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Research Article

Clinical Evaluation of Efficacy of 1.2% Atorvastatin Loaded in PRF with Collagen as a Barrier Membrane in Alveolar Ridge Preservation after Mandibular Molar Extraction

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Abstract

Introduction: Extraction of teeth accounts for loss in height and width of the tooth dependent alveolar process, which results in a significant structural and dimensional changes leading to the atrophy of the residual ridge. Most of the resorption occurs during the first 3 months of healing, although dimensional changes can be observed up to 1 year after tooth extraction. Therefore, regenerative or other surgical intervention appear to arrest the bone resorptive process, to restore the alveolar process thus preserving the natural contours and preparing the anatomical surroundings for the suggested prosthesis.

Aims and Objectives: To evaluate and compare the efficacy of 1.2% Atorvastatin loaded in PRF with collagen as a barrier membrane in alveolar ridge preservation versus controls after mandibular molar extraction, by measuring the following clinical parameters like relative coronal level of gingiva, mucogingival junction, crest of socket, socket depth, socket width at the most coronal level and to evaluate bone density changes radiographically by QDSR (Quantitative Digital Subtraction Radiography) technique in 1.2% Atorvastatin group and controls.

Materials and Methods: A prospective controlled clinical trial was conducted with a sample size of 20 subjects i.e., 20 sites, where mandibular molars were included in the study. Clinical parameters like relative coronal level of gingiva, MGJ, crest of socket, socket depth, socket width at the most coronal level were measured and bone density changes were recorded radiographically by Quantitative Digital Subtraction Radiography technique in 1.2% Atorvastatin group and control groups.

Results: Paired t-test and Unpaired t-test was used for intergroup comparison with in both the groups for SL, SM, SC, SD, W and radiographic density at different time intervals for various parameters at different time intervals. Unpaired t-test was also used to calculate the mean change and standard deviation of various clinical and radiographic parameters between control and test groups. Extraction sockets treated with 1.2% ATV together with PRF sealed with collagen barrier membrane resulted in significantly less

changes in respect of hard and soft tissue parameters in test group when compared to control group with spontaneous healing from baseline to 4 months after tooth extraction. Also, on evaluation with QDSR technique, there was a significant increase in the bone density in extraction sockets, which received 1.2% ATV and PRF than control group from baseline to 4 months after tooth extraction.

Conclusion: This study may give a new insight into the use of hydrophilic statins i.e. Atorvastatin together with PRF in the alveolar ridge preservation procedure to limit the resultant dimensional changes of tooth socket after extraction. Further longitudinal multicenter, and histological clinical trials are required for more conclusive interpretations of the results and to explore the additional possibility of using synergistic action of platelet concentrates and statins in alveolar preservation.

Keywords: Atorvastatin; PRF; Collagen; Barrier Membrane; Alveolar Ridge Preservation; Mandibular Molar Extraction

Introduction

Extraction of teeth accounts for loss in height and width of the tooth dependent alveolar process, which results in a significant structural and dimensional changes leading to the atrophy of the residual ridge. Most of the resorption occurs during the first 3 months of healing, although dimensional changes can be observed up to 1 year after tooth extraction. These structural alterations affect the outcome of the therapies which are aimed to restore the lost dentition, either by limiting the bone availability or by compromising the aesthetic result of the prosthetic restorations [1].

Therefore, regenerative or other surgical intervention appear to arrest the bone resorptive process, to restore the alveolar process thus preserving the natural contours and preparing the anatomical surroundings for the suggested prosthesis [1].

Ridge preservation is one such intra-socket osseous procedure advocated to counteract the early tissue changes following tooth extraction, for an undisturbed socket healing. Hence limiting the resorptive process of the alveolar crest, further improves the outcomes of the different rehabilitation approaches after tooth loss. Socket preservation therapy is a therapeutic approach which is carried out immediately after tooth extraction, to preserve the alveolar socket architecture and to provide the maximum bone availability for implant placement" [1].

This alveolar ridge preservation technique involves filling the socket with autogenous bone grafts or bone substitutes, guided bone regeneration (GBR) with resorbable or non-resorbable barriers and the use of various bone promoting molecules such as enamel matrix derivative recombinant growth and differentiation factors and autologous platelet concentrates.

Though statins (e.g. Simvastatin (SMV), Atorvastatin (ATV) and Rosuvastatin (RSV)) are well known as cholesterol lowering drugs, they are also effective in influencing bone turn over by stimulating bone formation. These are most commonly prescribed in patients with hypercholesterolemia. They function by inhibiting the 3-hydroxy-3-methylglutaryl coenzyme A reductase, which in turn is the rate-limiting enzyme in the Mevalonate pathway.

