

AN EVALUATION OF THE EFFECT OF LOW INTENSITY PULSED ULTRASOUND ON THE HEALING OF MANDIBULAR FRACTURES A RANDOMIZED CLINICAL TRIAL

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ABSTRACT

INTRODUCTION: Mandibular fractures are considered a significant percentage of maxillofacial trauma. Multiple techniques, have been used to improve mandibular fracture healing over the years. Low Intensity Pulsed Ultrasound (LIPUS) has recently been used in orthopaedic surgery for improvement of bone union, but was rarely investigated for facial bones.

OBJECTIVE: The aim is to compare the efficacy of the use of LIPUS in accelerating bone healing of jaw fractures after open reduction versus the use of conventional miniplates only, investigated both radiographically and clinically.

MATERIALS AND METHODS: In an interventional study, 18 cases with jaw fractures were assigned to two groups at random: the study group and the control group, having 9 participants in each group. Both groups underwent open reduction and internal fixation using two conventional miniplates but only the study group received LIPUS stimulation (1.5MHz, 30W/cm²) for 20 minutes on postoperative days 4, 8, 14 and 20. The control group did not receive LIPUS. Clinical evaluation included wound healing, occlusion and pain intensity. Radiographic evaluation using immediate Cone Beam Computerized Tomography (CBCT) and postoperative CBCT after 12 weeks were used to determine the efficacy by measuring various variables, including bone density and radiographic fracture healing.

Results After twelve weeks, both groups had normal occlusion and normal sensory function. The wound healing was measured using landry's score index, there was a significant difference in both groups along the follow up period ($p < 0.001$) and a statistically significant reduction in pain intensity ($p < 0.001$). The average bone density improved statistically significantly in both groups A ($p < 0.001$) and B ($p < 0.001$) when comparing post-operative 12 week values to preoperative values.

CONCLUSION: Based on the favourable clinical and acceptable radiographical outcomes of our study, it is concluded that the application of low intensity pulsed ultrasound in mandibular fractures could potentially speed up the healing process, decrease the pain and postoperative complications.

KEYWORDS: Low intensity pulsed ultrasound, Ultrasound, Anterior mandibular fracture.

RUNNING TITLE: Low intensity pulsed ultrasound application in mandibular fractures.

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INTRODUCTION

The process of bone healing involves various biochemical and biomechanical processes. It includes various direct and indirect techniques to promote fracture healing and reduce the need for surgery have been introduced, including the use of lasers(1), drugs (2), extracorporeal shock wave (3), and ultrasound bio-stimulation (4).

Ultrasound waves have been widely used as both for diagnosis and therapy in the medical and surgical fields.

It has been used to treat various pathologies. In maxillofacial field, both intensities in ultrasound waves (high and low) are used to treat a range of clinical conditions, such as temporomandibular joint disorders (5). Ultrasound refers to waves with a frequency greater than 20 kHz. The power intensity of an ultrasound

wave is a measure of the energy it produces and is typically measured in W/cm². Therapeutic and surgical ultrasound intensities can range from 1 to 3 W/cm². Ultrasound devices used for diagnosis typically use a much lower intensity of only 10 to 50 mW/cm² (6).

Studies have shown that low-intensity ultrasound can decrease healing time in both animal and human trials, particularly for long bones, providing further evidence for its effectiveness (7, 8).

In this study, the research and the utilization of low-intensity ultrasound for jaw fractures was clinically measured and analysed due to the positive and notable outcomes found in the previous researches (9, 10) using LIPUS. In the literature (9) there is evidence that LIPUS aids in the bone healing in mandibular fractures after closed reduction, but its effect on bone healing is still not fully known after open reduction and internal fixation with minimal movement between the bone segments. And, it has been found that the natural process of bone fracture healing, despite being a simple process, is capable of supporting clinically significant loads.

Therefore, the aim of our trial was to assess the effectiveness of low intensity pulsed ultrasound (LIPUS) in enhancing bone healing for patients with mandibular fractures, with a focus on both radiographic and clinical outcomes.

The null hypothesis is there is no dissimilarity in the clinical and radiographic performances on bone healing and density between using LIPUS with reduction and fixation using miniplates without LIPUS.

MATERIAL AND METHODS

This clinical trial followed a prospective randomized controlled design with an allocation ratio of 1:1. The study was performed according to the CONSORT guidelines (<http://www.consort-statement.org>) for setup and reporting. The sample size was determined assuming a 5% alpha error and 80% study power, with a calculated sample size of 9 patients per group to account for potential patient loss to follow-up (15 patients in total). The enrolled patients were divided into two groups equally: Group I, which underwent open reduction and internal fixation using conventional miniplates and received subsequent LIPUS treatment (1.5 MHz, 30 mW/cm²), and Group II, which was treated using two conventional miniplates without LIPUS.

