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Regeneration of Maxillary Cystic Bone Defects with Low Level Laser Therapy Versus PRF (Comparative Study)

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Abstract

The purpose of this research was to evaluate the regeneration of maxillary cystic bone cavities using low-level laser therapy (LLLT), Plasma rich fiber (PRF) and the combination of them using radiographic assessment. The present study was performed on twenty-four healthy male patients with cystic lesion in the anterior maxillary region with maximum size 3x4cm, endodontic treatment was done to the affected teeth, then surgical enucleation of cystic lesion. PRF was prepared in the centrifuge machine for 10 minutes running at 3,000 rpm. Bone cavities were grouped into three groups, group A subjected to LLLT, group B filled with PRF, Group C filled with PFR and irradiated with diode laser. Radiographic assessment of area density index was performed using Digora software toolbox. After 3 months evaluation period, group C showed the highest mean difference to base line records with 77.94% followed by group A with 29.60% followed by Group B with 24.18. LLLT could induce bone formation in bone defects at a faster rate than PRF. However, the combination of both LLLT and PRF as treatment modalities could induce bone formation in bone defects more than that of LLLT or PRF alone.

Keywords: Diode laser, RPF, radicular cyst, endodontics, radiograph

Full-length article *Corresponding Author*, e-mail: dr.nohaeladl@yahoo.com

1. Introduction

Cystic cavities are one of the most commonly seen pathologies of the head and neck region, especially in the maxilla [1, 2]. Treatment of such cysts is based on the removal of the cystic lining and filling of the defect with a suitable material when it is larger than the critical size [3-5]. The hollow defect that is left after cystic enucleation is always a challenge to treat with the possibility of infection, inflammation and surgical dehiscence when autogenous grafting is used [6, 7]. The anterior maxillary region is of specific clinical significance due to the thin ridge and the challenges that adds to the rehabilitation and the esthetic and phonetic issues that arise due to the pathologies in this area [8, 9].

Several management options have been proposed for the management of maxillary cystic cavities to avoid complex risky grafting procedures. These include the use of allografts [10] which adds risks of infection and inflammation and surgical dehiscence. Platelet rich fibrin (PRF) has also been reported to be used to help regeneration of these maxillary defects [11]. PRF has widely been documented as a stimulant for bone filling of defects in preprosthetic surgeries [12-14]. This bone regenerating capacity has been attributed to the abundance of stem cells, growth factors, cytokines and wound healing proteins such as TGF-β, PDGF and VEGF). These have been shown to promote bone fill of cystic cavities with some cases of failure of complete healing reported [15]. Low level laser Therapy (LLLT) on the other hand has been reported to enhance tissue heling response [16-18]. These effects have been attributed to the mitochondrial energy absorption which causes biostimulation of a multitude of processes including enzymatic transport and ATP production which are crucial for cellular proliferation and regeneration. LLLT has already been reported to be used in several maxillofacial applications with significant results.

These applications include orthodontic cases, Temporomandibular disorders and periodontal management. All these applications for LLLT support the idea that it improves healing of both hard and soft tissues and reduces inflammation and infection risk. Researchers have also proposed the use of combinations of such techniques to synergistically improve hard and soft tissue healing of bony defects.

2. Subjects and Methods

2.1. Patient selection

The present study was performed on twenty-four healthy male patients of middle age range from 20 - 44. All patient presented to the National Research Center, Giza, Egypt for evaluation and management of painful maxillary teeth. All patients were selected based on the following inclusion and exclusion criteria: Inclusion criteria

- Cystic lesion in the anterior maxillary region with maximum size 3x4cm.
- Treatment by enucleation without using bone grafting materials Exclusion criteria
- Aggregate systemic pathologies such as diabetes, thyroid disorders, and bone metabolism diseases
- Patients taking calcium, bisphosphonates, glucocorticoids, or other drugs that can interfere with bone metabolism.

