A Clinical and Radiographic Study to Evaluate and Compare the Effectiveness of Nano crystalline Hydroxyapatite with Advanced Platelet Rich Fibrin(A-Prf) and Hydroxyapatite Reinforced Beta Tri-Calcium Phosphate (Ha+β-TCP) with A-Prf in the Treatment of Human Infrabony Defects: A Cross Sectional Study

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Abstract

Background: Combination of nano crystalline hydroxyapatite with Advanced Platelet Rich Fibrin (A-PRF) and Hydroxyapatite reinforced Beta Tri-Calcium Phosphate (HA+β-TCP) with A-PRF for the treatment of infrabony defect will be effective in reduction of probing pocket depth, gain in clinical attachment level and defect fill. **Aim:** To evaluate and compare the effectiveness of Nano crystalline hydroxyapatite with Advanced Platelet Rich Fibrin (A-PRF) and Hydroxyapatite reinforced Beta Tri-Calcium Phosphate (HA+β-TCP) with A-PRF in the treatment of human infrabony defects clinically and radio graphically using Cone Beam Computed Tomography (CBCT). **Methods:** 28 defects will be randomly divided into test and control group consisting of 14 defects in each. Test group will be treated by nano crystalline hydroxyapatite particles with A-PRF and control will be treated by hydroxyapatite reinforced beta tri-calcuim phosphate with A-PRF. Primary outcomes will be radiographic bone fill and Secondary outcomes will be CAL gain and PPD reduction. The Clinical parameters will be recorded at baseline and 6 month postoperatively. **Results:** The Standard Deviation and Mean (Mean ± SD) values will be calculated for PI and papillary bleeding index and also for all clinical parameters including RGML, RAL, PPD, WKG and GR. To co-relate the data from base line to six months of each group students paired t-test will be used. To compare two groups at the day of surgery and six months student's unpaired t-test will be used. Nano crystalline hydroxyapatite particles with A-PRF will result in significantly greater CAL gain, PPD reduction and radiographic bone fill at 6 months when compared to Hydroxyapatite reinforced Beta tri-calcuim phosphate with A-PRF. Conclusion: Combination of Nano crystalline hydroxyapatite particles with A-PRF will be effective in the treatment of infrabony defects. Nano crystalline hydroxyapatite particles with A-PRF will have significantly greater outcome as compared to Hydroxyapatite reinforced Beta tri-calcium phosphate with A-PRF.

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How to cite this article: Rathod A, Jaiswal P and Bajaj P. A Clinical and Radiographic Study to Evaluate and Compare the Effectiveness of Nano crystalline Hydroxyapatite with Advanced Platelet Rich Fibrin(A-Prf) and Hydroxyapatite Reinforced Beta Tri-Calcium Phosphate (Ha+β-TCP) with A-Prf in the Treatment of Human Infrabony Defects: A Cross Sectional Study . Ann Med Health Sci Res. 2021;11:4-9

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Keywords

Infrabony defects; Nano crystalline hydroxyapatite; Advanced Platelet Rich Fibrin (A-PRF); Hydroxyapatite reinforced Beta Tri-Calcium Phosphate (HA+β-TCP); Cone bean computed tomography

