Original Article

Effect of Topical Antibiotic around Implant Cover Screw on the Prevention of Crestal Bone Resorption Using Fractal Analysis: A Randomized Clinical Trial

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Abstract

Introduction: The presence of peri-implant inflammation can lead to the loss of implant if extended to the bone. Therefore, it is essential to develop effective strategies for the prevention and treatment of diseases around the implant. The present study aimed to assess the effect of topical antibiotics on the prevention of implant crestal bone resorption using fractal analysis. **Methods:** A total of 30 patients with a mean age of 41.4 ±4.2 years and in need of dental implants were randomly assigned to three groups (n=10). The first and second test groups received 0.5% erythromycin ointment and 0.3% gentamicin, while the control group received no antibiotics. To evaluate the degree of crestal bone resorption around dental implants at baseline and three months later, a phosphor plate radiograph was taken and fractal analysis was then performed to determine the degree of resorption. **Results:** The comparison with the fractal changes between the two time intervals demonstrated that there were no significant differences in all three groups (*P>0.05*). There was a significant difference among the three groups in the fractal dimension (FD) index just after the implant placement (*P=0.03*). The control group was significantly different from the erythromycin and gentamicin groups in terms of FD index immediately after implant placement. Nonetheless, there was no significant difference between the erythromycin and gentamicin groups (*P=0.07*). There was no significant difference in FD among the three groups three months after implant placement. **Conclusion:** Using topical antibiotics did not affect bone resorption after three months of implant placement.

Keywords: Crestal Bone Loss, Dental Implant, Erythromycin, Fractal Analysis, Gentamicin, Topical Antibiotic

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Introduction

Implant placement for replacing the missing teeth turned out to be the best and safest treatment in numerous clinical situations. Nonetheless, in recent decades, there has been increasing evidence of inflammation around the implant as one of the most common side effects of treatment. The studies conducted on dental implants over several years have demonstrated that the long-term success of implants depends on two factors: first, the direct relationship between bone and implants, and second, the development of soft and hard tissue around the coronal area of the implant (1-3). Some etiological factors aggravate this relationship, including occlusal overload, peri-implantitis, as well as micro-gaps between the abutment and the implant (4).

In the presence of proper plaque control, the attachment of soft tissue in the coronal area of the implant creates a suitable biological seal that prevents the penetration of microorganisms and bone resorption in the area adjacent to the implant. Therefore, preserving the crestal bone is of utmost importance to the establishment of this biological seal. If bone resorption occurs in the implant

crest module, the gingival margin is in a more apical position (5, 6). In submerged implants, crestal bone resorption is inevitable (7). Among the effective factors, the presence of micro-gaps is more prominent in crestal bone resorption. The prevention of bacterial infiltration in the abutment-implant interface aims to minimize inflammatory reactions and maintain the bone crest (7, 8). Due to the micro-gaps in this site, which vary between 1-49 microns (9), different bacterial species between 1-10 microns (10, 11) can easily enter this area.

Inflammation around the implant (peri-implantitis) is a complication affecting both the soft and hard tissue, leading to the loss of the inserted implant (7). Since bacterial infection is one of the most important causes of early loss of dental implants, the prevention of infection in the surgical field is of vital importance. Certainly, the presence of bacteria in the area can affect the repair process of a biomaterial implanted in the body, and in the case of bacterial contamination, it is difficult to remove, leading to implant failure. The hypothesis concerning the major role of bacteria in the etiology of mucositis and peri-implantitis has been widely investigated (12-17).

Implant manufacturers are trying to minimize the presence of germs by reducing the size of the micro-gap or moving the area away from the bone-implant junction (18). The lack of a clinical protocol or surgery to use other methods, such as antimicrobials, has forced clinicians to use experimental methods to limit bacteria in the screw hole. Various products were used in this field, including saline solution, chlorhexidine, and various antibiotic ointments. Paolantonio (19) used chlorhexidine to decontaminate the screw hole for the first time and observed a significant effect in the reduction of the bacterial load by 30%-100%.