The criteria for patients' selection specified that adult patients between the ages of 20-40, regardless of gender, who had uninfected mandibular fractures (symphyseal, parasymphseal, or body) and agreed to be present for follow-up visits for 3 months were eligible for enrolment.

Materials

The Miniplates 2.0-mm System Plates used in the study were manufactured by Stema Medizintechnik

GmbH in Stockach, Germany (www.stema-medizintechnik.de). The plates were paired with 2.0 mm diameter screws made of titanium alloy (Figure 1). Both groups received the same miniplates for reduction and fixation of the fracture line. LIPUS (Physioled low intensity pulsed ultrasound) (LED SpA // Via Selciatella, 40 // 04011 Aprilia (LT) // ITALY), is a newer method that can speed up the healing fractures. In this trial, LIPUS was applied to patients using a frequency of 1.5 MHz, a signal burst width of 200 ms, a signal repetition frequency of 1 kHz, intensity 30 mW/cm², with a time of approximately 20 minutes per day (Figure 2). It's important to note that therapeutic and operative ultrasound intensities are typically much higher, ranging from 1 to 3 W/cm².

Methods

I. Preoperative assessment

Patients medical history was taken, then underwent a comprehensive clinical examination, which included both intra-oral and extra-oral assessments. Prior to surgery, a computed tomography (CT) scan was conducted to assess the extent and displacement of the fracture line, as well as the presence of vital structures in the fracture site. (Figure 3 A)

II. Surgical procedure

1. Before surgery, patients received prophylactic antibiotic treatment with Cefotaxime 1 gm/12 hours (Cefotax, E.I.P.I.C.O., Egypt) prior to the surgical procedure.
2. General anaesthesia and nasal intubation were applied to all patients whom underwent the surgery.
3. The surgical site was prepared using sterile towels and swabs soaked in povidone-iodine solution (Betadine 7.5 percent; Purdue Products L.P.)
4. Fracture line was exposed through intra-oral approach or the existing extra-oral wound according to each one.
5. The fracture was mobilized, and any soft tissue that was caught within the fracture line was removed. The treatment of teeth in the fracture line involved either extraction or preservation, depending on the individual case.
6. After the bone was reduced into its proper anatomical position, intermaxillary fixation (IMF) was temporarily secured to ensure proper occlusion.
7. Two conventional miniplates were applied according to Champy's osteosynthesis lines. (Figure 3 B).
8. Removal of the inter maxillary fixation.
9. Suturing was done.

III. Ultrasound treatment

For Group A LIPUS treatment was done on day 4, 8, 14, 20 for 20 minutes with a frequency of 1.5 MHz and a wavelength of 30mW/cm² (Figure 4). Group B received no treatment.

IV. Postoperative care

All patients were advised to apply an ice pack

extra-orally for 12 hours immediately following the surgery. Sutures were removed on the 8th day postoperative.

Postoperative medication

- The patient will receive medication through a vein called cefotaxime, 1 gram every 12 hours for the first 3 days, and then they will switch to Amoxicillin and clavulanate (Augmentin: Amoxicillin 875 mg + Clavulanic acid 125 mg: GlaxoSmithKline, UK) 1 gram twice a day for the following 5 days. Metronidazole (Flagyl: metronidazole 500mg: GlaxoSmithKline, UK) 500mg every eight hours for 5 days.
- α -chemo-trypsin (α -chemo-trypsin: Leurquin France, packed by Amoun pharmaceutical CO.S.A.E-Egypt) ampoules as anti-oedematous once daily for 5 days.
- Diclofenac potassium (Cataflam: Diclofenac Potassium 50mg: Novartis-Switzerland) 50mg every eight hours for 5 days.

Follow up phase

A thorough follow-up was performed after the LIPUS treatment on days 5, 9, 15, 21 for the measurement of the following clinical variables. For all patients, evaluation of postoperative pain using a 10-point Visual Analogue Scale (VAS), and wound healing, using modified Landry's index table were performed (11), occlusion checking the centric occlusion, which is the maximum intercuspal position, is used to ensure that the teeth are in the correct position in relation to each other (12), Nerve function was evaluated by asking patient if they noticed any changes in sensation (subjective assessment) and by using dental probe with pressure to notice sensory nerve change (objective assessment) (13), wound infection, Wounds that were closed with sutures were checked for any indications or symptoms of infection (14).

V. Radiographic evaluation

Immediate CBCT scan was used to evaluate if the alignment of the fractured bones is satisfactory and fixation, and then another CBCT was taken at 12th week determine the average density of the bone at the site of the fracture and compare it with the bone density measured in the immediate postoperative CBCT scan (15) (Figure 5 A, B). Six measurements were made along the fracture line, and the average bone density was calculated for each measurement (16).

