Original Article

IMPACT OF PHOTOBIOMODULATION ON POSTOPERATIVE PAIN AND BONE HEALING FOLLOWING CYCT ENUCLEATION A RANDOMIZED CLINICAL TRIAL

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ABSTRACT

Aim of the study: is to assess the influence of low-level laser therapy (LLLT) on post-operative pain and bone healing when used prior to and following enucleation of cystic lesions.

Participants and methods: twenty healthy patients of either gender aged from 2050- years who were seeking cyst enucleation of intra-bony maxillary cystic lesions approximately 2 x 3 cm in size equally and randomly allocated to either test group or control group. Group was treated Pre and post-operative low level laser treatment at the site of cyst enucleation of intra-body maxillary cystic lesions. Post- operative pain assessment was recorded on visual analog scale (VAS) every 24h for 7 days in addition to radiographic assessment via CBCT scan obtained immediately post-operative, 3 and 6 months postoperative.

Results: Regarding postoperative pain at 24 hours, no significant difference between the two groups at p value of (0.190). Yet, at 48 hours a significant differences emerged with p value of (0.012) and at 7 days a p value of (0.010), with the test group showing lower pain scores. As for The bone density measurements a significant difference emerged at 3 months (p=0.008), with the test group showing a higher mean bone density. By 6 months, the difference became non-significant (p=0.186), though the test group maintained a higher mean value.

Conclusion: Application of low level laser therapy prior to and after enucleation of intra-body cystic lesions is beneficial in postoperative pain relief and early bone healing.

Key Words: Enucleation, Intra-bony maxillary cyst, Low level laser therapy, Bone healing

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INTRODUCTION

Osseous defects (dead spaces); are well-known concern faced by oral and maxillofacial surgeons in the facial regions. Osseous defects of the jaw occur due to a variety of pathological conditions such as infectious diseases, neoplasms, cystic lesions or iatrogenic reason inflected by the surgeon during surgical procedures of preexisting per-radicular bony lesions. These defects complicate prosthetic rehabilitation and implant application [1].

Management of these osseous defects face surgeons with great challenges and demand continually exploring ways to find new modalities. This unique mineralized connective tissue continuously undergoes remodeling via alternating bone resorption and bone formation cycles [2], once local injury of osseous structure occurs an inflammatory immune reaction; which has great impact and influence on the overall outcome of the bone healing process; starts [3].

Many treatment modalities have been suggested to positively influence and accelerate the healing process as Low-Level Laser Therapy (LLLT). This novel mode of phototherapy involves employing low power monochromic light to site of boney defects or lesions. Moreover, previous study has shown that LLLT was able to initiate wound healing in osseous defects that were not healing [4]. It is undoubted that normal bone tissues are able to regenerate; osseous defects heal spontaneously however; The process is a time consuming process [5].

The modulation influence of low-level laser therapy (LLLT) on osseous tissue metabolism is positive [6]. Not only does low intensity laser enhance and accelerate bone matrix secretion- as an initial stage -but also further boosts calcification. [7] In an animal study when applying 980-nm low level laser irradiation to bony defects with a daily dose of 13.95 J/cm for sixty seconds in both normal and diabetic rats. Histological results showed that (LLLT) is not only advantageous in accelerating initial stages of bone healing but also in late stage enhances more calcification in normal as well as diabetic rates. [8]

Thus; the null hypothesis of the current study is that no difference is found regarding postoperative pain and bone healing following enucleation of intra-body maxillary cystic lesions with and without application of (LLLT).

PARTICIPANTS AND METHODS:

Ethical regulations:

An ethical clearance was attained from Ethics Committee,

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Faculty of Dentistry, Minia University under ID number (110/ 973). The research was operated in accordance with Helsinki Declaration for human research. Registration on the clinical trials website (www.clinicaltrials.gov) was done with ID (NCT06759571). Following a detailed explanation of all aspects of the study; participating patients signed a consent.

Sample size calculation

Employing a power analysis; according to a previous study [9]; to the null hypothesis that there is no difference found between the two groups of the study using G*Power-version 3.1.9. Sample size calculation was determined at 16 patients which was increased to 20 patients (10 for each group) to account for dropout.