Furthermore, statins have been reported to stimulate the expression of bone anabolic factors, such as vascular endothelial growth factor and BMP-2 and to promote osteoblast differentiation and mineralization [2]. In addition, it has been suggested that statins directly affect osteoclasts through mechanisms analogous to those of bisphosphonates [3].

Statins can modulate the inflammatory response by affecting the profile of inflammatory mediators, leukocyte-endothelial cell interaction as well as the major histocompatibility complex-II (MHC-II) expression [4].

Among statin drugs, Atorvastatin (ATV) has been demonstrated to exhibit favorable effects in the treatment of bone remodeling disorders and bone fractures through the promotion of osteogenesis and the reduction of bone resorption [5].

To use Atorvastatin (ATV) for promotion of bone regeneration, a suitable delivery system is required. One promising autologous delivery system for tissue regeneration is the platelet rich fibrin (PRF). This is due to its angiogenic property and ability to activate release of growth factors from platelets and also to promote formation of a suitable fibrin network [6].

This system is now widely accepted as a successful scaffold system because of its favorable mechanical properties that improves biological characteristics which improve/facilitate the osseointegration process [7].

Using PRF as a vehicle for carrying ATV enables a constant release of growth factors such as Plasma Derived Growth Factors (PDGF), Transforming Growth Factor (TGF), Vascular Endothelial Growth Factor (VEGF), and Insulin-like Growth Factor (IGF) for 7 - 14 days [8,9].

Covering the orifice of the extraction socket with a free gingival graft or membrane may reduce postoperative external contour shrinkage. The use of an occlusal membrane for a ridge preservation procedure also prevents particle loss and migration of epithelial and connective tissue cells into the defect area [10,11].

Using a manufactured barrier membrane is more convenient than using a soft tissue graft because a donor site is not required. Successful gain of alveolar bone volume has been reported and greater improvement in clinical parameters has been shown when statins like Simvastatin, Atorvastatin and Rosuvastatin are delivered sub-gingivally as adjuncts to SRP and in the treatment of intra bony defects, management of furcation involvement. However, the clinical efficacy of 1.2% Atorvastatin together with PRF in the alveolar ridge preservation is unknown.

Hence, in the present study an attempt was made to evaluate the efficacy of 1.2% Atorvastatin loaded in PRF with collagen as a barrier membrane in alveolar ridge preservation after mandibular molar extraction.

Aims and Objectives

1. To evaluate and compare the efficacy of 1.2% Atorvastatin loaded in PRF with collagen as a barrier membrane in alveolar ridge preservation versus controls after mandibular molar extraction, by measuring the following clinical parameters:

- Relative coronal level of gingiva (SL).
- Relative level of MGJ (SM).
- Relative crest of socket (SC).
- Relative socket depth (SD).
- Relative socket width at the most coronal level (W).

2. To evaluate bone density changes radiographically by QDSR (Quantitative Digital Subtraction Radiography) technique in 1.2% Atorvastatin group and controls.

Materials and Methods

A prospective controlled clinical trial was conducted with a sample size of 20 subjects i.e., 20 sites, where mandibular molars were indicated for extraction from the Department of Periodontics, Lenora Institute of Dental Sciences, Rajamahendravaram, Andhra Pradesh.

The study sample included the mandibular first or second molars which were indicated for extraction. To standardize the clinical measurements of SL, SMG, SC, SD, W a custom-made acrylic stent was used. Bone density changes were assessed radiographically by QDSR technique and by using Image J software.

Digital standardized periapical x-ray films with paralleling long cone technique using XCP film holder were used for standardization of radiographs. The nature of the study was explained to all the patients and written informed consent forms were obtained. 20 patients with 20 sites were randomly selected and divided into control and test groups.

Inclusion criteria

1. Patients of age between 18 to 55 years.
2. Mandibular first and second molars which are indicated for extraction (badly decayed non restorable tooth, tooth contraindicated for crown preparation like tooth with sub-gingival caries, root caries, broken roots).
3. Traumatized teeth.

Exclusion criteria

1. Smokers and use of tobacco in any other form.
2. Patients with systemic disorders.
3. Pregnant, lactating or intending to become pregnant women.
4. Known hypersensitivity to statin drugs.
5. Previous radiation, chemotherapy or immunosuppressive treatments.
6. Patients under intramuscular or intravenous bisphosphonates.
7. Patients with coagulation defects, anticoagulant therapy.

Study Method:

Patients were included in the study after taking precise case history and hematological examination will be done at baseline. SL is the distance between the margin of stent and coronal level of gingiva in 3 points namely mesiobuccal (SLm), midbuccal (SLmid) and distobuccal (SLd). SL is the mean of SLm, SLmid, and SLd.SMG is the distance between the margin of stent and MGJ in 3 points namely Mesiobuccal (SMGm), midbuccal (SMGmid) and distobuccal (SMGd) are measured. SMG is the mean of SMGm, SMGmid, and SMGd. Before any intervention, first SL and SMG were measured with UNC 15 probe.

