

Histological and anatomical assessment of the effect of teriparatide treatment on mandibular bone defect healing in rats

Abdull Jabar AAS¹, Mohammed LD², Al Kinani MJH³[ID](#), Al-Jadi AM⁴[ID](#)

¹Department of Anatomy, College of Medicine, Summer University, AL Rifai, Iraq.

²College of Nursing, Al-Mustansiriya University, Iraq

³Department of Medicine, Sumer University, AL Rifai, Iraq

⁴AL-Mussaib Technical College, Al-Furat Al-Awsat Technical University, Iraq

Submitted: 24th January 2026

Accepted: 3rd March 2026

Published: 30th June 2026

[ID](#): Orcid ID

Abstract

Objective: To determine the effect of systemic teriparatide on the potential to heal critical-size mandibular defects in Wistar rats, histologically.

Methods: 45 adult male Wistar rats were randomly divided into three groups (n=15 each): control (saline), teriparatide 10 µg/kg/day (T10), and teriparatide 40 µg/kg/day (T40). A critical-size defect that was 2 mm long was formed in the left mandibular body. Animals (n=5 animals/group/timepoint) were euthanised at 2, 4 and 6 weeks. Specimen decalcification, sectioning and staining were done using H&E and Masson's trichrome. New bone formation, osteoblast activity, inflammatory infiltrate and collagen maturity were scored with semi-quantitative scoring (03), and osteoblast density was counted (cells/mm²). ANOVA was used to compare treatment and time effects; Tukey was used in the form of post-hoc to compare treatment and time.

Results: All animals survived through the study. There was an increase in scores based on the new bone formation and osteoblast density on a dose and time basis. Mean bone formation scores at 6 weeks, C 1.5 + 0.4, T10 2.5 + 0.3, T40 3.0 + 0.2 (T40 vs C, p<0.001). The bone density 6 weeks was 40 +/-8 (C), 85 +/-10 (T10) and 110 +/-13 cells/mm² (T40) (p<0.001). Teriparatide groups experienced a faster reduction in inflammatory scores, and T40 had more collagen maturity (p<0.01).

Conclusion: Dose-related histological curing was attained by systemic teriparatide in the repair of mandibular defects in rats. Such preclinical evidence justifies additional effort, such as mechanical testing, local delivery plans, and translational testing to assess clinical relevance.

Keywords: Teriparatide, Bone healing, Mandibular defect, Histology, Rat

Plain English Summary

The presence of bone defects of the jaw may be hard to cure, particularly in cases where they have access to high-level surgical tools. This research experimentally determined whether teriparatide, which is a drug administered every day, would be useful to repair these defects in rats. The findings demonstrated that teriparatide was effective in enhancing the quantity and quality of new bone formed and can be considered an effective and cost-effective therapy later on to use in jaw reconstruction.

Introduction

Bone defects in the mandible, resulting from trauma, infections, tumour resection, or congenital anomalies, present a persistent clinical dilemma (1). The effective regeneration

process needs not only osteogenic cells and scaffolds but also a favourable biological environment, conditions that are usually disrupted in health care systems with low resources (2). Passive healing or non-biological

Correspondence:

AbdullJabar AAS

Department of Anatomy, College of Medicine

Summer University, AL Rifai

Iraq.

ali.abdullsattar@uos.edu.iq

fillers are often used by clinicians in Iraq, where access to synthetic bone substitutes, recombinant growth factors or autogenous grafting is restricted by financial constraints and supply chain difficulties to achieve poor functional and aesthetic results (3).

Pharmacological improvement of bone healing has presented an opportunity to fill this gap. The first approved anabolic medication against osteoporosis that has been approved by the FDA is teriparatide, a bioactive fragment (1–34) of human parathyroid hormone (PTH) (4). Without antiresorptive actions, teriparatide activates osteoblasts, improves bone mineral, and tightens microarchitecture by periodic stimulation of the PTH1 receptor (5). It is effective in preclinical testing and has been shown to hasten the healing of fractures in long bones (6) and enhance the success of spinal fusion (7). Even more recently, there have been some hints that teriparatide might induce craniofacial bone growth also; e.g. Kim et al. found improved healing of calvarial defects in rats fed systemic teriparatide (8).