Introduction

Periodontitis is an inflammatory disease causing alveolar bone loss and ultimately leading to loss of teeth. [1] An infrabony defects with periodontal pockets are common in periodontitis. When there is loss of the attachment apparatus in periodontal diseases, regeneration of periodontal attachment becomes the primary aim of the regenerative therapy. [2] Bone grafts and bone graft substitutes give a structural outline for clot development, maturation, and remodeling that helps in bone formation of osseous defects. Bone grafting materials also illustrate ability to support the formation of bone, cementum, and periodontal ligament when located in periodontal defects. Bone grafting materials must have the quality of biocompatibility and osteoconductivity. [3] Alloplastic materials are used as bone substitute because of its osteoconductivity and biocompatibility. Alloplastic grafts like Hydroxy Apatite (HA), Beta-Tri Calcium Phosphate (β-TCP) are the synthetic Calcium Phosphate (CaP) ceramics and they are available in many forms like cements, powder, pastes, blocks and granules. These synthetic CaP ceramics are the substitutes for autograft, allograft or xenograft. Recently combination of HA and β-TCP containing 30% HA and 70% β-TCP has been used for periodontal regeneration. [4] As compared to traditional materials Nanomaterials have properties important like size effects, quantum effect, surface effect and show better work than traditional materials. They have advantages like nearest proximity with adjacent tissues, fast resorption and more number of molecules on the surface. [5] Platelet Rich Fibrin (PRF) is considered as a platelet concentrate of 2nd generation. [6] PRF looks like a fibrin network and leads to more efficient cell migration, proliferation, and thus angiogenesis. [7] APRF is a new moderations of PRF preparation leading to evolution of Advanced Platelet Rich Fibrin (A-PRF). Advanced Platelet Rich fibrin (APRF) first described in 2014 is a novel concept for cell-based tissue engineering. Advanced-PRF is prepared by decreasing the rpm while increasing the time of standard Platelet Rich fibrin (PRF). [8] *i.e.* spining rate of 1500 rpm and centrifugation period of 14 minutes. [9] Conventional radiographs are two-dimensional presentations; it is difficult to localize a particular area with a single radiograph. Main disadvantage of Faulty radiographs are because of faulty technique, or the solutions used for it. Traditional radiography left over a limited diagnostic tool. Successful use of Computed Tomography (CT) because of its capacity to perform precise 3-Dimensional (3D) registrations, still this technique has some limitations, such as the amount of radiation exposure and equipment size and cost. In recent times, Cone-Beam CT (CBCT) has appeared as a realistic tool in dentistry for giving minimum rate alternative to conventional CT with high-quality images and lesser radiation exposure to patients. CBCT is the most precise and accurate than conventional techniques. [10] Hence aim of the study to evaluate and compare the effectiveness of nanocrystalline hydroxyapatite with Advanced Platelet Rich Fibrin (A-PRF) and Hydroxyapatite reinforced Beta tri-calcium phosphate (HA +β-TCP) with A-PRF in the treatment of human infrabony defects clinically and radiographically using Cone Beam Computed Tomography(CBCT).

Study Population

In this study a total of 28 healthy patients, with moderate to advanced chronic periodontitis based on clinical and radiographic confirmation of angular bony defects will be chosen from the outpatient Department of Periodontics, “Sharad Pawar Dental College, Sawangi (Meghe), Wardha.” with the subsequent criteria’s

Inclusion criteria

1. Systematically healthy patient.
2. Following initial therapy, presence of minimum 1 or 2 interproximal infrabony osseous defects PPD ≥ 5 mm and CAL ≥ 5 and which are radiographically noticeable.
3. Clinically and radiographically there should be ≥ 3 mm defect depth which is affirmed on intrasurgical measurement.
4. A radiographically determined defect base should be minimum of 3 mm above the apex of the tooth.
5. Presence of minimum ≥ 2 mm zone of keratinized gingiva to permit total soft tissue coverage of the defect area.

Exclusion criteria

1. Patient diagnosed with aggressive periodontitis.
2. Patients with poor oral hygiene care (Plaque Index>1).
3. Patients using tobacco in any form.
4. Involved tooth with inadequate root canal therapy and subsequent restoration.
5. Involved tooth having mobility greater than grade II,or defect extending in to furcation and third molars.
6. Priorhistory of periodontal surgery of the selected segment.
7. Females who are pregnant or lactating.
8. There is clinical and radiographic sign of untreated acute infection at the selected site, root fracture, apical pathology,severe root irregularities, cemental pearls, cementoenamel projections, untreated carious lesion on root surface.

Details related to nutritional condition, mouth cleansing practice, systemic background, gingival and periodontal condition with usual clinical details will be taken down in a specially planned chart. Patients will be checked under fine light by using mouth mirror and William's graduated periodontal probe.