Study design and Selection of participants and Recruitment strategy:

A parallel arm 1:1 Single blind randomized control clinical trial was executed at outpatient clinic – Faculty of Dentistry- Minia University. Consecutive sampling was preformed till the target population was selected according to predetermined inclusion criteria: healthy patients -class I category according to ASA- of either gender and with age ranging between 20 to 50 years, who need cyst enucleation of painful intra-body maxillary cystic lesions approximately 2 x 3 cm in size. While patients suffering any systemic disease that impede bone healing or alcoholic individuals were excluded.

Randomization, blinding

Participants were allocated randomly by choosing one card of a set of prepared cards with a series of numbers from 1 to 20 and the sequenced intervention was then retrieved from the excel sheet. One blinded radiologist; who was not notified of the type of treatment; evaluated radiographically the outcome.

Grouping

Twenty healthy participants were randomly allocated equally to one of the study groups: Group A (10 patients), served as test group. These patients were exposed to low level diode laser ("perto- laser SL202" 47, Saint Petersburg, Russia) prior to cyst enucleation (2 times per week for 2 weeks) and then following surgical procedure (for 3 times per week for 4 weeks). With the following parameters [9]: the dosage of 24 J/cm2, that of power 50 mW and a wave length of 870nm for 60 seconds / session. On the other hand, Group B (10 patients), served as control group. the patients under went conventional surgical enucleation of intra-body maxillary cystic lesions without any laser application.

Surgical procedure:

All teeth that were involved in the lesion received root canal treatment which was performed by one specialist prior to surgery. Regarding the surgical procedure, thorough disinfection of the oral mucosa with 10% iodine solution (Betadine/ Nile Pharmaceuticals, Cairo, Egypt) was established then profound local anesthesia was applied. A full thickness muco-periosteal flap was raised of sufficient dimensions to allow good accessibility to the lesion's site. Osteotomy was performed using fissure surgical bur under copious irrigation till the cyst was exposed followed by thorough enucleation of the cyst using surgical curettes then apicectomy of root apices. Careful debridement of the osseous cavity and smoothening of bone margins subsequently ample irrigation with sterile saline was performed. The flap was repositioned and sutured.

Post-operative instructions:

All patients were given instruction to; apply intermittent extra-oral cold packs and prohibited from ingesting hot food and /or drinks for 24 hours while on the second day patients were advised to switch to hot fomentation. All patients received prescription of Augmentin 1 gm (Smithline Beecham Pharma Co., England) every 12 hours for 5 days post-operatively and 50 mg diclofenac potassium (Cataflam; Novartis Pharma, Switzerland) every 8 hours for 3 days.

Outcome assessment:

Regarding Primary outcome; patients were educated to record Pain score utilizing a visual analog scale (VAS) were 0 indicates no pain and 10 indicates the worst pain the patient had ever experienced. The records were taken every 24h for 7 days. For a secondary outcome Radiographic assessment of bone density via CBCT scan (Planmeca Promax 3DMid machine, Helsinki Finland) which was obtained immediately postoperative, 3 and 6 months postoperatively

Data collection and statistical analysis

All data were entered electronically and all Patients' files were stored in numerical order and tabulated then sent for statistical analysis using commercially available software program (SPSS Chicago, IL, USA). Data were collected and analyzed using Mann Whitney test for not normally distributed data (pain scoring) between the two groups and Independent Samples T test for quantitative data (bone density) between the two groups.

RESULTS:

The CONSORT flow diagram of patient selection and allocation is shown in Figure (1). For demographic data; No significant difference between the test and control groups was demonstrated. Tab. (1)

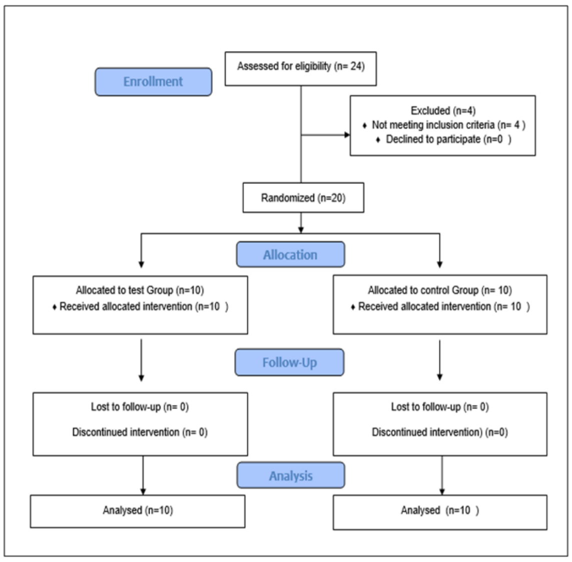

Figure (1): CONSORT flow diagram of patients' selection, allocation and follow up

