The Local Effect of Alendronate with Intra-alveolar Collagen Sponges on Post Extraction Alveolar ridge Resorption: A Clinical Trial

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Abstract

Introduction Extraction of teeth is followed by resorption of the residual alveolar ridge that continues throughout life resulting in loss of alveolar height and width. Of the numerous techniques that have been used to arrest post extraction alveolar ridge resorption, the placement of a graft material inside the socket immediately after extraction has been mostly followed. Type I collagen is one of the commonly used graft material that prevent resorption by providing dimensional stability to the socket.

Bisphosphonates are an anti-osteoclastic drug that prevent resorption by disrupting the membrane ruffling of the osteoclasts. Alendronate a bisphosphonate, is primarily used in diseases with bone loss. It has been used to reduce active bone resorption significantly without interfering with bone mineralization and quality. The need for the study is to examine the inhibitory effect of alendronate on residual ridge resorption when applied locally in combination with type I collagen on alveolar bone immediately following tooth extraction.

Materials and Methods Twenty patients with age between 30 and 65 years were selected from the out patient department of The Oxford Dental College and Hospital. The patients were divided into two groups. In the first group after extraction of teeth from premolar to midline the sockets were irrigated with saline and sutured. On the left side type I collagen sponge was placed and sutured. In the other group the right side was treated the same way after extraction as in first group where as in the left side sockets type I collagen soaked in 20 mg/ml of alendronate was placed and sutured. Patients were evaluated clinically for any local irritation as well as radiologically with orthopantomograph X-rays were taken immediately after the extraction, 1 month after extraction and 4 months after extraction to determine the amount of bone loss prevented.

Results The statistically significant bone loss prevented by the collagen alone was 22.8 % and in collagen with alendronate group was 44.38 % at the end of 4 months.

Conclusion Type I collagen soaked with alendronate when placed in the socket immediately after extraction of teeth prevents post-extraction alveolar ridge resorption.

Keywords Alendronate · Collagen sponges · Extraction sockets · Ridge preservation

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Introduction

Extraction of tooth by various local and systemic factors often causes reduction of the residual alveolar ridge height and width. The most striking feature of the extraction wound healing is that even after the healing of wound, the residual ridge alveolar bone undergoes life-long catabolic changes. This unique phenomenon has been described by Jahangari as residual ridge reduction [1].

The remodelling of the woven bone to mature bone would naturally determine a tridimensional contraction of the wound after extraction [2]. This reduction is mainly due to extensive resorption of the buccal walls.

Some authors have stated that due to the increased matrix content of cancellous bone compared to compact bone, the process of resorption is four times more in the mandible than in maxilla. Also the resorption is at its maximum in the immediate post-operative period accounting to about 15–25 % of the bone height above the base of the socket by the end of the first year [3].

To counteract this phenomenon, numerous techniques have been advocated. Of them local ridge preservation techniques are the most frequently used procedures to maintain the bone mass and density [1].

The ridge can be prepared by locally grafting a biomaterial into the socket immediately after an extraction. The grafted material must have the capability to conduct bone formation and provide dimensional stability to the socket. Of the different biomaterials that are used to prevent post extraction ridge resorption, collagen is the most popularly used to maintain the socket width and height preventing about 60 % of the immediate resorption [1].

These graft materials have been combined with various drugs like bisphosphonates and antibiotics and placed directly on the bone to prevent periodontal/alveolar bone loss in both animal and human models. The graft materials in combination with these drugs cause a prolonged release of the drug over an extended period of time [4].

Bisphosphonates are antimetabolite drugs that are analogous to pyrophosphonates that bind selectively to bone hydroxapatite crystals. They are frequently used in post-menopausal women to prevent bone loss. The rationale of their use is based on their osteoclastic activity and their probable inhibitory effects on the matrix metalloproteinases. Alendronate is a widely used bisphosphonate that has been administered systematically to reduce post extraction alveolar ridge resorption to 50 % of the original loss in animals as well as in humans [1, 2].

It has also been administered locally to prevent bone loss due to periodontitis in animal models [5–8]. Nevertheless the effect of bisphosphonates on ridge preservation by local application in humans remains poorly investigated. Therefore when alendronate is combined with collagen in

small acceptable doses and applied locally, immediately after extraction of teeth, it helps both by supporting the extraction socket as well as by inhibiting the resorption process of the alveolar ridge by slow release of the drug in the extracted tooth region.