2.2. Pre-operative assessment

- Dental and medical history were recorded.
- Clinical examination and digital periapical radiographs were performed for all patients. 2.2. Pre-operative preparation
- Strict instructions for good oral hygiene were advised to all patients.
- Endodontic treatment or retreatment was done to the affected teeth. (Fig.1)

2.3. Operative procedure

- Surgical tray was prepared. (Fig.2).
- All the procedures were performed under local anesthesia using Mepecaine-L∗ (2% mepivacaine hydrochloride –1:20, 0000 Levonordfrin).
- A careful aseptic technique was employed throughout the surgical procedures.
- A full-thickness mucoperiosteal flap was performed with Bard Parker blade no. 15 extending from 1 or 2 teeth mesial and distal to the lesion and reflected using a mucoperiosteal elevator. (Fig.3).
- Bone overlying the cystic cavity was removed with bone rongeur and a medium size (5 or 6) carbide round bur was then used to create a window in the buccal bone and expose the apical tissues.
- Enucleation of cystic lesion was performed carefully using a surgical bone curette. (fig.4).

2.4. Preparation of platelet concentrates

Following Dohan et al(19) (- Dohan DM, Choukroun J, Diss A, Dohan SL, Dohan AJ, Mouhyi J. Platelet-rich fibrin (PRF): a second-generation platelet concentrates. Part II: platelet-related biological features. Oral Surg Oral Med Oral Pathol Oral RadiolEndod 2006;101: e45e50) protocol venous blood withdrawn from the antecubital vein was transferred to (10ml) sterile test tubes without the addition of any anticoagulant. The test tubes were then placed in the centrifuge machine for 10 minutes running at 3,000 rpm. At the end of the centrifuge cycle, blood was divided into three characteristic layers: a bottom layer of red blood cells, a middle layer of platelet-rich plasma, and the uppermost layer composed of platelet-poor plasma. (fig. 5(a, b).

2.5. PRF preparation

Tissue forceps were used to hold the middle layer that contains the fibrin clot. It was then separated from the underlying layer with scissors. Following this fibrin clot was compressed between two glass slabs to obtain PRF.

2.6. Patients grouping

The patients were divided into three equal groups, eight patients each; Group A (Laser group): Eight patients were subjected to low-intensity diode laser application after surgery to the area of the enucleated lesion. (fig.5). The irradiation technique used was the application of low intensity diode laser immediately after surgery and then for three times per week, on the buccal surface of the surgical site. using a therapeutic laser apparatus"soft-laser-SL-202" manufactured by scientific-and-production allegation "PERTO LASER"∗∗ with the following technical features: (Fig 7). Laser radiation power of 1-100mW, Emitted wavelength of 870 nm, Type of radiation continuous modulated mode, Exposure time range1-99 sec.Group B (PRF group): In Eight patients the cystic cavities were filled with PRF after surgery to the area of the enucleated lesion. Group C (PRF + laser group): In Eight patients the cystic cavities were filled with PRF and were subjected to low-intensity diode laser application after surgery to the area of the enucleated lesion.

2.7. Post-operative care

2.7.1. Post-operative instructions

- The patients were instructed to bite on oral gauze pressure pack for one hour
- Cold application for 15 minutes/hour was prescribed the day of operation.
- The patients were advised to take fluids and soft diet the day after surgery
- Hot saline and mild antiseptic mouth wash were prescribed from the next day of surgery and till the time of suture removal.

2.7.2. Postoperative medication

1-Antibiotics: Co_Amoxiclave ****tablet every 8 hours for seven days.

2-Analgesic: Ibuprofen 600 mg ******tablets 2 times per day.

3-Anti-edammotous drug: Betamethasone 7mg ***** ampoule once postoperatively. The sutures were removed on the seventh day postoperatively.

2.7.3. Postoperative evaluation (Radiographic evaluation)

To obtain radiographic images, an x-ray machine MINRAY® (Soredex, Tuusula, Finland) operating with tube voltage 70 kVp and tube current 7 mA at 0.08 second was used. The machine was set at the same exposure parameters throughout the study period. The focal spot object distance was fixed for all of the samples. The radiographs were taken for each patient one day after operation and after 3 months.

2.8. Methods of Density Measurements

2.8.1. Area measurement (area density index)

**A rectangular area was marked including the area of enucleated cyst and apices of the affected teeth to measure the mean of density in the bone area. As the applied software does not allow hands-free measurements: only rectangular measurements, the sites were standardized for reproducibility of measurements on all serial images by using the “start and end” as well as the “x and y coordinate” options present within the Digora software toolbox. (Fig. (8).