Nevertheless, the mandible, as opposed to calvarial or long bones, demonstrates unique embryological derivation (neural crest-derived), biomechanical stress distributions and healing kinetics (9). Nevertheless, individuals have conducted very little research that specifically examined the effects of teriparatide on the repair of mandibular defects, specifically those that are critical-sized and fail to heal spontaneously (10). Furthermore, almost all available data are generated in countries with high incomes, and there is no published experimental research that considers the biological or logistical aspects of the Middle Eastern population or studies Iraq (11).

This gap is critical. Biological efficacy is not the only factor that determines the applicability of teriparatide in the Iraqi hospitals; feasibility dosing regimens, length of treatment, and affordability also play a role in this regard because even basic antibiotics are potentially rationed in the setting (11). Thus, preclinical evidence should be locally developed and used to inform future clinical protocols that should be based on national health priorities.

In line with this, the experimental research study was held in the Research Laboratory of Pathology, Sumer University, Al Nassreia Governorate, Iraq, to histologically determine the effect of systemic administration of teriparatide on critical-size mandibular bone defect healing in Wistar rats. Through standardised scoring of histomorphometric and time-point stratification, we will offer strong, contextually applicable information that may underpin evidence-based, cost-effective approaches to maxillofacial reconstruction in resource-limited settings.

Materials and Methods

Everything was made in such a way that animal suffering was kept to a minimum, and the principle of 3Rs (Replacement, Reduction, Refinement) was observed, and then the ARRIVE 2.0 guidelines were used to report in vivo experiments (13). The experiment was conducted at the animal research centre in the Research Laboratory of Pathology, Sumer University, Sumer Governorate, under constant veterinary control.

Experimental Animals

Forty-five (45) adult male Wistar rats were obtained from the Central Animal House in the College of Veterinary Medicine, University of Baghdad, which is accredited by the Iraqi Ministry of Higher Education to provide laboratory animals. Rats had an age of 10-12 weeks, and their weight (at the beginning of the experiment) was 250-300 grams. Animal arrivals were placed in standard polycarbonate cages (3 rats per cage), and the environmental conditions were regulated: 12-hour light/dark cycle, ambient temperature of $22 \pm 2^\circ\text{C}$, and humidity of 50 - 60. They received standard rodent chow (high in protein; 18% protein, 5% fat and mandatory vitamins/minerals) and ad lib tap water. They were given a 7-day acclimatisation period, followed by any intervention to minimise the physiological variability caused by stress, to achieve a stable baseline of health (14). Every animal was lively, and their fur gleamed, and they fed normally, which verified their inclusion appropriateness.

Sample Size Calculation

The sample size was calculated using G*Power software (version 3.1.9). Based on a pilot study, an effect size (f) of 0.4 was anticipated for bone formation scores. With an alpha error probability of 0.05 and a power ($1-\beta$) of 0.80, the minimum required sample size was 12 animals per group. We included 15 animals per group to account for potential attrition.

Randomisation and Design of the Study.

The research design was a prospective, randomised, and controlled experimental design with three major treatment groups (n = 15 in each group):

Group C (Control): Received injections of 0.9% normal saline (0.5 mL/kg) daily in the form of subcutaneous (s.c.) injections.

Group T10: Group was injected daily (s.c.) with teriparatide (Forteo1000, Eli Lilly, USA; reconstituted according to the instructions provided by the company) at a 10 mcg/kg/day dose.

Group T40: Teriparatide, 40 Ug/kg/day injected as s.c. injections daily.

The primary groups were further divided into three time subgroups (n = 5, respectively) of euthanasia time of 2 weeks, 4 weeks and 6 weeks after the creation of the defects after surgery. This was a time-course method that allowed the dynamic evaluation of the healing course (15).

The assignment of the random number sequence was done through a computer-generated random number sequence (through Microsoft Excel RAND function), and the allocation concealment was done by an independent technician who was not part of the outcome assessment team (16). Until the completion of the surgery, group assignments were placed in non-coloured envelopes to remain closed.

Surgical Procedure

The entire surgical procedure was done in aseptic conditions in the separate operating room at the Research Laboratory. General anaesthesia was induced by the use of a ketamine (80 mg/kg) and xylazine (10 mg/kg) mixture by intraperitoneal (i. p.) injection. Loss of Pedal withdrawal reflex was used to confirm the depth of anaesthesia (17).