Methodology

The study subjects consisted of twenty healthy adult patients who were selected from the Department of Oral and Maxillofacial Surgery, The Oxford Dental College and Hospital, Bangalore. The study protocol was approved by the ethical committee of The Oxford Dental College and Hospital, Bangalore. The study was conducted according to the guidelines for research principles involving patients, taking appropriate measures to minimize the pain and discomfort.

Inclusion criteria

1. Patients requiring extraction of teeth bilaterally from left to right premolar.
2. Patients who have given their consent for this trial.

Exclusion criteria

1. Patients should not have taken drugs, especially bisphosphonates or drugs altering bone metabolism, within 2 months before the inclusion in the study.
2. Patients having history of allergy to any drugs.
3. Patients who have a history of any concomitant major known medical problem and/or ongoing pharmacologic treatments.

The following materials and methods were used for the study.

Materials

- Collagen sponges (Fig. 2).
- 10 mg sodium alendronate tablet (OSTEOFOS 10 manufactured by CIPLA LTD) (Fig. 3).

Armamentarium (Fig. 1)

- Mouth mirror
- Probe
- Tweezer
- Cheek retractor
- 2 ml injection syringe
- No-15 surgical blade
- Stainless steel tray
- Kidney tray
- Stainless steel bowl

Dental extraction kit containing (Fig. 1)

Fig. 1 Armamentarium

- Howarths periosteal elevator
- Molt periosteal elevator
- Mandibular premolar forceps
- Mandibular anterior forceps
- Bard Parker handle (No-3)
- Adson tissue forceps (non-toothed)
- Needle holder
- Suture cutting scissor

Study Design

A total of twenty patients aged between 30 and 65 years were randomly divided into two groups, each group comprising of ten patients. In each group the experimental sites were divided into left and right study sites (Figs. 2, 3).

Group 1: Collagen sponge

- Left—Collagen sponge alone (active control).
- Right—Saline irrigation (passive control).

Group 2: 20 mg/ml Alendronate sodium soaked in collagen sponge

- Left—20 mg/ml Alendronate sodium soaked in collagen sponge (experimental site).
- Right—Saline irrigation (passive control).

Preoperative Evaluation of the Bone Height

A standardized digital orthopantomograph was taken immediately before the surgery at 100 % magnification. Vertical height of the mandible from the lower border to the deepest point in the sockets of the respective tooth was measured with a digital vernier caliper. Measurement for each tooth socket region was done. In the interdental areas,

Fig. 2 Type I collagen

Fig. 3 Alendronate

measurement was done from the lower border of the mandible to the superior most prominent point on the alveolar crest. Measurements were done both on left and right sides of the mandible. A mean of all at the respective sides was taken as the vertical height of the mandible on that side.

Preparation of Collagen Sponge Pellets Soaked in Alendronate

Two tablets, 10 mg, of alendronate sodium were taken in a steel bowl and one ml of sterile water was added to it with the help a 2 ml syringe. The solution was stirred until the tablets dissolve in the water. Four numbers of 5 mm × 5 mm of collagen sponge pellets were cut with the tissue dissector and immersed in the solution for 15 min for equal absorption. Then they were removed and kept in an empty steel bowl.

Surgical Procedure

In each patient preoperative analysis and diagnosis were done. Patient's history was recorded in the specially prepared proforma.

Using panoramic radiograph, a single stage surgical protocol was planned. The patient was draped and the site was prepared with povidone-iodine paint.

A bilateral inferior alveolar nerve block was achieved using 2 % Lignocaine Hydrochloride solution.

The full thickness flaps were reflected using Howarth's periosteal elevator.

Teeth were extracted atraumatically. The sockets were irrigated with saline solution.

In group 1 within the sockets of the extracted teeth on the left side the collagen pellets soaked in saline water were placed. The sockets on the right side were irrigated with saline water.

In group 2 in the sockets on the left side of the mandible collagen sponge soaked with alendronate sodium solution was placed, and the right side sockets were irrigated with normal saline. The mucoperiosteal flap was approximated and primary closure achieved with 3.0 mersilk suture material. Figure of eight suturings were done to secure the collagen pellets within the sockets.