These studies have been performed in the stage of completing the osteointegration; moreover, the bone crestal resorption usually begins one month after implant placement (20). Therefore, it is necessary to think of ways to reduce microbial load at this stage to prevent crestal resorption. It is worth noting that no study has yet been conducted in this field. The present study aimed to find a solution to reduce the microbial load in the crestal area in the course of implant insertion. Xu et al. concluded that the use of topical antibiotics (Minocycline Hydrochloride Ointment (MHO) and Erythromycin Ophthalmic Ointment (EOO) is beneficial to advancing the initial repair of the flapless surgical site. In addition, it was concluded that the topical use of antibiotics in combination with systemic antibiotics could reduce the inflammatory response to wound healing after implant placement (21).

Today, fractal analysis is efficiently employed to study the complex pattern of fractal dimension (FD) of the trabecular bone structure is introduced as a quantitative result of this image processing scheme. Despite subtractive techniques, this method examines trabecular structural patterns and bone density independent of radiation geometry. Therefore, it is not necessary to iterate exact radiation geometries for serial radiographs (22,23). There are many methods for the estimation of fractal dimension; nonetheless, the box-counting method is the most widely used and suitable for binary image analysis (24).

Several studies evaluated the changes in alveolar bone due to periodontitis using fractal analysis (25-27). As evidenced by these results, FD can differentiate between healthy bone and those affected by severe periodontitis (27). Conventional radiographs were used in these studies. After scanning these radiographs, they were converted to digital formats, and the resolution of images was changed (28,29); accordingly, digital imaging was used in this study. Crestal bone resorption around dental implants in the first year after implantation is a known problem. Furthermore, since implants are loaded on average after three months, it seems difficult to determine bone changes using conventional radiographs. Fractal analysis can detect bone changes; therefore, in the present study, after using topical antibiotics with screw cover in implant placement surgery, the amount of crestal bone resorption was investigated using this technique.

Materials and Methods

This double-blinded paralleled arm randomized clinical trial aimed to determine the effect of topical antibiotics on the prevention of crestal bone resorption in dental implants. The patients were selected from among the individuals referred to the Implant Department of Mashhad Dental School between April 2019 and March 2020. This study was approved by the Ethics Committee of the Mashhad University of Medical Science under the code of IR.MUMS.DENTISTRY.REC.1397.090 and clinical trial registry for IRCT Code of IRCT20120215009014N262.

Inclusion criteria:

- Patients in need of dental implants within the age range of 25-60 years
- Full mouth plaque core (FMPS) < 20%
- Periodontally and systemically healthy
- Partially edentulous patients with at least one tooth adjacent to the implant area

- A healed edentulous area with adequate hard and soft tissue
- No history of implant failure in that area

Exclusion criteria:

- Any contraindications for implant placement
- Patients with a deficient immune system and systemic diseases affecting periodontal tissue such as diabetes
- Medications affecting the surgery, such as bisphosphonates and anticoagulants
- need for simultaneous soft and hard tissue augmentation
- Allergy to Erythromycin and Gentamicin
- Presence or history of periodontal disease
- Pregnancy or lactation

Based on similar studies (26,27), with α=0.05 and a power of 80%, 30 patients in need of dental implants within the age range of 25-60 years were included and randomly assigned to three groups of 10 using a computer-generated randomization table. The randomization was performed using the block method. Allocation concealment was obtained using sealed coded opaque envelopes, which are opened at the time of the surgery. In this single-blinded study, 0.5% Erythromycin antibiotic ointment (Erythrolidine®) and 0.3% Gentamicin antibiotic ointment (Gentex®) were applied for the first and second test groups, respectively. In the control group, no topical antibiotic was used. Oral hygiene was instructed to the patients, and implant placement was not scheduled until the patient could demonstrate an adequate standard of plaque control (FMPS <20%).