Table 1: Comparison of demographic data between the test and control groups

		Test Group N=10	Control Group N=10	P value
Age	Range	(20-59)	(22-58)	0.654
	Mean ± SD	38.2±15.1	41.1±13.3	
Gender	Male	4(40%)	6(60%)	0.371
	Female	6(60%)	4(40%)	

- Comparison of quantitative data between the two groups with Independent Samples T test for
- for qualitative data Chi square test applied between the two groups
- Significant level set at P value < 0.05

Regarding pain scores reveal that at 24 hours, significant difference was not demonstrated between the two groups at a p value of 0.190. However, significant differences emerged at 48 hours (p=0.012) and 7 days (p=0.010), with the test group showing lower pain scores. Both test and control groups demonstrated a significant decrease in pain scores over time at p value < (0.001), with consistent significant differences between consecutive time points. Intra-group analysis shows a consistent and statistically significant pain reduction pattern for both groups. Tab (2), Fig (2)

Table 2: Comparison of pain score at different times between the test and control groups

Pain		Test Group N=10	Control Group N=10	P value
At 24 hr.	Median	7	7	0.190
	IQR	(6-7)	(6.8-8)	
At 48 hr.	Median	5	6	0.012*
	IQR	(4-5)	(5-7)	
At 72 hr.	Median	3	4	0.366
	IQR	(3-4)	(3-4.3)	
At 7 days	Median	1	2	0.010*
	IQR	(1-2)	(2-3)	
P value (between times)		<0.001*	<0.001*	
24 hr. versus 48 hr.		0.004*	0.006*	
24 hr. versus 72 hr.		0.004*	0.004*	
24 hr. versus 7 days		0.004*	0.004*	
48 hr. versus 72 hr.		0.004*	0.004*	
48 hr. versus 7 days		0.004*	0.005*	
72 hr. versus 7 days		0.004*	0.007*	

- Mann Whitney test for not normally distributed quantitative data between the test and control groups
- Friedman test for not normally distributed quantitative data between different times within each group, followed by Wilcoxon signed rank test between each two times
- *: Significant level was set at P value < 0.05

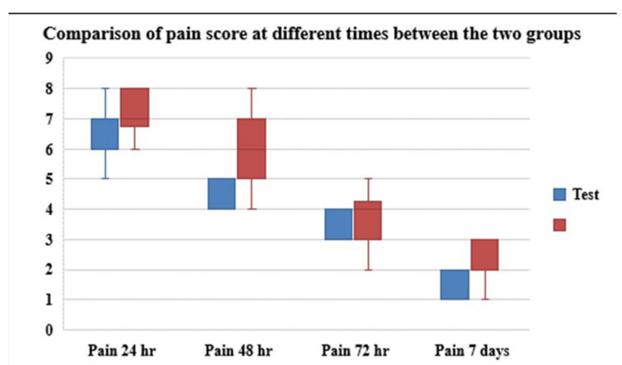

Figure (2): Box plot representation of comparison of pain score at different time periods for test and control group

The bone density measurements showed initial comparable postoperative values (p=1.000). A significant difference emerged at 3 months (p=0.008), with the test group showing a higher mean bone density (577.8 vs. 507.5). By 6 months, the significant difference was no longer sustained showing a p value of (0.186), though the test group maintained a higher mean value. Both groups demonstrated statistically significant increases in bone density over time (p<0.001), with significant improvements noted between postoperative, 3-month, and 6-month measurements.