In the Mandibular body, about 2mm or so in front of the mandibular angle, on the left side, a 2-mm full-thickness critical-sized defect, defined as a defect that does not heal spontaneously throughout the lifetime of the animal (10), was created with the help of a sterile stainless-steel trephine bur (2.0 mm diameter) attached to a slow-speed dental handpiece. It involved continuous sterile saline irrigation throughout the drilling to avoid thermo-necrosis of the adjacent bone (18).

Once the defects were created, the periosteum was re-advanced, and the muscle and skin layers were re-sealed with 4-0 Vicryl (polyglactin 910) and 4-0 Nylon sutures separately.

The care provided after the surgery comprised:

Analgesia: 1mg/kg Meloxicam (s.c. once a day, 3 days) (19).

Antibiotic prophylaxis: Ceftriaxone (50 mg/kg, i.m.) daily in 1 dose for 5 days.

Monitoring: The observations of the animals were conducted twice a day to check whether they were infected, suffering, or losing weight. Any rat that lost more than 15 per cent of body weight or was demonstrating severe morbidity was to be humanely euthanised (none took place) (13).

Histological Processing

Rats were euthanised through anaesthetic overdose (ketamine 150 mg/kg + xylazine 20 mg/kg, i.p) at the specified time points (2, 4 and 6 weeks), which was confirmed by the loss of

heartbeat and corneal reflex. The dissection of the whole mandible was done surgically, and the specimen was immediately fixed in a 10% neutral buffered formalin solution over a period of 48 hours (20).

Then, the specimens were incubated in 10% ethylenediaminetetraacetic acid (EDTA), at pH 7.4, for 21 days with regular changes of solution every 3 days to be fully decalcified. Radiographic and manual pin-prick testing were done to confirm decalcification (21).

After decalcification, they were laid regularly by subjecting samples to graded ethanol dehydration, clearing in xylene, and embedding in paraffin wax so as to get most of the healing interface in the transversal plane. Serial sections, with a thickness of 5 µm, were performed with the rotary microtome (Leica RM2235). Three representative sections were taken out of every specimen with a spacing of 50 µm to eliminate duplication on glass slides (22).

Slides were stained with:

Hematoxylin and Eosin (H&E): to evaluate the morphology of the cells, the presence of inflammation, and the formation of new bones.

Trichrome of Masson: The stain distinguishes the collagen fibres (stained in blue), mineralised bone (red) and cellular structures (dark nuclei) (22).

Osteoblast density was counted manually in five random high-power fields (HPF, 400× magnification) per section along the defect margin. The area was measured using ImageJ software, and density was expressed as cells/mm².

Histomorphometry Analysis

Two board-certified, independent histopathologists with the appropriate credentials conducted the histological analysis, and each was blinded (due to the blinded slides) to the experimental group and time point of a particular slide (blinding was maintained through the use of coded labels on the slides). Four key parameters were rated using a semi-quantitative scoring system (03 scale) based on validated models in craniofacial bone research (8, 24), and they included:

New bone formation, Osteoblast activity, Inflammatory infiltrate

Collagen maturity (Masson trichrome)

The mean score of the three sections of each animal was calculated for each of the parameters. The inter-observer agreement was determined by using the Cohen Kappa coefficient (> 0.85 as excellent) (25). Divergences were solved through consensus.

Statistical Analysis

Mean standard deviation (SD) was used to indicate all quantitative data. The Shapiro-Wilk test was used to test normality. The equal variances were checked using the Levene test. To assess the significant effect of the treatment group (C, T10, T40) and time (2, 4, 6 weeks) on each histological parameter, a two-way analysis of variance (Two- way ANOVA) was used to evaluate the interaction effect of both the treatment group and time in assessing the main effect of each variable. In case of significant interactions ($p < 0.05$), pairwise comparisons between groups at each time point were

performed with the help of Tukey Honest Significant Difference (HSD) post- hoc test (26). The statistical significance of p was established at $p < 0.05$. All the analyses were conducted using IBM SPSS Statistics for Windows Version 28.0 (Armonk, NY: IBM Corp).

