Original Article

Is Low-level Laser Therapy and Gaseous Ozone Application Effective on Osseointegration of Immediately Loaded Implants?

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ABSTRACT

Purpose: The purpose of this study was to investigate the effects of biostimulation lasers and ozone therapy on osseointegration of immediately loaded implants. **Materials and Methods:** A total number of 100 implants (DTI Implant Systems) were applied to 25 patients evenly. Temporary crowns were applied to each patient on the same session as the surgery. Implants were divided into four treatment groups (Group 1: low-level laser therapy (LLLT) group, Group 2: ozone therapy group, Group 3: different protocol of ozone therapy group, and Group 4: control group) each with 25 implants. The irradiations were performed with a gallium-aluminum-arsenide diode low-level laser (Laser BTL-4000) to Group 1. Ozone therapy was performed using an ozone generator (OzoneDTA) with an intraoral probe to Group 2 and Group 3. **Results:** In this study, the overall implant survival rate was 92% after a 6-month observation period. The implant stability quotient values were found significantly higher in Group 1 (LLLT group) and Group 3 (different protocol of ozone therapy group) than the other groups ($P < 0.05$). There was no significant difference in Group 2 (ozone therapy group) and the control group ($P > 0.05$). **Conclusions:** Our results suggest that both LLLT and ozone therapy with prolonged application time are promising methods to enhance bone healing around immediately loaded implants and increase implant stability; however, there is a need for more studies on this subject for these methods to become routine applications.

KEYWORDS: *Immediate loading, implant stability, laser therapy, ozone therapy, resonance frequency analysis*

INTRODUCTION

The immediate loading (IL) technique has been widely used in oral implant rehabilitations to reduce treatment time. This technique eliminates the necessity to wait during the healing time, permits the use of provisional prostheses after implant insertion, and keeps the implants in function during the healing process.[1] However, some trends suggest that immediately loaded implants have lower survival rates than conventionally loaded implants.[2,3] Success of IL depends on various factors such as primary stability, surgical technique, bone quality, systemic diseases, number of implants, and occlusal forces. Primary stability is one of the most important variables in IL.[4] Resonance frequency analysis (RFA) is the most common method for the evaluation of primary stability.[4] as the implant stability quotient (ISQ) that can range from 0 to 100. Higher ISQ values indicate the stability of an implant to be better.[3] It has also been suggested that ISQ values can be used to evaluate the stiffness of the implant-to-bone interface for IL.[3] Suggested criteria for IL include an ISQ of 50–65, as determined by RFA.[5] Recent studies have been focusing on bone healing. According to these studies, bone healing promotion has been achieved with

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physical stimuli, such as ultrasound, low-level laser therapy (LLLT), and ozone therapy.[6,7]

LLLT is a noninvasive treatment modality that uses low-level (low-power) lasers or light emitting diodes.[8-10] LLLT is known to improve bone healing.[10] In medicine, LLLT has been used for various effects such as biostimulation of wounds, collagen synthesis, and fibroblast proliferation.[10-12] Most studies focused on this subject to evaluate the biostimulation effect of lasers on osteoblast proliferation, collagen deposition, and bone formation compared to bone tissues that have not been exposed to laser light.[10,13,14] In the literature, there is insufficient data considering these effects of lasers on osseointegration of dental implants.[10]

Ozone therapy is another noninvasive treatment modality used for bone healing. Ozone is naturally present in gaseous form that consists of three atoms of oxygen, but it may also be in aqueous form.[15,16] Ozone therapy may lead to several effects on the human body. It can enhance blood circulation, and thus oxygen delivery to ischemic tissues. Ozone therapy also plays a role in increasing of cellular antioxidant enzyme and growth factor levels or activation of the immune system.[16,17]

Most studies addressing ozone therapy in dentistry has evaluated antimicrobial effects of ozone.[16,18-20] However, we have discovered through a broad search of the literature that there are no studies considering the use of ozone therapy in dental implants. Since ozone is known to have therapeutic effects on wound healing by improving blood supply, upregulation of antioxidant enzymes and growth factors and activation of the immune system; we hypothesized that ozone therapy may improve the stability and predictability of implants by promoting bone healing.

