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Is Low Intensity Pulsed Ultrasound (LIPUS) Effective in the Success Rate of Alveolar Cleft Graft?

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Abstract

Background: The aim of this study was to investigate the efficacy of the low intensity pulsed ultrasound in reconstruction of the alveolar cleft area after autologous bone grafting.

Methods: In this study, 14 patients with unilateral or bilateral cleft lip and palate aged between 9 to 13 years, were selected. Seven of the patients received only the autologous bone graft and the remaining seven underwent alveolar bone graft, and one week after transplantation were subjected to LIPUS waves for five minutes at a frequency of 1 MHz and 100 mW in the area of the graft for a period of five weeks (15 sessions). CBCT images were immediately taken after surgery and three months later. In CBCTs, bone mass was measured with two components of height and bone thickness and the quality was measured by evaluating the bone density by means of the Hounsfield Uniform (HU) mean. Data analysis was done via SPSS version 16 software and using paired t, independent t, and Mann-Whitney and Wilcoxon tests. A significance level of 0.05 was considered.

Results: The mean changes of the sagittal thickness (P=.944), sagittal height (P=.482), and axial thickness (P=.242) before and after surgery, in contrast to the axial height (P=.357) and density (P=.443), were less in the control group than the intervention group, but the differences were not significant for any of variables. In the intervention and control groups, in comparison to the immediate results after surgery, the mean values of the sagittal thickness, sagittal height, axial thickness, and axial height decreased significantly three months later; but the mean loss in density was not significant.

Conclusion: Ultrasound in repairing alveolar defect in patients with cleft palate has no significant effect on clinical success criteria.

Key Words: Alveolar bone graft, Cleft lip and palate, Low intensity pulsed ultrasound.

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1- INTRODUCTION

Orofacial clefts are one of the most common abnormalities in the craniofacial area (1). In general, the incidence of cleft lip and palate in different societies vary from 1 to 1.5 in 1,000 births (2, 3). Bone graft in the gap region is used as a common technique for repairing defects in patients with cleft lips and palates; however, there is uncertainty about the right time to do this (4). Sometime initial bone grafting is performed at the same time as lip reconstruction before the age of two years, but satisfactory results from this technique do not exist at this age range (5, 6). In the mixed dentition procedure, the secondary bone graft is performed within the age range of 7 to 12 years (7-14). In different studies, the use of alloplastic (12) and autogenous (6-20) transplants for the reconstruction of alveolar clefts has been studied and compared (12).

Among the methods used to better reconstruct bone tissue, low intensity pulsed ultrasound (LIPUS) has been widely used in medicine as a therapeutic tool (21). Unlike medical imaging (which transmits ultrasound waves to tissue and processes a reversible waveform for image production), ultrasound therapy is a one-way energy application that is performed by an appliance of an audio device with a frequency of 1 to 3 MHz and an intensity between 0.1 to 3 watts per square centimeter (22). The ultrasound energy causes the molecules to melt through acoustic waves. This increased molecular movement causes frictional heat and, as a result, an increase in the temperature of the tissue. These effects of ultrasound are said to increase the collagen's flexibility, increase the speed of nervous conduction, change in local perfusion, increase enzyme activity, change muscle contractility activity, and increase the nociceptive threshold (23). Ultrasound is often used for the benefits of heat generation, while some recent researches in this field have indicated that the non-thermal effects of ultrasound are also effective and even predominant (24). The mechanisms that are thought to be effective in generating these non-thermal effects include cavitation and acoustic streaming or micro-streaming. It has been said that these phenomena increase cell permeability and influence the process of cellular growth and thus improve tissue repair.

In previous studies, LIPUS has been accepted to promote and improve bone fractures. In addition, the effect of LIPUS on soft tissue repair has attracted much attention, and many studies have been conducted to evaluate the potential effects of LIPUS on hard and soft tissue engineering (25). Chen et al. investigated the effects of LIPUS as supplemental therapy on osteonecrosis of the alveolar bone graft and showed that LIPUS helps to prevent osteonecrosis as a biophysical technique (26). In addition, Toy et al. examined the effects of low pulsed ultrasound waves on bone formation after maxillary expansion in mice. They concluded that cell activation in the LIPUS group was greater than that in the control group, so LIPUS could be accepted as an effective strategy to improve the formation of sutural bone (27).

Since alveolar graft is one of the basic treatments for patients with cleft lip and palate, and due to the importance of the impact of therapeutic methods and techniques on the success of treatments of these patients, in this study we investigated the effect of the usage of low intensity ultrasound on the success of alveolar bone graft.