This suggests positive bone density progression for both groups, with the test group showing a potentially more favorable early bone density development. Tab (3), Fig (3)

Table 3: Comparison of bone density at different times between the two groups

Bone density		Test Group	Control Group	P value
		N=10	N=10	
Postop.	Range	(63-82)	(65-87)	1
	Mean ± SD	73.2±6.3	73.2±7.6	
At 3 months	Range	(460-631)	(398-599)	0.008*
	Mean ± SD	577.8±50	507.5±55.1	
At 6 months	Range	(801-970)	(801-920)	0.186
	Mean ± SD	905.8±43.2	882±33.6	
P value (between times)		<0.001*	<0.001*	
Postop. versus 3 months		<0.001*	<0.001*	
Postop. versus 6 months		<0.001*	<0.001*	
3 months versus 6 months		<0.001*	<0.001*	

- Independent Samples T test for quantitative data between the two groups
- Repeated measure ANOVA test for quantitative data between different times within each group, followed by post hoc LSD test between each two times
- *: Significant level at P value < 0.05

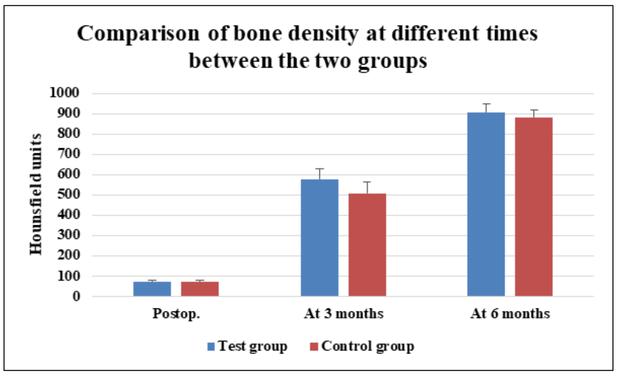

Figure (3): Bar chart representation of comparison of bone density at different periods between the test and control groups.

DISCUSSION:

Low-level laser therapy (LLLT), is a novel therapeutic modality, which has been introduced in a variety of medical fields producing low or insignificant temperature changes within the treated tissues. Many studies have shown that LLLT, in which the light energy is transformed to a chemical form of energy in the cell, imposes bio-stimulatory effects, stimulating cellular activities, enhancing positive tissue regeneration, and has pain alleviation, antimicrobial, anti-inflammatory effects and accelerated wound healing. (10) On a cellular level The target tissue absorbs specific wavelength which activate fibroblast and osteoblast differentiation as well as proliferation in addition to collagen secretion and granulation tissue formation during wound healing intern promotes the healing of tissues. [11]

Many factors affect the laser optimum healing effect and penetration depth as; type of tissue, anatomical features of the tissue, energy density, wavelength, duration of application, power density, pulse status and the number of therapeutic sessions. There is still no complete information about dosimetry that provides repeatable and reliable outcome therefore, most researchers considered the depth of laser penetration hypothetically. The aim of the current study is to evaluate the effect of (pre and post) operative application of 24 J/cm2, 50 mW power with an 870nm wavelength at the cystic lesions enucleation site on postoperative pain relief and bone healing [9]

Pain is one of the great challenges facing a surgeon following enucleation of jaw cysts surgically. Different means have long been used to alleviate pain postoperatively such as non-steroidal anti-inflammatory drugs (NSAIDs), opioid analgesic and epidural analgesia. Due to the side effects accompanied with excessive use of these medications; new methods were suggested as LLLT; which is a non-invasive modality with nearly no complications and a reasonable cost. [12, 13, 14]

For the results of the current study statistically significant differences emerged at 48 hours and 7 days postoperatively with the test group showing significantly lower pain scores. Indicating the positive benefits of low level laser therapy application pre and post-operatively at the enucleation site on pain relief.
Our results come in agreement with Dos Santos etal [15] in a previous animal immune-histochemical study who have documented the efficacy of laser on pain relief, owing this to its ability to reduce neutrophil migration during the early phase of inflammation and modulation of inflammatory cytokines and decreased bradykinin levels leading to attenuation of the general inflammatory process.