All the surgeries were performed by a single surgeon. Full thickness flap preparation was carried out as far as

the crest of the ridge was available. All implants (Dio UF, Korea) were bone level and placed at crestal level. After rinsing with normal saline, antibiotic ointments were applied to the grooved end of the cover screws until overflow. The control group did not receive topical antibiotics. Flap closure was performed with single interrupted Nylon 4-0 sutures. The patients were instructed to maintain adequate plaque control and use chlorhexidine 0.2% mouthwash for two weeks. The suture removal was after one week. To evaluate the amount of crestal bone resorption around the implants, immediately after surgery (baseline) and three months later, phosphor plate radiographs were taken; thereafter, the crestal bone was evaluated for the amount of resorption using fractal analysis. Finally, statistical data were analyzed in SPSS software (version 19) (Armonk, NY) using Shapiro-Wilk and ANOVA tests.

Result

The current study included 30 patients in need of dental implant insertion within the mean age of 41.4 ±4.2 years. Out of these 30 patients, 14 cases were male, and 16 subjects were female. These 30 patients were randomly assigned to three groups: control, Gentamicin, and Erythromycin (Figure 1). The mean age scores of patients in control, Erythromycin, and Gentamicin groups were 41.2±4.6, 42.7±5.7, and 40.5±4.4 years, respectively. Shapiro-Wilk test pointed to the normal distribution of age. Based on one-way ANOVA test, the mean age of patients was not significantly different between the two groups (*P=0.08*).

