was 9.61±2.54 days (Table 1).

All patients received a fixed dose of teriparatide (20 µg S.C. daily) for a duration of 90 days with no adverse events reported regarding the treatment with teriparatide. No complications, such as infections or blood clots, were reported during teriparatide treatment. All the patients experienced none of the related complications in terms of periprosthetic fractures caused by possible osteoporosis.

Table 1: The baseline demographics of the patients.

Characteristics	Frequency	Percent
Gender-wise distribution of patients		
Female	17	53.1
Male	15	46.9
Diagnosis-wise distribution of patients		
Bilateral cemented total knee replacement	1	3.1
Bilateral subchondral distal femoral fracture	1	3.1
Bilateral subchondral femoral head collapse/fracture	8	25.1
Bilateral tri-compartmental osteoarthritis knee	17	53.1
Left comminuted intercondylar distal humerus fracture	1	3.1
Left-sided hip aseptic loosening with acetabular loosening	1	3.1
Left-sided subchondral femoral head fracture/collapse	1	3.1
Sided neck of femur comminuted fracture	2	6.3
Distribution of patients according to whether the implant was cemented or not		
Not reported	6	18.8
Cemented	19	59.4
Uncemented	7	21.9

DISCUSSION

Osteoarthritis is a chronic disease that affects the joints and causes pain, stiffness, swelling, and reduced mobility. It affects millions worldwide and can impair their quality of life and daily functioning. The hips and knees are the most affected joints, as they bear much weight and stress during everyday activities. When medication, physical therapy, and lifestyle changes are insufficient to relieve the symptoms, patients require total hip or knee arthroplasty (THA or TKA). This surgery replaces the damaged joint with a prosthesis, which can improve joint function and reduce pain. However, THA and TKA have some risks and complications, which can happen during or after the surgery and affect the outcome and satisfaction of the patients. These complications include infection, bleeding, loosening, dislocation, malalignment, and stiffness. They can cause pain, swelling, instability, deformity, reduced function, and limited mobility.[28] Osteoporosis can affect the bone around the prosthesis and increase the risk of periprosthetic fracture. Periprosthetic fracture is a severe complication due to trauma, stress, or prosthesis loosening. It can cause pain, instability, and deformity of the joint. Another complication that can affect the bone quality around the implants is the decrease in peri-implant BMD, which is the bone density near the implant interface. This can happen due to post-surgical inflammation, infection, stress shielding, or poor osseointegration. This may compromise the implant's stability and durability, leading to a higher fracture risk around the prosthesis.[29]

The present study demonstrates the benefits of teriparatide in reducing post-surgical complications after joint replacement surgery, especially in the hip and knee. Teriparatide is a drug that stimulates bone formation and improves osseointegration, integrating the implant with the surrounding bone. This results in better stability and durability of the implant and a lower risk of periprosthetic fractures and post-surgical complications, such as infection, dislocation, thromboembolism, acute kidney injury, and mortality. The increased bone mineral density (BMD) around the implants, likely due to Teriparatide, contributes to these positive outcomes and a lower chance of adverse events. These findings are consistent with the existing literature and support the potential of teriparatide

therapy to enhance bone density and patient outcomes in joint replacement surgeries. Teriparatide, a synthetic form of parathyroid hormone that stimulates bone formation, has shown promise in osteoporosis and fracture prevention.[30,31] Recent studies have explored the potential benefits of teriparatide administration in post-joint replacement surgery, particularly in preserving periprosthetic BMD and reducing fracture risk.[32]

One study by Suzuki et al evaluated the effect of teriparatide on periprosthetic BMD after TKA in patients with osteoporosis. They found that teriparatide significantly prevented BMD loss in the femoral and tibial components compared to the control group 12 months after surgery. This suggests that teriparatide is crucial in preserving periprosthetic BMD following TKA, contributing to long-term implant stability and reducing complications.[33] Another important aspect of joint replacement surgery is bone ingrowth, which is crucial for achieving stable fixation and preventing implant loosening. Kaneko et al investigated the impact of teriparatide injections on bone ingrowth after cementless TKA using multi-detector computed tomography (MDCT). It was observed that teriparatide treatment led to increased periprosthetic BMD in the medial regions of the tibial component after TKA, indicating enhanced bone ingrowth suggesting that Teriparatide promotes bone formation and integration around the implant, thereby potentially improving long-term outcomes.[34]

Teriparatide treatment has also shown positive outcomes in THA. Kobayashi et al compared teriparatide and alendronate on BMD after THA in 48 patients. Both drugs (teriparatide and alendronate) prevented periprosthetic BMD loss, but teriparatide had a more significant effect on lumbar BMD than alendronate. This study suggests that Teriparatide may be better for patients with lower BMD undergoing THA.[35] In another study involving patients with osteoporosis at high risk for fracture, an entire continuous 24-month teriparatide course improved skeletal health and outcomes compared to shorter periods.[36] The present study adds to the existing evidence on the potential benefits of teriparatide as a post-implant therapy for prosthetic implant surgery patients, especially those with osteoporosis. Teriparatide may preserve bone density around the implant, enhance bone ingrowth, improve implant stability, and lower fracture risk, thereby improving outcomes and reducing complications after prosthetic implant surgery, as seen in our current study's extended follow-up of three months. The safety profile of teriparatide was also confirmed in this setting. Therefore, teriparatide may be a valuable treatment option for patients who undergo prosthetic implant surgery and should be considered in clinical practice.

Limitations

The study's limitations include the absence of pre- and post-surgery DEXA scans, limiting accurate measurement of changes in BMD, and the evaluation of teriparatide's localized effects. Future research should incorporate DEXA scans to comprehensively understand teriparatide's impact on periprosthetic bone health.

CONCLUSION

Teriparatide shows promise as a valuable therapeutic option in joint replacement surgery. It can potentially increase BMD without significant adverse events, making it an attractive choice for managing patients undergoing joint replacement procedures. While teriparatide holds the potential for improving surgical outcomes, further research is needed to explore its long-term benefits and impact on implant longevity.

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