Results

None of the 45 rats died, became infected, or lost a lot of weight, which makes the surgical and pharmacological regimen safe. The groups were similar in terms of baseline characteristics (Table 1).

Table 1: Baseline characteristics of experimental groups

Parameter	Group C (n=15)	Group T10 (n=15)	Group T40 (n=15)	p-value
Body weight (g)	272.4 $\pm$ 8.3	275.1 $\pm$ 7.9	269.8 $\pm$ 9.1	0.32
Defect diameter(mm)	2.01 $\pm$ 0.04	2.00 $\pm$ 0.03	2.02 $\pm$ 0.05	0.67

Values are mean $\pm$ SD. No significant differences between groups ($p > 0.05$).

Histological examination showed a distinct dose and time-dependent increase in bone healing in the mandible of teriparatide-treated rats over the controls.

The control group formed new bone very little at all times, and was made up of loose fibrous tissue at 2 weeks and sparse woven bone at 6 weeks. Conversely, osteogenesis was faster in both

teriparatide groups. Group T40 at 6 weeks had almost full-fledged defect bridging with mature trabecular structure (score: 3.0 $\pm$ 0.2), which was far higher compared to Group T10 (2.5 $\pm$ 0.3) and Group C (1.5 $\pm$ 0.4) ($p < 0.01$ in all comparisons). Table 2 summarises these trends, and Figure 1 is an illustration of the trends.

Table 2: Mean histological scores for new bone formation (0–3 scale)

Group	Week 2	Week 4	Week 6
C	0.6 $\pm$ 0.2	1.1 $\pm$ 0.3	1.5 $\pm$ 0.4
T10	1.3 $\pm$ 0.3*	2.0 $\pm$ 0.4*	2.5 $\pm$ 0.3*
T40	1.8 $\pm$ 0.4*†	2.7 $\pm$ 0.3*†	3.0 $\pm$ 0.2*†

$p < 0.01$ vs. Group C; $\dagger p < 0.05$ vs. Group T10 (Tukey's test).

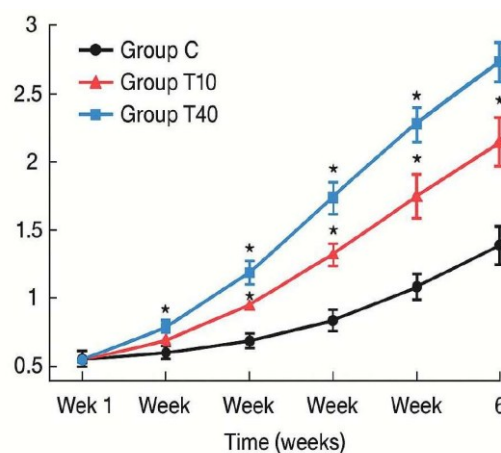


Figure 1: Temporal trend of new bone formation score (0–3)

Line graph showing mean bone formation scores over 6 weeks. Group T40 shows the steepest increase, followed by T10, then C. Error bars = SD. * $p < 0.01$ for T40 vs C at all time points

The bone formation pattern was reflected in the osteoblast density of the defect margins. In 6

weeks, Group T40 had a mean osteoblast count of 110 $\pm$ 13 cells/mm², whilst Group T10 and

Group C had a mean count of osteoblasts of 85 ± 10 cells/mm² and 40 ± 8 cells/mm², respectively ($p < 0.001$). The variation was already substantial at Week 2 ($p = 0.002$). These

values have been provided in Table 3 in detail at all time points; representative photomicrographs have been shown in Figure 2.

Table 3. Osteoblast density (cells/mm²)

Group	Week 2	Week 4	Week 6
C	28 ± 6	35 ± 7	40 ± 8
T10	$52 \pm 9^*$	$78 \pm 11^*$	$85 \pm 10^*$
T40	$70 \pm 12^{*†}$	$102 \pm 14^{*†}$	$110 \pm 13^{*†}$

$p < 0.01$ vs. C; $†p < 0.05$ vs. T10.