VI. Statistical Analysis

Descriptive statistics, plots, and the Shapiro-Wilk normality test were used to check the normality of all variables. Descriptive statistics were calculated as means, standard deviation (SD), median, interquartile range (IQR) and range (Min – Max) for quantitative variables. Comparisons between the two study groups were done using Mann-Whitney U test for quantitative (age, VAS, and bone density) and qualitative ordinal variables (Landry's index), while comparisons between different time periods within the same group were done using Wilcoxon signed rank test (two timepoints only) and Friedman test (three or more timepoints). Comparisons of qualitative nominal

variables between the two study groups were done using chi-squared along with Fisher exact tests (17).

RESULTS

Patients' ages varied between 20 to 40 years with the mean age of group A 28.56 ± 7.45 and group B 30.56 ± 6.92 . The included study population showed a higher percentage of males (66.7%) compared to females (33.3%). No notable difference between two groups as regarding age and sex.

Out of the eighteen cases in this study; in this study five patients had fractures in the right side, eight in the left side and five had midline fractures (sympheseal). Throughout our study, fifteen patients were presented with isolated mandibular fractures (sympheseal, parasympheseal and body) in both groups. On the other hand only three patients were presented with associated fractures in the maxillofacial area in both groups.

Clinical Evaluation

In relation to the 24h postoperative values, according to VAS, all patients had a notable reduction in pain level during the follow-up duration (P value <0.001) (Figure 6).

During the follow-up period, three patients were presented with malocclusion in group A and two patients in group B. MMF was done to restore the occlusion. Normal occlusion was achieved successfully without the need for selective grinding, selective extraction or any occlusal modification.

One patient in group (A) and two patients in group (B) presented with postoperative inferior alveolar nerve sensory disturbance. Nerve injury gradually decreased by the 21 day follow up postoperatively and completely resolved for patients in group B. In contrast, for group A patient the sensory nerve disfunction continued and did not resolve (Table 1). Which was due to the position of the fracture line crossing the mental foramen.

Two cases in group A and two in group B noted wound dehiscence and infection with a mild pus discharge which was traced back to the oral hygiene and a devitalized teeth due to trauma on the side of the fracture.

Postoperative wound healing was scored using Landry's scale index score, there was a notable difference between the two groups at day 15 ($p=0.01$). There was no notable difference observed between the groups at any other point in time. But there was a notable difference in both groups along the entire follow up period ($p<0.001$). However, at the 4th week of the follow-up period, the wound had healed due to secondary intention in both groups. (Table 2)

Radiographic Evaluation

Regarding the immediate post-operative scan, both groups showed statistically insignificant difference ($P= 0.73$). The mean immediate post-operative bone density for the study group was 441.14 ± 85.83 , while a mean of 439.42 ± 97.64 was reported in the control group. A mean three months postoperative

bone density calculation for the study group was 1007.04 ± 169.17 , while a mean reported value of 1023.93 ± 192.39 was revealed in the control group. The intergroup comparison regarding the three months mean bone density postoperatively was statistically insignificant ($P= 0.93$). In both groups, the difference between three months and immediate mean bone density was statistically significant ($P= 0.008^*$ and $P= 0.008^*$ respectively) (Table 3)

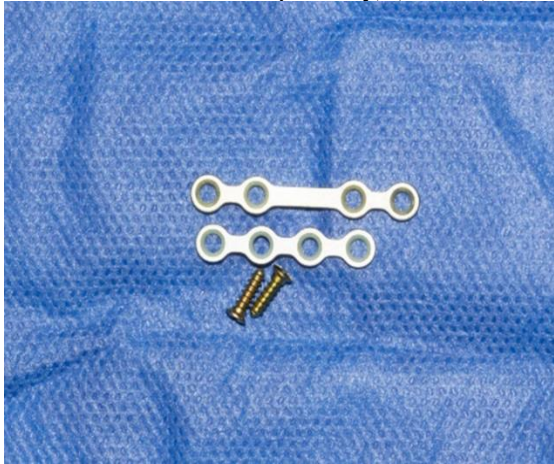


Figure (1): Miniplate and screws.



Figure (2): Physioled low intensity pulsed ultrasound.

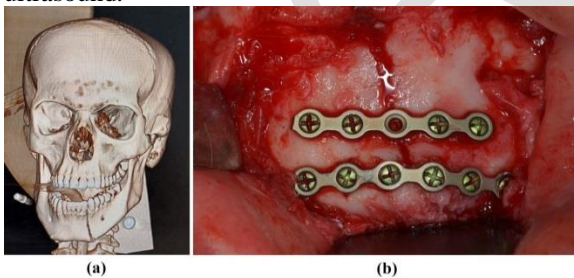


Figure (3): (a) Preoperative CT scan. (b) Reduction and fixation using miniplates.