2.8.2. Line measurement (line density index)

Six horizontal lines were drawn equidistantly inside the area of the defect. The mean of the six readings was taken. Fig. (9). **The mean of the six trials for each method of measurement (twelve trials in total) was pooled and included in further statistical analysis.

3. Results

The present study was performed on twenty-four healthy patients of middle age. All patients presented with intrabony maxillary cystic lesions approximately 3x3 cm in diameter. The patients were chosen from the Outpatient clinic of the National Research Center, Giza, Egypt. Patients were divided into three equal groups, eight patients each; Laser group (A) where eight patients were subjected to low-intensity diode laser application after surgery to the area of the enucleated lesion, PRF group (B) In Eight patients in the cystic cavities were filled with PRF and PRF + laser group(C) In Eight patients the cystic cavities were filled with PRF and were subjected to low-intensity diode laser application after surgery to the area of the enucleated lesion. Bone Density data showed parametric (normal) distribution. Paired-samples t-test was used to compare between dependent samples while one-way ANOVA followed by the Tuckey post hoc test was used to compare between more than two groups. The significance level was set at $P \leq 0.05$. Statistical analysis was performed with IBM® SPSS® Statistics Version 20 for Windows.

4. Discussion

Inflammatory jaw cysts known as periapical cysts develop at the base of infected teeth with necrotic pulps. Bay cyst and apical cyst were the two classifications for periapical cysts, depending on how the root canal opened or connected to the epithelial-lined cavity [20]. A cystic cavity that has complete epithelialization but no opening into the apical foramen and root canal is considered an apical cyst; on the other hand, a cystic cavity with epithelial linings that are open to the root canal is regarded as a bay cyst, which is now called “periapical pocket cysts” because of its similarities with the marginal periodontal pocket [21]. Radicular cysts were selected to be investigated in the current study due to the high incidence percentage 52%–68% of all the jaw cysts [22].

The anterior maxilla is more common as compared to the mandible due involvement of anterior maxilla may be due to trauma, caries, and old silicate restorations in the anterior teeth [23], with higher incidence percentage in males than females with 1.6:1 ratio [20], hence male patients with radicular maxillary anterior cysts were employed in the current study. Numerous factors, including the extent of the lesion and its clinical characteristics, the involvement of significant anatomical structures, the patient's desire, and their systemic condition, may influence the treatment of choice. Conventional root canal therapy can be used to treat the majority of radicular cysts without utilizing a surgical procedure [24, 25]. Bone metabolism is arranged with chemicals and electrical and mechanical stimulants; during bone healing, platelets, macrophages, and fibroblasts are known to secrete many growth factors [26]. Various methods, including drug therapy and surgery, have been proposed to accelerate bone healing [27]. The present study was designed as a randomized controlled clinical trial, which evaluated the effectiveness of LLLT, PRF and the combination of them in site modulated intra-bony defects in aim to increase bone density. After three months evaluation in comparison to baseline levels, group B (PRF group) showed the least bone density change with a percentage of 24.18 %, yet the healing process in this group could be explained due to the capacity of Platelet-rich fibrin (PRF) as biomaterial rich in growth factors, such as PDGF, TGF-β, IGF, EGF, fibroblast growth factor, and bone morphogenic protein [28]. These growth factors are crucial for hemostasis, angiogenesis, osteoblastic proliferation, and differentiation. PRF's structure and low thrombin concentration facilitate endothelial cell migration and postoperative site protection, accelerating integration, maturation, and remodeling [29]. Also various studies suggested that PRF accelerates the healing effect by keeping the particles of β-TCP together via its adhesive property and attaching them tightly to the walls of the bone defect’s cavity [30, 31]. On the other hand some studies found no effect of employing PRF in surgical site In the current study, low-intensity gallium arsenide laser with wavelength 870 nm was used as a regenerative approach to enhance osseointegration and increase the density of bone in the surgical bone defect. Although many researchers investigated the effect of LLLT in bone tissue in various branches of medicine and dentistry, with wavelengths varying from 670 to 1,064 nm [32, 33]. Group A (Laser group) showed higher bone density change with a percentage of 29.60 %, the high bone density after three months in comparison to baseline levels , Cold Lasing causes the activation of intracellular or extracellular photo-absorbable molecules, thereby initiating intra-cellular signaling through cell signaling pathways such as p38, MAPK/ERK pathways which stimulate osteoblastic differentiation, followed by BMP/ SMAD signaling pathways, thereby producing signals that promote osteoblastic proliferation [34, 35]. Immediately after injury, the bone repair process starts in the vascularized regions in tissue anoxia and is accelerated by the stimulatory effect of laser on bone matrix [36]. Furthermore, laser provide angiogenesis, improved vascularization and perfusion that facilitated the presence of high levels of such micronutrients and minerals in the wounded area, with a subsequent increase in mineral deposition and bone density during a relatively short period [37]. LLLT further promotes the entry of β-Catenin into the nucleus and thus it upregulates the Wnt pathway, which further stimulates osteoblastic differentiation fostering bone formation and inhibits osteoclastic differentiation, thereby causing the cessation of bone resorption [38]. This hypothesis is supported by a number of previous researches used a wide spectrum wavelength of LLLT [39-42]. The highest bone density change recorded in group C (the combination of PRF and Laser) with 77.94 %, that could be due to that, bone healing is a complex and lengthy process of inflammation, bone formation, and bone remodeling. The mechanisms of action of LLLT and PRF in accelerating the bone healing process are different [43]. The synergic effect of both LLLT and PRF should be superior to using them separately.

