

# Clinical update quiz: your free CPD hour



## Effect of recombinant human bone morphogenetic protein-2 (rhBMP-2) on the volumetric contraction of post-extraction sockets: a double-blinded randomized controlled clinical trial.

Araujo LML, Walterson MP, Zenobio EG, Faverani LP, Souza JGS, Fernandes GVO, Shibli JA. Quint Int 2025; 56(5): 364-374

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### Aim

After extraction of a tooth, alveolar bone loss is seen in both horizontal and vertical dimensions. The buccal plate may be lost due to the healing process or trauma from the extraction procedure. The most significant time of alveolar bone loss occurs in the first few months with 3-5mm loss in six months. Some studies have reported more than half the ridge is resorbed by six months and is greater at the buccal aspect of the alveolar bone which causes aesthetic issues for crowns and implant supported prostheses.

Studies have aimed to reduce this type of bone loss using bone grafts with xenografts and alloplastic grafts achieving good results for alveolar preservation. Bone morphogenic proteins (BMPs), in particular BMP-2 and BMP-7 have been studied to increase the available bone when used in conjunction with a bone graft. When a larger osteotomy was present, rhBMP-7 significantly increased bone formation, however it had little effect when a normal osteotomy was present for implant placement.

Non-glycosylated (ng)/rhBMP-2 has been used as a coating on titanium implants with and without hydroxyapatite (HA) coating. ng/rhBMP-2 resulted in a greater bone surface area compared with the HA implants and this was more significant than the combined HA and ng/rhBMP-2 coated implants. Implants soaked in 3.0mg/mL rhBMP-2 did not show an increase in bone formation compared with groups receiving 0.75 and 1.5mg/mL at 8 weeks. The objective of this human prospective randomised controlled trial was to evaluate the effect of 1.5mg/mL rhBMP-2 in socket preservation.

### Methods

Patients in good health who required an extraction of no more

than two adjacent teeth in the maxilla and sought dental implant treatment at the Dental Implant Clinic at Guarulhos University (Sao Paulo, Brazil) were included.

Exclusion criteria were patients that were under the age of 20 years, smokers, pregnant or breastfeeding patients, diabetes, blood dyscrasia, teeth with active infections, non-controlled systemic disease, bony defects in the area of interest or loss of a bony wall during extraction.

Clinical examination, general dental care including restorations, prophylaxis, oral hygiene instructions and scaling and root planing were undertaken prior to surgery. Pre-operative examination of blood count, blood coagulation, creatinine, blood calcium, fasting blood glucose and cone beam CT (CBCT) were performed.

The sample size calculation was based on a study which found horizontal bone changes of  $1.49 \pm 0.45\text{mm}$  in the control group and  $0.82 \pm 0.11\text{mm}$  in the rhBMP-2 group at a level of 3mm from the marginal bone. Twenty patients were recruited based on a power of 90% and considering dropouts.

Patients were split into two groups - control group (CG- Blood clot) and test group (TG- socket preservation with rhBMP-2) using a randomisation tool. The surgeon was not blinded but was not involved in data analysis.

Minimally traumatic flapless extractions were performed. Teeth were sectioned when required. In the CG, the socket was curetted and irrigated with saline and a horizontal cross mattress or interrupted nylon suture was placed across the socket with only a blood clot present. In the TG group, after irrigation and socket curettage, rhBMP-2 (Infuse, Medtronic) was prepared at a concentration of 1.50mg/mL in a collagen sponge and soaked for 20 minutes. Collagen strips soaked with

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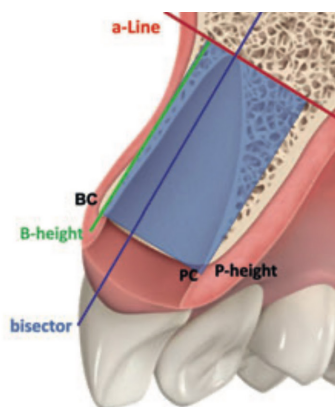


rhBMP-2 were inserted into the socket with slight pressure and the socket was closed with a free gingival graft (FGG) from the palate in the area of the first premolar to mesial of the first molar.

Preoperatively 1g amoxicillin was administered 12 hours before the procedure and then 500mg every eight hours for seven days. Chlorhexidine gluconate mouthwash (0.12%) was prescribed every 12 hours for seven days, 100mg nimesulide (NSAID) was prescribed every 12 hours for three days and 750mg paracetamol for pain control. Sutures were removed at 12-14 days. Follow-up examinations were performed at 30, 60, 90 and 120 days post-surgery.

CBCT scans were performed on day two (T0) and day 120 (T1) after the surgical procedure. Parasagittal slices 1mm in thickness with 1mm spacing were obtained in Digital Imaging and Communications in Medicine (DICOM) files and the images were evaluated using digital image analyser software.