Figure (4): LIPUS application.

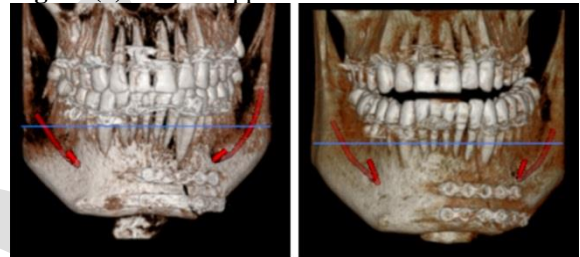


Figure (5): (a) Immediate postoperative. (b) 3 months postoperative.

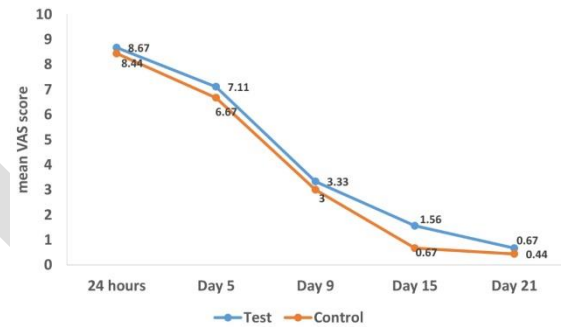


Figure (6): VAS in the two study groups at different timepoints (same figure different type).

Table (1): Comparison of sensory nerve function between two studied groups at different time points

		Test (n= 9)	Control (n= 9)	Fisher exact test P value
		N (%)		
24 hours	Normal	8 (88.9%)	7 (77.8%)	$X^2= 0.40$ $P_{FE}= 1.00$
	Numbness	1 (11.1%)	2 (22.2%)	
Day 5	Normal	8 (88.9%)	7 (77.8%)	$X^2= 0.40$ $P_{FE}= 1.00$
	Numbness	1 (11.1%)	2 (22.2%)	
Day 9	Normal	8 (88.9%)	7 (77.8%)	$X^2= 0.40$ $P_{FE}= 1.00$
	Numbness	1 (11.1%)	2 (22.2%)	
Day 15	Normal	8 (88.9%)	7 (77.8%)	$X^2= 0.40$ $P_{FE}= 1.00$
	Numbness	1 (11.1%)	2 (22.2%)	
Day 21	Normal	8 (88.9%)	9 (100%)	$X^2= 1.06$ $P_{FE}= 1.00$
	Numbness	1 (11.1%)	0 (0%)	
Cochran's Q test P value		Q= 0.0001 P= 1.00	Q= 8.00 P= 0.09	

X^2 : Chi-square, P_{FE} : Fisher exact test

Table (2): Comparison of Landry's index between the two groups at different timepoints.

		Test (n= 9)	Control (n= 9)	MWU test P value
		N (%)		
24 hours	Very poor (1)	7 (77.8%)	6 (66.7%)	Z= 36.00 P= 0.73
	Poor (2)	2 (22.2%)	3 (33.3%)	
	Good (3)	0 (0%)	0 (0%)	
	Very good (4)	0 (0%)	0 (0%)	
	Excellent (5)	0 (0%)	0 (0%)	
	Mean (SD)	1.22 (0.44)	1.33 (0.50)	
	Median (IQR)	1 (1, 1.5)	1 (1, 2)	
Day 5	Very poor (1)	4 (44.4%)	7 (77.8%)	Z= 25.00 P= 0.19
	Poor (2)	3 (33.3%)	2 (22.2%)	
	Good (3)	2 (22.2%)	0 (0%)	
	Very good (4)	0 (0%)	0 (0%)	
	Excellent (5)	0 (0%)	0 (0%)	
	Mean (SD)	1.78 (0.83)	1.22 (0.44)	
	Median (IQR)	2 (1, 2.5)	1 (1, 1.5)	
Day 9	Very poor (1)	2 (22.2%)	3 (33.3%)	Z= 30.00 P= 0.39
	Poor (2)	4 (44.4%)	5 (55.6%)	
	Good (3)	2 (22.2%)	1 (11.1%)	
	Very good (4)	1 (11.1%)	0 (0%)	
	Excellent (5)	0 (0%)	0 (0%)	
	Mean (SD)	2.22 (0.97)	1.78 (0.67)	
	Median (IQR)	2 (1.5, 3)	2 (1, 3)	
Day 15	Very poor (1)	0 (0%)	0 (0%)	Z= 13.50 P= 0.01*
	Poor (2)	2 (22.2%)	6 (66.7%)	
	Good (3)	1 (11.1%)	3 (33.3%)	
	Very good (4)	6 (66.7%)	0 (0%)	
	Excellent (5)	0 (0%)	0 (0%)	
	Mean (SD)	3.44 (0.88)	2.33 (0.50)	
	Median (IQR)	4 (2.5, 4)	2 (2, 3)	
Day 21	Very poor (1)	0 (0%)	0 (0%)	Z= 24.00 P= 0.16
	Poor (2)	0 (0%)	0 (0%)	
	Good (3)	3 (33.3%)	6 (66.7%)	
	Very good (4)	0 (0%)	1 (11.1%)	
	Excellent (5)	6 (66.7%)	2 (22.2%)	
	Mean (SD)	4.33 (1.00)	3.56 (0.88)	
	Median (IQR)	5 (3, 5)	3 (3, 4.5)	
Friedman test P value		$\chi^2= 31.57$ $p < 0.001^*$	$\chi^2= 29.22$ $p < 0.001^*$	

