Original Article - Prospective Study

Evaluation of Efficacy of Low-Intensity Pulsed Ultrasound on Comorbidities Following Mandibular Impacted Third Molar Surgery: A Prospective Study

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Abstract

Introduction: Despite several *in vitro* and *in vivo* applications of low-intensity pulsed ultrasound (LIPUS), it remains an under-studied feature of the oral and maxillofacial region. The goal of this *in vivo* study was to objectively investigate the efficacy of low-intensity pulsed ultrasound on wound healing and related morbidities following surgical removal of an impacted third molar. **Materials and Methods:** The following *in vivo* prospective, comparative, randomised controlled clinical study was carried out amongst 56 patients who reported to the Department of Oral and Maxillofacial Surgery fulfilling the inclusion criteria. Group A received sham ultrasound, whereas Group B received LIPUS therapy. Based on the group allocated LIPUS 1 MHz, pulsed 20% and dose 1.0 watts/square centimetre (W/cm^2)/sham, ultrasound therapy was given on 1st, 2nd and 3rd post-operative days. The assessment of post-operative pain, oedema, trismus and wound healing on preoperative, first, third and seventh postoperative days. **Results:** The quantitative variables of the study were assessed using independent sample *t*-test, and qualitative variables were assessed using the Chi-square test. The $P < 0.05$ on third and seventh post-op days for pain, trismus and wound healing in the LIPUS group compared to control group making it statistically significant. There was no statistically significant difference in the reduction of oedema amongst the two groups. **Discussion:** Post-LIPUS application in the patients, postoperative pain was significantly reduced, trismus was noticeably improved and wound healing was satisfactory and can be employed as a complementary technique.

Keywords: Low-intensity pulsed ultrasound, oedema, third molar extraction, trismus, wound healing

Introduction

The surgical removal of impacted mandibular third molars produces a significant degree of trauma to soft tissues and bony structures of oral cavity, resulting in inflammatory reaction.[1] This produces postoperative signs and symptoms of pain, oedema and trismus. Several therapeutic protocols such as preoperative antibiotic administration, use of different kinds of flaps, use of postoperative ice packs, postoperative administration of several antibiotics, cortisone administration by systemic route or topical application, low level laser therapy and low-intensity pulsed ultrasound (LIPUS) are used.[2]

Duarte was the first to develop LIPUS (30 mW/cm^2) in the year 1976 through an animal study in 45 rabbits for fracture repair where he demonstrated a significant increase in callus formation during the healing phase.[3] Thereafter, it has been used extensively in the field of orthopaedic surgery and oral and maxillofacial surgery (OMFS) to improve fracture healing, for relief of myofascial pain, gingival and periodontal ligament regeneration and implant osseointegration.[4-6] Despite various *in vitro* and *in vivo* studies on LIPUS, it is a less explored aspect in oral and maxillofacial region. Therefore, the present *in vivo* study was designed to objectively assess the efficacy of LIPUS in wound healing and associated morbidities after surgical removal of impacted third molar.

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The investigators hypothesise that there exists a statistically significant difference in the effect of LIPUS therapy on wound healing and associated morbidities following surgical extraction of impacted mandibular third molar.

Materials and Methods

The following *in vivo* prospective, comparative, randomised controlled clinical study was carried out after obtaining the institutional ethical committee clearance (SSMC/Dent/IEC-9; December 2020). A sample size of 56 patients was estimated, and those fulfilling the inclusion criteria were taken up for the study and were randomly allocated in Group A (Control Group) which received sham ultrasound and Group B (LIPUS Group) which received LIPUS therapy (Alpha Meditronics mini analogue ultrasound) [Figure 1] by picking lots. All the disimpactions were carried out by a single operator. The patient and the evaluator (single) were blinded to the group the patient belonged.

Patients of (a) age group of 18–45 years undergoing extraction of impacted mandibular third molar without any localised acute or chronic infections in the third molar region; (b) patients giving consent for multiple follow-up visits and (c) patients having any lower third molar impactions with Pederson difficulty index of 5–7 (moderately difficult) were included in the study.[7] Patients with acute or chronic infections, uncontrolled systemic conditions, chronic smokers, alcoholics and pregnant patients were excluded from the study.

