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BASIC SCIENCE

Dose-Dependent Enhancement of Spinal Fusion in Rats With Teriparatide (PTH[1–34])

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Study Design. Controlled animal experiments.

Objective. To test the dose and efficacy of teriparatide in a rat spinal fusion model.

Summary of Background Data. Teriparatide was shown to enhance spinal fusion in rats and rabbits previously, but the dose-dependent effect of teriparatide in spinal fusion in rats was not well characterized.

Methods. A 0.5 × 0.5 cm trabecular bone graft was taken and implanted onto the L5 and L6 transverse processes of the same rat. Rats were randomly assigned into 3 groups: saline vehicle control (Vehicle), teriparatide 4 μg/kg per day (PTH4), and teriparatide 23 μg/kg per day (PTH23) subcutaneous injections for 4 weeks (5 d per wk). The L5–L6 spinal segments were harvested at week 4, and assessments included radiography, micro-computed tomography, manual palpation, and histomorphometry. L3 vertebra, femurs, and serum bone markers were examined.

Results. The average radiographical score of L5–L6 fusion in Vehicle, PTH4, and PTH23 groups was 1.53, 2.87, and 4.11, respectively, with the PTH23 being significantly higher ($P = 0.001$ *vs.* Vehicle). The average micro-computed tomographic score of L5–L6 fusion in Vehicle, PTH4, and PTH23 groups was 1.53, 2.40, and 3.74, respectively ($P = 0.001$, PTH23 *vs.* Vehicle and PTH4). Manual palpation showed that fusion rate was 20%, 50%, and 67.7% in Vehicle, PTH4, and PTH23 groups, respectively. The bone mineralization apposition rate at the fusion site was significantly increased in a dose-dependent manner among the groups. Teriparatide significantly increased vertebral and femoral bone mineral density, bone mineral content, and trabecular area in a dose-dependent manner relative to Vehicle. No difference was found between the circulating Procollagen type I N-terminal propeptide and intact osteocalcin levels in the serum at 4 weeks after treatments.

Conclusion. Teriparatide at 23 μg/kg per day for 4 weeks showed anabolic skeletal effects and significantly enhanced spinal fusion rate in rats, whereas teriparatide at 4 μg/kg per day had also anabolic effects but did not significantly enhance spinal fusion rate. Higher doses of teriparatide may be needed to promote spinal fusion in short-term application.

Key words: teriparatide, rat, spinal fusion, autograft. **Spine 2012; 37:1275–1282**

Spinal fusion is known as a surgical technique to join 2 or more adjacent vertebral segments. This surgical procedure is used primarily to stabilize the spinal column and alleviate pain caused by spinal deformity, trauma, vertebral compression fracture, or degenerative disc disease. Supplementary bone tissue is often used in the surgery from the patient (autograft), demineralized bone matrix (allograft), or synthetic biomaterials.

Teriparatide (rhPTH[1–34]) is a bone anabolic agent that is approved to treat osteoporosis in women and men.[1,2] Teriparatide has been shown to replace lost bone mass, restore bone microarchitecture, and enhance bone strength by stimulating osteoblast activity and apposition of newly synthesized bone matrix.[1–5] Therefore, teriparatide may provide greater benefits to patients with established osteoporosis than antiresorptive therapies, especially in patients who do not respond well to antiresorptive therapies. Human and animal studies have shown that teriparatide stimulates new bone formation by increasing osteoblast number, by enhancing differentiation of precursors and improving cell survival, and by increasing activity. Teriparatide induces bone formation at inactive

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bone surfaces and further stimulates bone formation at active remodeling surfaces, resulting in increased bone mass, trabecular thickness, trabecular connectivity, and eventually trabecular number. [1,3,5–14]

Previously, teriparatide was shown to enhance spinal fusion in rats and rabbits.[15–18] However, the doses used previously in rats were 20[16] and 40 μg/kg per day,[15] and a dose of 10 μg/kg per day[17,18] was used in rabbits. The doses of parathyroid hormone (PTH) used in animals and humans may not be comparable due to different metabolic status; for instance, the serum level of PTH(1–34) in rats receiving 5 μg/kg per day teriparatide was approximately 3-fold greater than the serum PTH(1–34) level in women receiving 20 μg/kg per day teriparatide therapy; hence, the need of effective PTH dose may be much higher in rats than in humans.[19] Therefore, we conducted a dose-response analysis to ascertain systemic efficacy of PTH(1–34) in inducing posterior-lateral spinal fusions at 4 and 23 μg/kg per day. Assessments included radiography, micro-computed tomography (μCT), manual palpation, and histomorphometry. Analyses of nonfractured skeletal sites and serum bone markers (Procollagen type I N-terminal propeptide [PINP] and osteocalcin) were also used to assess the systemic skeletal effects of PTH(1–34).