PRF preparation protocol

PRF clots were prepared as described by Choukroun., *et al* [12]. At the time of surgery, 10 ml of intravenous blood was collected from each patient by vein puncturing of the ante-cubital vein. Blood was collected in a sterile glass vacutainer (10 ml) without any anti-coagulant. Immediately blood was centrifuged using a centrifugal machine at 3000 rpm for 10 minutes. PRF clots were removed from the tubes and separated from the red element phase at the base with scissors.

Formulation of 1.2% atorvastatin gel

A concentration of 1.2% ATV gel was prepared at Lenora Pharmacy College [13]. A weighed amount of ATV is added to the accurately weighed amount of methylcellulose and dissolved completely to obtain a homogeneous phase of polymer, solvent, and drug. Thus, the ATV in situ gel was prepared with a concentration of 1.2%.

Surgical protocol

On completion of the baseline examination the patients who were advised for extraction of lower first and second molars were randomly assigned to either control group or Test group. Patients were seated comfortably on the dental chair and then asked to rinse the mouth with 10 ml of 0.12% chlorhexidine digluconate solution. The extraoral antisepsis was done with 0.5% povidine iodine solution.

The operative site was anaesthetized with 0.2% Lignocaine HCI with adrenaline (1:80,000) using Inferior alveolar nerve block and long buccal nerve block techniques. In control group, after administration of local anesthesia, a mucoperiosteal flap was elevated to expose both the labial and palatal/lingual aspects of the alveolar ridge.

Extraction was done in control group with extraction forceps. And in test group atraumatic extraction was done using periotome. At this stage, the measurements for SC, SD, W were carried out using the previous stent, UNC 15 probe and a caliper. SC is the distance between the margin of stent and the crest of socket in 3 points namely mesio-buccal (SCm), mid-buccal (SCmid), and disto-buccal (SCd).SC is mean of SCm, SCmid, and SCd. SD is the distance between margin of stent and socket depth. W is socket width. Both the measurements were taken from the midpoint of the mesio-distal span of the edentulous site.

Immediate extraction socket radiograph was taken with paralleling long cone technique using XCP film holder. After extraction replaced (without obtaining complete closure) and figure of 8 suture was performed using a 3/8 circle, reverse cutting needle and 3-0 black braided silk sutures and left to heal.

In test group, PRF was prepared as described above and was combined with 10 µl of 1.2% ATV and placed into the extraction socket. Periocol collagen membrane was placed over the socket and flaps were replaced (without obtaining complete closure). Suturing was performed and the area was protected with a non-eugenol (Coe-pak) dressing. Post extraction instructions were given. All patients were prescribed systemic antibiotics (Amoxicillin 500 mg tablets every 8 hours for 5 days) along with analgesics (Aceclofenac 100 mg tablets daily for 3 days) and 0.2% chlorhexidine digluconate rinse.

Post surgical protocol

All subjects were seen weekly until soft tissue closure over the site occurs. Periodontal dressing and sutures were removed after 2 weeks post operatively. The post-operative clinical and radiographic evaluations were performed 4 months after the extraction.

All parameters were measured again with earlier prepared respective acrylic stent, UNC 15 probe and caliper. Post-operative digital periapical radiographs were taken with paralleling long cone technique using Dentsply Rinn XCP® film holder. In QDSR [14], radiographs were digitized and density changes were calculated using Image J® software.

Region of interest (ROI) was measured at the middle third of the empty socket to prevent the superimposition of anatomic landmarks like submandibular fossa at apical one third and external oblique ridge at coronal one third of tooth socket. 10 points were considered in ROI and those 10 digital values at 10 X and Y coordinates of ROI were taken and numerical mean is obtained. “ROC” corresponds to the region of control and was measured around the region of interest, i.e. out of the empty socket of the same film. The numerical mean of ROC was obtained by measuring 10 numerical values at 10 X/Y coordinates.

The numerical mean of these numbers in ROI and ROC were subtracted in each film. The numerical difference of means of ROI and ROC in the 4 month post-operative radiographs was also calculated in the similar way as described above. The respective X/Y

coordinates were used to reproduce the same position of the ROI and ROC in all radiographic images at baseline and 4th month radiographs. The statistical analysis of this mean value helps in determination of bone density changes after 4 months of ridge preservation. The results were subjected to statistical analysis.

Results

The following statistical tests were employed to analyze the clinical and radiographic parameters using SSPS version 20 software.