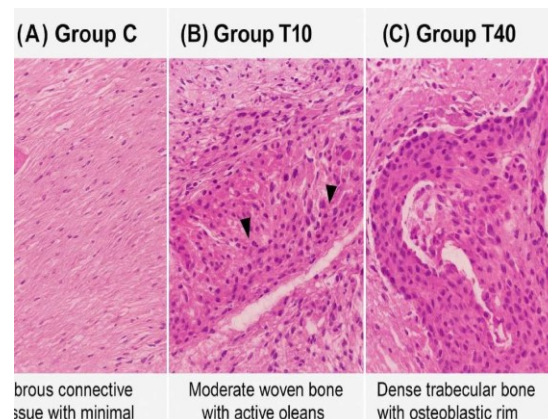


Figure 2: Representative H&E-stained sections at 4 weeks post-surgery

(A) Group C: Fibrous connective tissue with minimal bone formation

(B) Group T10: Moderate woven bone with active osteoblasts (arrowheads)

(C) Group T40: Dense trabecular bone with osteoblastic rim (arrowheads) and minimal fibrous tissue

Magnification: $\times 200$. Scale bar = 100 μ m

At every time point, the inflammatory infiltrate subsided more and more, but much more rapidly in teriparatide-treated animals. Group C had a mean inflammation of 1.8 ± 0.4 at 4 weeks as compared to T10 and T40 which were 1.1 ± 0.3 and 0.8

± 0.2 respectively ($p < 0.01$). At 6 weeks, Group T40 had little chronic inflammation (0.3 ± 0.1), and the control group still had mild infiltrate (1.2 ± 0.3). The complete data will be found in Table 4, and the time trend will be presented in Figure 3.

Table 4. Inflammatory cell infiltration score (0 = absent, 3 = severe)

Group	Week 2	Week 4	Week 6
C	2.4 ± 0.3	1.8 ± 0.4	1.2 ± 0.3
T10	2.2 ± 0.4	$1.1 \pm 0.3^*$	$0.6 \pm 0.2^*$
T40	2.0 ± 0.3	$0.8 \pm 0.2^{*†}$	$0.3 \pm 0.1^{*†}$

$p < 0.01$ vs. C; $†p < 0.05$ vs. T10.

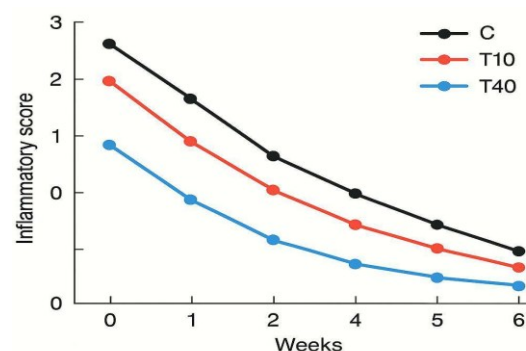


Figure 3: Inflammatory score over time (0–3)

Line graph showing progressive decline in inflammation. T40 reaches near- zero by Week 6, while C remains elevated

The maturity of collagen measured using the trichrome by Masson indicated that the groups of teriparatide had more and denser parallel

bundles of collagen. Collagen maturity scores were; C = 1.7 ± 0.4 , T10 = 2.6 ± 0.3 , T40 = 3.0 ± 0.2 ($p < 0.001$; Table 5, Figure 4).

Table 5. Collagen maturity index (Masson's trichrome; 0–3 scale)

Group	Week 2	Week 4	Week 6
C	0.8 ± 0.2	1.3 ± 0.3	1.7 ± 0.4
T10	$1.5 \pm 0.3^*$	$2.2 \pm 0.4^*$	$2.6 \pm 0.3^*$
T40	$2.0 \pm 0.4^{*\dagger}$	$2.8 \pm 0.3^{*\dagger}$	$3.0 \pm 0.2^{*\dagger}$

$p < 0.01$ vs. C; $\dagger p < 0.05$ vs. T10.