MATERIALS AND METHODS

Animals

Animal surgery procedures were performed under the approval of the Animal Experimentation Ethics Committee of the Chinese University of Hong Kong. Thirty Sprague Dawley male adult rats (age, 12 wk; body weight, 400–450 g) were used in this study. Animals were randomized into 3 different treatment groups after spinal fusion surgery.

Posterior Spinal Fusion Model

In animals under general anesthesia and using sterile conditions, a 0.5 × 0.5 cm bone block was removed from the left iliac crest as autograft material to be used in spinal fusion. Then, the vertebral column was exposed by elevating all paraspinal muscles and periosteum from the posterior elements to expose the L5 and L6 transverse processes of the lumbar vertebrae. The dorsal side of the cortical bone of L5 and L6 transverse processes was carefully removed, using an air-driven power drill with a burr attachment (Synthes; Mathys AG, Bettlach, Switzerland). Autograft material (0.5 × 0.5 cm iliac trabecular bone graft) was then placed onto the L5 and L6 transverse processes. The muscle and skin were closed in layers. One day postsurgery, animals were subcutaneously administered teriparatide (Eli Lilly Corporation, Indianapolis, IN) or saline. Rats were randomly assigned into 3 groups, with 10 per group. Treatment groups included saline vehicle control (Vehicle), teriparatide 4 μg/kg per day (PTH4), or teriparatide 23 μg/kg per day (PTH23) subcutaneous injection in a total volume of 0.5 mL for 4 weeks (5 d per wk). Animals were necropsied at 4 weeks postsurgery, and the spinal segments as well as other bones and sera were harvested for further assessments.

Radiographical Assessments

Digital radiographs (MX-20; Faxitron X-Ray, Inc., Wheeling, IL) were taken at the day of surgery and at 4 weeks after the surgery. Radiographs were used as a guide to check graft position, in that a line between the 2 iliac crest tops passed through the L7 vertebral body, which was used as a reference guide to check whether the graft was in position between L5 and L6 transverse processes. Digital radiographs were graded using a scoring system according to the reference (Table 1).[18] Scoring was performed in a blinded manner by 3 independent observers, and the average scores were compared.

Computed Tomographic Analysis

L5–L6 vertebral samples were fixed with 4% phosphate buffered formaldehyde for 24 hours and were then transferred to 70% ethanol. Specimens were scanned by μCT (μCT40; Scanco Medical, Bassersdorf, Switzerland), using a resolution of 36 μm per voxel. The 3-dimensional (3D) reconstruction was performed with a standardized segmentation parameter (sigma: 1.2, support: 1, threshold: 143). The 3D images were generated by machine's built-in software and were used to assess osseous tissue fusion between the 2 processes, using a scoring system (Table 1).[18] Scoring was performed in a blinded manner by 3 independent observers, and the average score was compared.

In addition, L3 vertebra and left femur were excised from each animal, fixed in 70% ethanol, and scanned using a quantitative computed tomography scanner (Aloka LaTheta LTC-100 model; Tokyo, Japan). Bone mineral density (BMD) and bone mineral content (BMC) of the distal left femur metaphysis and diaphysis as well as the L3 lumbar vertebra were recorded. In brief, bones were mounted on modeling clay for positioning, and scans of the femora were taken at 2 and 10 mm from the end of the epiphysis for distal and femoral diaphysis analyses, respectively. L3 vertebrae were scanned at approximately the midpoint, using radiographical landmarks. Data were calculated by manufacturer's software package (SYS-C320 version 1.5; Aloka).

TABLE 1. Radiographical and μCT Scoring System

Description	Score
No bone	0
Poor new bone formation	1
Moderate new bone formation and definite pseudarthrosis	2
Moderate new bone formation and possible pseudarthrosis	3
Good new bone formation and probable fusion	4
Definite fusion	5

μCT indicates micro-computed tomographic.