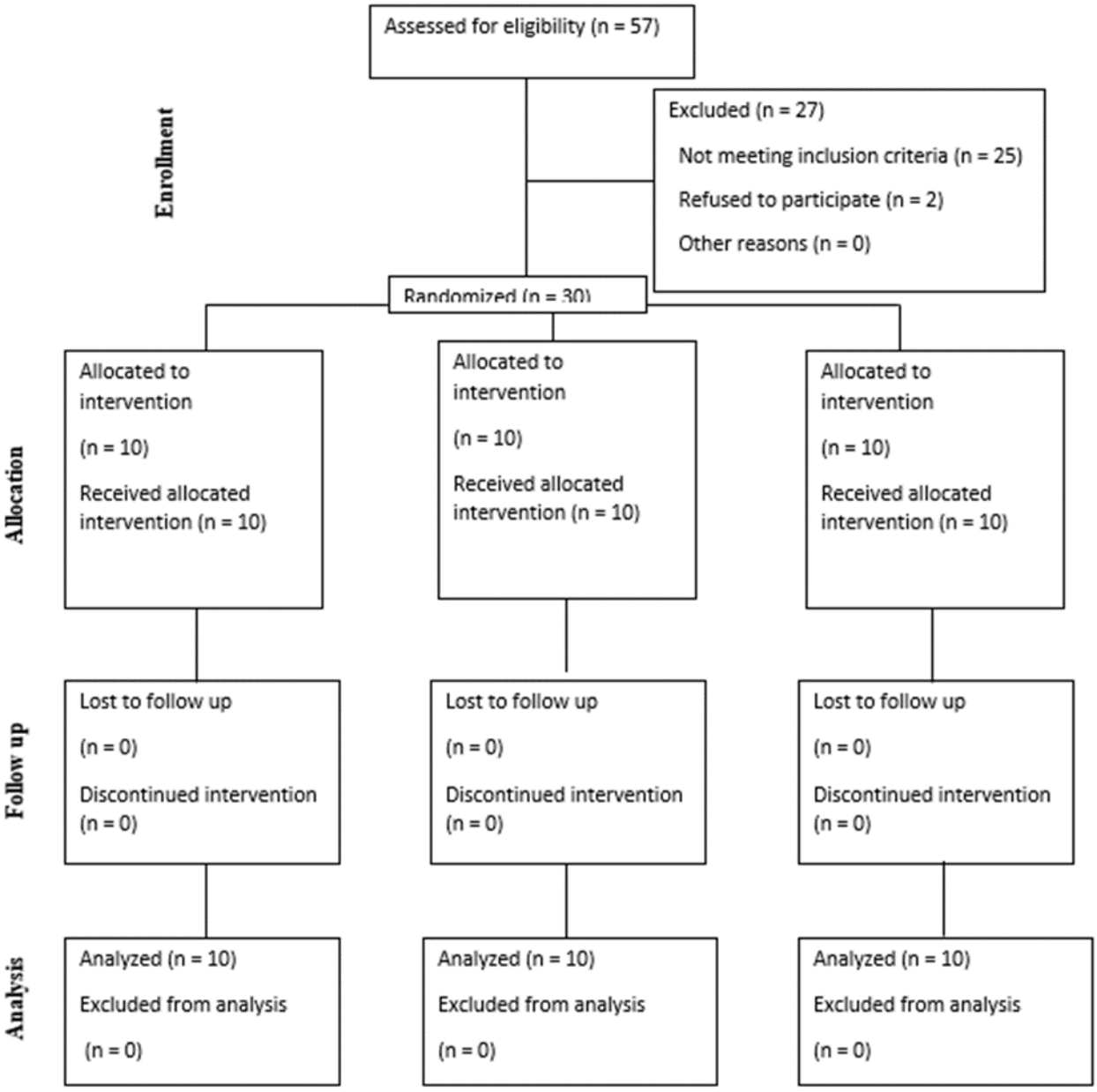

Figure1. CONSORT diagram

There were five male and five female patients in the control group, five male and five female patients in the Erythromycin group, and four male and six female patients in the Gentamicin group. In Table I, we compared the mean fractal dimension (FD) index between two time periods (baseline and three months) in each of the three groups. Based on the Shapiro-Wilk test, all data in the groups had a normal distribution; therefore, the paired t-test was used and revealed that the mean crestal bone resorption did not differ significantly between time periods in all three groups ($P>0.05$).

Table I. Mean fractal dimension index in three groups at two time points

Group	Immediately after implant placement	three months after implant placement	*P value*
Control	0.075±0.02	0.069±0.15	*P=0.08*
Erythromycin	0.08±0.54	0.072±0.23	*P=0.23*
Gentamicin	0.076±0.36	0.079±0.17	*P=0.31*

In Table II, we compared the mean FD index among the three groups in each of the two time periods using the one-way ANOVA test and found that the mean fractal values were significantly different among the three groups only in the time interval immediately after implant placement (*P=0.03*).

Table II. Mean fractal dimension index among the three groups in each of the two time periods

Time period	Control	Erythromycin	Gentamicin	*p-value*
Immediately after implant placement	0.075±0.02	0.08±0.54	0.076±0.36	*P=0.03*
three months after implant placement	0.069±0.15	0.072±0.23	0.079±0.17	*P=0.68*

In the pairwise comparison of groups immediately after implant placement, we use the Post-hoc Tukey test. It was revealed that the control group was significantly different from both Erythromycin and Gentamicin groups in terms of FD index immediately after implant placement (*P=0.01, P=0.02*). There was no significant difference between Erythromycin and Gentamicin groups (*P=0.07*).

Discussion

As evidenced by the results of this study, the use of topical antibiotics exerted no effect on bone resorption after three months of implant placement. Although pre- and postoperative antibiotics are strongly supported, their effects are unclear (30). It has been recently reported that systemic use of antibiotics in implant surgery is helpful in the reduction of postoperative complications and infections. Some studies have reported that topical application of antibiotics has a better effect on initial wound healing than systemic antibiotics (30-32).