Postoperative antibiotics i.e. Amoxicillin 500 mg thrice daily for 5 days and non steroidal anti inflammatory drugs i.e. Ibuprofen 400 mg twice daily were prescribed for all patients for 5 days.

After 24 h gargling with chlorhexidine mouthwash twice daily for 7 days was advised.

The patients were advised to report to the institution if any discomfort was experienced at any time. Sutures were removed after 7 days.

Clinical Evaluation

All patients were clinically evaluated for any signs of pain, swelling, healing and ulceration after the extraction and at the end of 1 and 4 months respectively from the day of the surgery.

Radiographic evaluation was done according to the following methods:

- Three standardized digital orthopantomographs were taken. 1st radiograph—immediately after the surgical procedure, 2nd radiograph—1 month after the surgical procedure and 3rd radiograph—4 months after the surgical procedure.
- All radiographs were recorded at 100 % magnification with the same orthopantomogram.

Method of Measurements in the First Postoperative Radiograph

Measurements of height were done both on left and right sides of the mandible in the same way it was done in the preoperative radiograph and the amount of loss of vertical bone height was calculated by comparing the mean with the pre-operative bone height.

Method of Measurements in the Second and the Third Postoperative Radiographs

Here the vertical height of the mandible was measured with a digital vernier caliper from the lower border to the most prominent and the superior-most point on the alveolar ridge. Readings were taken from ten different areas on each side in antero-posterior dimension. A mean of all at the respective sides was taken as the vertical height of the mandible on that side. The amount of loss of vertical bone height was calculated in the same way it was calculated in the first post-operative orthopantomogram.

Results

Study Design

A comparative clinical study with 20 patients using collagen alone and collagen soaked with alendronate having ten patients in each group was undertaken to evaluate the efficacy of alendronate with intra-alveolar collagen sponges in reducing alveolar bone resorption after teeth extraction, and to observe any signs and symptoms of adverse effects like local irritation and pain.

Interpretation of the Result

In the present study the mean age of the patients (Table 1; Graph 1) in both the study groups and the control are

Table 1 Comparison of age distribution in the three groups

Age in years	Control		Collagen		Collagen + alendronate	
	No	%	No	%	No	%
Up to 50	8	40.0	5	50.0	3	30.0
51–60	8	40.0	3	30.0	5	50.0
>60	4	20.0	2	20.0	2	20.0
Total	20	100.0	10	100.0	10	100.0
Mean $\pm$ SD	50.85 $\pm$ 11.51		50.20 $\pm$ 11.78		51.50 $\pm$ 11.84	

Samples age matched with $P = 0.969$

Graph 1 Age distribution of patients in the control group

Table 2 Gender distribution in three groups

Gender	Control		Collagen		Collagen + alendronate	
	No	%	No	%	No	%
Male	10	50.0	5	50.0	5	50.0
Female	10	50.0	5	50.0	5	50.0
Total	20	100.0	10	100.0	10	100.0

Samples are gender matched with $P = 1.000$

Graph 2 Age distribution of patients in study groups

almost same and the difference in the groups is statistically insignificant ($P = 0.969$).

The sex distribution in both the groups was the same (Table 2; Graph 2) comprising of 50 % male patients and 50 % female patients.

Pain (Table 3; Graphs 3, 4, 5) was mostly present in the immediate post-operative period. More pain was seen in

the group containing collagen soaked with alendronate 100 % when compared with the other two groups which is of statistical significance ($P < 0.001$).

There was no swelling in any of the patients.

The healing was also satisfactory at the three follow ups.

Ulceration (Table 4; Graphs 6, 7, 8) was seen in only 10 % of the patients treated with collagen with alendronate and 5 % of the patients in the control group which is statistically insignificant ($P > 0.1$).

The bone loss seen (Table 5; Graph 9) in the group receiving the collagen sponge alone was maximum in the post operative period (0.028 ± 0.02) followed by the controls (0.0215 ± 0.010) and then the group receiving alendronate only, But the finding is not of statistical significance with $P = 0.385$.