Histomorphometry Analysis

To evaluate bone formation activity and measure the newly formed callus/bones, 2 fluorochromes, xylenol orange (90 mg/kg) and calcein green (5 mg/kg), were injected intraperitoneally at days 12, 11 (xylenol orange) and days 3, 2 (calcein green) before killing. After nondestructive examinations, the vertebrae samples (at least 5 from each group) were then embedded with methyl methacrylate according to previous methods.[19] Samples were then sectioned at 300-μm thickness by a saw microtome (SP1600; Leica Microsystems GmbH, Wetzlar, Germany) sagittally and perpendicular to the plane of transverse process. Three sections from middle one-third of each sample were further ground and polished to 100 ± 10 μm thickness using a grinder/polishing machine (Phoenix 4000; Buehler Ltd., Lake Bluff, IL). The newly formed bone was determined by the distance between the 2 fluorochrome labels using epifluorescent microscopy (DMRXA2 imaging system; Leica Microsystems GmbH). Measurements of distance were performed within well-organized trabeculae. Five regions were randomly measured for each sample, and epifluorescent micrographs were taken under a red and green filter separately (16× magnification) and merged by PhotoStitch 3.1 (Canon Inc., Tokyo, Japan). Image was recorded by 2 investigators in a blinded manner. The bone mineralization/apposition rate was calculated by the distance (between the 2 labels) divided by 9 days (the time between the 2 labels) and expressed as mm per day.

Serum Markers for Bone Formation Activity

Sera (3 aliquots, 2 × 150 μL, 1 × 100 μL) were collected at necropsy and stored at −80°C. Serum osteocalcin was measured by radioimmunoassay using a kit from Biomedical Technologies Incorporated (Stoughton, MA) with modifications to a 96-well format. Each well of a multiscreen plate (MAHV N45; Millipore, Bedford, MA) contained 2.5-μL rat serum, 2.5-μL goat antirat osteocalcin (BT-413), 0.625-μL normal goat serum (BT-415), and 119.375-μL RIA buffer (0.1225M NaCl; 0.01M NaH_2PO_4, pH 7.4; 0.025M Na_4EDTA; 0.1% [w/v] BSA; and 0.1% [w/v] Tween-20). Plates were incubated for 18 hours at 4°C on an orbital shaker at 80 rpm. After the addition of 0.2 μCi/mL [125I] rat osteocalcin (BT-411R) in 25-μL RIA buffer to each well, plates were incubated for 24 hours at 4°C on an orbital shaker at 80 rpm. The complex was precipitated for 2 hours at 25°C by the addition of donkey antigoat immunoglobulin G (1:30; BT-414) in 0.2 M Na_2HPO_4, pH 7.4; 5% (w/v) polyethylene glycol, 125 μL/well. The precipitate was collected by vacuum filtration and washed once with 100 μL/well dH_2O. Filters were punched from the plate, and the radioactivity was quantified on a gamma counter (Cobra II; Packard Instruments, Meriden, CT). A standard curve of purified rat osteocalcin (BT-412) was used to calculate unknown samples.

Serum PINP was analyzed using a commercially available kit (RatLaps, Immunodiagnostic Systems Limited, Fountain Hills, AZ) following the manufacturer's protocol. The assay employed an antibody raised against the C-terminal telopeptide α1 chain of rat type I collagen. Briefly, biotinylated peptide was immobilized by binding to the streptavidin-coated wells. After washing, 20-μL standards, controls, or unknown samples were added along with the primary antibody. After an overnight incubation at 4°C and another wash step, a horseradish peroxidase–conjugated secondary antibody was added. After another wash step, the assay was developed with 3,3′,5,5′-tetramethylbenzidine substrate. A standard curve of the synthetic peptide was used to determine unknown samples.

Statistical Analysis

The scores of radiographical and μCT 3D reconstructive images and the clinical fusion rate were compared by Fisher exact test. The bone mineralization apposition rate was compared by Mann-Whitney test. The statistical analysis was carried out using SPSS (version 11; SPSS Inc., Chicago, IL), and the level of significance was set at a P value of less than 0.05. The data of systemic effects on nonfractured skeletal sites were assessed using Dunnett's corrected t test, with statistical significance defined as a P value of less than 0.05 (JMP version 5.1; SAS Institute, Inc., Cary, NC).

RESULTS

General Observations

After the first week postsurgery, all the skin incision wounds had healed with no sign of infection. During the last 3 weeks postsurgery, no apparent difference in body weight or general well-being was noticed among animals in all groups. One animal in PTH23 group died at day 1 after surgery, which was likely due to failure to recover from anesthesia.

Radiographical Assessments

Radiographical images at the day of surgery showed that the iliac crest autograft material was properly positioned at the L5 and L6 transverse processes, and no difference of graft position was observed among the 3 groups (Figure 1). Mineralization activity was evident at week 4 postsurgery in all 3 groups. Radiographs showed that bone formation activity had increased in a dose-dependent manner in the teriparatide-treated groups, with a significantly larger amount of bone with definite fusion observed in PTH23 group (Figure 1). The average radiographical scores of L5–L6 fusion in Vehicle, PTH4, and PTH23 groups at 4 weeks were 1.53, 2.87, and 4.11, respectively (Fisher exact test, $P = 0.001$, relative to Vehicle; Table 2).