Our hypothesis was that laser and ozone therapies will enhance bone healing around immediately loaded implants. The aim of the present study is to test this hypothesis on enhancing the osseointegration of immediately loaded dental implants using biostimulation lasers and ozone therapy.

Materials and Methods

Patient selection and study design

In this study, data were collected in Gazi University, Faculty of Dentistry, Department of Oral and Maxillofacial Surgery and Department of Prosthodontics between January 2016 and December 2016. The protocol of this study was approved by the Ethical Committee of Gazi University. The patients were informed in detail about the surgical procedure and were instructed about postoperative care, follow-up examinations, and alternative treatment options available to them. Informed written signed consent was obtained from all participants according to the Declaration of Helsinki.

Inclusion criteria were as follows – patients with a noncontributory medical history, patients older than 18 years of age, adequate amount of bone height (minimum 12 mm above the mandibular canal), and width (minimum 5.0 mm) for placement of implants, implant site with no signs of acute infection.

The following exclusion criteria were applied – patients under 18 years of age, patients who were nursing or pregnant, if the treatment could somehow affect the patient's health condition (diabetic patients and smokers were excluded), patients whose cooperation appeared questionable, patients whose systemic condition was not suitable for ozone and LLLT or patients who did not give his/her informed consent to participate.

A total number of 100 implants (DTI Implant Systems, Istanbul, Turkey) were applied in 25 patients who referred to our department with proper indications. Four dental implants (with a diameter of 4 or 4.5 mm and a length of 10 mm) were placed in the posterior mandible of each patient. Dental implants placed in proper locations and angulations in the posterior mandible.

Implants were divided into four treatment groups, each with 25 implants (three study groups [Group 1: LLLT, Group 2: ozone therapy, and Group 3: different protocol of ozone therapy) and a control group (no LLLT or ozone therapy]).

All patients were subjected to a standardized surgical protocol, ozone and laser therapy by a surgeon with 25 years of experience. Another surgeon with 4 years of experience carried out the measurements and was blind to the groups of patients included. Pain levels of the patients were determined by visual analog scale (VAS) postoperatively and at 1, 3, 5, and 7 days after surgery. Plaque index and bleeding on probing scores were also evaluated on the 3rd and 6th months postoperatively.

Surgical procedures

After administering local anesthesia, the initial surgical incision was made, and a mucoperiosteal flap was elevated. By means of a surgical guide, appropriate implant positions were marked with a round bur. Drills of increasing diameters were used in preparing the implant site. Proper-sized implants were placed to the correct depth with the final placement torque values of 35–50 N cm. All implants were placed using the nonsubmerged technique. The flaps were sutured with 3-0 silk sutures (Dogsan 3.0, 16 mm, 3/8, cutting suture, Trabzon, Turkey). Patients were informed with postsurgical instructions.

Postoperatively, the patients were prescribed 1000 mg amoxicillin and 25 mg dexketoprofen orally and 0.2% chlorhexidine mouth rinse (1 min, three times daily) every day for 1 week. After implant placement, immediate prosthetic loading was performed.

Prosthetic procedures

Immediately after implant placement, provisional fixtures for the four treatment groups were delivered as single-unit crowns that were slightly out of occlusion.

After implant placement, single screw-retained provisional acrylic (Telio CS, C and B [A2] Ivoclar, Vivadent Amherst, NY, USA) crowns were fixed over the four treatment group implants 2 h after surgery. The titanium abutments and provisional crowns were screwed as one unit and tightened to 10 N cm.

Provisional crowns were adjusted to any vertical load or proximal contact for slight occlusion or articulation on the implants.

Six months following implant placement, the final impressions were taken (Impregum 3M ESPE, St. Paul, MN, USA), within 2 weeks after impression taking, permanent screw-retained implant-supported metal-ceramic crowns were placed on the same titanium abutments. The titanium abutments' screws were torqued in place to 30 N cm so that cement failure was avoided.