Table (3): Comparison of bone density between the two studied groups

		Test (n= 9)	Control (n= 9)	MWU P value
Immediate	Mean (SD)	441.14 (85.83)	439.42 (97.64)	Z= 36.00 P= 0.73
	Median (IQR)	435.33 (382.60, 483.33)	422.30 (381.75, 474.61)	
	Min – Max	318.33 – 483.33	311.89 – 662.50	
3 months	Mean (SD)	1007.04 (169.17)	1023.93 (192.39)	Z= 42.00 P= 0.93
	Median (IQR)	1007.17 (859.64, 1119.18)	976.76 (929.70, 1014.36)	
	Min – Max	849.70 – 1337.50	871.85 – 1521.80	
Percent change	Mean (SD)	134.27 (52.90)	142.80 (69.53)	Z= 46.00 P= 0.67
	Median (IQR)	116.47 (99.21, 171.59)	124.43 (110.95, 174.66)	
	Min – Max	64.47 – 241.46	41.75 – 295.48	
WSR p value Immediate vs. 3 months		Z= 2.67 P= 0.008*	Z= 2.67 P= 0.008*	

χ^2 : Chi-square, P_{FE} : Fisher exact test

*statistically significant at p value <0.05

DISCUSSION

The study was conducted only on fractures of the anterior mandible (sympheseal, parasympheseal) and body to make sure no differences in results or variations in the treatment outcomes.

In addition, the study included cases with displaced fractures that needed reduction and fixation using the conventional miniplates using the principles of Champy (18) which gained popularity over the time. They were introduced into the management of mandibular fractures, which resulted in a significant reduction in surgical soft tissue damage, improved handling, gave reasonable stability, and repair of mandibular fractures (18, 19). Gopalan et al., (10), as mentioned before, used LIPUS on displaced fractures. Patel et al., (9) study involved patients who had undisplaced fractures that were treated solely with intermaxillary fixation.

Demographic outcomes of this work revealed a mean age of 28.56 ± 7.45 with a male to female ratio 2:1. The literature shows several reports with alike demographic data (20, 21). The epidemiology of maxillofacial trauma in Egypt was investigated by Mabrouk et al., (22) in 2014, it reported a mean age of 25.6. Despite being lower than the reported value, still it is within range.

The sensory nerve sensation is an important aspect in the evaluation of any treatment modality used to manage mandibular fractures. Sensory nerve disruption could be caused due to severe fracture line displacement, poor anatomical reduction, entrapped or over compressed nerve or due to iatrogenic screw insertion into the canal (23). A subjective and objective appraisal was performed to every patient in the group and was found that 1 case yielded inferior alveolar nerve dysfunction in the first follow up 11.1% and 22.2% in group B. The case in group A suffered from a body fracture line that went exactly crossing the foramen, so on reduction and plate fixation the nerve was compressed and this explains the numbness that had occurred and did not resolve until the last follow up on day 21. These findings agree with Tay et al (24) stated that the overall prevalence of IAN injury was 33.7% before treatment and 53.8 after treatment which shows that after treating mandibular fractures there is a higher risk of numbness and loss of sensation due to nerve injury.

The presence of postoperative malocclusion using conventional miniplates is not noted in many studies, but postoperative malocclusion depends mainly on the degree of displacement of the fracture, site of the fracture, the presence of more than one fracture line and the time of immobilization of present (25). Of course malocclusion can occur with a minimal displaced fracture. IMF is the only treatment that gives good occlusion with good anatomical relation but at the expense of prolonged functional limitation. In this study 2 cases in group A had malocclusion and 2 from group B also. There was no significant

difference between the 2 groups. All cases were treated with IMF to restore the occlusion as been mentioned it is the only way to ensure a good occlusion (25).