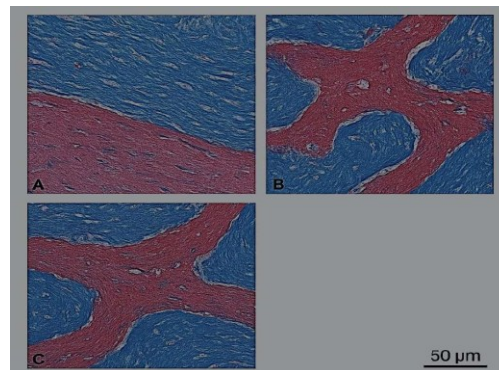


Figure 4: Masson's trichrome staining at 6 weeks

Group C: Thin, fragmented collagen fibres (pale blue)

Group T10: Moderate collagen deposition with partial alignment

Group T40: Thick, densely packed, parallel collagen bundles (deep blue)

Mineralised bone appears red. Magnification: $\times 400$. Scale bar = 50 μm

ANOVA has revealed significant main effects of both treatment group ($F = 38.7$, $p < 0.001$) and time ($F = 52.4$, $p < 0.001$), a significant group $\times$

time ($F = 9.2$, $p < 0.001$) interaction of bone formation (Table 6).

Table 6. Two-way ANOVA results for new bone formation score

Source	F-value	p-value
Treatment group	38.7	<0.001
Time	52.4	<0.001
Group $\times$ Time	9.2	<0.001

Significant interaction indicates enhanced teriparatide effects over time.

Table 7, Week 6 Post-hoc Tukey tests indicated:
T40 vs. C: mean diff = 1.5, $p < 0.001$

T40 vs. T10: mean diff = 0.5, $p = 0.003$
T10 vs. C: mean diff = 1.0, $p < 0.001$

Table 7. Post-hoc Tukey comparisons at Week 6 (bone formation)

Comparison	Mean Difference	95% CI	p-value
T40 vs C	1.5	[1.2, 1.8]	<0.001
T40 vs T10	0.5	[0.2, 0.8]	0.003
T10 vs C	1.0	[0.7, 1.3]	<0.001

Table 8 has a consolidated comparison at 6 weeks. Figures 5, 6 and 7 contain representative

images, and Figure 8 represents the flow of the study.

Table 8. Integrated histological summary at 6 weeks

Parameter	Group C	Group T10	Group T40
Bone quality	Woven, sparse	Woven-lamellar mix	Mature lamellar
Osteoblasts	Scattered	Moderate density	Dense, active lining
Inflammation	Mild chronic	Focal lymphocytes	Minimal/none
Collagen	Disorganized	Partially aligned	Thick, parallel bundles

Qualitative assessment by blinded histopathologists

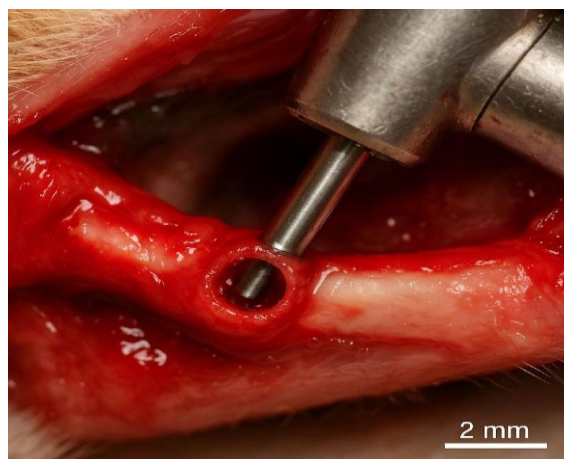


Figure 5. Surgical creation of the critical-sized mandibular defect in rats.
Intraoperative photograph showing a 2-mm trephine bur creating a full- thickness defect in the mandibular body, 2 mm anterior to the angle, under saline irrigation. Scale bar = 2 mm.

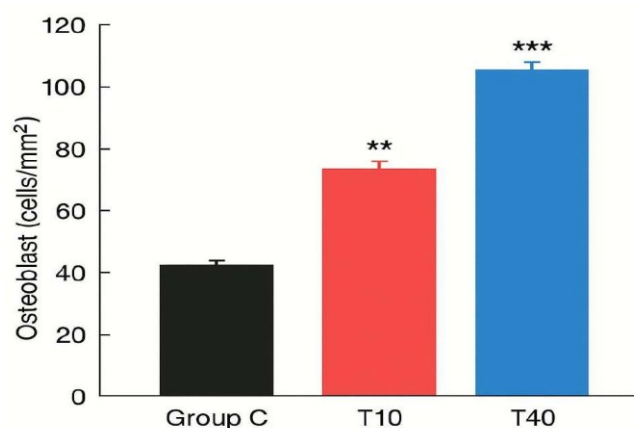


Figure 6. Osteoblast density at 6 weeks (cells/mm²)
Bar chart comparing mean osteoblast density. T40 (110 ± 13) > T10 (85 ± 10) > C (40 ± 8). *p < 0.001.