2- METHODS

2-1. Sampling

Using purpose-oriented sampling and random allocation, in two treatment centers (Orthodontic Department of Mashhad Dental School and Cleft Lip and

Palate Clinic of Akbar Children's Hospital), 14 patients with unilateral or bilateral non-syndromic alveolar cleft between the ages of 9 to 13 years, who were candidates for alveolar graft, were selected. The type of intervention was explained to the patients and their parents; and informed consent was obtained from them.

2-2. Patient preparation before surgery

For all patients, standard records including facial and intraoral photographs, panoramic radiographs and study models were prepared. In all patients expansion was considered before surgery. Expansion was performed via quad helix or hyrax. Quad helix was made if the width of the palate was narrow to accommodate hyrax. Hyrax or quad helix were cemented with glass ionomer cement. Patients were instructed to open the hyrax screw every other day and quad helix was made of 0.8 mm SS wire, which was activated 3 mm on each side. The treatment continued until the dental relationships were overcorrected and the appliances were kept in the mouth for another three months for retention.

2-3. Surgery

In both groups, standard alveolar bone grafting was performed, with the mucoperiosteal flap being excised in the cleft region. The nasal floor and buccal flaps were prepared (**Fig. 1**) and the defect area was prepared for transplantation. The autogenous bone (cortical and spongy) was then removed from the iliac region and inserted into the affected area. It should be noted that in patients with bilateral clefts, only one side underwent surgery and the same side was examined. All surgeries were performed by one surgeon.

Fig. 1: Alveolar bone grafting

2-4. Ultrasound application

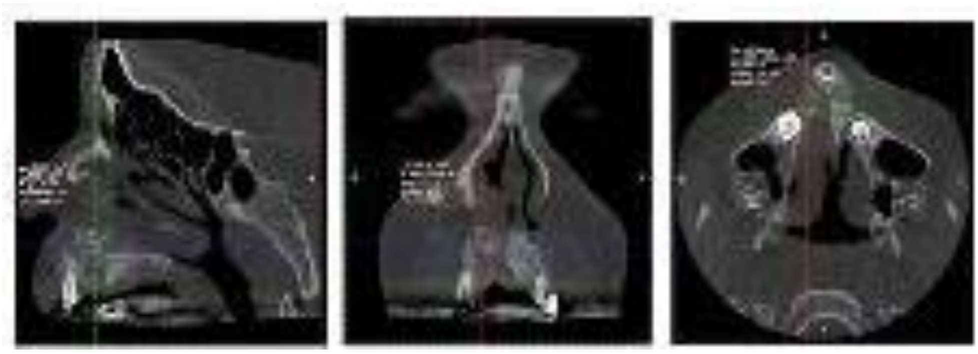
In seven patients, one week after surgery, the low-intensity pulsed ultrasound waves were used every other day for five minutes at 1 MHz frequency and 100 mW in rotational movements on the skin of the lips of the operated side (**Fig. 2**). This application continued for a total of fifteen sessions in five weeks. The waves were applied with a standard head size of 5 cm^2 using COMBINED 200 (EME, Italy). This step was performed according to the method proposed by Robertson et al (28).

2-5. Radiographic evaluation

Radiographic examination was performed to evaluate the quality and quantity of bone formed in the graft area. CBCT diagnostic radiography was used and the results were interpreted by an expert oral radiologist.

Fig. 2: LIPUS application

CBCT images were taken about one week and three months after surgery. In radiographic examination, bone quantity was measured with two components of height and bone thickness of the area and quality was measured by means of the Hounsfield Unit (HU). All CBCT images were acquired by PLANMECA Promax 3D Max (Helsinki, Finland) with a voxel size of 200 µm and FOV (field of view) dimension of 100 * 90 * 90 mm^3. The PLANMECA Romexis 4.4.3 software was used to examine CBCT images and superimposition (**Fig. 3** and **4**).



(a) (b) (c)

Fig. 3: CBCT images immediately after alveolar bone graft a: Axial view, b: Frontal view, c: Occlusal view

(a) (b) (c)

Fig. 4: CBCT images 3 months after alveolar bone graft a: Axial view, b: Frontal view, c: Occlusal view

The superimposition method was that the two CBCT images were matched in three coronal, axial, and sagittal views, and the joint locations including skull base, orbit and other joint points were automatically matched by the software and it was then reviewed by the user for possible troubleshooting. Sites that may have changed during treatment or over time were not considered during superimposition. This method compared the image one week after surgery with the image three months later. The graft in the CBCT was distinct from the surrounding bone.

Mid-sagittal cut was done on the superimposition and images of one week and three months after surgery were displayed separately. On the sides of this mid-sagittal cut, the cuts were struck down 2 mm apart. Height of the graft was measured in different cuts and averaged. Buccolingual thickness was also evaluated and averaged. The mean density was measured in a circle that was adjustable in size. If resorption was seen in the circumferential margins of the circle bone, the smaller circle would be adjusted. However, the diameter of the circle was quite similar in the radiographs after one week and three months after surgery.