Computed Tomographic Analysis

Three-dimensional reconstructed images showed increased new bone formation activity in a dose-dependent manner in the teriparatide-treated groups. Vehicle group had the least callus whereas PTH23 group had the largest callus. In Vehicle and PTH4 groups, clear pseudarthrosis was still seen in some of the animals, but none was found in PTH23 group (Figure 2). The average scores of L5–L6 fusion in Vehicle, PTH4, and PTH23 groups at 4 weeks postsurgery were 1.53, 2.40, and 3.74 ($P = 0.001$ relative to Vehicle, Fisher exact test; Table 2).

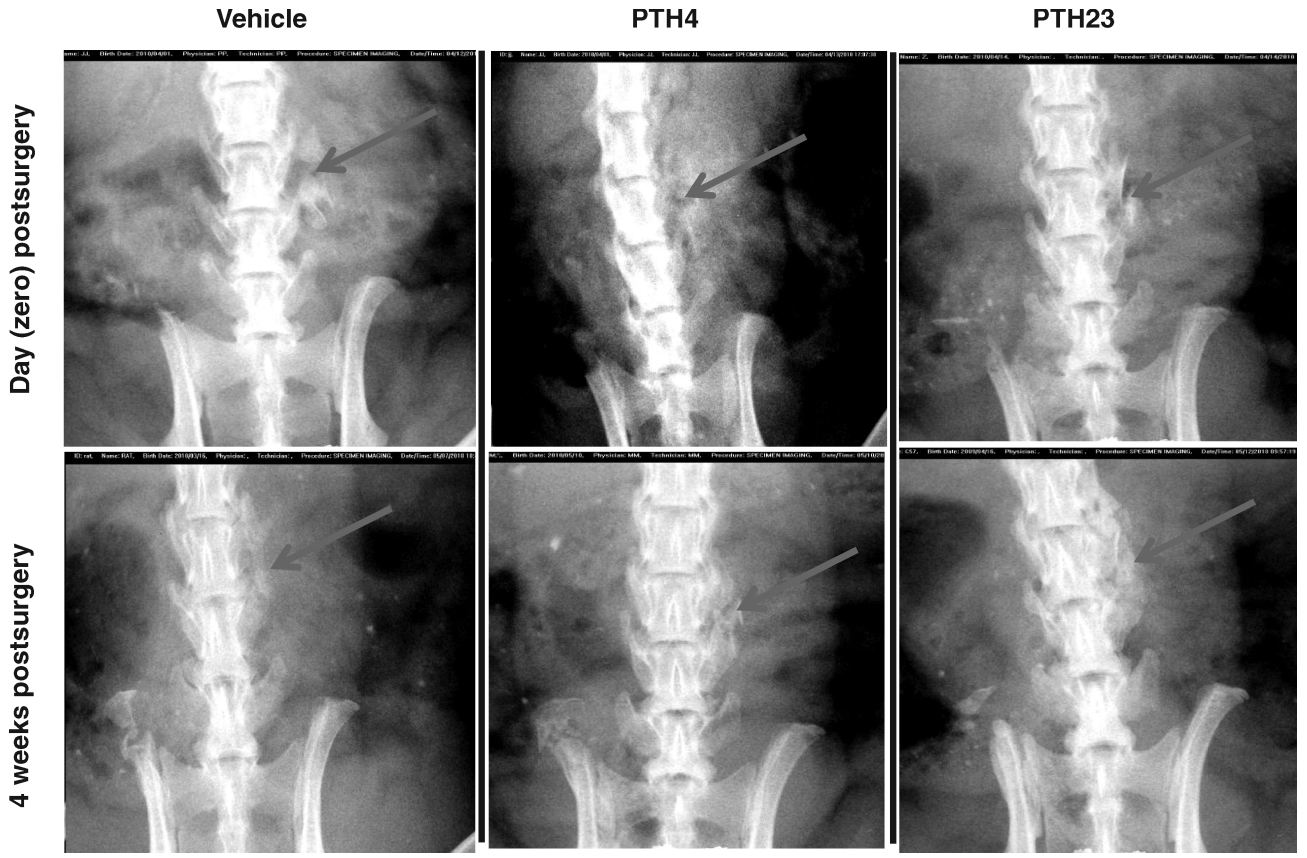

Figure 1. Representative radiographs of all experimental groups at day 0 and week 4 postsurgery. The radiographical images at the day of surgery showed that the iliac crest autograft material was between the L5 and L6 transverse processes (arrows), and the position of the graft was consistent among the 3 groups. At 4 weeks postsurgery, the callus volume in Vehicle group was smaller than that of PTH4 group. In PTH4 group, there was a moderate amount of new bone formation, but gaps at the fusion site were seen in some animals, suggesting that there was pseudarthrosis formation. In contrast, PTH23 group had the largest callus formation, and there was no gap seen at the fusion sites in any animal. PTH indicates parathyroid hormone.