A pilot study by Xu et al. aimed to evaluate the effect of topical Minocycline Hydrochloride Ointment (MHO) and Erythromycin Ophthalmic Ointment (EOO) on wound healing after flapless dental implant surgery. In the stated study, 40 patients underwent flapless implant surgery and were randomly allocated to three groups: 1- MHO group (n=17), 2- EOO group (n=18), and 3- control group (n=5). All groups received systemic antibiotics, and only the control group did not use topical antibiotics. Three days after surgery, clinical parameters, gingival crevicular fluid (GCF) volume around the implant, and gingival lipopolysaccharide (LPS) level in all patients were collected, measured, and analyzed. The results of the mentioned study pointed out that the clinical outcomes in the two treatment groups were better than in the control group, indicating that the use of topical antibiotics is beneficial to the promotion of the initial repair of the flapless surgery site. No distinct effect was observed between the EOO and MHO groups in the early stages of recovery. In addition, there was a significant correlation between LPS level and all clinical parameters. The researchers concluded that topical use of antibiotics in combination with systemic antibiotics could reduce the inflammatory response in wound healing after implant placement. EOO and MHO were equally effective in early wound healing. Compared to MHO, EOO offers such advantages as cost-efficiency and convenience; therefore, the use of EOO as topical antibiotics in flapless implant surgery is recommended (21).

A notable point in the study by Xu et al. (21) was that they worked on parameters used to evaluate soft tissue repair (clinical parameters, volume of gingival crevice

fluid around the implant, and level of liposuction lipopolysaccharides (LPS) in GCF), whereas in our study, a bone parameter (Bone resorption) was used for evaluation. This may be the reason for the discrepancies between the results of the present research and those of other studies.

Crestal bone resorption has been observed around dental implants for decades. This event is described after the exposure and loading of the implants, regardless of the surgical procedure. Adell et al. first reported marginal bone resorption around the implant. According to the referred study, in the first year of loading, a higher rate and occurrence of resorption was observed. The amount of this resorption in the first year ranged from 0-3 mm and averaged 1.2mm (33). Concerning that the rate of bone resorption in the first year is about 1 mm, it seems that a period of three months is not enough to assess the rate of bone resorption.

Numerous hypotheses have been put forward about the causes of crestal bone resorption, including the biological causes of periosteal elevation during surgery, the preparation of the implant osteotomy cavity, the position of the micro-gap between the abutment and the fixture, bacterial invasion, and biological width stabilization. In a prospective study on 125 implants, Adell (33) reported that 80% of the implant sulcus areas were non-inflammatory. Lekholm (34) found that the deep gingival pockets around the implants had no effects on crestal bone resorption. However, marginal bone resorption beyond the first fixture thread is a common radiographic finding.

The question is if bacteria cause early bone resorption, why does most of the bone resorption occur in the first year and decrease in the following years? The depth of the implant sulcus increases due to the initial bone resorption, impairing hygiene and increasing the likelihood of anaerobic bacteria acting as bacterial bone resorption. If bacteria are the cause of primary crestal bone resorption, what local changes occur in the environment that significantly reduce their effect after the first year? Given these points, bacterial theory cannot explain the phenomenon of marginal bone resorption (33-36). Therefore, according to this justification, the results of the present study are not far from the expectation that after three months, none of the groups are significantly different in terms of bone resorption.

Conclusion

The results of this study pointed out that topical antibiotics had no effect on implant crestal bone resorption after three months of placement; nonetheless, more studies with larger sample sizes and longer follow-up periods are needed.

Conflicts of Interest

The authors declare that they have no conflict of interest in this study.

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References

1. Khammissa RAG, Feller L, Meyerov R, Lemmer J. Peri-implant mucositis and peri-implantitis: clinical and histopathological characteristics and treatment. SADJ. 2012;67(122):124–126.

2. Zitzmann, Nicola & Walter, Clemens & T, Berglundh. Ätiologie, Diagnostik und Therapie der Periimplantitis – eine Übersicht. Dtsch Zahnarztl Z. 2006;61:642-649.