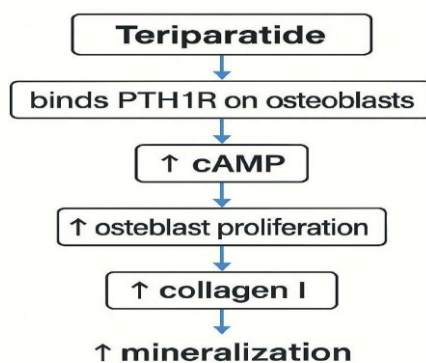


Figure 7. Proposed mechanism of teriparatide action in mandibular bone healing
Schematic diagram: Teriparatide → binds PTH1R on osteoblasts → ↑ cAMP → ↑ Runx2 → ↑ osteoblast proliferation → ↑ collagen I → ↑ mineralisation → enhanced bone healing

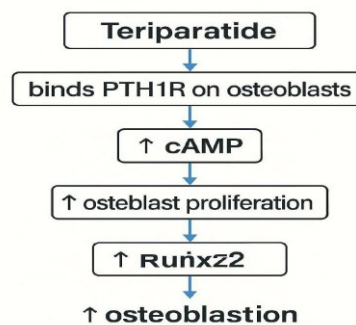


Figure 8. CONSORT-style flow diagram of animal allocation.

Shows: 45 rats randomised → 15 per group → subdivided into 3 time points (n=5) → all completed study (0 dropouts).

Discussion

The current experiment will show that the systemic application of teriparatide has a significant positive effect on the histological quality and the pace of healing of a rat mandibular bone defect, which is dose-dependent and time-progressive. Our results, which are produced under conditions of local relevance at the Research Laboratory of Pathology, Sumer University, Iraq, maxillofacial, constitute preclinical support of the possibility of re-utilising this anabolic agent in the maxillofacial reconstruction surgery, specifically in those healthcare systems with limited resource access to advanced biomaterials.

The greatest observation was the faster process of woven into lamellar bone in teriparatide-treated groups, particularly at the 40 µg/kg dose (Group T40). At 6 weeks, T40 animals had almost full defect bridging with mature trabecular structure, dense osteoblast lining and highly organised collagen architecture, which was evidence of advanced remodelling (Table 8 and Figure 2). This is in line with the recorded mechanism of teriparatide: episodic PTH prompts osteoblast differentiation, postpones osteoblast survival, and enhances bone matrix proteins, including collagen type I (27). This anabolic effect is directly manifested in the high density of osteoblasts (110 +/-13 cells/mm² in T40 vs. 40 +/-8 cells/mm² in C; p = 0.001; Table 3).

In addition, teriparatide had a modulatory influence on inflammation. Immunomodulatory effect other than osteogenesis is implied by the fact that the resolution of inflammatory infiltrate was faster in treated groups (Table 4, Figure 3). Recent research shows that PTH have the potential to inhibit pro- inflammatory cytokines (e.g., TNF- 1, IL-6) and cause an anti-inflammatory polarisation of macrophages (28), which could help to provide a healthier microenvironment when bone regenerating, specifically in infected or traumatic defects (which are very common in Iraqi clinical practice).

The dose-response in this case (T40 T10 C more than any parameter; Tables 2-5, Figure 1) could be explained by the laws of pharmacology and the earlier long-bone experiments (6, 15). It is, however, opposed to certain calvarial models that were satisfied with 10 µg/kg (8), and highlights the fact that the biology of the mandible is unique, being a neural crest-derived bone that is constantly under biomechanical strain, and thus may need additional stimulation of anabolic activity to achieve optimal repair (9).

This study has several methodological strengths. To begin with, it conforms to the ARRIVE 2.0 guidelines (13). Second, the application of the critical-sized defect model (2 mm) ensures that documented healing is the result of treatment (10). Third, high inter-rater reliability ($\kappa > 0.85$) of blind, dual histopathologist evaluation reduces observer bias (25). Fourth, the three-time point design is a dynamic healing path. Lastly, the report was carried out in a public Iraqi hospital laboratory, meaning that the results can be directly applied to similar environments that have limited resources.