The level of postoperative pain was evaluated using the visual analogue scale (VAS). These findings support that acute post trauma injury cause's inflammation that causes postoperative pain. Therapeutic ultrasound has been demonstrated to be a valuable modality in the treatment of musculoskeletal disorders and is widely used in physiotherapy. It has also been utilized to address pain dysfunction syndrome and temporomandibular joint disorders. These findings are consistent with those of Patel et al., (9) and Gopalan et al., (10), which indicate that LIPUS accelerates pain reduction by decreasing the inflammation. Ultrasound has thermal and mechanical effects on the target tissue resulting in an increased local metabolism, circulation, extensibility of connective tissue and tissue regeneration and thus decreasing the inflammation (26).

The result findings of landry's score index to assess wound healing agrees with those of Gopalan et al., (17). The findings support that LIPUS is mechanical vibration with frequencies above the limit of human sound detection, and can be transmitted into the body as high-frequency acoustic pressure waves (27-29). It has been recognized that such waves produce mechanical stimuli in living tissues, resulting in biochemical events promoting tissue healing(30, 31).

In this study there was a great correlation between the grey scale values in the CBCT and the bone density. This suggests that quantitative radiological methods for assessing bone density using CBCT scans are dependable. In this study bone density in both groups was statistically significantly increased through the follow up period ($p= 0.008^*$), comparing the immediate CBCT with the 3 months postoperative CBCT. A similar increase in average bone density was reported by several studies (9, 10) using LIPUS treatment to accelerate bone healing, which agrees with these results.

This study did not find any notable difference in the radiographic bone density between the two groups. However, a clinical study conducted in 2015 by Patel et al., (9) showed that ultrasound therapy using 1 MHz and 1.5 W/cm² on alternate days for 12 days and 5 minutes per session resulted in increased radiographic bone density in the study group compared to the control group. In contrast, we used LIPUS (1.5 MHz, 30 mW/cm²) for 20 minutes daily for only 4 days (on postoperative days 4, 8, 14, and 20) for surgically treated fractures, which was based on a study conducted in 2020 by Gopalan et al., (10). Ahmed et al., (32) used CBCT to measure the bone density after treating mandibular fractures using extracorporeal shockwaves on group A, LIPUS treatment in group B and group C received nothing.

The results in group B and group C increased significantly through the follow up period which was the same as our study (3months) but did not show significant increase compared to each other. Which agrees with our study findings that showed no significant difference between both groups.

Patel et al., (9) evaluated the radiographic density of the fracture site using five points in six different radiographs taken at weekly intervals. There was a notable difference in the radiographic density on 3rd and 5th week between the two groups ($p>0.01$). Radiographic density was 21.64% in the LIPUS treated group than the control group. This does not agree with our findings in this study. May be because in the former study they used a different measuring method and measured the fracture zone every week for six weeks immediately after the treatment.

Our results disagreed with Gopalan et al., (10) who stated in there study that on assessing radiographic bone density on week 4, 8 and 12 found notable increase in bone density. In the former research the method of measurement is different. They used Moed's scale (ultrasonography) for measuring the callus formation at the fracture site, which gave different measurements than those found in our study.

In conclusion, our study suggests that LIPUS treatment applied on mandibular fractures has favourable contributions in aiding in bone healing in healthy patients. Ultrasound may have positive effects in treating delayed unions, aiding in callus formation using distractors or in cases of osteoradionecrosis (33). Given access to the former studies, LIPUS treatment is of huge effect on the callus formation which in turn aids in bone healing.

This research is limited by limited amount of patients with only a single anterior or body mandibular fracture. Associated fractures may be a confusing factor, that may lead to occlusal instability that can interfere with the bone healing (23). Furthermore, this study was limited by the way of measuring of the bone density after the treatment, which did not measure the callus formation which is mainly the main stage affected by the LIPUS treatment. The CBCT only allowed for measurement of the degree of mineralization of bone (BMN) (34), which in turn does not measure the callus formation. Turunen et al., (35) evaluated the mineral content of callus and cortical bone and found that callus has a lower mineral content.

These findings support the constraint of this study which did not estimate the callus but in turn only measured the bone mineral density which is not really affected by LIPUS treatment. Callus is better measured by ultrasonography device as stated by Wawrzyk et al., (36) that ultrasonography showed high efficacy in measuring or diagnosis of callus formation.

LIPUS increases bone mineralization and stimulates fracture repair by converting the cartilaginous soft callus into mineralized callus, improving the stability of fracture union (37). LIPUS waves create nanomotion at the fracture site, where the mechanical signal is converted into biochemical signals intracellularly. It stimulates the production of cyclooxygenase 2, which promotes prostaglandin E2(PGE2) production. PGE2 triggers osteogenic genes, which facilitate mineralization and endochondral ossification, thereby aiding in fracture healing (38).