Paired t-test was used for intra group comparison with in both the groups for SL (Relative coronal level of gingiva), SM (Relative level of MGJ), SC (Relative crest of socket), SD (Relative socket depth), W (Relative socket width at the most coronal level) and radiographic density at different time intervals. Unpaired t-test was used for intergroup comparison with in both the groups for SL, SM, SC, SD, W and radiographic density at different time intervals for various parameters at different time intervals. Unpaired t-test was used to calculate the mean change and standard deviation of various clinical and radiographic parameters between control and test groups.

Variable	Time interval	Group 1 Control Group	Group 2 Test Group
		Mean ± SD	Mean ± SD
SL (Relative coronal level of gingiva)	Baseline	8.8 ± 1.32	8.80 ± 2.35
	Baseline to 4 months	11.53 ± 0.96	9.70 ± 2.35
SM (Relative level of MGJ)	Baseline	13.55 ± 0.62	13.60 ± 0.98
	Baseline to 4 months	15.27 ± 1.27	15.16 ± 1.05
SC (Relative crest of socket)	Baseline	12.20± 2.20	12.15 ± 1.59
	Baseline to 4 months	14.20 ± 1.93	12.75 ± 1.44
SD (Relative socket depth)	Baseline	12.35 ± 1.34	12.48 ± 1.53
	Baseline to 4 months	14.43 ± 0.96	14.20 ± 1.93
W (Relative socket width at the most coronal level)	Baseline	7.90 ± 1.79	7.90 ± 2.025
	Baseline to 4 months	6.0 ± 1.63	7.15 ± 2.15

Table 1: Means and SD of relative coronal level of gingiva (SL), relative level of MGJ (SM), relative crest of socket (SC), relative socket depth (SD), relative socket width at the most coronal level (W) in control group and test group at different time intervals.

Statistical Analysis: Paired t-test.

Variable	Group 1 Control Group	Group 2 Test Group	p value
	Mean ± SD	Mean ± SD	
SL (Relative coronal level of gingiva)	11.53 ± 0.95	9.7 ± 2.3	0.035 (S)
SM (Relative level of MGJ)	15.27 ± 1.27	15.16 ± 1.05	0.035 (S)
SC (Relative crest of socket)	14.20 ± 1.93	12.75 ± 1.43	0.043 (S)
SD (Relative socket depth)	14.43 ± 0.96	14.20 ± 1.93	0.040 (S)
W (Relative socket width at the most coronal level)	6.00 ± 1.63	7.15 ± 2.14	0.045 (S)

Table 2: Comparison of means of relative coronal level of gingiva (SL), relative level of MGJ (SM), relative crest of socket (SC), relative socket depth (SD), relative socket width at the most coronal level (W) within control group and test group from baseline to 4 months.

Statistical analysis: Independent t-test. Statistically significant if $p < 0.05$.

S = Significant.

Variable	Group 1 Control Group	Group 2 Test Group	p value
	Mean ± SD	Mean ± SD	
SL (Relative coronal level of gingiva)	2.73 ± 1.32	0.9 ± 0.23	0.000 (S)
SM (Relative level of MGJ)	1.72 ± 1.75	1.56 ± 1.09	0.046 (S)
SC (Relative crest of socket)	2.0 ± 0.67	0.6 ± 0.94	0.001 (S)
SD (Relative socket depth)	2.08 ± 1.3	1.72 ± 1.67	0.047 (S)
W (Relative socket width at the most coronal level)	-1.9 ± 0.87560	-0.75 ± 0.29	0.005 (S)

Table 3: Comparison of mean difference of relative coronal level of gingiva (SL), relative level of MGJ (SM), relative crest of socket (SC), relative socket depth (SD), relative socket width at the most coronal level (W) between control group and test group from baseline to 4 months.

Statistical analysis: Independent t-test. Statistically significant if $p < 0.05$.

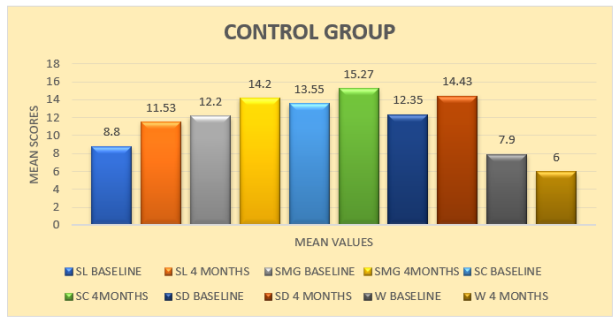
S = Significant.