Resonance frequency analysis

A wireless magnetic-based Osstell Mentor RF Analyzer (Osstell USA, Linthicum, MD, USA) was used to evaluate primary implant stability. The designated transducer (SmartPeg) was tightened to the fixture. Three measurements were done for both buccal and lingual sites. From these three measurements, the mean value was obtained for one site (buccal or lingual), and as a result, two ISQ values were recorded to assess the stability of each implant. RFA measurements were done immediately after the surgery and 6 months postoperatively. The screw-retained provisional acrylic crowns were removed for the 6th-month measurements and replaced with the final prostheses after. Prognoses of dental implants in the study and control groups were investigated by these measurements.

Low-level laser therapy

The irradiations were performed with a gallium-aluminum-arsenide diode low-level laser with continuous emission of 830-nm wavelength (Laser BTL- 4000, Brno, Czech Republic). The laser power was of 86 ± 2 mW and the laser spot size was 0.0028 cm^2, resulting in a calculated energy density of 92.1 J/cm^2, and an energy of 0.25 J per point. The irradiation time was three seconds per point, in contact. The total delivered energy was 5 J, equally divided by 20 irradiation points. The first irradiation was performed in the immediate postoperative period at 20 points: nine points at the vestibular region, nine at the lingual, one at the distal, and one at the mesial region of the implant. The LLLT was repeated every two days for 2 weeks [Figure 1].

Ozone therapy

Ozone therapy was performed using an ozone generator (OzoneDTA; Apoza, Taiwan, ROC) with an intraoral probe according to information given by the manufacturer. The ozone generator was applied intraorally with an intensity of 80% for 3 min in Group 2 and 6 min in Group 3 patients, three times a week for 2 weeks [Figure 2].

Statistical analysis

The data obtained in this study were analyzed by SPSS (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp). After the data were subjected to normality tests, Wilcoxon-signed rank test was used to assess statistically significant differences among the parameters within the groups, and Kruskal–Wallis H test was used for group comparisons. The level of significance was set at 0.05. There was no significant difference when $P > 0.05$ and there was a significant difference when $P < 0.05$.

Results

This study involved 25 patients (11 males and 14 females) with bilaterally edentulous posterior mandible, and their mean ± standard deviation age was 51.2 ± 2.3 years (range 36–64 years). A total of 100 dental implants were inserted without any complication. In this study, the overall implant survival rate was 92% after a 6-month observation period. Eight implants failed for unknown reasons, and as a consequence of these failures, new implants were placed to the same regions after adequate bone healing occurred. All the other implants and related prostheses were stable, and no complication was observed during the follow-up period.

Patients were recalled postoperatively on days 1, 3, 5, and 7 and evaluated for pain. There was no significant difference between study groups and the control group on VAS scale [Table 1]. Plaque index and bleeding on probing scores at the 3rd and 6th months showed no significant difference between study groups and the control group [Tables 2 and 3].

In the present study, the level of primary implant stability exceeded 65 ISQ in all study and control groups. The lowest measured value of primary implant stability was