In the 1 month post operative period both the study groups showed bone loss lesser than the controls (Table 5; Graph 9). Of the two study groups the group containing the collagen sponge showed less bone loss (76.7 % of controls) when compared with group containing collagen with alendronate (89.9 % of controls). The values are of moderate statistical significance ($P = 0.004$).

At the end of 4 months follow up the group containing both collagen and alendronate showed only 55.62 % bone loss followed by collagen which had 77.2 % of the controls (Table 5; Graph 9). The difference in the values are also of strong statistical significance with a P value of <0.001 .

Discussion

Intra alveolar socket healing is a complex process that comprises intense bone remodeling starting from a provisional connective tissue matrix to the formation of lamellar bone. This process naturally determines a contraction of tissue as wounds tend to contract. This results in an increased reduction of socket height and width in the immediate post operative period. Although this resorption process continues throughout life, the maximum resorption takes place in the first few months after extraction [1].

In the present study an anti-osteoclastic drug of bisphosphonate group (Alendronate) was administered locally by using collagen sponge that acts as a carrier to decrease this immediate post-operative resorption of bone.

The type I collagen when placed inside the extraction socket, provides dimensional stability to the socket and prevents the collapse of the socket walls. Moreover collagen when used as a carrier causes slow release of the drug over a prolonged period of time [9].

Table 3 Comparative evaluation of pain in patients studied

Pain	Immediate postoperative		1 Month post-operative		4 Months post-operative		% Change	P value
	No	%	No	%	No	%		
Controls (n = 20)								
Absent	1	5.0	19	95.0	20	100.0	+95.0	<0.001
Present	19	95.0	1	5.0	0	0.0	−95.0	<0.001
Collagen (n = 10)								
Absent	3	30.0	10	100.0	20	100.0	+70.0	<0.001
Present	7	70.0	0	0.0	0	0.0	−70.0	<0.001
Collagen + alendronate (n = 10)								
Absent	0	0.0	9	90.0	20	100.0	+100.0	<0.001
Present	10	100.0	1	10.0	0	0.0	−100.0	<0.001
Significance	0.106		1.000		1.000		−	−

Graph 3 Percentage of pain in control group **Graph 4** Percentage of pain in collagen alone group

The Type-1 Collagen Sponge (HEALIGUIDE, Manufactured by Advanced Biotech Products (P) Ltd)

Healiguide is purely a type I collagen sponge which is obtained from selected animal tissues and has been sterilized using ethylene oxide gas.

Graph 5 Percentage of pain in collagen + alendronate group

The type-I collagen is the purest, least immunogenic and highly bio-active, which makes it the ideal choice for the treatment, therapy and regeneration of tissue system(s) as it applies to various medical applications.

The type-I collagen which is one of the main constituents of human tissue conducts bone formation and provides dimensional stability to the socket by preventing the socket walls from collapsing. Exogenous collagen is chemotactic for fibroblasts and improves fibroblast migration through its scaffold-like fibrillar structure. It also creates a thrombogenic surface that stimulates platelet attachment which may accelerate fibrin and clot attachment.

Moreover collagen is hemostatic, a property that enhances wound healing [2]. Li et al. demonstrated the advantage of the semi-permeable property of collagen sponge, which allows diffusion of nutrient molecules from the external environment into the repair site and permits the diffusion of important wound-derived neurotrophic factors [10].

Collagen when used as a carrier of a drug causes slow release of the drug over a prolonged period of time [9] till the time it is degraded by the enzyme collagenase within the body after 6–8 weeks.

The bisphosphonates are antimetabolite drugs that are analogous to pyrophosphonates that prevent osteoclastic

Table 4 Comparative evaluation of ulcerations in patients studied

Ulcerations	Immediate postoperative		1 Month post operative		4 Months post operative		% Change	<i>P</i> value
	No	%	No	%	No	%		
Controls (n = 20)								
Absent	19	95.0	20	100.0	20	100.0	+5.0	0.437
Present	1	5.0	0	0.0	0	0.0	−5.0	
Collagen (n = 10)								
Absent	10	100	10	100.0	10	100.0	0	NS
Present	0	0.0	0	0.0	0	0.0	0	NS
Collagen + alendronate (n = 10)								
Absent	9	90.0	10	100.0	10	100.0	+10.0	0.411
Present	1	10.0	0	0.0	0	0.0	−10.0	
Significance	1.000		1.000		1.000		−	−