Histomorphometry Analysis

Xylenol orange and calcein green bands revealed new bone formation activity and permitted measurement of mineral apposition rate. Bone mineral apposition rate (mm per day) at the fusion site in Vehicle, PTH4, and PTH23 groups at 4 weeks postsurgery was 0.042 ± 0.004, 0.093 ± 0.009, and 0.246 ± 0.009, respectively. Significance was observed for PTH4 and PTH23 relative to Vehicle and between PTH4 and PTH23 groups (Figure 3). Therefore, teriparatide enhanced mineral apposition rate in a dose-dependent manner, with significance observed between the 3 groups ($P < 0.05$, Mann-Whitney test; Vehicle *vs.* PTH4, Vehicle *vs.* PTH23, and PTH4 *vs.* PTH23; Figure 4).

TABLE 2. Scores of Radiography and 3-Dimensional Reconstructive Images (Mean ± SD)

Group	Group A (Control)	Group B (Low PTH)	Group C (High PTH)
Radiographical score	1.53 ± 0.92	2.87 ± 1.62	4.11 ± 0.69*
CT score	1.53 ± 0.98	2.40 ± 1.44	3.74 ± 1.05*

**P < 0.05, Fisher exact test when compared with group A.*

PTH indicates parathyroid hormone; CT, computed tomography.

Systemic Effects of PTH(1–34)

Quantitative computed tomographic analyses were conducted for excised lumbar vertebra L3 and the distal femoral metaphysis (Table 3). Teriparatide dose dependently increased vertebral BMD (7% Vehicle group *vs.* 14% PTH23 group), BMC (11% Vehicle group *vs.* 28% PTH23 group), and trabecular area (4% Vehicle group *vs.* 12% PTH23 group), with significance observed comparing with the PTH23 group (Table 3). Analyses of the distal femoral metaphysis showed that teriparatide dose dependently increased BMD (7% Vehicle group *vs.* 30% PTH23 group) and BMC (8% Vehicle group *vs.* 36% PTH23 group), with significance observed for the PTH23 group (Table 3). Teriparatide administration had no effect on trabecular area at the distal femoral metaphysis. Analyses of the femoral midshaft showed that teriparatide administration had no effect on BMD for this site. At 4 weeks postsurgery, no differences were observed in serum PINP and osteocalcin levels between groups (Table 4).