Evaluation of the 2D changes was performed using the two CBCT scans. Alveolar area ( $\text{mm}^2$ ) was defined using software. The apical length of the alveolar ridge was defined as a line that crossed the apical area of the socket (a-Line) which was perpendicular to the line that divided the socket into palatal and buccal portions (bisector). The coronal length of the socket was identified by the line that linked BC (buccal bone crest) and PC (palatal bone crest) (BC-PC Line); the buccal bone wall height (B-height, mm) was used to determine the measure of the distance from buccal crest (BC) to the a-Line; the palatal bone wall height (P-height, mm) to determine the distance from the palatal crest (PC) to the a-Line. Fig 2 shows the schematic drawing of the landmarks used for measurements.



**Fig 2** Schematic drawing illustrating the landmarks used for the measurements in the CBCT scans (slices on the sagittal plane). The blue rectangle represents the alveolar area ( $\text{mm}^2$ ), from the buccal bone crest (BC) to the palatal bone crest (PC), limited by the coronal length of the socket (BC-PC Line), buccal wall height (B-height, mm), palatal bone wall height (P-height, mm), and apical length of the alveolar ridge (a-Line). The bisector line is a perpendicular line dividing the socket into palatal and buccal portions with reference to the apical portion of the alveoli.

The evaluation of the 3D changes was performed by the same investigator at T0 and T1 on plaster casts. The casts were then scanned and stereolithic (STL) files were created. The STL files were overlaid using software. The STL were converted to DICOM files and segmented. The segmented areas were transformed into a volumetric scale to measure and map bone remodelling (loss, gain or unchanged). The 3D overlap was compared between CG and TG.

### Results

Twenty-five teeth were extracted in the maxilla in 20 subjects (11 women and nine men). Teeth were extracted due to periodontal disease (seven), root fracture (six) and extensive caries (twelve). No fistula or suppuration was present at the time of extraction. No inflammatory complications were reported in the post-operative period. No dropouts were reported.

Results for the average area of the alveolar ridge showed better results in the TG than the CG during the experimental period as showed in Table 1. The CG had a loss of area of approximately 39% and the TG had a reduction of 15%. There was no statistically significant difference when comparing the area for both groups in the same time interval. (*Refer Table 1, page 40*)

Similar results were seen for buccal and palatal crest height where TG showed less ridge resorption with a statistically significant difference from CG at T1. The 3D reduction obtained by overlaying the images was  $2150.63 \pm 548.32\text{mm}^3$  to  $1956.51 \pm 214.5\text{mm}^3$ , meaning 9.02% reduction for the TG, whereas in the CG the change from  $2234.54 \pm 497.36\text{mm}^3$  to  $871.47 \pm 79.21\text{mm}^3$  equated to 39% alveolar bone loss.

**Table 1** Data (mean ± SD) for the buccal and palatal crest heights (mm) and alveolar ridge area (mm<sup>2</sup>) for both study groups

Group	Buccal crest height (mm)		Palatal crest height (mm)		Area (mm <sup>2</sup> )	
	T0	T1	T0	T1	T0	T1
Blood clot (control group)	7.64 ± 2.09 <sup>Aa</sup>	4.26 ± 1.68 <sup>Bb</sup>	8.04 ± 2.92 <sup>Aa</sup>	5.70 ± 2.33 <sup>Bb</sup>	75.52 ± 32.32 <sup>Aa</sup>	45.82 ± 25.35 <sup>Ab</sup>
rhBMP2 (test group)	7.54 ± 4.16 <sup>Aa</sup>	6.93 ± 4.06 <sup>Aa</sup>	8.52 ± 2.68 <sup>Aa</sup>	8.13 ± 2.85 <sup>Aa</sup>	63.42 ± 20.51 <sup>Aa</sup>	53.85 ± 18.35 <sup>Aa</sup>

<sup>ABC</sup>Difference among groups in the same time interval.<sup>abc</sup>Difference among groups in the same time interval.

## Discussion

After four months of healing, this study showed better healing with use of rhBMP-2 in extraction sockets. Different patterns were seen with the buccal and palatal plates. Previous studies have shown despite bone grafting, alveolar ridge resorption still occurs, with greater bone loss at the buccal aspect. Less height loss has been shown on the buccal side which is reflected in this study.

Other studies have suggested an autogenous bone graft as the ideal biomaterial for new bone formation with the least remnants of biomaterial, followed by HA, xenograft and bioglass. Non-significant increases in new bone were found among the experimental groups and using an e-PFTE barrier did not alter the formation of new bone.

Another study has compared rhBMP-2 alone (control), autograft with rhBMP-2, absorbable collagen sponge with rhBMP-2,  $\beta$ -TCP with rhBMP-2, bovine xenograft with rhBMP-2 and HA with rhBMP-2. The rhBMP-2 showed no difference in bone formation when combined with bovine bone,  $\beta$ -TCP or HA. There was also no difference at eight weeks between the groups.

rhBMP-2 has been used after cyst removal, post-extraction, sockets with buccal defects  $\geq 50\%$ . All had favourable results. rhBMP-2 groups concentrations have been considered- high if  $>1.1$  mg/mL, moderate if 0.7 to 1.1 mg/mL, and low at  $<0.7$  mg/L. Bone formation was found to be higher in groups that had rhBMP-2 applied regardless of dose.