On the first visit, a signed written informed consent was obtained, and proper medical and dental history, demographics and intraoral findings were recorded. An orthopantomogram was also obtained. On the second visit, surgical extraction of impacted mandibular third molar was done. The patients of both the groups were prescribed capsule amoxicillin with clavulanic acid 625 mg thrice daily and tablet aceclofenac 100 mg twice daily post-procedure. LIPUS therapy for Group B was given at 1 MHz, pulsed 20% and dose 1.0 W/cm^2 on 1st, 2nd and 3rd post-op days extraorally with light contact of the skin along the part of mandible corresponding to the lower third molar region and along the course of masseter muscle [Figure 2]. Pain, trismus, swelling and wound healing were evaluated on the first, third and seventh postoperative days for both the groups.

Pain was evaluated using Visual Analogue Scale (VAS-[Horizontal]) in a combined numerical and descriptive pattern of 10 points on numerical aspect and 'no pain, mild pain, moderate pain, severe pain and excruciating pain' from descriptive aspect. Facial oedema was measured using a measuring tape in millimetres from (a) the tragus to the corner of mouth and (b) from the lateral canthus of eye to the angle of mandible. Facial oedema = Preoperative value (in mm) – Postoperative value (in mm). Trismus will be assessed by measuring the interincisal distance in millimetres from mesioincisal angle of the right maxillary central incisor to opposing incisal edge of the mandibular teeth in midline. Comparison of the pain, oedema and trismus was done between the groups using the independent sample *t*-test. The wound healing [Figure 3] parameters were assessed post-operatively using a modified Landry's index.[8]

Statistical Package for the Social Sciences (SPSS, Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.) was used to perform the statistical analysis. Data was entered in the excel spread sheet. Descriptive statistics of the explanatory and outcome variables were calculated by frequency and proportion for qualitative variables, mean and standard deviation for quantitative variables. Inferential statistics like Chi-square test was applied to find the association of qualitative variables with the groups. Independent sample *t* test was applied to compare the quantitative variables between the groups at different time intervals.

Results

In our study, 56 patients who required extraction of impacted mandibular third molars were included. The age of patients ranged from 19 to 42 years in control group and 19 to 41 years in LIPUS group with a mean age of 28.43 and 28.46 years, respectively. The difference in mean age of both groups was statistically insignificant (P = 0.98). Of 56 patients, 53.6% (15) were male and 46.4% (13) were female in the control group, whereas 57.1% (16) were male and 42.9% (12) were female in the LIPUS group and was statistically not significant (P = 0.78).

Outcome measurements

Pain was assessed pre-operatively, first, third and seventh postoperative days and the P = 0.438, 0.408, 0.012 and 0.036, respectively. P values were statistically significant on

Figure 1: Low-intensity pulsed ultrasound device

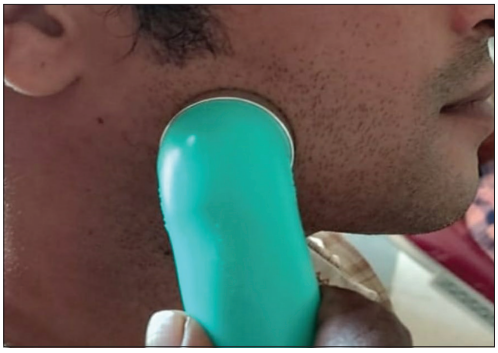

Figure 2: Extraoral application of low-intensity pulsed ultrasound with light contact of the skin along the part of mandible corresponding to lower third molar region and along the course of masseter muscle

the third and seventh postoperative days, suggesting decrease of pain in the LIPUS group after two applications [Table 1]. For postoperative oedema, *P* values for baseline, first, third and seventh day postoperative comparison for T-cm were 0.82, 0.96, 0.37 and 0.78, respectively, and 0.54, 0.53, 0.87 and 0.82 for Lc-Am, respectively, making a statistically insignificant difference between the study and the control groups, suggesting that LIPUS has a minimal role in the decrease of oedema after surgical removal of mandibular third molar [Figure 4].