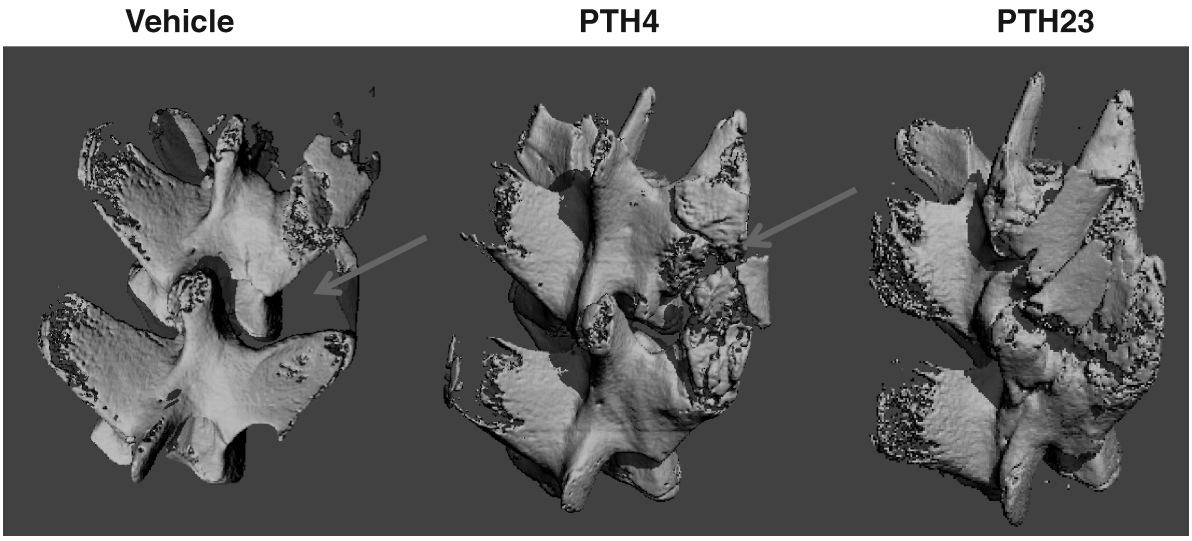

Figure 2. Representative micro-computed tomographic 3-dimensional reconstructive images of the L5–L6 fusion mass from the 3 groups. There was increased new bone formation in a dose-dependent manner in the 3 groups. The Vehicle group had less callus volume, PTH4 group had moderate callus volume, and PTH23 group had the maximum callus volume compared with Vehicle and PTH4 groups. There were still visible gaps in the fusion sites in both Vehicle and PTH4 groups (arrows) suggesting pseudarthrosis formation, whereas no gap was seen in the fusion site in PTH23 group. PTH indicates parathyroid hormone.

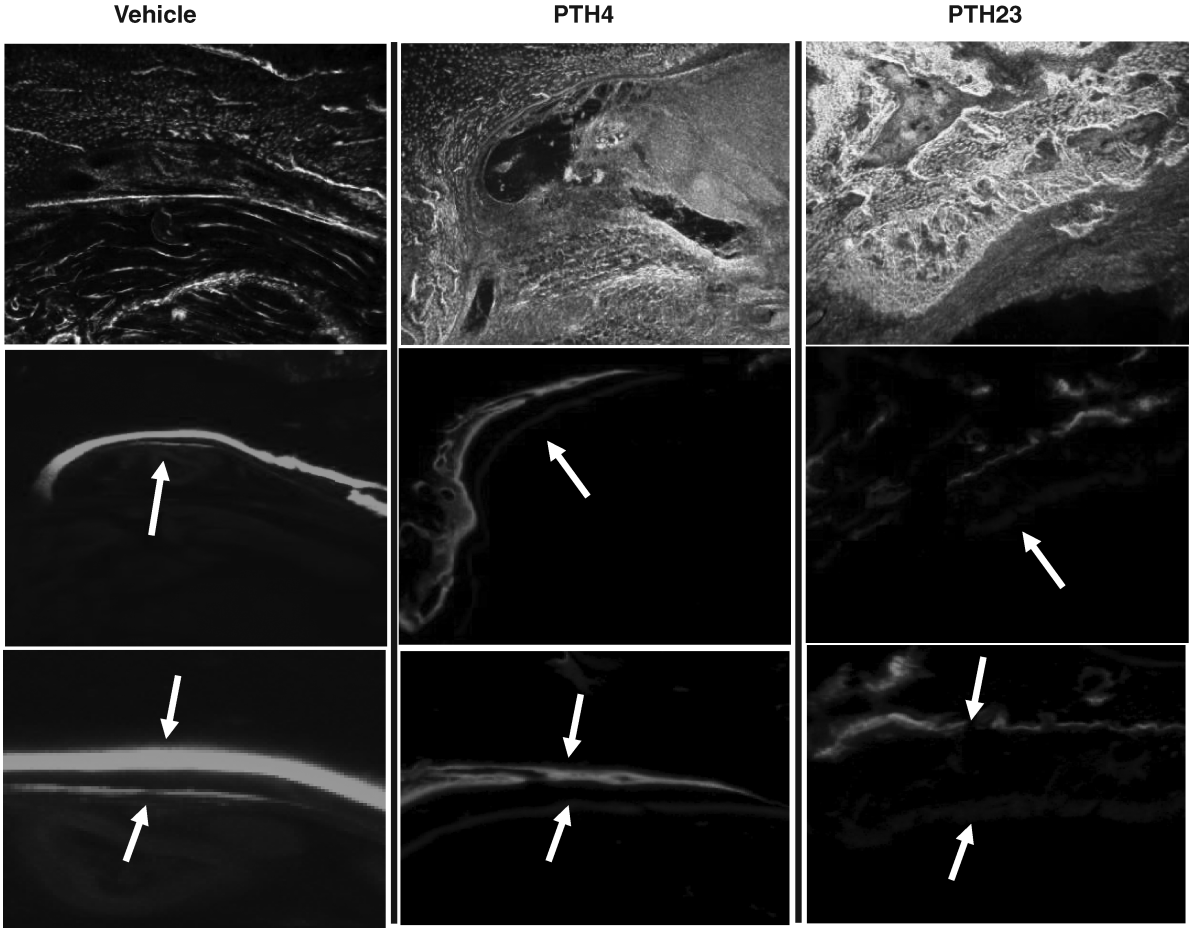

Figure 3. Histomorphometry data of fusion site callus at week 4 postsurgery. The xylenol orange and calcein green provided easily identified fluorescent bands in newly deposited bone within the fusion site. The distance between xylenol orange band and calcein green band demonstrated new bone formation (as shown by 2 arrows). The mineral apposition rate was calculated from the distance between bands. Teriparatide enhanced new bone apposition rate in a dose-dependent manner. (Top) Light microscopy; (Middle) fluorescent microscopy (100×); and (Bottom) fluorescent microscopy (400×). PTH indicates parathyroid hormone.