NS Not significant

Graph 6 Evaluation of ulceration in controls **Graph 7** Evaluation of ulceration in the collagen group

bone resorption. The activity of the bisphosphonate is related to the number of carbons in the aliphatic chain. In

Graph 8 Evaluation of ulceration in the collagen + alendronate group

these derivatives the optimal number of carbon is four. They are being used clinically to treat metabolic bone diseases in humans which involve increased bone resorption, such as Paget's disease and hypercalcemia of malignancy. Animal studies have indicated that bisphosphonates are also effective in preventing bone loss in other metabolic diseases, such as osteoporosis, related to immobilization and oestrogen deficiency [11].

After conducting animal studies using bisphosphonates they are recently being used on human models to prevent the bone loss after periodontal surgeries. They were also successful in reducing the resorption process after distraction osteogenesis and placement of autogenous free bone grafts [12].

Alendronate which is a four carbon compound with an amino-group side chain is one of the most potent bisphosphonates which reduces the resorption. In some recent studies it has been demonstrated that, alendronate when administered systematically was successful in reducing alveolar bone loss after extraction of teeth in both animal [1] and human [2] models.

Table 5 Comparative evaluation of bone loss in three groups of patients studied

Bone loss	Control (n = 20)	Collagen (n = 10)	Collagen + Aledronate (n = 10)	Over all significance
Immediate post operative	0.125 ± 0.010	0.028 ± 0.02	0.020 ± 0.011	0.385
% of bone loss	–	130.2 %	93 %	–
1 Month post operative	0.378 ± 0.056	0.29 ± 0.06	0.34 ± 0.06	0.004
% of bone loss	–	76.7 %	89.8 %	–
4 Month post operative	1.717 ± 0.07	1.326 ± 0.074	0.955 ± 0.115	<0.001
% of bone loss	–	77.2 %	55.62 %	–

Graph 9 Comparison of bone loss (in mm) between all the three groups at different follow up periods

Chemical Structure of Alendronate

Pharmacodynamic Properties

Bisphosphonates like alendronate are deposited mainly in the bone lacunae [13] and are released locally during the resorption process in the acidic pH [14]. Although, the exact mechanism of action of alendronate is still under investigation it is stated by some authors that alendronate can inhibit several protein tyrosine phosphatase in the osteoclasts thus disrupting the formation of cytoskeleton [15].

Some authors have stated that alendronate disrupts the membrane ruffling thus inhibiting the resorption process [16]. It was seen that osteoclasts seeded on the bone causes resorption by extrusion of acids by a sodium-independent mechanism and this process is inhibited by alendronate [14].

Pharmacokinetic Properties

Till date, no metabolites of alendronate have been identified in humans. This may be due to the metabolic stability of the compound. Limited human studies have confirmed that the elimination of alendronate is almost exclusively via the urine [13].

Tolerability

On local administration the adverse effects included ulceration and pain when administered at a dose more than 40 mg/ml.

Although osteomalacia has been reported with the use of other bisphosphonates, no such problems have been found with local administration of alendronate in clinical trials over 2–3 years.

Dosage and Administration

Alendronate is most effective at the dose of 20 mg/ml of saline, in reducing bone loss when used locally [6–8, 17, 18]. It was demonstrated that alendronate at pharmacologically active dose (20 mg/ml), shows higher uptake on resorptive surfaces than on formative surfaces [18].

The present study takes into account the clinical parameters like pain; swelling, healing and ulceration which were not recorded in the study conducted by Altundal and Guvener [1].

Pain that was elucidated by the patients at the surgical site in the immediate post-operative period may be because of inflammatory reaction to foreign body. The only adverse reaction seen in the study was ulceration over the alveolar ridge, buccal mucosa and lip commissure in one of the patients who also gave a history of ulceration in the past with analgesic. This reaction may be due to the adverse drug reaction of the analgesic which regressed after the analgesics were withdrawn and the ulcers were absent at the end of the first week follow up. There was no incidence of swelling or any other adverse effects in any of the patients in either group. The healing was also satisfactory

in all the cases without any post-operative complications. The study showed no statistically significant difference ($P = 0.385$) in the bone loss between all the three groups in the immediate post operative period.