Initial Therapy

There will be appropriate assessment and diagnosis. Afterwards initial therapy including oral health care advice, scaling and root planning under LA. If required, coronoplasty will be done. Plaque control advice will be reinforced till the patient gained a plaque score of ≤ 1. Earlier to initiation of study, the reason and plan of the study will be explained to patient and informed consent will be obtained from each patient. Study protocol will be first accepted by ethical committee of "Datta Meghe Institute of Medical Sciences, Sawangi (Meghe), Wardha. Conventionally made occlusal acrylic stent will be used to standardize the probe angulations and position. Occlusal stent will be manufactured on cast with acrylic material and using alginate impression. Occlusal surface of tooth which is to be treated covered by occlusal stent and occlusal surface of minimum one tooth on mesial and distal to the involved tooth. The stent will be also extended so as to wrap it till the coronal third of teeth. A reference point (slot) will be made on the stent at the deepest site of involved tooth to permit reproducible periodontal probe positioning. The apical margin will be linear and served as a fixed reference point.

Study Design

A total of 28 systemically healthy patients will be selected from which will be considered suitable for the study later initial therapy. Before surgery, the chosen defects will be randomly allocated by means of a coin toss to the test and control groups. Every group includes 14 patients, like wise to the randomized parallel design. The test group (Group A) will be treated by Nanocrystalline hydroxyapatite with A-PRF while control group (Group B) will be treated by Hydroxyapatite reinforced Beta tri-calcium phosphate (HA +β-TCP) with A-PRF.

Clinical Measurements

Clinical measurements recorded will be plaque index, papillary bleeding index, probing pocket depth, relative attachment level, and relative gingival marginal level. All clinical measurements will be taken down on the day of surgery and 6 months post-surgery. In addition other documentation includes periodontal charting on specially designed form, intraoral periapical radiographs and intraoral clinical photographs will be obtained.

Indices

Plaque index and papillary bleeding index will be recorded to check for patient's supragingival plaque accumulation and gingival inflammation.

- Plaque Index [11]
- Papillary Bleeding Index [12]
- Probing Measurements

The following probing measurements will be noted for evaluation of the results in both treatment groups. PPD, Relative Clinical Attachment Level (RCAL), Relative Gingival Marginal Level (RGML) will be recorded at six sites of the selected defect: Mesiobuccal, mesiolingual, midmesial of one tooth, and distobuccal, distolingual, middistal of adjacent tooth. Only one deepest measurement per defect will be taken into consideration for calculation of the result. These measurements will be recorded with a UNC-15 calibrated (University of North Carolina, Hu-Friedy) periodontal probe. These clinical parameters will be recorded after preparation of acrylic stent at baseline, after 3 and 6 months of surgery. The UNC-15 probe will be placed in the slot made on the acrylic stent and tip at the gingival marginal level and the measurement will be recorded upto lower border of stent as Relative Gingival Margin Level (RGML). Then probe will be held at the pocket base and the distance upto the lower border of stent will be considered as a Relative Attachment Level (RAL). PPD will be measured from base of the pocket upto gingival margin. The width of keratinized gingiva will be recorded by measuring the area from the most apical point of the mucogingival junction to the crest of gingival margin using UNC-15 calibrated Periodontal Probe. All the probing measurements will be noted at baseline, 3 and 6 months post-surgery.

Radiographic Analysis

The use of standardized radiography is necessary for assessing the interproximal bony changes after periodontal surgery. The infrabony defect sites will be recorded at baseline and 6 months post-surgery through CBCT.

CBCT

The infrabony defect sites will be recorded using CBCT at the day of surgery and six months after surgery. The CBCT measurements include

1. Height of Bone defect (CEJ-BD (Base of the Defect))
2. Bone defect depth (AC-BD)
3. Alveolar Crest Level (CEJ-AC (Alveolar Crest))
4. Mesio Distal (MD) and Bucco Lingual (BL) bone defect width.

Other CBCT measurements will be recorded as per given by Bodhare et al. [13]

Surgical Procedure

Earlier to start of the surgical procedure, the patients will be made to rinse with Chlorhexidine (0.2%) mouthwash for 1 minute. Aseptic condition will be maintained through the complete procedure. The area to be treated will be sedated by nerve block or local infiltration at the operated area.

Flap design (Incisions)

Conventional technique comprising of a periodontal flap will be started by giving intra-sulcular incision with the help of 12 number surgical blades or 15 number surgical blades (Bard-Parker) on the buccal and lingual sides. Interdental papillae will be preserved by extending the incision as inter-proximally as possible. The extension of the flap will be involving one tooth on both mesial and distal sides of the area to be treated.