2-6. Data analysis

Sample size: According to Alonso et al. (29), at the first type error of 5% and the second type error of 20%, the number of samples in each group was calculated as six patients. However, to increase confidence, the number of samples was increased to seven patients. Statistical methods: Paired t test, Mann-Whitney and Wilcoxon tests were used for statistical analyses via SPSS software version 16.

3- RESULTS

In this study, 14 orthodontic patients with cleft lip and palate, including eight males (57.1%) and six females (42.9%) aged 10 to 13 years were evaluated. First, their demographic information was reviewed. Seven patients were placed in the intervention group and seven patients in the control group. In the intervention and control groups, three females (42.9%) and four males (57.1%) were present. According to the statistical test results, the gender distribution of the two groups was quite similar (p=1.00). The age range was 10-12 years in the intervention group and 10-13 years in the control group, and there was no significant difference between the groups (p=0.390).

Table 1 presents the mean, standard deviation, minimum, maximum, and median of all the variables in the intervention and control groups, respectively. According to the table, immediately after surgery, the means of sagittal thickness, sagittal height, axial height, and density in the control group were higher than those in the intervention group, but the mean of the axial thickness in the intervention group was higher than that in the control group. Only the difference of density was significant between the two groups (p=0.045). Thus, the two groups were homogeneous for all variables except density.

Table 2 presents the mean, standard deviation, minimum, maximum, and median of all the variables in the intervention and control groups, respectively. As seen, three months later, the means of all variables of sagittal thickness, sagittal height, axial thickness, axial height, and density were higher in the control group than those in the intervention group. However, the difference between the two groups was significant only for sagittal height (p=0.05, 0.021) and was not significant for the other variables.

Table 3 shows that the mean changes of sagittal thickness, sagittal height, and axial thickness in the control group were lower than those in the intervention group, but the mean changes of axial height and density in the intervention group were lower than those in the control group, but the difference between the two groups was not significant for any of the variables. The two groups were similar in terms of changes during time (one week and three months after surgery).

4- DISCUSSION

Bone repair is one of the most amazing homeostatic activities in the body (30). Following fracture or transplantation, inflammation, repair, and reconstruction are performed consecutively to restore bone mineralization. The process is slow; so it can cause problems such as fractures and disruption of the treatment process (31). This has prompted researchers to look for different therapies to accelerate the bone healing process (32).

Table-1: Comparing the variables of sagittal thickness, sagittal height, axial thickness, axial height and density immediately after surgery between the intervention and control groups

variable	group	N	mean	Standard deviation	Min	Max	Median	Independent T. test results
Sagittal thickness (mm)	intervention	7	9.88	2.28	7.73	14.70	9.53	Z^*=0.96
	control	7	12.40	4.33	6.40	18.37	13.35	P=0.338
Sagittal height (mm)	intervention	7	9.84	3.21	6.80	15.23	8.13	T=1.61
	control	7	12.86	3.80	9.75	20.53	11.20	P=0.134
Axial thickness (mm)	intervention	7	10.71	2.40	6.70	13.50	11.18	T=1.01
	control	7	9.27	2.92	5.00	12.83	10.37	P=0.334
Axial height (mm)	intervention	7	8.35	1.83	6.63	12.23	8.05	Z^*=1.34
	control	7	10.64	3.51	5.15	15.15	11.90	P=0.180
Density (Hounsfield unit)	intervention	7	266.53	57.62	163.83	349.86	270.45	T=2.24
	control	7	403.47	151.26	170.71	668.08	390.50	P=0.045

*: Mann-whitney test

Table-2: Comparing sagittal thickness, sagittal height, axial thickness, axial thickness and density three months after the surgery between the intervention and control groups

variable	group	N	mean	Standard deviation	Min	Max	Median	Independent T. test results
Sagittal thickness (mm)	intervention	7	6.00	3.67	0.00	10.85	7.20	Z*=0.57 P=0.565
	control	7	8.65	4.68	5.20	18.27	6.75	
Sagittal height (mm)	intervention	7	5.21	2.29	0.00	10.63	4.30	Z*=2.31 P=0.021
	control	7	9.66	3.55	6.60	15.03	7.80	
Axial thickness (mm)	intervention	7	5.93	2.84	0.00	8.13	7.10	Z*=0.32 P=0.749
	control	7	6.40	2.36	4.30	10.45	4.83	
Axial height (mm)	intervention	7	5.76	1.72	3.07	8.13	5.63	T=1.30 P=0.219
	control	7	7.11	2.15	3.80	9.50	7.20	
Density (Hounsfield unit)	intervention	7	229.49	120.99	78.79	445.26	204.12	T=1.20 P=0.254
	control	7	317.67	152.56	155.32	615.37	336.34	