Based on the favourable clinical and acceptable radiographical outcomes of our study, it may be concluded that the utilization of low intensity pulsed ultrasound in mandibular fractures, decreases the pain and postoperative complications. Given the limitations of this study, we suggest conducting further studies with a larger sample size and a more extended follow-up period to confirm and validate the current findings and the use of moed scale for callus measurements in Future studies to show more accurate results and also the use of LIPUS in medically compromised patients.

CONFLICT OF INTEREST

The authors state that they have no conflicts of interest.

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REFERENCES

- Ebrahimi T, Moslemi N, Rokn A, Heidari M, Nokhbatolfoghahaie H, Fekrazad R. The influence of low-intensity laser therapy on bone healing. *J Dent (Tehran)*. 2012;9:238-48.
- Einhorn TA, Gerstenfeld LC. Fracture healing: mechanisms and interventions. *Nat Rev Rheumatol*. 2015;11:45-54.
- Xu ZH, Jiang Q, Chen DY, Xiong J, Shi DQ, Yuan T, et al. Extracorporeal shock wave treatment in nonunions of long bone fractures. *Int Orthop*. 2009;33:789-93.
- Erdogan O, Esen E. Biological aspects and clinical importance of ultrasound therapy in bone healing. *J Ultrasound Med*. 2009;28:765-76.
- Karumuri SK, Rastogi T, Beeraka K, Penumatcha MR, Olepu SR. Ultrasound: A Revenant Therapeutic Modality in Dentistry. *J Clin Diagn Res*. 2016;10:Ze08-12.
- Jiang X, Savchenko O, Li Y, Qi S, Yang T, Zhang W, et al. A review of low-intensity pulsed ultrasound for therapeutic applications. *IEEE Trans Biomed Eng*. 2018;66:2704-18.
- Raza H, Saltaji H, Kaur H, Flores-Mir C, El-Bialy T. Effect of low-intensity pulsed ultrasound on distraction osteogenesis treatment time: a meta-analysis of randomized clinical trials. *J Med Ultrasound*. 2016;35:349-58.
- Warden SJ, Fuchs RK, Kessler CK, Avin KG, Cardinal RE, Stewart RL. Ultrasound produced by a conventional therapeutic ultrasound unit accelerates fracture repair. *Phys Ther*. 2006;86:1118-27.
- Patel K, Kumar S, Kathiriya N, Madan S, Shah A, Venkataraghavan K, et al. An Evaluation of the Effect of Therapeutic Ultrasound on Healing of Mandibular Fracture. *Craniomaxillofac Trauma Reconstr*. 2015;8:299-306.
- Gopalan A, Panneerselvam E, Doss GT, Ponvel K, Raja Vb K. Evaluation of Efficacy of Low Intensity Pulsed Ultrasound in Facilitating Mandibular Fracture Healing-A Blinded Randomized Controlled Clinical Trial. *J Oral Maxillofac Surg*. 2020;78:997.e1-.e7.
- Panneerselvam E, Balasubramanian S, Raja VBK, Kannan R, Rajaram K, Rajendra Sharma A. 'Plain lignocaine' vs 'Lignocaine with vasoconstrictor'-Comparative evaluation of pain during administration and post-extraction wound healing by a double blinded randomized controlled clinical trial. *Acta Odontol Scand*. 2016;74:374-9.
- Glória JCR, Fernandes IA, Silveira EMD, Souza GM, Rocha RL, Galvão EL, et al. Comparison of Bite Force with Locking Plates versus Non-Locking Plates in the Treatment of Mandibular Fractures: A Meta-Analysis. *Int Arch Otorhinolaryngol*. 2018;22:181-9.
- Nayak SS, Kamath AT. Surgical Management of Double/Triple Mandibular Fractures Involving the Condylar Segment: Our Perspective. *J Int Soc Prev Community Dent*. 2018;8:87-91.
- Ristow O, Pautke C, Victoria K, Koerdt S, Schwärzler K, Hahnefeld L, et al. Influence of kinesiologic tape on postoperative swelling, pain and trismus after zygomatico-orbital fractures. *J Craniomaxillofac Surg*. 2014;42:469-76.
- Cassetta M, Stefanelli LV, Pacifici A, Pacifici L, Barbato E. How accurate is CBCT in measuring bone density? A comparative CBCT-CT in vitro study. *Clin Implant Dent Relat Res*. 2014;16:471-8.
- El Halawani GN, Ayad SS, Darwish SA, Hassan RS. Evaluation of rhombic three dimensional plate in treatment of mandibular subcondylar fractures in adult patients from alexandria. *Alex Dent J*. 2017;42:56-61.
- Petrie A, Sabin C. *Medical statistics at a glance*. 4th ed. Wiley-Blackwell; 2020.
- Budhreja NJ, Shenoi RS, Badjate SJ, Bang KO, Ingole PD, Kolte VS. Three-dimensional locking plate and conventional miniplates in the treatment of mandibular anterior fractures. *Ann Maxillofac Surg*. 2018;8:73.