Variable	Time interval	Group 1 Control Group	Group 2 Test Group
		Mean ± SD	Mean ± SD
ROC (Region of Control)	Baseline	148.29 ± 11.91	148.30 ± 10.09
	Baseline to 4 months	152.09 ± 14.58	152.51 ± 11.56
	p value	p = 0.609(NS)	p = 0.484(NS)
ROI (Region of Interest)	Baseline	74.72 ± 5.82	74.77 ± 6.62
	Baseline to 4 months	113.84 ± 17.41	140.94 ± 11.61
	p value	p = 0.000(S)	p = 0.000(S)
Difference Between ROC and ROI	Baseline	73.57 ± 12.64	73.53 ± 14.97
	Baseline to 4 months	38.25 ± 7.27	11.57 ± 4.29
	p value	p = 0.000(S)	p = 0.000(S)

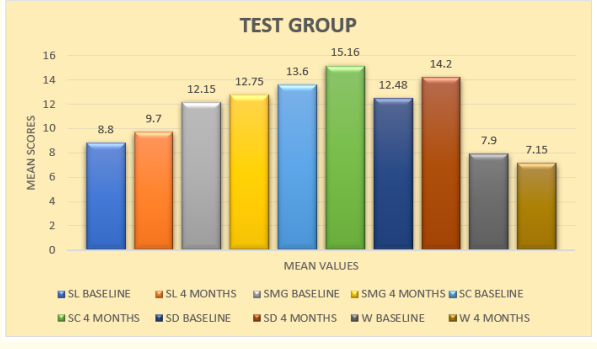
Table 4: Comparison of means of ROC (region of control), ROI (region of interest) and difference between ROC and ROI within control group and test group at different time intervals.
Statistical analysis: Paired t-test. Statistically significant if p < 0.05.
S = Significant.
NS = Non significant.

Variable	Time interval	Group 1 Control Group	Group 2 Test Group	p value
		Mean ± SD	Mean ± SD	
ROC (Region of Control)	Baseline to 4 months	152.09 ± 14.58	152.51 ± 11.56	p = 0.944 (NS)
ROI (Region of Interest)	Baseline to 4 months	113.84 ± 17.4	140.94 ± 11.60	p = 0.001 (S)
Difference between ROC and ROI	Baseline to 4 months	38.25 ± 7.27	11.57 ± 4.29	p = 0.000 (S)

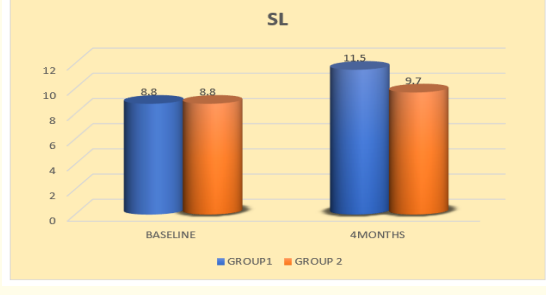
Table 5: Comparison of means of ROC (region of control), ROI (region of interest) and difference between ROC and ROI between control group and test group at different time intervals.
Statistical analysis: Independent t-test. Statistically significant if p < 0.05.
S = Significant
NS= Non Significant.



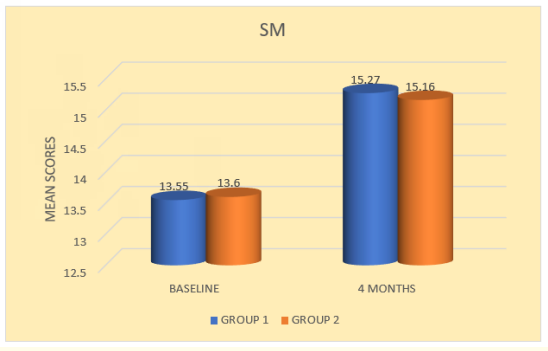
Graph 1: Means of relative coronal level of gingiva (SL), relative level of MGJ (SM), relative crest of socket (SC), relative socket depth (SD), relative socket width at the most coronal level (W) in control group at different time intervals.



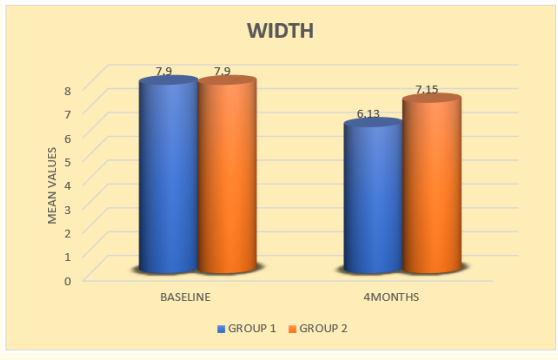
Graph 2: Means of relative coronal level of gingiva (SL), relative level of MGJ (SM), relative crest of socket (SC), relative socket depth (SD), relative socket width at the most coronal level (W) in test group at different time intervals.