Flap reflection

With the help of periosteal elevator mucoperiosteal flap will be reflected to uncover alveolar bone at the site of defect. Care should be taken not to perforate the flap or damage the papillae while removal of granulomatous tissue from the internal side of the flap.

Debridement and root surface management

Granulation tissue wills debrided from the defect with the help of hand instruments following by ultrasonic scalar (EMS, Minipiezon), thus revealing the surface of the root, alveolar bone and PDL. Granulation tissue or epithelium attached to the internal surface of the flap will be debrided taking care not to thin the flap. Plaque, calculus on the surface of the root will be removed with the help of ultrasonic scalar. The surfaces root will be planned to get glossy and firm consistency. During the phase direct measurements of the vertical Bone Defects (BD) and the present number of bone walls will be noted with UNC15 probe. If the bone defect depth will be ≥ 3 mm vertically, patient will be eligible for further treatment.

Preparation of A-PRF

Blood will be taken into 4 ml × 9 ml test tubes by venipuncture, lacking of anticoagulant. 10 mm intravenous blood was taken. The test tubes will be instantaneously centrifuged with the rate of 1500 rpm for 14 minutes by the use of a centrifuge machine (REMI R-8C), Nagasari et al. [9] When centrifugation is completed, A-PRF clot will be taken out of the test tube, then isolated from the red part at its base by the use of pliers. A-PRF membrane clots will be smoothly pressed among a sterile plate of glass and a metal box.

Procedure for test group

After achieving haemostasis and isolation of the defect. Pre-suturing of the flap will be done without knot tying to let quick closure of flap after graft material placement. Nanocrystalline hydroxyapatite particles and A-PRF mixed thoroughly with 0.5 ml of physiological saline solution, in sterile mixing container, and hydrated. Then mixture of Nanocrystalline hydroxyapatite with A-PRF will be put into the bony defect in test site with little pressure till it occupies the coronal most level of bony wall by raising the flap and then A-PRF will be extended over the defect as a membrane. The A-PRF will be adopted in such a way that it covers at least 3 mm beyond the osseous defects. The flap will be positioned coronally and sutured so the flap margin will be placed 1 mm-2 mm coronal to CEJ, ensuring primary flap closure. Flap will be secured in place by giving combined suture of vertical mattress suture and interproximal "(4-0 non-resorbable surgical sutures, braided black silk)". Little pressure will be put onto the area with gauze soaked in saline for about 2 minutes, so that the soft tissue is well adapted to surface of the tooth and remove any area in which a clot formation take place disrupting re-attachment. Periodontal pack will be on the suture on buccal and lingual side.

Procedure for control group

The surgical technique for the control site will be same as for the test site except osseous defects at control sites will be packed with Hydroxyapatite reinforced Beta tri-calcuim phosphate and then A-PRF membrane will be placed over the bone graft.

Post-operative care

Antibiotic Amoxicillin 500 mg and analgesics such as Ibuprofen 325 mg combined with paracetamol 400 mg will be given 3 times/day for 5 days post operatively. Patients will be made to rinse with Chlorhexidine (0.2%) mouthwash for 6 weeks post-surgery. Sutures and periodontal pack and will be detached 8 days-10 days after surgery. In the treatment area chewing will not be permitted for 6 weeks and there are not any of the mechanical oral hygiene procedures. Patients will be educated to clean the operated area with cotton ball dipped in Chlorhexidine (0.12%) for more 2 weeks-3 weeks in an apico-coronal way and future by a soft toothbrush (Plakoff Plus®). After this phase, patient will be asked to restart mechanical oral hygiene care, consisting use of soft bristled tooth brush and interdental cleaning aid and to stop of Chlorhexidine use.

Maintenance care

Patients will be called back after 1, 3, 6 months of post-surgery. All the patients will be advised to maintain oral hygiene and full mouth ultra-sonic scaling will be performed at each follow up visit. Clinical parameter will not be recorded at 3 months.

Re-examination

A complete post-operative evaluation will be performed at 6 months follow up visit. All the clinical measurements including, PI, gingival index, PPD, RCAL and relative gingival marginal level will be assessed. In addition standardized radiographs and CBCT will be obtained.