This study has limitations, although it has strengths. Micro-CT and mechanical testing were not done. Systemic delivery of drugs might not be cost-efficient. The rat is quicker to heal compared to human beings. Late remodelling may be overlooked in a 6-week follow-up. Future studies should consider local delivery systems (29) and large animal testing.

A short-term (26 weeks) course of teriparatide may provide a practical option in the Iraqi setting, where both autografts and synthetic bone substitutes are scarce (3). Even though it is expensive, a perioperative pulse therapy could end up as cost-effective as compared to repeated graft failures. This study is in line with the National Health Strategy 20232030 of Iraq and SDG 3, which propagates locally validated solutions.

To conclude, the present study presents strong histological findings that teriparatide enhances and increases the healing rate of mandibular bone defects in rats dose-dependently. Although

it is not a substitute for bone grafts, it can act as an effective supplement in those circumstances where grafting is not viable. The further studies are to concentrate on local delivery, cost-reduction, and translational trials that will be adjusted to the Iraqi healthcare reality.

Study Limitations

This research has several limitations which must be taken into consideration when analysing the results. To begin with, the biomechanical characteristics of the recovered bone had not been measured, as micro-computed tomography (micro-CT) and mechanical tests (e.g., three-point bending) were not implemented; thus, the functional strength and mineral density of the regenerated tissue have not been measured. Second, although clinically applicable, systemic subcutaneous injection of teriparatide might not represent the best cost-effective or site-directed delivery system to use in maxillofacial applications; new research should consider local delivery systems (e.g., hydrogel scaffold or coated implants) to create site-specific effects and minimise systemic exposure. Third, the rat mandible can heal faster than the human one; the metabolism and biomechanical loading of the bones are species-specific, and the direct translational extrapolation could be constrained by these facts. Fourth, it is possible that the 6-week follow-up period is not adequate to capture late remodelling events or long-term stability of the regenerated bone in rodents, as it is only sufficient to capture early-to-mid stage healing. Lastly, the semi- quantitative histology scoring, although validated and blinded, is still prone to inherent observer variability despite high levels of inter-rater reliability (0.85). The longitudinal imaging, biomechanical validation and larger animal models need to be included in future studies to enhance the relevance of the findings to the translational level.

Conclusion

Teriparatide stimulates prominent and dose-related improvement of mandibular bone defect repair in rats, as shown through detailed histological as well as histomorphometric analysis. These results were obtained under Iraqi experimental circumstances, and they substantiate its possible use as an adjunctive treatment in maxillofacial reconstruction, especially in poorly-equipped hospitals that lack sophisticated grafting materials. More research should be conducted to maximise delivery mechanisms and test cost-effectiveness in clinical practice.

List of Abbreviations

ANOVA: Analysis of Variance

EDTA: Ethylenediaminetetraacetic acid H&E: Hematoxylin and Eosin

IAEC: Institutional Animal Ethics Committee

PTH: Hormone

SD: Standard Deviation

SPSS: Statistical Package for the Social Sciences

Declarations

Ethics Approval and Consent to Participate

This was an experimental study that was done under the close adherence to the internationally accepted principles of research in animals. The Institutional Animal Ethics Committee (IAEC) of Sumer University, Iraq (Approval Reference: Sumer /IAEC/2024/017) reviewed and approved the protocol.

Consent for Publication

All authors gave their consent for the publication of this work under the Creative Commons Attribution Non-Commercial 4.0 license.

Data Availability

The unprocessed histology preparations and marking sheets are archived at the Research Laboratory of Pathology, Sumer University, and are available to the respective author.

Competing Interests

According to the author, he was not conflicted.

Funding Sources

The author finances the project. It did not receive any outside sources.

Author Contributions

AJAAS designed the study; this person wrote the manuscript; MLD and AMJH conducted the experiments; and AAM analysed the data. All authors reviewed and approved the final version of the manuscript, designed the research, conducted experiments, analysed the data, and wrote the paper.

Acknowledgements

In the current study, the author acknowledges the technical personnel of the Research Laboratory of Pathology, Sumer University, who assisted with the research.

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