Table 1: Comparison of postoperative visual analog scale scores between groups

Treatment groups	*n*	Mean	Median	Minimum	Maximum	SS	Kruskal-Wallis H		
							Mean rank	*H*	*P*
VAS (postoperative)									
Laser	25	3.0	3.0	1.0	7.0	1.43	49.74	0.232	0.972
Ozone (3 min)	25	3.0	3.0	1.0	7.0	1.40	52.78		
Ozone (6 min)	25	3.0	3.0	1.0	7.0	1.43	49.74		
Control	25	3.0	3.0	1.0	7.0	1.43	49.74		
Total	100	3.0	3.0	1.0	7.0	1.40			
VAS (day 1)									
Laser	25	4.9	4.0	2.0	9.0	2.03	50.76	0.009	1
Ozone (3 min)	25	4.8	4.0	2.0	8.0	1.95	50.36		
Ozone (6 min)	25	4.8	4.0	2.0	9.0	2.08	50.12		
Control	25	4.9	4.0	2.0	9.0	2.03	50.76		
Total	100	4.9	4.0	2.0	9.0	1.99			
VAS (day 3)									
Laser	25	4.0	3.0	2.0	8.0	1.72	50.44	0.022	0.999
Ozone (3 min)	25	4.0	3.0	2.0	8.0	1.71	49.84		
Ozone (6 min)	25	4.0	4.0	2.0	8.0	1.70	50.86		
Control	25	4.0	4.0	2.0	8.0	1.70	50.86		
Total	100	4.0	3.5	2.0	8.0	1.68			
VAS (day 5)									
Laser	25	2.6	2.0	1.0	5.0	1.16	50.50	0	1
Ozone (3 min)	25	2.6	2.0	1.0	5.0	1.16	50.50		
Ozone (6 min)	25	2.6	2.0	1.0	5.0	1.16	50.50		
Control	25	2.6	2.0	1.0	5.0	1.16	50.50		
Total	100	2.6	2.0	1.0	5.0	1.14			
VAS (day 7)									
Laser	25	1.8	2.0	1.0	4.0	0.85	50.50	0	1
Ozone (3 min)	25	1.8	2.0	1.0	4.0	0.85	50.50		
Ozone (6 min)	25	1.8	2.0	1.0	4.0	0.85	50.50		
Control	25	1.8	2.0	1.0	4.0	0.85	50.50		
Total	100	1.8	2.0	1.0	4.0	0.84			

VAS=Visual analog scale; SD=Standard Deviation

Table 2: Comparison of plaque scores between groups at different observation times

Treatment groups	*n*	Mean	Median	Minimum	Maximum	SS	Kruskal-Wallis H		
							Mean rank	*H*	*P*
Plaque score (3 months)									
Laser	25	0.5	0.0	0.0	2.0	0.59	52.42	2.54	0.467
Ozone (3 min)	25	0.4	0.0	0.0	1.0	0.49	45.78		
Ozone (6 min)	25	0.6	1.0	0.0	2.0	0.70	56.10		
Control	25	0.4	0.0	0.0	1.0	0.50	47.70		
Total	100	0.5	0.0	0.0	2.0	0.58			
Plaque score (6 months)									
Laser	25	0.5	1.0	0.0	1.0	0.51	47.48	6.57	0.087
Ozone (3 min)	25	0.7	1.0	0.0	2.0	0.56	54.50		
Ozone (6 min)	25	0.8	1.0	0.0	2.0	0.52	58.42		
Control	25	0.4	0.0	0.0	1.0	0.50	41.60		
Total	100	0.6	1.0	0.0	2.0	0.53			

SD=Standard Deviation

68 ISQ in 100 implants. Over the observation time, the implant stability increased in all groups. The ISQ values were found significantly higher in the Group 1 and Group 3 than the other groups after 6-months ($P < 0.05$). There was no significant difference between Group 2 and the control group at the 6th-month follow-up [$P > 0.05$] [Table 4].

Table 3: Comparison of bleeding on probing scores between groups at different observation times

Treatment groups	*n*	Mean	Median	Minimum	Maximum	SS	Kruskal-Wallis H		
							Mean rank	*H*	*P*
Bleeding on probing (3 months)									
Laser	25	0.8	1.0	0.0	3.0	0.87	49.54	4.48	0.214
Ozone (3 min)	25	1.0	1.0	0.0	2.0	0.71	59.50		
Ozone (6 min)	25	0.7	1.0	0.0	1.0	0.48	48.26		
Control	25	0.6	1.0	0.0	1.0	0.50	44.70		
Total	100	0.8	1.0	0.0	3.0	0.66			
Bleeding on probing (6 months)									
Laser	25	0.6	1.0	0.0	2.0	0.64	47.66	0.523	0.914
Ozone (3 min)	25	0.7	1.0	0.0	2.0	0.54	52.08		
Ozone (6 min)	25	0.7	1.0	0.0	2.0	0.56	50.18		
Control	25	0.7	1.0	0.0	2.0	0.54	52.08		
Total	100	0.7	1.0	0.0	2.0	0.56			