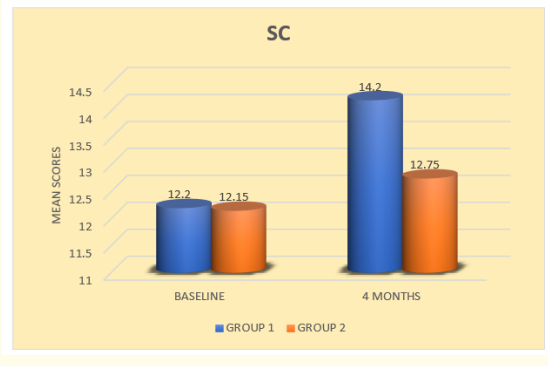
Graph 3: Comparison of means of relative coronal level of gingiva (SL) between control group and test group at post operative 4 months.



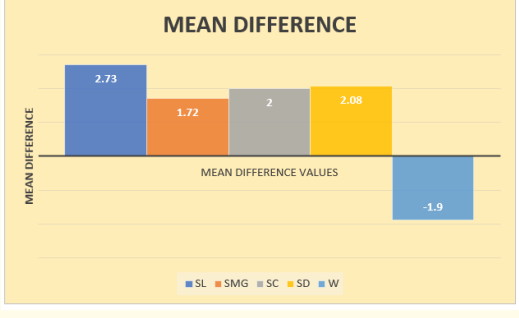
Graph 4: Comparison of means of relative coronal level of mucogingival junction (SM) between control group and test group at post operative 4 months.



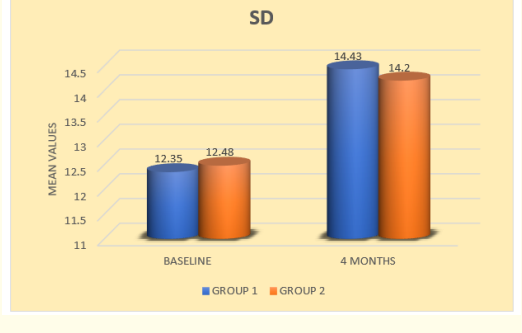
Graph 7: Comparison of means of relative socket width (W) at the most coronal level (W) between control group and test group at post operative 4 months.



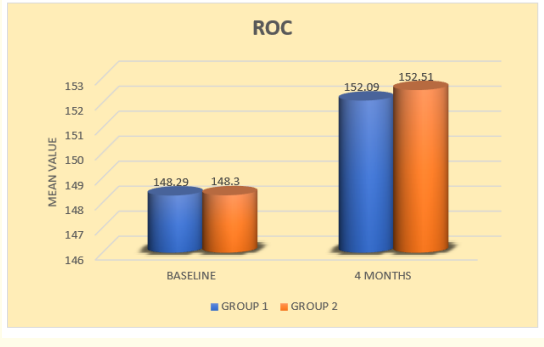
Graph 5: Comparison of means of relative crest of socket (SC) between control group and test group at post operative 4 months.



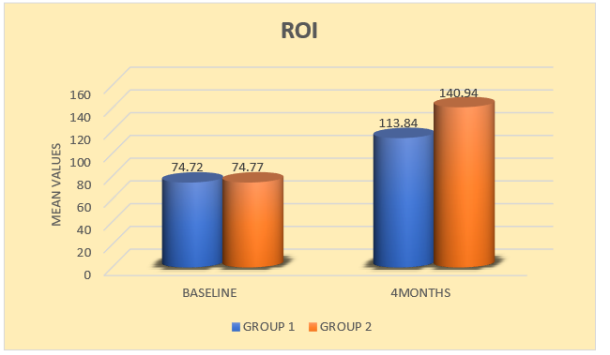
Graph 8: Comparison of mean difference of relative coronal level of gingiva (SL), relative level of MGJ (SM), relative crest of socket (SC), relative socket depth (SD), relative socket width at the most coronal level (W) between control group and test group from baseline to 4 months.



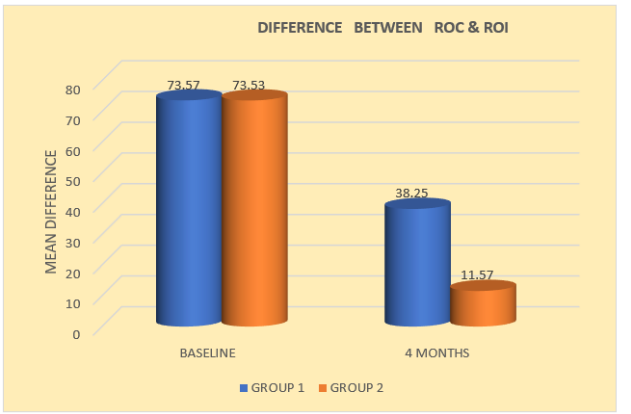
Graph 6: Comparison of means of relative socket depth (SD) between control group and test group at post operative 4 months.



Graph 9: Comparison of means of ROC (Region of Control) in control group and test group at different time intervals.



Graph 10: Comparison of means of ROI (Region of Interest) in control group and test group at different time intervals.