Preoperatively, mouth opening ranged from 17 to 49 mm in control group and 17 to 48 mm in LIPUS group with a mean of 34.71 and 33.93, respectively. *P* values were 0.65, 0.307, 0.004 and 0.047 on pre-op, first, third and seventh postoperative, respectively. $P < 0.05$, on third and seventh postoperative days suggesting the values are statistically significant, suggestive of improvement in mouth opening in the LIPUS group [Table 2]. *P* values were 0.408, 0.002 and 0.021 on first, third and seventh postoperative, respectively. The $P < 0.05$, on third and seventh postoperative days suggesting the values are statistically significant for wound healing [Table 3 and Figure 5].

Discussion

Ultrasound refers to a form of sound wave whose frequency is higher than that of the average human sound. In reality, a simple sound source is frequently a ceramic disc with a finite radius that shows the piezoelectric effect. They are essentially mechanical vibrations with higher frequencies that span from 0.5 to 5 MHz, with 1–3 MHz being the most often employed range in the therapeutic field.[9] In medical and dental field, ultrasound is used in two different ways. The first is pulsed ultrasound, which only uses ultrasonic waves for a portion of the treatment, whereas the second is continuous ultrasound, which has a thermal effect.

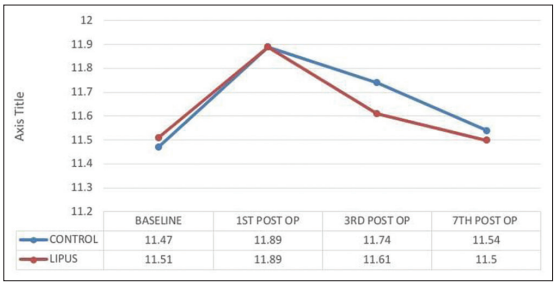

Figure 3: Comparison of oedema (T to cm) between the groups at different time intervals

Biophysical non-thermal effects of ultrasound

Usually perceived as a synthesis of:

- Micro massage – When a sound wave travels across a medium, molecules vibrate as a result, potentially affecting tissue fluid exchange and tissue movement
- Cavitation – Happens at therapeutic ultrasonic levels and causes gas-filled cavities to form in tissues or fluids that take 1000 cycles to grow to their largest size
- Acoustic streaming – Fluids eddying on a tiny scale close to a vibrating structure can modify membrane permeability and diffusion rates, which changes the synthesis of proteins and physiological secretion.[10]

Application settings for LIPUS that is most frequently utilised are intensity at 0.03 W/cm^2 (or 30 mW/cm^2), pulse ratio at 1000 Hz (1:4) and frequency at 1.5 MHz. Moreover, for regular therapeutic applications, the intensity of LIPUS applied can range from about 0.03 to 1.00 W/cm^2.[9] The setting of frequency and Watts differs for each application site, the commonly used settings being 1 W/cm^2, 3 MHz as adjunct treatment in osteoradionecrosis, 30 m W/cm^2 and 1 MHz in fracture healing and 1 W/cm^2, 1.5 MHz as adjunct treatment in orthognathic surgery.[11-13] In our study, we used 1 MHz, pulsed 20% and dose 1.0 W/cm^2. Areas other than OMFS, where it has been used include healing of long bone fracture, osteoarthritis, erectile dysfunction, soft-tissue regeneration, chronic pelvic or prostate pain and inflammation and stress urinary incontinence to name a few.[3]

Its applications in oral and maxillofacial region are limited to muscle spasm relief in temporomandibular joint, adjunct therapy in fracture healing and very few studies on extraction sockets.[2,3,12,14] The different outcomes assessed in the present study were pain, oedema, trismus and wound healing pre- and post-application of LIPUS. Pain is a distressing experience that is typically triggered on by intense or harmful stimuli. The majority of the time, pain starts after the anaesthetic from the treatment wears off and peaks 6–12 hours later. For the first 24–48 hours, it is often mild and brief. The progressive release of mediators from mast cells, the vasculature and other cells following tissue injury or inflammation may help to explain the pathophysiology of pain. The first substances to be detected are histamine and serotonin, which are soon followed by bradykinin and prostaglandins.[15]