At 1 month follow up there was maximum resorption in the controls (0.378 ± 0.056 mm) followed by the collagen soaked in alendronate group (0.34 ± 0.06). Resorption was least (0.29 ± 0.06) in the group containing collagen alone, preventing 23.3 % of the resorption seen in the control group. With $P = 0.004$ this finding is of moderate statistical significance because of a very less difference in bone resorption.

At the end of 4 months, bone loss was maximum in the control group (1.717 ± 0.07). Collagen when grafted into the socket prevented the bone loss by 22.8 % whereas in the group grafted with both collagen and alendronate, the bone loss was 44.38 % less, with a statistically significant P value of <0.001 .

This coincides with the study conducted by Altundal and Guvener [1] where alendronate was administered systematically and collagen sponge was placed after third molar surgeries.

In a similar animal study conducted by H. Altundal the author found that systematically administered alendronate reduces the rate of alveolar bone resorption to about 95 % and the lingual bone resorption to about 98 % [1].

The reduction in anti-resorptive property of collagen in between the first and fourth month follow up may be due to its degradation in the body between the sixth and the 8th week of placement, after which it is not much effective in prevention of the resorption process where as the alendronate even when the collagen is resorbed is deposited in bone resorptive lacunae and released whenever there is any resorption, even at the end of 4 months [16].

In this study the type I collagen was more effective in combination with alendronate than collagen alone (at the end of 4 months), which was in conformity with the study conducted by Sowmya et al. on regenerative potential of type I collagen with xenogenic bone grafts in the treatment of infrabony defects [9]. The resorption process in both the study groups was slowed down but was not arrested completely.

It was maximum in the controls, followed by the area which received collagen alone. However at the sites receiving collagen with alendronate, resorption was present but in much lesser extent. None of the patients had any

signs of new bone formation or any increase in the bone height after extraction.

Conclusion

Patients receiving type I collagen soaked with alendronate showed lesser loss of bone height.

The amount of bone loss prevented in patients treated with collagen soaked with alendronate was maximum after a period of 4 months followed by the patients treated with collagen alone whereas there were insignificant changes of bone loss in the immediate post-operative period and at the end of 1 month.

Thus, it can be concluded that collagen prevents the collapse of the socket in the post-operative period while alendronate slows down the late stage of osteoclastic bone resorption that continues throughout life.

Additional research is required for understanding the mechanisms by which alendronate or type I collagen or in combination inhibits the resorption process when applied locally in the extraction socket. Since in the present study the samples have been selected based on some inclusion criteria with smaller sample size, studies with larger sample size and longer follow up periods are required to determine the effects of the drug even under prolonged forces of mastication.

Summary

The effects of a bisphosphonate, alendronate with type I collagen on post extraction alveolar ridge resorption has been evaluated in the present study.

There was no adverse reaction with the drug or the collagen. The bone loss prevented by collagen soaked with alendronate group was maximum at 4 months post operative in comparison to the controls. The difference of bone loss between the control, collagen alone and collagen soaked with alendronate in the immediate post operative and 1 month post operative period was not of much significance.

This provides a solution to prevent bone loss before placing prosthesis or implants, thus resulting in a better function of the prosthesis. Collagen sponge and alendronate are economical, easily available and the surgical procedure is not technique sensitive which makes them a promising combination for bone preservation after extraction.

Appendix

Patient Consent form

I, _____, do hereby declare in my complete consciousness that I have decided on my own accord, and wish to undergo examination / investigation / treatment or any other necessary procedures carried out by _____

And further state that neither the dentist nor the assistants will be held responsible for any consequences as regard to the treatment rendered or any work executed. I also agree to co-operate fully, realizing that failure to do so could result in less than optimal results.

