EGYPTIAN DENTAL JOURNAL
www.eda-egypt.org
VOL. 69, 2619:2625, OCTOBER, 2023
PRINT ISSN 0070-9484 • ONLINE ISSN 2090-2360
ORAL SURGERY
Submit Date : 12-07-2023 • Accept Date : 16-09-2023 • Available online: 01-10-2023 • DOI : 10.21608/EDJ.2023.221678.2628

BONE GAIN IN ALVEOLAR CLEFT REPAIR COMBINING HYALURONIC ACID WITH ANTERIOR ILIAC CREST CORTICOCANCELLOUS GRAFT

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ABSTRACT

Purpose: This study aims to evaluate the osteogenic effect of adding Hyaluronic acid (HLA) gel to anterior iliac crest corticocancellous graft for secondary alveolar cleft repair.

Methods: The study included forty patients with unilateral alveolar cleft scheduled for repair using autogenous bone graft from the iliac crest. The included patients were divided into two groups. HLA group underwent alveolar bone grafting mixed with Hyaluronic acid gel while the control group underwent alveolar bone grafting alone from the iliac crest. CBCT images were obtained at 1 week and at 6 months following the procedure. The gained bone volume and density were assessed and compared between the two groups.

Results: At the end of the follow up period, the HLA group showed more bone gain with higher density compared to the control group.

Conclusion: The addition of Hyaluronic acid to bone graft showed uneventful healing and showed an osteogenic potential with increased amount of bone gain.

Keyword: Alveolar cleft grafting; HLA; CBCT; Hyaluronic acid

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INTRODUCTION

The craniofacial development of the oral cavity plays a critical role in the maxillofacial region with its components. It plays an outstanding role in feeding, speech, breathing and immunity. The risk of the development of the oral cavity becomes very much evident if any disturbance occurs. This may result in palatal and alveolar cleft. Nutrition, oral hygiene, respiratory infections, speech functions, maxillofacial deformity and psychological problems will be problematic during the long period of management of the cleft patient. Therefore, the management is made with a multidisciplinary approach[1].

Alveolar cleft reconstruction can be described as the procedure to be performed on alveolar cleft patients to close the oronasal fistula, provide sufficient bone for the erupting permanent canine and/or the lateral incisor, unify the dental arch, reconstruct the nasal floor and lift the alar base up, restore the continuity of gingival and alveolar tissues closing the periodontal defect, creating the vestibule and providing a hygienic oral environment along with minimal scarring and maxillary growth restriction[1,2].

Bone grafting is the golden standard in the management of the patient with alveolar cleft. An inappropriate or delayed primary intervention can lead to a defect that could be detrimental for the quality of life. A complete bony alveolar arch integrity should be aimed to facilitate stability of the dentition and tooth eruption. In addition to its important role as a pillar for the facial aesthetics in the face, lips, and nose.[3]

Autogenous bone grafts are used greatly in oral and maxillofacial surgery to reconstruct bony defects. Many donor sites have been suggested including the iliac crest, proximal tibia, rib, mandibular symphysis, and calvaria bone. However, every site has its potential drawbacks[4,5]. Previous studies concluded that the use of corticocancellous blocks as grafts for restoring facial bony defects as an onlay can maintain their volume when a membranous bone source is involved in comparison to endochondral bone[6]. The alveolar process defect in cleft patients is a marginal defect affecting the continuity of the nasal pyriform and the alveolus. Therefore, alveolar cleft grafting is considered to be an inlay graft between the osseous segments, rather than an onlay graft[6,7].

The use of iliac crest bone grafting is considered as the "gold standard". The anterior iliac crest has the superiority of providing an increased volume of cancellous bone in addition to its accessibility. The use of cancellous bone is more preferable because of its ease in harvesting, reduced intraoperative time, and higher content of osteogenic precursor cells. However, the surgical approach involves the reflection of musculo-periosteal flaps during surgical exposure of the iliac crest. This can result in significant post-operative complications including hematoma, pain, discomfort and gait disturbances[2,8–10].

Hyaluronic acid (HLA, also known as hyaluronan or hyaluronate) was first discovered and isolated from the vitreous body of cow's eyes. The proposed name "hyaluronic acid" was derived from "hyalos," meaning glass in Greek word, and "uronic acid". HLA is the simplest glycosaminoglycan (GAG) and the only GAG that is not synthesized in the Golgi apparatus, and it is a major component in the extracellular matrix and HLA is found in several soft connective tissues, including synovial fluid, vitreous body of eye, cartilage, and skin and it is also found in lung, kidney, brain, and muscle tissues. The wide existence throughout all mammals suggests that HLA is a biomolecule of considerable importance. Hyaluronic acid (HLA) is a polysaccharide containing D-glucuronic acid and N acetylglucosamine and it is rich in the human body especially in the extracellular space and load-bearing joints. In addition, HLA is also involved in skin moisture due to its hydrophilic nature and it has been reported that HLA plays a role in the treatment of knee and temporomandibular osteoarthritis[11–14].