SD=Standard Deviation

Table 4: Comparison of implant stability quotient values between groups at different observation times

Treatment groups	*n*	Mean	Median	Minimum	Maximum	SS	Kruskal-Wallis H			
							Mean rank	*H*	*P*	Paired comparison
Postoperative (B-L) (immediately postoperative)										
Laser	25	73	74	68	80	3.25	42.93	2.12	0.548	-
Ozone (3 min)	25	75	75	69	82	4.58	49.65			
Ozone (6 min)	25	73	73	68	81	3.60	39.88			
Control	25	73	73	68	80	3.13	40.13			
Total	100	73	73	68	82	3.66				
Postoperative (B-L) (6 months)										
Laser	25	79	80	75	84	2.51	53.50	11.96	0.008	1-3
Ozone (3 min)	25	77	75	72	84	4.29	36.19			1-4
Ozone (6 min)	25	80	80	74	84	3.01	54.76			2-3
Control	25	77	77	74	82	2.14	34.43			2-4
Total	100	78	78	72	84	3.24				

B-L=Bucco-lingual; SD=Standard Deviation

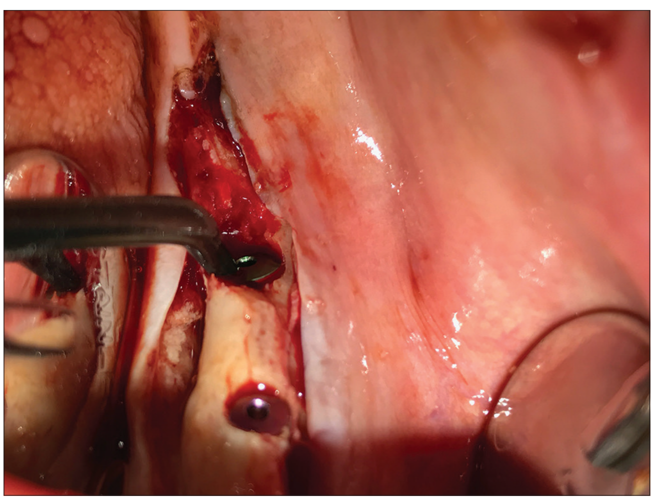

Figure 1: Immediately postoperative low-level laser therapy application

Figure 2: Immediately postoperative ozone application

Discussion

Many studies have reported promising outcomes of LLLT and ozone therapy regarding the bone-healing process; still, little data exist relating to these effects on implant osseointegration.[6,10,16,21-23] The aim of this study was to evaluate the effect of LLLT and ozone therapy on immediately loaded implant osseointegration.

Implant stability has been assessed by RFA in many studies.[24-27] Although, ISQ values are not a perfectly reliable source of information for implant success; it is widely used in the literature.[28-30] Therefore, RFA was used to measure implant stability in this study. Recent data indicate that an ISQ value of primary implant stability between 60 and 65 is sufficient for IL.[25,26,31] In the present study, primary implant stability was sufficient in all study groups. The lowest measured value of primary implant stability was 68 ISQ in 100 implants.

In this study, the overall implant survival rate was 92% after a 6-month observation period. Eight implants failed in this period for unknown reasons, and as a consequence of this failure, new implants were placed to the same regions after adequate bone healing was obtained. All the other implants and related prostheses were stable, and no complication was observed during the follow-up period. In the literature, immediately loaded implants showed a high survival rate (96.8%) in the posterior part of the mandible as in this study (92%).[29,32,33] During the observation time, the implant stability increased in all survived implants. The ISQ values were found significantly higher in the LLLT group than the other groups after 6 months. This increase in osseointegration could be referred to an improvement in the bone-healing phase around the implants. There are several studies that focus on IL in posterior maxilla which report lower survival rates when compared to conventionally loaded implants.[3,34,35] However, the standardized protocol of this study only included patients with bilaterally edentulous mandibles; a different study may be planned to observe the effects of LLLT and ozone therapy on immediately loaded implants in the maxilla.