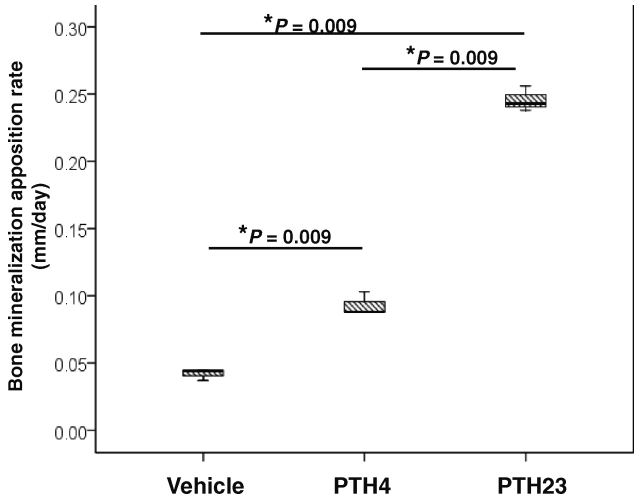

Figure 4. The bone mineralization apposition rate (mm per day) at the fusion site in Vehicle, PTH4, and PTH23 groups at 4 weeks postsurgery was 0.042 ± 0.004, 0.093 ± 0.009, and 0.246 ± 0.009, respectively, which was significantly increased in a teriparatide dose-dependent manner ($P = 0.009$ compared with Vehicle group). Data are expressed as mean ± SD, with significant difference indicated by $*P < 0.05$, Mann-Whitney test, N = 5. PTH indicates parathyroid hormone.

DISCUSSION

Teriparatide (rhPTH[1–34]) is an amino-terminal fragment of PTH that has been shown to stimulate new bone formation by increasing osteoblast activity and numbers by enhancing differentiation of precursors and improving cell survival. Teriparatide induces new bone formation at inactive bone surfaces and further stimulates mineral apposition at active remodeling surfaces, resulting in increased bone mass, trabecular thickness, and improved trabecular connectivity in animals and patients.[3,5–14] In rats, skeletal efficacy was shown to be dose- and duration-dependent.[8,20–25]

Previous studies demonstrated that systemic administration of teriparatide enhanced spinal fusion in rats and rabbits: effective PTH(1–34) dose used in rats was 40[15] and 20 μg/kg per day[16] and the dose used in rabbits was 10 μg/kg per day.[17,18] In our study, teriparatide was evaluated at 4 and 23 μg/kg per day in rats. The reason we evaluated a low-dose PTH at 4 μg/kg per day is that previously we have demonstrated that systemic exposure of 5 μg/kg per day in rats achieved serum level of PTH(1–34) approximately 3-fold greater than the serum PTH(1–34) level in women receiving 20 μg/kg per day teriparatide.[19] We have initially planned to use a dose of 5 and 25 μg/kg per day for comparison, but due to the growth of the rats during the experimental period, and when we finally adjusted the actual dose against body weight, the mean dose tested became 4 and 23 μg/kg per day. Nonetheless, 4 μg/kg per day is a near clinically relevant dose, which has never been properly tested in rats in the context of spinal fusion before. Because of the high costs of PTH and the complexity of the spinal fusion model, instead of using more groups with various PTH dosing, we decided to test the clinically relevant dose (4 μg/kg per d) and compare it with a known effective dose (23 μg/kg per d). Our radiographical, μCT, and histomorphometry data showed that the spinal fusion rate and the bone mineral apposition rate at the fusion sites were significantly enhanced in PTH23 group (23 μg/kg per d) as compared with that in the PTH4 group (4 μg/kg per d). Both PTH doses showed systemic effects on enhancing trabecular bone mass, but the enhancing effect on the cortical bone was modest (not significant) after 4 weeks of PTH treatment. The data indicated that 4 μg/kg per day dose was not sufficient to enhance spinal fusion in rats, suggesting that the doses of PTH used in rats and humans may not be comparable due to different metabolic status. The current finding will form a useful guideline for further study of best PTH dosing in rats (it shall be between 4 and 23μg/kg per d).