Brosseau etal [16] investigated the effect of LLLT for osteoarthritis and rheumatoid arthritis the results showed significant pain relief which was attributed to the increased secretion of neurotransmitters such as serotonin. In addition, Fekrazad [17] studied the efficacy of LLLT in relieving pain caused by orthodontic elastomeric separators.
They found a significant decrease in pain which was explained by the ability of LLLT to boost up blood circulation with in tissues, thus increasing oxygen level available for tissues and wash away the pain-causing factors.

Many studies have investigated the reasons behind the analgesic effects of LLLT. It was found to be mostly related to the increase in secretion of endorphin and enhanced circulation at the site of inflammation. Furthermore, it was also suggested that LLLT aids the release of neurotransmitters, as serotonin that boosts up endorphin's performance. Furthermore, it reduces the level of prostaglandin E2 and cyclooxygenase-2 and nociceptor signal transduction all which contribute in the analgesic influence of low level laser therapy. [18, 19, 20]

Following enucleation of cysts from maxilla or mandible a bony defect is created. The normal spontaneous reaction to this osseous defects is osteogenesis which initiates with formation of a blood clot, granulation tissue then replaced later by osteogenic tissue unfortunately this process is a slow one [21]. Regarding our results, a superior bone density was demonstrated when laser was applied. A significant difference emerged at 3 months with p value of 0.008, where the test group showing a higher mean bone density than the control group indicating that the test group showed a more favorable early bone density development.

The results were in accordance with Park and Kang [8] who investigated the influence of (LLLT); in diabetic and healthy rats; on the healing of extraction sockets in an immunohistochemical study. The authors found that LLLT gave beneficial effect in early stages of alveolar bone healing and calcification of the secreted osseous matrix in both diabetic and normal rats when applying a dose of 13.95 J/cm2 every day for 60 seconds.

In a clinical investigation by Zaky etal 2016 [9] to evaluate the effect of (LLLT) on osseous tissue healing in cystic defects following cyst enucleation. They concluded that this adjunctive treatment modality enhanced bone healing in maxillary cystic defects. Moreover, it was suggested that it prevented possible delayed healing. They even recommended that This may be helpful for application in implant placement and provide possible early dental implant osseointegration.

Further Momeni etal [22] evaluated in a randomized clinical study the influence that LLLT on osseointegration of immediately loaded implants. The researchers found the application of LLLT significantly increased secondary stability of implants in the bucco-lingual dimension which indicative of the enhanced bone healing and accelerated osseointegration.

The finding of the current study may be explained by that LLLT stimulate runx2 expression which intern provides more osteoblast differentiation, stimulate their function and accelerated bone formation. Runx2 as the first marker of osteoblastic differentiation and a transcription factor that belongs to the runt-domain gene family is expressed in the initial period of osteogenesis moreover it activates other genes related to secretion of bone matrix [23, 24]

In a immunohistochemical study by Tanaka etal [25] revealed that a significant high density of bone was related to the high levels of runx2 mRNA at days 5, 7, and 14. Moreover, Collagen type I; a major organic matrix component in the bone and has major role in calcification; was also related. They came to conclude the strong relation of Runx2 and collagen type I and bone healing. Low level laser therapy was shown to increase the expression of runx2 and collagen type I mRNA than when LLLT was not applied. Indicating that LLLT promotes in initial stages of osseous healing. [8]

On the other hand, calcification of bone begins when osteocalcin is secreted from osteoblasts. [25] The osteocalcin level is significantly higher in osseous tissues that have received LLLT than in the control group and increased significantly by time and up to 2 weeks after application. Park and Kang [8] concluded that LLLT was effective in promoting bone calcification. This provides evidence that LLLT not only enhances the bone formation in its early stages but also promotes faster bone maturation and calcification which are comparable to the findings of our study where bone density was notably higher for test group at the three months' mark. Furthermore, the application of such treatment (LLLT) prior to and following enucleation of intra-body maxillary cystic lesions provided a favorable environment for better healing of the enucleation site. Thus; the null hypothesis that no difference is demonstrated regarding postoperative pain and bone healing following enucleation of intra-body maxillary cystic lesions with and without application of LLLT was rejected.

CONCLUSION:

Application of low level laser therapy prior to and following enucleation of intra-body maxillary cystic lesions is beneficial in postoperative pain relief and early bone healing.

CONFLICT OF INTEREST

the authors declare that there are no conflict of interest.

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