Table 1: Comparison of the pain between the groups at different time intervals using independent sample *t*-test

Time intervals (pain)	Groups	*n*	Minimum	Maximum	Mean	SD	Mean difference	*P*
Baseline	Control	28	0	2	0.71	0.763	−0.14	0.438
	LIPUS	28	0	2	0.85	0.563		
1st postoperative	Control	28	1	8	5.68	1.634	−0.32	0.408
	LIPUS	28	3	8	6.0	1.127		
3rd postoperative	Control	28	1	6	5.00	1.7	−1.07	0.012*
	LIPUS	28	1	6	3.93	1.359		
7th postoperative	Control	28	0	3	1.68	0.965	−0.50	0.036*
	LIPUS	28	0	3	1.18	0.772		

*Significant. LIPUS: Low-intensity pulsed ultrasound, SD: Standard deviation

Table 2: Comparison of the trismus between the groups at different time intervals using independent sample *t*-test

Time intervals (trismus)	Groups	*n*	Minimum	Maximum	Mean	SD	Mean difference	*P*
Baseline	Control	28	17	49	34.71	6.25	0.78	0.65
	LIPUS	28	17	48	33.93	6.97		
1st postoperative	Control	28	17	42	30.21	5.15	1.5	0.307
	LIPUS	28	15	43	28.71	5.71		
3rd postoperative	Control	28	25	45	34.43	5.11	−4.25	0.004*
	LIPUS	28	25	48	38.68	5.55		
7th postoperative	Control	28	30	50	37.04	4.90	−2.94	0.047*
	LIPUS	28	29	50	39.98	5.91		

*Significant. SD: Standard deviation, LIPUS: Low-intensity pulsed ultrasound

Table 3: Distribution of the patients based on healing

Healing	Count (%)			χ^2	*P*
	Groups		Total		
	Control	LIPUS			
1st postoperative					
2	16 (57.1)	19 (67.9)	35 (62.5)	0.68	0.408
3	12 (42.9)	9 (32.1)	21 (37.5)		
3rd postoperative					
2	7 (25.0)	0	7 (12.5)	12.87	0.002*
3	15 (53.6)	11 (39.3)	26 (46.4)		
4	6 (21.4)	17 (60.7)	23 (41.1)		
7th postoperative					
3	8 (28.6)	1 (3.6)	9 (16.1)	7.72	0.021*
4	15 (53.6)	16 (57.1)	31 (55.4)		
5	5 (17.9)	11 (39.3)	16 (28.6)		

*Significant. LIPUS: Low-intensity pulsed ultrasound

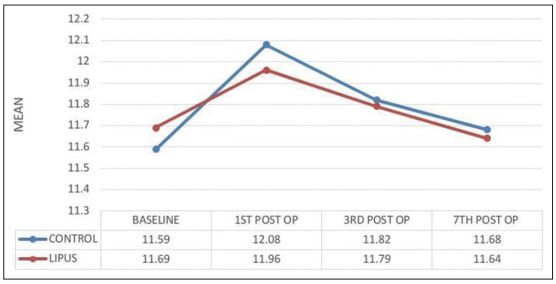

Figure 4: Comparison of oedema (Lc to Am) between the groups at different time intervals

In our study, pain was evaluated pre- and post-administration of LIPUS using VAS of scale 10. *P* values were statistically significant on third and seventh postoperative days. The LIPUS operates on the cavitation and acoustic streaming concept. By increasing the blood flow and membrane permeability, this microstreaming flushes away harmful metabolites and stored chemical mediators, reducing discomfort to the nerve endings.[15] In a study conducted by Gopalan *et al*., 40 patients participated in a blinded randomised controlled clinical trial to assess the effectiveness of LIPUS in promoting healing of mandibular fractures. Internal fixation and open reduction were used to treat fractures. On postoperative days, four, eight, 14 and 20 following fixations, the study group received LIPUS stimulation (1.5 MHz, 30 mW/cm^2) for 20 min each day, whereas the control group received no LIPUS stimulation. On days five, nine, 15 and 21, postoperative outcome criteria including postoperative pain, wound healing, tooth mobility and radiographic and ultrasound fracture healing were evaluated. According to the study, LIPUS application helped fracture healing in patients with impaired healing capability by reducing postoperative discomfort. The pain score was reduced in the study group on all postoperative days.[12]