In dentistry, HLA showed anti-inflammatory, antioxidant, and antibacterial features in treating periodontal diseases and provided its viscoelastic properties, it played a role as a space maintainer during the treatment of periodontal diseases. Recently HLA has played a role in tissue engineering as a biomaterial while several studies established the ability of HLA to enhance extracellular matrix production and accelerating new bone formation by enhancing mesenchymal cells differentiation. These findings encouraged several researchers to use HLA as implant surface treatment and residual ridge preservation after tooth extraction with favourable results[11–13,15–20]

The aim of this study is to assess that osteogenic potential the HLA may have when added to the iliac crest corticocancellous bone graft in unilateral alveolar cleft repair.

MATERIALS AND METHODS

From December 2019 to November 2021, 40 patients with unilateral alveolar cleft in the mixed dentition stage prior to permanent maxillary canine (if present) eruption were enrolled and assigned to two groups. The patient allocation was done based on patient enrolment numbers where patients with odd numbers were assigned to HLA group while those with even numbers were assigned to the control group.

All patients had their alveolar clefts repaired during the mixed dentition period as soon as radiographic evidence of having their permanent maxillary canine (if present) roots half formed. Careful patient and family history, clinical examination to assess patient's fitness for surgery were performed. A preoperative Cone Beam Computed Tomography scan (CBCT) for the alveolar cleft was obtained, in addition to plain pelvic radiograph to exclude any pathologic condition that would interfere with the graft harvesting procedure from the anterior iliac crest (Figure 1).

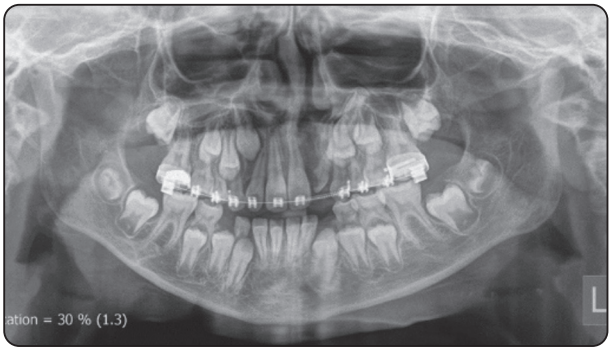

Fig. (1): Preoperative panoramic X-ray Scan x ray showing a unilateral alveolar cleft

The surgical procedure involved mucosal flap repair using lateral sliding flap in the standard fashion (Figure 2). Particulate corticocancellous bone was taken from the anterior iliac crest using trephine bone collector. In HLA group, corticocancellous iliac bone graft was placed at the alveolar cleft defect mixed with around 1 cubic centimetre of Sodium Hyaluronate while control group patients received only corticocancellous iliac bone (Figure 3). Then the flaps were closed with sutures to obtain the best seal possible over the graft (Figure 4). The patients' wounds were assessed for the first week for hygiene and healing progress. Postoperative CBCT scans were obtained within a week after surgery and at the end of the 6 months follow-up period

Volumetric measurements

On the preoperative CBCT, the volume of the defect was measured from the nasal spine to the level of the interdental bone of the teeth adjacent to the cleft. To measure the volume of the defect, the bony structure on the scan was segmented and the volume of the segment was calculated directly by the software. On the postoperative CBCTs (immediate and 6 months), the same software was used to measure the amount of bone fill as follows: the bone structure was segmented (this included the graft), and the volume of the segment was then automatically calculated. Subtracting the volumes from each other gave the volume of the unfilled area. The volume of the graft can now be

Fig. (2): Showing surgical exposure of the unilateral cleft borders

Fig. (4): showing closure of the alveolar cleft after alveolar grafting

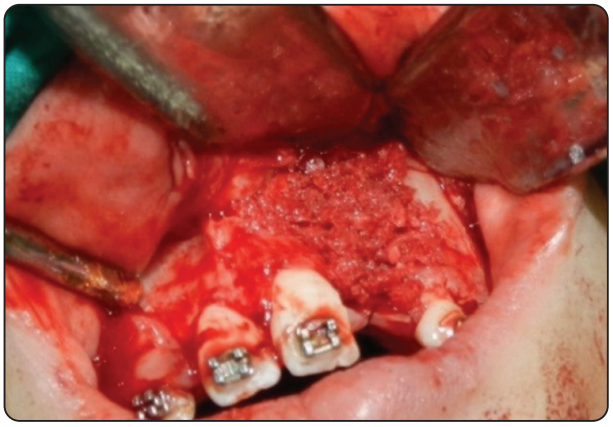

Fig. (3): The graft mixed with sodium hyaluronate gel packed in place

easily calculated by subtracting the volume of the unfilled area from the original volume of the defect which was obtained from the preoperative CBCT (Figure 5).