A previous study had similar design with rhBMP-2 and collagen sponge resulting in better socket fill. This previous study did not find significant differences in the alveolar crest height. The severity of the defect likely affected the results, suggesting that osteo-induction of the growth factor was limited by the socket bone walls and did not extend above the defect or involved above-bone gain.

Studies have shown in extraction sockets, 1.50mg/mL rhBMP-2 and collagen achieved better results than 0.75mg/mL rhBMP-2 and collagen sponge, collagen sponge alone and water. The no treatment group had an average loss of  $1.17 \pm 1.23$ mm. The 1.50mg/mL rhBMP-2 and collagen group had an increase in the average bone length next to the crest of  $3.27 \pm 2.53$ mm. This study used vertical releasing incisions to close the socket in comparison with this study where an FGG was used.

rhBMP-2 activates signalling pathways to stimulate the osteogenic differentiation of bone marrow-derived stem cells (BMSCs) using the mitogen-activated protein kinase pathways.

This leads to increased osteoblasts and expressions of biomarkers alkaline phosphatase (ALP), osteocalcin and type I

collagen. The signalling cascade initiated by BMP-2 can interact with other pathways such as Wnt/ $\beta$ -catenin<sup>1</sup> amplifying the effects of osteoblast differentiation. Wnt signalling can then synergistically enhance rhBMP-2 mediated differentiation. BMP-2 attracts progenitor cells to the site of action where they can migrate, proliferate and differentiate into osteoblasts.

Other studies have used acrylic stents and titanium pins to help with the reproducibility of the measurements. Others have used radiography or tomography. This study used linear measurements for length and buccal and palatal bone crests and measured the socket area.

Limitations of this study included lack of positive control with a collagen sponge only, inclusion of both single rooted and multi-rooted teeth, the low number of patients and the use of only one dose of rhBMP-2 (1.5mg/mL). Future studies are needed considering the above factors and histologic images and analysis.

## Conclusion.

This current RCT showed rhBMP-2 in extraction sockets resulted in the maintenance of 2.5 times more bone available in the test group. This is important when maintaining dimensions when immediate implant placement is not possible. Healing time is reduced for new bone formation for subsequent implant placement using rhBMP-2, the cost- benefit ratio, case selection and the higher risk of osteonecrosis need to be considered.

## Footnote

1. Wnt/ $\beta$ -catenin signalling pathway is involved in crucial parts of tissue homeostasis.

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1. A B C D
2. A B C D
3. TRUE or FALSE
4. A B C D
5. A B C D
6. A B C D
7. TRUE or FALSE
8. A B C D
9. A B C D
10. A B C D

### August QUIZ 2025 answers

1. B
2. A
3. FALSE
4. B
5. C
6. D
7. TRUE
8. C
9. A
10. C

## Questions

1. Previous studies of use of rhBMP-2 in combination with  $\beta$ -TCP with a resulted in:
  - a. Better bone preservation than rhBMP-2 and HA
  - b. Less bone preservation than rhBMP-2 and bovine xenograft
  - c. No difference compared with rhBMP-2 and HA or bovine xenograft
  - d. Less bone preservation than rhBMP-2 and collagen sponge
2. The buccal crest height (mm) in the Control Group (CG) at T1 was:
  - a.  $4.26 \pm 1.68$
  - b.  $5.70 \pm 2.33$
  - c.  $6.93 \pm 4.06$
  - d.  $8.13 \pm 2.85$
3. In this study, a collagen sponge was used as a positive control.
  - TRUE
  - FALSE
4. The Test Group (TG) had a reduction in 3D volume by:
  - a. 50%
  - b. 39%
  - c. 15%
  - d. 9.02%
5. The Control Group (CG) had the socket closed with:
  - a. Collagen sponge
  - b. Suture across the socket
  - c. Free gingival graft
  - d. rhBMP-2 placed directly in the socket
6. CBCT scans were performed at:
  - a. Day 1
  - b. Day 30
  - c. Day 90
  - d. Day 120
7. Previous studies have shown 1.50mg/mL rhBMP-2 and collagen placed in a socket results in better bone preservation than 0.75mg/mL rhBMP-2.
  - TRUE
  - FALSE
8. The sample size was based on a power of :
  - a. 60%
  - b. 70%
  - c. 80%
  - d. 90%
9. rhBMP-2 has been shown to activate signalling pathways to stimulate bone marrow-derived stem cells and also works with which other pathway:
  - a. Alkaline Phosphatase
  - b. Wnt/ $\beta$ -catenin
  - c. rhBMP-7
  - d. BMSC
10. After extraction, approximately how much alveolar bone loss is seen?
  - a. 3-5mm in 1 month
  - b. 3-5mm in 3 months
  - c. 3-5mm in 6 months
  - d. 3-5mm in 12 months