The use of lasers to achieve biostimulation for bone regeneration has become popular in medicine, and many researchers have reported that LLLT has positive effects on bone healing.[10,16,21,36,37] LLLT has an anti-inflammatory effect through several mechanisms such as induction of ascorbic acid uptake by cells, enhancement of mitochondrial adenosine triphosphate production, stabilization of the cell membrane, lymphocyte stimulation, mast cell activation, and proliferation of various cell types. It also promotes local cell circulation, cell proliferation, and collagen synthesis.[38] LLLT is known to demonstrate biomodulary effect of the laser light by regulating cell physiology or stimulating the proliferation and differentiation of undifferentiated cells.[39] This information leads us to think that it may also enhance the bone healing process.

There are several variations in the literature regarding the choice of the power, density, and wavelength when using low energy level laser therapy in bone healing.[10,40-47] Khadra *et al*.[41] reported that a standard protocol for laser irradiation in dental implant procedures has not yet been identified. It has been suggested that the 830 nm wavelength laser has a positive effect on the recovery of both fibroblasts and osteoblasts by different authors.[42-47] García-Morales *et al*.[10] used 830 nm wavelength, at 86 mW power and 92.1 J/cm^2 density. The laser settings chosen in this study were based on clinical trials, in which positive effects of LLLT on wound healing after wisdom tooth extraction and bone healing after dental implant application were shown.[10,21]

In the many studies that determine adjunctive therapies to the bone healing mechanisms, LLLT promotes the healing process in bone defects.[6,10,36,48-50] Garcia *et al*.[48] have reported that the diode laser is effective in inducing bone formation in the calvarium defects of osteoporosis-induced rats. Likewise, Pretel *et al*.[36] and Fávaro-Pípi *et al*.[49] reported that LLLT administration had positive effects on bone healing. In another study, laser application is found to accelerate fracture repair process by providing increased callus volume and bone mineral density.[6] Renno *et al*.[50] reported that laser application at a wavelength of 830 nm provided a significant increase in the proliferation of osteoblasts. Sella *et al*.[44] found that low-level laser application to fractured rat femurs increased the amount of bone tissue in the fractured area. In the present study, ISQ values revealed a significant increase in low-level laser therapy group at 6 months. This result was consistent with the results of those studies mentioned above,[6,10,36,48-50] and low-level laser therapy was found to have a positive effect on the stability of dental implants.

Clinical evidence for ozone application in dentistry is not adequate.[6] Ozone therapy has positive effects on oxygen metabolism, cell energy, immune system, antioxidant defense system, and microcirculation.[21] In this study, ozone therapy was applied to two different groups for different durations. In Group 2, a protocol used in a previous study[21] that indicate a positive effect of ozone therapy on wound healing after tooth extraction was utilized. Another protocol of ozone therapy with a longer application time was described in the user guide of the ozone device as applicable to oral mucosa, and this protocol was used in Group 3. A statistically significant increase in ISQ values was observed in Group 3 at the end of 6 months compared to Group 2 and the control group. No statistically significant difference was found between Group 2 and the control group. According to this result, it is observed that maximum dose of ozone application had a positive effect on implant stability, but no comparison was made in the literature since there is no study evaluating the effect of ozone application on osseointegration.

It is important to point out that this study is limited to one anatomic site, a single type of implant, a particular type of prosthetic appliance (single crowns) and a specific methodology, and results may differ in different anatomic sites (maxilla), prosthetic appliances (dentures or bridges) and implants when using different LLLT, and ozone therapy protocols with other methodologies and different lengths of follow-up. Thus, more studies similar to this one should be planned and conducted with different methodology to contribute to the literature.

Conclusions

Within the limitations of this study, it is concluded that both laser therapy and ozone therapy with prolonged application time increase implant stability in the immediate slightly functional loading of single implants in the posterior mandible. However, the standard application of ozone did not seem to have any effect on implant stability. Our data suggest that both ozone and laser therapies provide additional new insights into therapeutic strategies in improving implant stability in dentistry, but further experimental and clinical evaluations are needed.

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Conflicts of interest

There are no conflicts of interest.

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