Densitometric measurements

Bone density was measured for each case on the postoperative CBCTs (immediate and 6 months) using the same software and measurements were also made on the axial cuts. Several axial cuts were selected for each case to cover varying areas of the graft material. On these cuts the density of the graft and the density of the native alveolar bone on the contralateral side were measured and the mean density of all recorded values was calculated and included into further analysis.

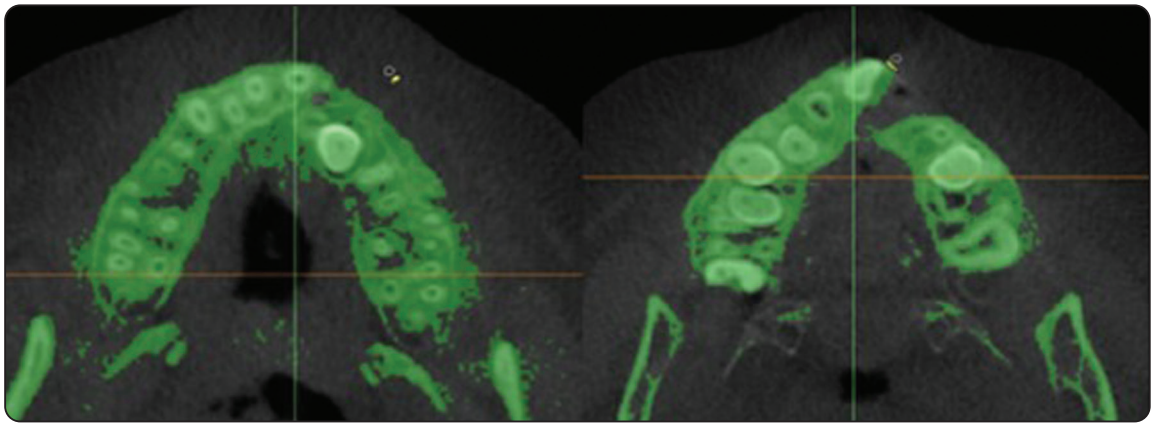

Fig. (5): Calculating the volume of the defect

The volumetric and densitometric measurements were performed by the same examiner twice in two weeks interval and the average of the two trials was taken and involved in the statistical analysis

Statistical Analysis

Statistical analysis was performed using SPSS (Statistical package for the social sciences). Data were represented as mean ± standard deviation and explored for normality using Kolmogorov-Smirnov and Shapiro-Wilk tests. For normally distributed data, Student's t-test will be used to compare variables between the two groups while non- normally distributed data, Mann-Whitney U test will used to compare variables between the two groups and the test result was considered statistically significant if the P- value was equal or less than 0.05.

This study was approved by the research ethics committee of the Faculty of Dentistry, Future University in Egypt.

RESULTS

This study was conducted on 40 patients with mean age 10.15 ± 0.95. The average defect size was 516.1 mm ± 77.5. All patients tolerated the procedure well with the early postoperative period indicating closure of the oronasal fistula. No complications were reported by any of the patients till the end of the follow up period. Healing at the alveolar cleft area was uneventful in all patients of both groups, except for a minimal area of dehiscence on the labial flap that was noted on patient number 3 of the control group. Saline irrigation was repeatedly done for this area 3 times a week along with oral hygiene measures. Spontaneous healing occurred after 2 weeks without further complications and no additonal intervention was needed. As regards to morbidity of the donor site, no long term sensory or functional deficits were reported by any of the patients. The normal gait was restored completely by the second week and all patients were able to return to their normal daily activity.

Percentage of bone gain was higher for HLA group (120.3±16.4 %) compared to the control group (92.2±3.4 %), (P value <0.001). Graft density after 6 months was higher for HLA group (438.69 + 89.21) compared to the control group (361.27+12.89) (P value <0.001) as shown in Table 1, (Figure 6,7).