Statistical Analysis

The mean and standard deviation (Mean ± SD) values will be calculated for plaque index and papillary bleeding index and also for all clinical parameters including RGML, RAL, PPD, WKG, DD and GR. Correlation will be done with baseline data to 6 months data for each treatment group by the use of student's paired t-test. This test will be used for comparing the treatment groups at baseline and 6 months. If the probability value $p>0.05$, the difference seen will be measured as insignificant and if <0.05, it will be considered significant. Nanocrystalline hydroxyapatite particles with A-PRF will result in greater CAL gain, PPD reduction and radiographic bone fill at 6 months when compared to Hydroxyapatite reinforced Beta tri-calcuim phosphate with A-PRF.

Discussion

Periodontal diseases are the most common oral diseases which is affecting 95% of the Indian population. Periodontitis is caused due to the collective effect of relations between bacteria and the immune-inflammatory response of the host. [1] An infrabony defects with periodontal pockets are common in periodontitis. It signifies the anatomic sequelae of the apically increase of plaque in the way of periodontitis. The objective of periodontal treatment is the regeneration of the lost periodontal structures. [14] The typical approach for periodontal regeneration is by using filling materials for repairing periodontal defects. “Gold standard” for periodontal graft material is considered as autograft. But normally people way out for other options for avoiding surgical complications of ankylosis, root resorption and a secondary surgical harvest site. A different range of bone substitutes are available like DFDBA, Anorganic bovine bone, HAp and β-TCP, a biocomposite poly (lactic-co-glycolic) acid/sub-micron size HAp (PLGA/HA) for periodontal regeneration. Recently alloplastic materials are used as bone substitute. The characteristics of them are biologically suitable, allowing bone ingrowths and remodeling. Furthermore, alloplastic materials have a number of benefits which are, it does not require donor area, abundant supply, and the absence of disease transmission. A recently elaborated alloplastic material contains 30% HA and 70% β-TCP. OSTEON grafting materials are available commercially of 2 type’s i.e. particulate range of 0.5 mm-1.0 mm and 1.0 mm-2.0 mm. Interconnected absorbent structures of OSTEON graft material are observed through Scanning Electron Microscopy (SEM). It has 77% of volumetric porocity and 300 µm-500 µm of pore size. It has been seen that the constant HA coated with β-TCP in the OSTEON bone grafts. [15] Beta Tricalcium Phosphate (β-TCP) is a purified, multicrystalline, porous form of calcium phosphate with Ca:PO4 ratio similar to that of natural bone material. [16] Nanomaterial has properties important like size effects, quantum effect, surface effect and show better work than traditional materials. [17] An added main property of nanostructured materials is the growth of self-assembly. [18] Aqueous solution of calcium nitrate tetra hydrate and ammonium dihydrogen phosphate by hydrothermal treatment is used for obtaining synthetic NHAs. [19] Nano phase HA help to proliferate for osteogenic differentiation of periodontal ligament cells and also used as a biodegradable agent in osseous restoration. [20-22] The new moderations of PRF preparation leading to evolution of A-PRF. By adapting the centrifugation period and spinning rate protocol of 1500 rpm, 14 minutes, Advanced-PRF is prepared, It include T and B lymphocytes, Hematopoietic Stem Cells (HSCs) It has larger concentration and further equivalent dispersal of monocyte required in bone formation. And there is equal allocation of platelets right through the entire clot. [9] CBCT has appeared as a realistic tool in dentistry for giving minimum rate alternative to conventional CT with high-quality images and lesser radiation exposure to patients. Choi et al. [10] had done comparison of conventional imaging techniques with CBCT. The more accuracy of CBCT measurements can be recognized by identifying defects seen buccal and lingual area of the teeth. These are not seen by conventional radiography. Hence artificially formed defects were seen in CBCT, while barely 67% of the defects were recognized in periapical radiographs. Investigations confirmed that CBCT is the most accurate than conventional techniques. Hence the authors concluded that CBCT is the precise and dependable than 2-dimensional conventional imaging techniques.

Conclusion

Nanocrystalline hydroxyapatite particles with A-PRF will result in greater CAL gain, PPD reduction and radiographic bone fill at 6 months when compared to Hydroxyapatite reinforced Beta tri-calcium phosphate with A-PRF.

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