One of the main discomforts for patients following the extraction of a third molar is oedema, which is the swelling of a region of the body as a result of fluid accumulation in the tissues and typically peaks two to three days after surgery and should start to reduce by four days and takes around seven days to go away. This is linked to damage to the soft tissue during the reflection of the flap and during bone removal which leads to the stagnation of toxic metabolites and inflammatory mediators in the area.[16] The waves of compression and rarefaction induce micro massage which reduces swelling in the LIPUS group by altering the permeability of cell membranes and enhancing lymphatic circulation through the pulsation effect.[10] In a similar clinical trial by Xu *et al*., LIPUS has been shown to alleviate inflammatory responses efficiently at the cellular level by affecting some signalling pathways. This in turn contributes to the decrease in pain and oedema of the patients.[17]

Trismus, or difficulty opening the mouth, is frequently the result of surgical trauma and follows lower third molar surgery-related masticatory muscle inflammation. The medial pterygoid muscle is the most frequently injured muscle due to a needle injury, oedema, haemorrhage or inflammation.[15] In our study, $P < 0.05$, on third and seventh postoperative days suggesting the values are statistically significant. In a study conducted by Muragod *et al*. for evaluating the comparative effectiveness of ultrasound therapy (1 MHz, pulsed 20% and dose 1.0W/cm^2 for seven minutes for the first three days after surgery) and laser therapy on pain, swelling and trismus following third molar surgeries in thirty patients, there was a significant difference between pain, swelling and trismus within the groups, but no significant difference in the intergroup comparison stating that LIPUS is as efficient as laser.[18]

Increased local tissue temperature, abundant blood flow and improved tissue elasticity and extensibility with reduced fluid viscosity significantly relieve the muscles of mastication of the collected inflammatory mediators and strain, thereby improving

Figure 5: Wound healing on 1st, 3rd and 7th postoperative days

mouth opening.[15] All four phases of wound healing must take place in the right order and amount of time for healing to be successful.[16] One of the mechanisms of LIPUS is increased rates of ion diffusion, thereby increasing calcium influx which acts as secondary messenger in release of histamine from mast cells and increases the growth factor levels, stimulates fibroblasts, induces angiogenesis and bone remodelling, thus scaling up the efficiency of wound healing. In our study, *P* values were 0.408, 0.002 and 0.021 on first, third and seventh postoperative, respectively. The $P < 0.05$, on third and seventh postoperative days suggesting the values are statistically significant.

The use of LIPUS is contraindicated in tumours, pregnant uterus, epiphyseal plates, eyes, gonads and areas of radiotherapy.[16] The cost of a portable therapeutic ultrasound unit range from 98.5 US $ to 147 US $, which is very less compared to the expensive laser units making it a cost-effective alternative.[18] Our study did have certain restrictions. The literature evidence available for the usage of LIPUS is very minimal for understanding the exact protocol to be followed. Following the disimpaction of the mandibular molars, LIPUS therapy needs to be applied on three consecutive days, on an outpatient basis; however, patients who lived in remote locations found it challenging to travel to the hospital for the same. The LIPUS unit is available in various frequency and watts; in our study, we have only analysed LIPUS 1 MHz, pulsed 20% and dose 1.0 W/cm^2. Further studies with different settings are necessary to have a greater knowledge about the efficacy and disadvantages of the equipment.

Conclusion

In this study, it was observed that postoperative pain was significantly reduced, trismus notably improved and wound healing was satisfactory after application of LIPUS in the patients. When compared to the control group, the LIPUS group showed a minimal reduction in oedema. Thus, we can conclude that LIPUS can be used as an adjunctive method in routine management of post-surgical morbidities. Further randomised controlled prospective studies with different settings are necessary to have a greater knowledge about the efficacy, different applications, modes and disadvantages of the equipment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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