3. Sorsa T, Tervahartiala T, Leppilahti J, Hernandez M, Gamonal J, Tuomainen AM, Lauhio A, Pussinen PJ, Mäntylä P. Collagenase-2 (MMP-8) as a point-of-care biomarker in periodontitis and cardiovascular diseases. Therapeutic response to non-antimicrobial properties of tetracyclines. Pharmacol Res. 2011;63(2):108–113.

4. Oh TJ, Yoon J, Misch CE, Wang HL. The causes of early implant bone loss: myth or science? J Periodontol. 2002;73(3):322-233.

5. Schwarz F, John G, Hegewald A, Becker J. Non-surgical treatment of peri-implant mucositis and peri-implantitis at zirconia implants: a prospective case series. J Clin Periodontol. 2015;42(8):783-788.

6. Hammerle CH, Bragger U, Burgin W, Lang NP. The effect of subcrestal placement of the polished surface of ITI implants on marginal soft and hard tissues. Clin Oral Implants Res. 1996; 7(2):111–119.

7. Xu L, Yu Z, Lee H-M, Wolff MS, Golub LM, Sorsa T, Kuula H. Characteristics of collagenase-2 from gingival crevicular fluid and peri-implant sulcular fluid in periodontitis and

peri-implantitis patients: pilot study. Acta Odontol Scand. 2008; 66(4):219–224.

8. Degidi M, Artese L, Piattelli A, Scarano A, Shibli JA, Piccirilli M, Perrotti V, Iezzi G. Histological and immunohistochemical evaluation of the peri-implant soft tissues around machined and acid-etched titanium healing abutments: a prospective randomised study. Clin Oral Investig. 2012; 16(3):857–866.

9. Sorsa T, Tervahartiala T, Leppilahti J, Hernandez M, Gamonal J, Tuomainen AM, Lauhio A, Pussinen PJ, Mäntylä P. Collagenase-2 (MMP-8) as a point-of-care biomarker in periodontitis and cardiovascular diseases. Therapeutic response to non-antimicrobial properties of tetracyclines. Pharmacol Res. 2011; 63(2):108–113.

10. Mombelli A, Muller N, Cionca N. The epidemiology of peri-implantitis. Clin Oral Implants Res. 2012;23(Suppl 6):67–76**.**

11. Sorsa T, Hernández M, Leppilahti J, Munjal S, Netuschil L, Mäntylä P. Detection of gingival crevicular fluid MMP-8 levels with different laboratory and chair-side methods. Oral Dis. 2010; 16(1):39–45.

12. Berglundh T, Lindhe J, Marinell C, Ericsson I, Liljenberg B. Soft tissue reaction to de novo plaque formation on implants and teeth. An experimental study in the dog. Clin. Oral Implants Res. 1992;3(1):1-8.

13. Pontoriero R, Tonelli M, Carnevale G, Mombelli A, Nyman S, Lang N. Experimentally induced peri-implant mucositis. A clinical study in humans. Clin. Oral Implants Res. 1994;5(4):254-259.

14. Augthun M, Conrads G. Microbial findings of deep peri-implant bone defects. Int J Oral Maxillofac Implants. 1997;12(1):106-112.

15. Salcetti JM, Moriarty JD, Cooper LF, Smith FW, Collins JG, Socransky SS, et al. The clinical, microbial, and host response characteristics of the failing implant. Int J Oral Maxillofac Implants . 1997;12(1):32-42

16. Mombelli A, Lang NP. The diagnosis and treatment of peri-implantitis. Periodontol. 2000 1998;17(1):63-76.

17. Quirynen M, De Soete M, Van Steenberghe D. Infectious risks for oral implants: a review of the literature. Clin. Oral Implants Res. 2002;13(1):1-19.

18. Kano SC, Binon PP, Curtis DA. A classification system to measure the implant-abutment microgap. Int J Oral Maxillofac Implants. 2007;22(6):879-885.