TABLE (1) Analysis of the volumetric and densitometric measurements

		Volume						Density			
		Age	Defect	Immediate	% Bone fill	6m	% Bone fill 6	% Bone gain	Graft 0	Graft 6	Graft 6-0
HLA group	Mean	10.15	493.35	360.63	73.44	426.30	86.48	120.29	360.92	438.69	77.76
	St. Dev	0.95	34.67	70.83	15.34	59.96	11.14	16.41	96.75	89.21	68.77
Control group	Mean	9.99	538.85	499.40	92.56	459.35	85.26	92.17	348.44	361.27	12.83
	St. Dev	0.97	100.24	97.72	3.88	88.79	3.75	3.43	15.64	12.89	9.47
	t	0.613	0.063	0.000	0.000	0.176	0.645	0.000	0.572	0.000	0.000
	P value	0.61	0.06	< 0.001	< 0.001	0.18	0.64	< 0.001	0.57	< 0.001	< 0.001

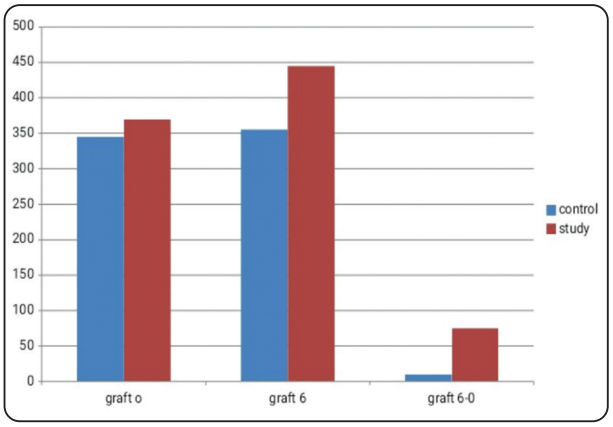

Fig. (6) Histogram showing changes in bone density

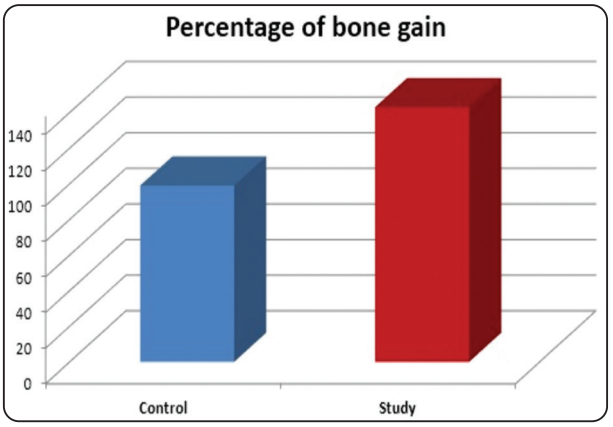

Fig. (7) Histogram showing changes in bone volume

DISCUSSION

The reconstruction of alveolar cleft defects is an inevitable procedure in the overall management of a cleft patient and it is generally agreed upon that autogenous bone grafts are superior to any other type of bone graft as they are osteogenic, supplying living cells that aid in new bone formation, osteoinductive, inducing new bone formation, and osteoconductive, acting as a scaffold upon which new bone is formed. Moreover, autogenous bone eliminates the risk of disease transmission and they lack the possibility of inducing antigen-antibody reaction[2,21].

A recent In Vivo study suggested the hyaluronic acid can also increase angiogenesis and bone remodelling as well as healing capacity when used with bone substitutes[22]. Another animal study suggested using hyaluronic acid with tricalcium phosphate particles for calvaria bone defects with similar findings[23]. Although these results were encouraging to use a bone substitute with hyaluronic acid for alveolar cleft reconstruction, the authors opted this out. The highly specialized nature of the alveolar bone and the need to orthodontically move teeth through the grafted defect or the need to insert dental implant were the main concern that opposed the idea of using any material other than autogenous bone.

Around one cubic centimetre of Sodium Hyaluronate was mixed with the bone and this amount was slightly more in relatively larger defects as the amount of the graft increased. The HLA improved workability of the mix making it easier to handle and to apply into the defect. These findings are similar to other studies' that also reported histological evidence of increased angiogenesis and bone remodelling[12,13,24].

The results are in accordance with previous studies which found out that the bone regeneration and healing occurs in less time when hyaluronic acid was used with autogenous bone. It is documented that after alveolar cleft repair, loss of the grafted bone volume progressively occurs to the extent that implant placement might need additional ridge augmentation prior to implant placement. The amount and quality of gained bone might reduce that need to augment the residual ridge[14,24–26].

The authors concluded that HLA gel addition to autogenous bone grafts plays a role in augmentation of newly formed bone and thus decreases the need of harvesting larger volumes of bone from donor sites and this decreases the morbidity and side effects of bone harvesting while improving bone quality and enhancing bone remodelling.

Authors declare no conflict of interest

This study was self-funded

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