Figure 1. A photograph showing preoperative radiograph illustrating the cystic cavity and the root canal treatment of related upper right central and lateral teeth

Figure 2. Photograph showing surgical tray for enucleation of cystic lesion

Figure 3. Photograph showing labial pyramidal mucoperiosteal flap and apical lesion perforation

Figure 4. Photographs showing the bony cavity after removal of the cyst

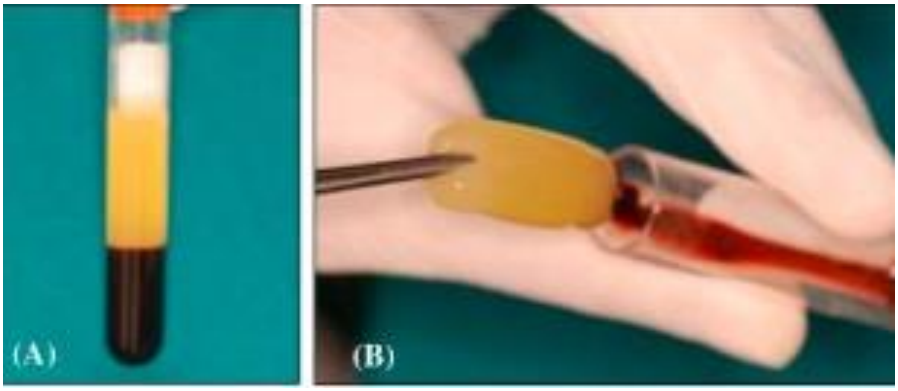

Figure 5. PRF preparation

Figure 6. Photograph showing soft-laser sl-202

Figure 7. Photograph showing the application of laser

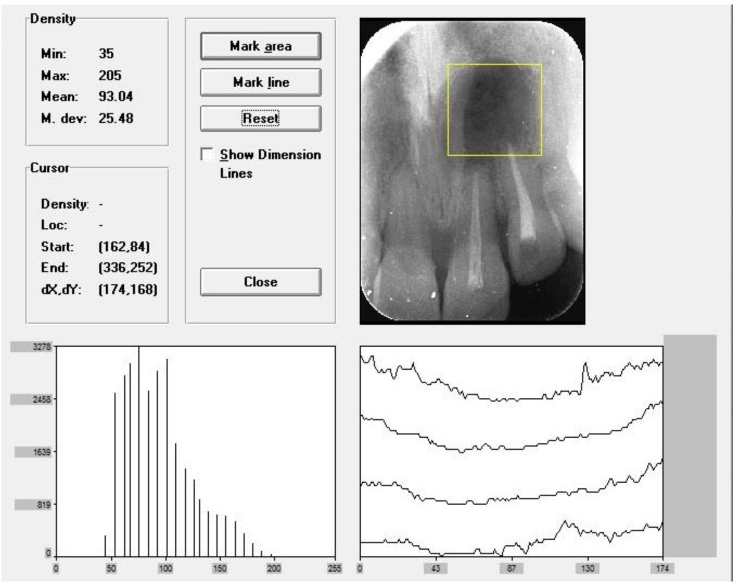

Figure 8. A digital radiograph of one of the investigated cases demonstrating rectangles drawn to calculate the mean of area density measurement

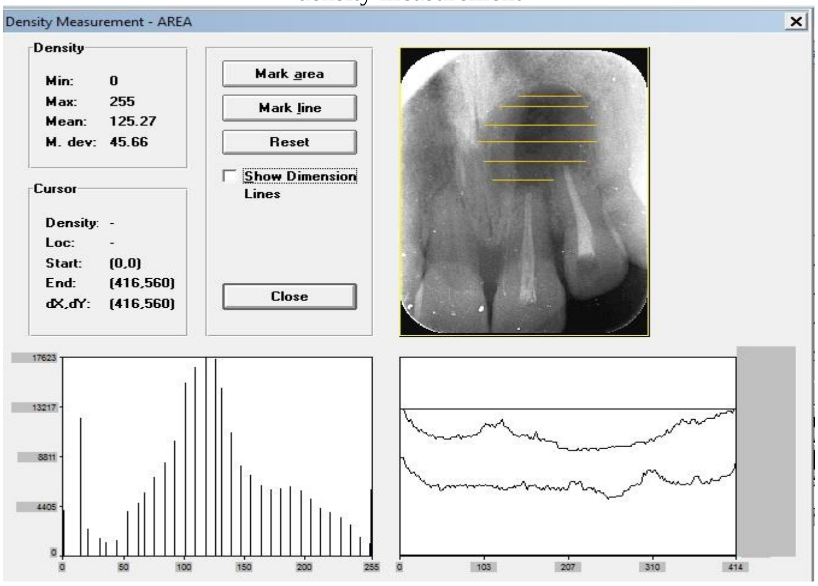

Figure 9. A digital image for the same case demonstrating six horizontal lines covering the investigated area. The six readings were taken individually and their mean was adopted

Table 1. Comparison of the mean, standard deviation (SD) of Bone density of all groups using one way ANOVA followed by Tuckey post hoc test

Groups / *Period*	*laser (A)*		*PRF(B)*		*PRF+Laser (C)*		*P-value*
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	
1Day	55.76	±7.06[a]	56.39	±8.74[a]	56.26	±9.73[a]	**0.9ns**