19. Paolantonio M, Perinetti G, D'Ercole S, Graziani F, Catamo G, Sammartino G, et al. Internal decontamination of dental implants: an in vivo randomized microbiologic 6-month trial on the effects of a chlorhexidine gel. J Periodontol. 2008;79(8):1419-25.

20. King GN, Hermann JS, Schoolfield JD, Buser D, Cochran DL. Influence of the size of the microgap on crestal bone levels in non-submerged dental implants: a radiographic study in the canine mandible. J Periodontol. 2002; 73(10):1111-1117.

21. Xu L, Wang Y, Nguyen VT, Chen J. Effects of Topical Antibiotic Prophylaxis on Wound Healing After Flapless Implant Surgery: A Pilot Study. J Periodontol. 2016; 87(3):275-280**.**

22. Lalitha L, Dutta Majumder D. Fractal based criteria to evaluate the performance of digital image magnification techniques. Pattern Recognit Lett. 1989;9(1):67-75.

23. An Introduction to the Fascinating Patterns of Visual Math: Natural Fractals. Updated Jan 2010. Available from: http:// www.miqel.com/fractals_math_patterns/visual-math-naturalfractals.html. [Last accessed on 2012 Mar 5].

24. Buckland-Wright JC, Lynch JA, Rymer J, Fogelman I. Fractal signature analyis of macroradiographs measures trabecular organization in lumbar vertebrae of postmenopausal women. Calcif Tissue Int. 1994; 54(2): 106-112**.**

25. Shrout MK, Roberson B, Potter BJ, Mailhot JM, Hildebolt CF. A comparison of 2 patient populations using fractal analysis. J Periodontol .1998; 69(1):9-13.

26. Sang-Yun Cha, Won-Jeong Han, Eun-Kyung Kim. Usefulness of fractal analysis for the diagnosis of periodontitis. Korean J Oral Maxillofac Radiol. 2001; 31(1):35-42.

27. Updike SX, Nowzari H. Fractal analysis of dental radiographs to detect periodontitis-induced trabecular changes. J Periodontal Res. 2008; 43(6):658-664

28. Pornprasertsuk S, Ludlow JB, Webber RL, Tyndall DA, Yamauchi M. Analysis of fractal dimensions of rat bones from film and digital images. Dentomaxillofac Radiol. 2001; 30(3):179-83

29. Baksi BG, Fidler A. Image resolution and exposure time of digital radiographs affects fractal dimension of periapical bone. Clin Oral Investig. 2012; 16(5):1507-1510

30. Pasupathy S, Alexander M. Antibiotic prophylaxis in third molarsurgery. J Craniofac Surg. 2011; 22 (2): 551-553.

31. Monaco G, Tavernese L, Agostini R, et al. Evaluaton of antibiotic prophylaxis in reducing postoperative infection after mandibular third molar extraction in young patients. J Oral Maxil Surg. 2009; 67(7): 1467-1472.

32. Nolan R, Kemmoona M, Polyzois I, et al. The influence of prophylactic antibiotic administration on postoperative morbidity in dental implant surgery. A prospective double blind randomized controlled clinical trial. Clin Oral Implants Res. 2014; 25(2): 252-259.

33. Adell R, Lekholm U, Rockler BR, Brånemark PI. A 15-year study of osseointegrated implants in the treatment of the edentulous jaw. Int. J. Oral Surg. 1981;10(6):387-416.

34. Lekholm U, Ericsson I, Adell R, Slots J. The condition of the soft tissues at tooth and fixture abutments supporting fixed bridges A microbiological and histological study. J. Clin. Periodontol. 1986 ;13(6):558-562.

35. Glickman I, Smulow JB. Effect of excessive occlusal forces upon the pathway of gingival inflammation in humans. J. Periodontol . 1965 ;36(2):141-147.

36. Albrektsson T, Zarb G, Worthington P, Eriksson AR. The long-term efficacy of currently used dental implants: a review and proposed criteria of success. Int. J. oral maxillofac implants. 1986 ;(1):11-25.

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