Graph 11: Comparison of means of difference between ROC and ROI (Region of Control and Region of Interest) in control group and test group at different time intervals.

Discussion

Extraction is generally indicated when a tooth cannot be restored or maintained for long-term health, function and/or aesthetics. The alveolar ridge bone resorption and soft tissue shrinkage always occur after tooth extraction, which compromises the alveolar ridge esthetics and function. Tan., *et al*. [15] showed that, 6 months after tooth extraction, there were approximately 29% to 63% of alveolar ridge bone width loss and 11% to 22% of bone height loss.

Bone resorption rate is rapid in the first 3 months and in the subsequent days, the resorption rate slows down [16]. Alveolar ridge atrophy may have a considerable impact on tooth replacement therapy, particularly when implant-supported restorations are planned [17]. Therefore, alveolar ridge preservation (ARP) has become a key component of contemporary clinical dentistry.

The first therapeutic attempts to prevent alveolar ridge resorption were performed by root retention, with the primary goal of maximizing the stability of removable prostheses [18]. But, root retention was not always feasible because of fracture, caries and/or strategic reasons. Hence, ARP via "socket grafting" emerged in the mid-1980s as a therapeutic alternative to root submergence. Its use was rationalized on the notion that "filling" the space left by the extracted tooth with a biomaterial would emulate a "root retention effect" conducive to bone preservation, which would subsequently facilitate endosseous implant placement by reducing the need of additional grafting procedures [19].

The major way of alveolar ridge preservation is socket bone graft combined with GBR techniques. Cardaropoli., *et al*. [20] reported that filling the socket with bone graft was an effective method to reduce alveolar ridge bone resorption. The main purpose of the bone graft material is to provide a scaffold to conduct the formation of blood vessels, socket space maintenance, improve the quality and quantity of the newly formed bone, protect blood clots and support the soft tissue flap. Meanwhile, the barrier membrane can guarantee the stability of the bone graft material and blood clots in the socket, to prevent bone graft material loss or premature resorption [16].

Several grafting materials have already been investigated alone or with membranes for alveolar ridge preservation, such as autogenous bone, allografts, xenografts and alloplasts. Among the alloplastic bone grafts, statins have been recently evaluated for bone regeneration in intra-bony defects and socket preservation techniques. A widely used statins in periodontal therapy include simvastatin, atorvastatin, rosuvastatin, etc.

Statins are competitive inhibitors of the rate limiting enzyme 3- hydroxy-3-methylglutaryl coenzyme A reductase. Statins stimu-

lates osteoblast-derived BMP-2 expression and directly affect osteoclasts through mechanisms, which closely resemble the mode of action of nitrogen-containing bis-phosphonates and osteoblast paracrine pathway, which acts through osteoclast cross-talks and involves the RANKL/OPG system. Cellular and animal investigations have demonstrated that non-lipid benefits of statins include the up regulation of endothelial nitric oxide synthase (eNOS), reduction of oxidative stress, and antagonism of isoprenoid-mediated activation of small GTP-binding proteins. ATV has recently been found to have a beneficial effect on periodontal disease.

Goes., *et al*. demonstrated that ATV was able to prevent alveolar bone loss by over 47% on a ligature-induced periodontitis in Wistar rats. He also inferred that ATV anti-inflammatory action and bone anabolism characteristic must be considered on alveolar bone protection [21].

Platelet-rich fibrin (PRF) is a second generation platelet concentrate with a rich source of autogenous cytokines and growth factors thus can be considered as a healing biomaterial. The three-dimensional network of PRF is proposed to be associated with effective and early organization of bone substance and bone volume percentage [12].

It is suggested that incorporation of PRF increases the efficiency of cell proliferation (PDGF), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), thrombospondin-1 (TSP-1), transforming growth factor-beta (TGF-β) influencing angiogenesis, epithelialization, stem cell trapping and immune control. However, to the best of our knowledge, there are no studies evaluating the efficacy of 1.2% ATV loaded with PRF as scaffold and collagen as a barrier membrane for alveolar ridge preservation in the mandibular first and second molar extraction.

Hence, the present study was undertaken to evaluate and compare relative coronal level of gingiva (SL), relative level of MGJ(SM), relative crest of socket (SC), relative socket depth (SD), relative socket width at the most coronal level (W) with controls after mandibular molar extraction at baseline and after 4 months.

Bone density changes were evaluated radiographically by QDSR (Quantitative Digital Subtraction Radiography) technique in 1.2% Atorvastatin group and controls at baseline and after 4 months. In the present study, when comparison of means of relative coronal level of gingiva (SL) between groups was done at different time intervals, there was statistically significant decrease in the test group. This means, coronal level of marginal gingiva was preserved comparatively and shifted greatly towards the occlusal surface in the test group. The reason could be due to atraumatic extraction and socket grafting which could have supported soft tissue and prevented its collapse.