19. Scolozzi P, Martinez A, Jaques B. Treatment of linear mandibular fractures using a single 2.0-mm AO locking reconstruction plate: is a second plate necessary? *J Oral Maxillofac Surg.* 2009;67:2636-8.
20. Jadhav A, Mundada B, Deshmukh R, Bhutekar U, Kala A, Waghvani K, et al. Mandibular Ramus Fracture: An Overview of Rare Anatomical Subsite. *Plast Surg Int.* 2015;2015:954314.
21. Sakr K, Farag IA, Zeitoun IM. Review of 509 mandibular fractures treated at the University Hospital, Alexandria, Egypt. *Br J Oral Maxillofac Surg.* 2006;44:107-11.
22. Mabrouk A, Helal H, Mohamed AR, Mahmoud N. Incidence, etiology, and patterns of maxillofacial fractures in ain-shams university, cairo, egypt: a 4-year retrospective study. *Cranio-maxillofac Trauma Reconstr.* 2014;7:224-32.
23. Guimond C, Johnson JV, Marchena JM. Fixation of mandibular angle fractures with a 2.0-mm 3-dimensional curved angle strut plate. *J Maxillofac Surg.* 2005;63:209-14.
24. Tay ABG, Lai JB, Lye KW, Wong WY, Nadkarni NV, Li W, et al. Inferior alveolar nerve injury in trauma-induced mandible fractures. *J Maxillofac Surg.* 2015;73:1328-40.
25. Moreno JC, Fernández A, Ortiz JA, Montalvo JJ. Complication rates associated with different treatments for mandibular fractures. *J Maxillofac Surg.* 2000;58:273-80.
26. van der Windt D, van der Heijden G, van den Berg SGM, Ter Riet G, de Winter AF, Bouter LM. Ultrasound therapy for musculoskeletal disorders: a systematic review. *Pain.* 1999;81:257-71.
27. Al-Daghreer S, Doschak M, Sloan AJ, Major PW, Heo G, Scurtescu C, et al. Effect of low-intensity pulsed ultrasound on orthodontically induced root resorption in beagle dogs. *Ultrasound Med Biol.* 2014;40:1187-96.
28. Azuma Y, Ito M, Harada Y, Takagi H, Ohta T, Jingushi S. Low-intensity pulsed ultrasound accelerates rat femoral fracture healing by acting on the various cellular reactions in the fracture callus. *J Bone Miner Res.* 2001;16:671-80.
29. Bosshardt DD, Degen T, Lang NP. Sequence of protein expression of bone sialoprotein and osteopontin at the developing interface between repair cementum and dentin in human deciduous teeth. *Cell Tissue Res.* 2005;320:399-407.
30. Chen YJ, Wang CJ, Yang KD, Chang PR, Huang HC, Huang YT, et al. Pertussis toxin-sensitive Galphai protein and ERK-dependent pathways mediate ultrasound promotion of osteogenic transcription in human osteoblasts. *FEBS Lett.* 2003;554:154-8.
31. Claes L, Willie B. The enhancement of bone regeneration by ultrasound. *Prog Biophys Mol Biol.* 2007;93:384-98.
32. Ahmed EAE, Eldibany MM, Melek LF, Abdelnaby HM. Comparative study between the effect of shockwave therapy and low-intensity pulsed ultrasound (lipus) on bone healing of mandibular fractures (clinical & radiographic study). *Alex Dent J.* 2022;47:29-35.
33. Rice N, Polyzois I, Ekanayake K, Omer O, Stassen LF. The management of osteoradionecrosis of the jaws--a review. *Surgeon.* 2015;13:101-9.
34. Kim DG. Can dental cone beam computed tomography assess bone mineral density? *J Bone Metab.* 2014;21:117-26.
35. Turunen MJ, Lages S, Labrador A, Olsson U, Tägil M, Jurvelin JS, et al. Evaluation of composition and mineral structure of callus tissue in rat femoral fracture. *J Biomed Opt.* 2014;19:025003.
36. Wawrzyk M, Sokal J, Andrzejewska E, Przewratil P. The Role of Ultrasound Imaging of Callus Formation in the Treatment of Long Bone Fractures in Children. *Pol J Radiol.* 2015;80:473-8.
37. Saito M, Fujii K, Tanaka T, Soshi S. Effect of low- and high-intensity pulsed ultrasound on collagen post-translational modifications in MC3T3-E1 osteoblasts. *Calcif Tissue Int.* 2004;75:384-95.
38. Harrison A, Lin S, Pounder N, Mikuni-Takagaki Y. Mode & mechanism of low intensity pulsed ultrasound (LIPUS) in fracture repair. *Ultrasonics.* 2016;70:45-52.