90 Days	71.53	± 5.89[b]	70.04	± 6.48[b]	100.11	± 5.73[b]	**0.001***
P-value	**0.006***		**0.001***		**0.0001***		

Mean with different letters in the same column indicate statistically significance difference *; significant ($p<0.05$) ns; non-significant ($p>0.05$)

Table 2. The mean, standard deviation (SD) and percentage of Bone density change after different methods of treatments

Groups \ Variables	Change in bone density		% of change	
	Mean	**± SD**	**Mean**	**± SD**
Laser (A)	16.51	±1.48[a]	29.60 %	±6.18%
PRF(B)	13.64	±1.34[a]	24.18 %	±5.98%
PRF+ Laser (C)	43.85	±11.06[b]	77.94 %	±17.94%
P-value	**0.001***			

Mean with different letters in the same column indicate statistically significance difference *; significant (p<0.05) ns; non-significant (p>0.05)

This finding is supported by the histological study of El-Hays et al 2016 that confirmed the superiority of combining the bioactive surgical additive PRF and LLLT in bone repair and bone density [43].

5. Conclusion

In conclusion, LLLT could induce bone formation in bone defects at a faster rate than PRF. However, the combination of both LLLT and PRF as treatment modalities could induce bone formation in bone defects more than that of LLLT or PRF alone.

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