Moreover, the loss in buccal cortical bone influences stability in the horizontal direction of soft tissue. When the buccal cortical bone is reabsorbed, the soft tissue cannot be stabilized and therefore collapses into this new gap, occupying the place that used to be occupied by the cortical bone. This results in bucco-lingual retraction [14]. On comparison of means of relative level of MGJ (SM) between groups was done at different time intervals, there was statistically significant decrease in the test group. This could be inferred as width of keratinised tissue was better maintained in the test group due to well preserved marginal gingiva and buccal cortical bone due to atraumatic extraction and grafting of socket.

The present study results were in accordance with studies by Barone., *et al*. [23,24] though measuring technique and type of graft material were different from the present study. When relative crest of socket (SC) parameter was compared between both groups at different intervals of time, there was statistical decrease of buccal crestal bone height in test group than control group. This finding was in correlation with clinical trials done in mandibular molar sites by Pang., *et al*. [16] and Guarnieri., *et al* [25]. Though there were differences in biomaterials used and measuring method of buccal bone height changes when compared to present study, these studies reported significantly lower values of buccal crestal bone loss in test groups.

Systematic review by De Risi V., *et al*. [26] also concluded that there is more post-extraction ridge height loss in control sites compared with test sites with a follow-up time of at least 3 months. The atraumatic extraction and grafting in test group might have acted synergistically, in maintaining the blood supply and reducing the crestal bone resorption.

When comparison of relative socket depth (SD) parameter was done, between both groups at different intervals of time, there was statistical decrease of depth in test group than control group. This could be due to adequate bone fill by the graft material and also

collagen membrane might have prevented the migration of soft tissue into the socket space and also preventing the loss of bone graft material, thus promoting the osteogenic potential cells for wound colonizing.

On comparison of relative socket width at the most coronal level (W) parameter was done, between both groups at different intervals of time, there was more decrease of width in control group than test group. These results were comparable to the study results by El hamid., *et al* [27]. This may be due to space maintenance and resultant bone fill in the extraction socket by the grafted material, and atraumatic extraction in test group. This inference was also in accordance with the review by De Risi V., *et al*. [26] who concluded that there is more post-extraction ridge width loss in control sites compared with test sites with a follow-up time of at least 3 months, irrespective of the technique used.

In the present study, QDSR (Quantitative Digital Subtraction Radiography) technique was used to evaluate bone density changes radiographically in both the groups at different time intervals. When the difference between ROC and ROI from baseline to 4 months was compared between groups, the results showed significant increase in the bone density values in test group. This finding was in accordance with Goes., *et al*. [21], Haghighat A., *et al* [14]. This significant result in the test group may be attributed to combined effect of ATV and PRF.

ATV also reduces osteoclast mediated bone resorption by mechanisms related to bisphosphonates. ATV is a lipophilic statin that appears to have a more potent bone-sparing effect. It stimulates BMP-2 expression, which in turn increases osteoblast differentiation and enhances bone formation. [2] ATV gel combined in dense fibrin matrix of PRF was hypothesized to form an exciting prospect in periodontal regeneration [28].

Though there is difference in defect type (IBDs) when compared to present study, the synergistic effect of PRF and 1.2% ATV in treatment of intrabony defects has shown significantly greater periodontal benefits [28]. From the present study, it can be inferred that 1.2% ATV loaded in PRF with collagen as barrier membrane was effective in socket preservation as this combination was effective in improving the bone density, bone fill and limiting the soft and hard tissue contour changes after mandibular first or second molar extraction.

It can be delineated as cost effective treatment and can reduce the need for additional bone augmentation procedures during further prosthetic rehabilitation. This study was not a split mouth study, which can be considered as a limitation. However, further long term studies are needed in this aspect for evaluation of these materials and to affirm the findings of this trial for considering the limitations.

Conclusion

Extraction sockets treated with 1.2% ATV together with PRF sealed with collagen barrier membrane resulted in significantly less changes in respect of hard and soft tissue parameters in test group when compared to control group with spontaneous healing from baseline to 4 months after tooth extraction. Also, on evaluation with QDSR technique, there was a significant increase in the bone density in extraction sockets, which received 1.2% ATV and PRF than control group from baseline to 4 months after tooth extraction.

The results of this study may give a new insight into the use of hydrophilic statins i.e., Atorvastatin together with PRF in the alveolar ridge preservation procedure to limit the resultant dimensional changes of tooth socket after extraction. Further longitudinal multi-center, and histological clinical trials are required for more conclusive interpretations of the results and to explore the additional possibility of using synergistic action of platelet concentrates and statins in alveolar preservation.

Source(s) of Support

Nil.

Conflicts of Interest

Nil.

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