*: Mann whitney – test

Table-3: Comparing the changes in the variables of sagittal thickness, sagittal height, axial thickness, axial height and density immediately and three months after surgery between the intervention and control groups

variable	group	N	mean	Standard deviation	Min	Max	Median	Independent T. test results
Sagittal thickness changes(mm)	intervention	7	3.88	3.03	0.45	9.53	3.85	T=0.07 P=0.944
	control	7	3.75	3.60	0.10	9.46	2.08	
Sagittal height changes(mm)	intervention	7	4.62	3.50	1.23	12.07	3.83	Z*=0.70 P=0.482
	control	7	3.20	1.76	0.25	5.50	3.50	
Axial thickness changes(mm)	intervention	7	4.78	2.81	1.60	10.25	5.17	T=1.23 P=0.242
	control	7	2.87	3.01	0.35	8.00	1.80	
Axial height changes(mm)	intervention	7	2.54	1.37	0.35	4.10	3.23	T=0.96 P=0.357
	control	7	3.53	2.35	0.15	6.30	3.90	
Density changes (Hounsfield unit)	intervention	7	37.08	76.96	-95.40	106.92	67.52	T=0.79 P=0.443
	control	7	85.80	143.18	-165.63	262.16	65.19	

*: Mann-whitney test

One of the procedures that have recently received attention is the use of ultrasound waves. Although many studies have been conducted to evaluate the potential effects of low intensity pulsed ultrasound on soft and hard tissue engineering (25), there has been no study on alveolar cleft reconstructions. To evaluate and compare the therapeutic outcomes in different techniques, evaluation of the amount of bone formed and the height and location of the bone in the alveolar cleft area is necessary. Given the alveolar cleft and considering that there is not enough clinical studies done to evaluate and compare the aforementioned methods, we aimed to investigate the use of low-intensity ultrasound compared to autogenous bone in the repair of alveolar cleft defect. In the present study, similar to other studies, 1 MHz frequency of ultrasound waves was used. The depth of penetration of LIPUS waves is approximately 10 mm, so the application of the head on the skin is appropriate for reaching the bone and graft site (28).

According to the present study, the mean difference between pre- and postoperative variables of sagittal thickness, sagittal height, and axial thickness was less in the control group than that in the intervention group; but the difference between the two groups was not significant for any of the variables. This result indicates that in general, the two groups were similar in terms of changes between the pre- and postoperative methods.

There was no similar research to compare in this area, but our results were not consistent with those studies that showed a positive effect of ultrasound on the fracture healing process (33-35). On the other hand, our results are consistent with the findings of some other researchers reporting no effect for ultrasound on bone repair (36-39).

Differences in the results of research studies investigating the effect of ultrasound on bone tissue and bone fracture healing may be due to differences in the use of different doses and times, the use of ultrasound in human or animal models, and sometimes the use of ultrasound in vitro.

The use of ultrasound in the culture of cells isolated from the body and from other tissues and the general circulation process and various factors including hormones as well as immune and growth factors that flow through the bloodstream and tissue cells can be very different from the effect of ultrasound on the bone tissue in the living organism. Therefore, the positive or negative effects of one or more factors, including ultrasound on the cell or living tissue, can be confirmed in the studies launched in vivo.

Using different methods that produce bone defects or fractures and the use of different intensities of ultrasound cause the results of the research to be different. In selecting the effective intensity of ultrasound, the results have not been uniformly reported and each researcher has suggested a dose according to his/her experience.

Research on the repair of femoral fractures using ultrasound has shown that osteopontin mRNA levels are significantly increased (40). On the other hand, histological examination of tissues after receiving ultrasound at the time of tissue repair and bone healing have shown that the ultrasound effect may be restricted to soft tissues and has no effect on cells located in hard and calcified tissues (41).

5- CONCLUSION

Given the limitations of this study, the following results were obtained:

a) Mean changes in sagittal thickness, sagittal height, and axial thickness were lower in the control group than those in the intervention group, but the difference between the two groups was not significant for any of the variables.

b) In the intervention and control group, mean sagittal thickness, sagittal height, axial thickness, and axial thickness were significantly decreased three months after surgery, but the mean decrease in density was not significant.

c) Low intensity pulsed ultrasound with the frequency of 1 MHz and intensity of 0.1 W/Cm^2 has no significant effect on the clinical success criteria in repairing alveolar defects in patients with cleft palate.

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