Date:

Place:

Signature:

PROFORMA:

THE OXFORD DENTAL COLLEGE AND HOSPITAL BANGALORE DEPARTMENT OF ORAL AND MAXILLOFACIAL SURGERY

Title of the study:

“THE LOCAL EFFECT OF ALENDRONATE WITH INTRA-ALVEOLAR COLLAGEN SPONGES ON POST EXTRACTION ALVEOLAR RIDGE RESORPTION- A CLINICAL TRIAL”

I) IDENTIFYING DATA:

OP NO:

NAME:

SEX:

AGE:

DATE:

WHEATHER COLLAGEN SPONGE IS USED ALONE OR WITH ALENDRONATE IN THE STUDY SIDE:

II) PRE- OPERATIVE VARIABLES

RADIOGRAPHIC:

A. Height of the mandible (in mm) from the lower border of the mandible to the upper border of mandible on the study site

1, 2, 3, 4, 5, 6, 7, 8, 9, 10

MEAN

B. Height of the mandible (in mm) from the lower border of the mandible to the upper border of mandible on the control site

1, 2, 3, 4, 5, 6, 7, 8, 9, 10

MEAN

III) POST-OPERATIVE VARIABLES:

a) CLINICAL:

A) IMMEDIATE POST-OPERATIVE

SYMPTOM	CONTROL	STUDY
PAIN		
SWELLING		
HEALING		
UNCERATION		

B) ONE MONTH POST OPERATIVE

SYMPTOM	CONTROL	STUDY
PAIN		
SWELLING		
HEALING		
UNCERATION		

C) FOUR MONTHS POST OPERATIVE

SYMPTOM	CONTROL	STUDY
PAIN		
SWELLING		
HEALING		
UNCERATION		

b) RADIOGRAPHIC:

i) Height of the mandible (in mm) from the lower border of the mandible to the upper border of mandible on the study site.

A. IMMEDIATE POST OPERATIVE:

1, 2, 3, 4, 5, 6, 7, 8, 9, 10

MEAN-I:

MEAN-II: ONE MONTH POST-OPERATIVE-1, 2, 3, 4, 5, 6, 7, 8, 9, 10

MEAN-III: FOUR MONTHS POST-OPERATIVE-1, 2, 3, 4, 5, 6, 7, 8, 9, 10

ii) Height of the mandible (in mm) from the lower border of the mandible to the upper border of mandible on the control site.

1, 2, 3, 4, 5, 6, 7, 8, 9, 10

MEAN I:

MEAN-II: ONE MONTH POST-OPERATIVE-1, 2, 3, 4, 5, 6, 7, 8, 9, 10

MEAN-III: FOUR MONTHS POST-OPERATIVE-1, 2, 3, 4, 5, 6, 7, 8, 9, 10

B. ONE MONTH POST OPERATIVE:

1, 2, 3, 4, 5, 6, 7, 8, 9, 10

MEAN-I:

MEAN-II: ONE MONTH POST-OPERATIVE-1, 2, 3, 4, 5, 6, 7, 8, 9, 10

MEAN-III: FOUR MONTHS POST-OPERATIVE-1, 2, 3, 4, 5, 6, 7, 8, 9, 10

ii) Height of the mandible (in mm) from the lower border of the mandible to the upper border of mandible on the control site.

1, 2, 3, 4, 5, 6, 7, 8, 9, 10

MEAN I:

MEAN-II: ONE MONTH POST-OPERATIVE-1, 2, 3, 4, 5, 6, 7, 8, 9, 10

MEAN-III: FOUR MONTHS POST-OPERATIVE-1, 2, 3, 4, 5, 6, 7, 8, 9, 10

C. FOUR MONTHS POST OPERATIVE:

1, 2, 3, 4, 5, 6, 7, 8, 9, 10

MEAN-I:

MEAN-II: ONE MONTH POST-OPERATIVE-1, 2, 3, 4, 5, 6, 7, 8, 9, 10

MEAN-III: FOUR MONTHS POST-OPERATIVE-1, 2, 3, 4, 5, 6, 7, 8, 9, 10

ii) Height of the mandible (in mm) from the lower border of the mandible to the upper border of mandible on the control site.

1, 2, 3, 4, 5, 6, 7, 8, 9, 10

MEAN I:

MEAN-II: ONE MONTH POST-OPERATIVE-1, 2, 3, 4, 5, 6, 7, 8, 9, 10

MEAN-III: FOUR MONTHS POST-OPERATIVE-1, 2, 3, 4, 5, 6, 7, 8, 9, 10

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