TABLE 3. QCT Measurements of BMD, BMC, and Trabecular Area (Mean ± SEM)

Location	Group	BMD	BMC	Trabecular Area
L3 vertebra	Group A (control)	456 ± 7	0.876 ± 0.021	0.320 ± 0.004
	Group B (low PTH)	488 ± 14	0.973 ± 0.033	0.332 ± 0.004
	Group C (high PTH)	521 ± 8*	1.120 ± 0.044*	0.358 ± 0.011*
Distal femoral metaphysis	Group A (control)	478 ± 10	0.664 ± 0.018	0.232 ± 0.006
	Group B (low PTH)	512 ± 11	0.716 ± 0.021	0.233 ± 0.004
	Group C (high PTH)	619 ± 16*	0.905 ± 0.046*	0.243 ± 0.009
Femural midshaft	Group A (control)	747 ± 14	0.554 ± 0.008	0.124 ± 0.002
	Group B (low PTH)	737 ± 13	0.581 ± 0.010*	0.132 ± 0.002*
	Group C (high PTH)	737 ± 19	0.578 ± 0.015	0.132 ± 0.006

$P < 0.05$, Dunnett test, comparing with control group.

QCT indicates quantitative computed tomographic; BMD, bone mineral density; BMC, bone mineral content; PTH, parathyroid hormone.

TABLE 4. Serum Levels of PINP and Osteocalcin at 4 Weeks Postsurgery (Mean ± SD)

Group	Group A (Control)	Group B (Low PTH)	Group C (High PTH)
Osteocalcin, ng/mL	17.5 ± 4.1	18.6 ± 5.1	15.6 ± 2.1
PINP, ng/mL	13.8 ± 2.1	16.9 ± 2.2	17.3 ± 4.3

PTH indicates parathyroid hormone.

Previously, Abe *et al*[15] reported that PTH 40 μg/kg per day (obtained from Asahi Kasei Corporation, Tokyo, Japan) significantly upregulated expression of multiple genes, enhanced early spinal fusion, improved bone microstructure, accelerated new bone mineral apposition rate, and expanded the mineralized surfaces and osteoclast surfaces. Lawrence *et al*[16] also reported that PTH 20 μg/kg per day (obtained from Eli Lilly Co.) enhanced the fusion rate after 6 weeks and significantly increased serum osteocalcin levels in the control group (59.8 ± 12.4 ng/L) and in the PTH group (88.57 ± 17.27 ng/L) ($P = 0.00014$).

Although the osteocalcin and PINP levels between groups in this study were not different, other data are consistent with previous findings that PTH 23 μg/kg per day has significantly enhanced spinal fusion rate after 4 weeks of treatment. Although the spinal fusion rate did not improve significantly in the PTH4 group, the anabolic effects were seen in the PTH4 group, such as enhanced mineral apposition and trabecular bone formation. The limitation of this study is that we did not test other dosing levels of PTH treatment apart from the 2 doses tested, and it is known clearly that the effective PTH dose for enhancing spinal fusion in rats will be between 4 and 23 μg/kg per day for at least 4-week administration. This will provide useful guidelines for future investigation.

In conclusion, significant improvement in spinal fusion rate was observed after 4 weeks of systemic administration of teriparatide at 23 μg/kg per day, 5 days per week, in rats. Mechanistically, systemic administration of teriparatide was observed to enhance mineral apposition rate onto trabecular bone surfaces. The data taken together suggest that a high dose of teriparatide administered for short term may be beneficial to promote bone healing in patients. Alternatively, a low dose of teriparatide administered during a longer duration may also be beneficial because increased mineral apposition rate in trabecular bone was seen in the PTH4 group as well as in the PTH23 group. Further studies are needed to clarify the optimal dose and duration for enhancement of bone healing such as spinal fusion with PTH(1–34).

➢ Key Points

- ❑ Systemic administration of teriparatide (PTH[1–34]) at 23 μg/kg per day significantly enhanced spinal fusion rate with autologous bone graft implantation in rats.
- ❑ Teriparatide at 4 and 23 μg/kg per day enhanced trabecular bone formation at vertebra and the distal femur metaphysis sites in a dose-dependent manner during a period of 4 weeks.
- ❑ Teriparatide had the systemic osteogenic efficacy on trabecular bone sites, including vertebra body and the distal femur metaphysis, but the effects on cortical bones were modest.
- ❑ Teriparatide significantly promoted bone mineralization apposition rate at the trabecular bone sites.
- ❑ The study showed that systemic administration of teriparatide in a short duration could significantly enhance the spinal fusion rate after autologous bone graft implantation in rats and suggest its potential clinical applications in spinal fusion surgery.

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