Evaluating the Efficacy of Bone Marrow Aspiration Added to Grafts in Oral defects: 2 Clinical Reports

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Abstract

Background: Autogenous bone has long been considered the "gold standard" in bone grafting materials. A novel technique has been developed to harvest patients own bone marrow aspirate from the iliac crest as the source for obtaining adult stem cells, progenitor cells for osteoblasts, growth factors and cytokines. The aim of this study is to introduce and evaluate the bone marrow aspirating technique as it is described and applied to oral bone grafting surgery.

Materials and methods: A maximum of 4 cc bone marrow was aspirated from a single site for two patients. In the first patient, two block allograft sources for scaffolding were used for the anterior ridge augmentation procedure. The blocks were shaped, injected with heparinized marrow aspirate, and secured in the surgical site with bone screws. In the second patient, pure phase β-tricalcium phosphate particulates were mixed with bone marrow aspirate for augmentation of the right and left maxillary sinuses.

Results: After approximately 5 months of healing, a bone core biopsy sample was taken from the sinus augmentation site with a trephine drill. Histomorphometric analysis of the sample revealed 36% new vital bone formation. Dental implants were delivered and ultimately restored without complication. In the patient treated with block allografts, the grafts integrated with the host bone demonstrating good vitality, vascularity, and adequate thickness to place 3 dental implants. Neither patient experienced any complications from the intraoral surgical sites or at the bone marrow aspiration sites.

Conclusion: Histomorphometric analysis supports the clinical findings that bone marrow aspirate combined with allograft or alloplast grafts are effective alternatives to autogenous bone grafts in the oral region. While it does require a secondary harvest site for acquisition of marrow aspirate, patient morbidity is minimal and offers an alternative to the conventional method of harvesting autogenous bone.

KEY WORDS: Autogenous bone, Iliac crest, bone marrow aspirate, adult stem cells, bone graft

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INTRODUCTION

There are a plethora of grafting options to support bone grafting as an adjunct to dental implant therapy. While a large variety of grafting techniques have been developed, the bone grafts used to accomplish these techniques are not created equally. Autogenous bone is still considered to be the "gold standard" in the realm of grafting materials as it is the only material that provides all three fundamental mechanisms of osteoconduction, osteoinduction, and osteogenesis. However, autogenous bone may increase morbidity and complications for the patient as it requires a second surgical site for harvesting donor bone.

To avoid secondary surgical donor sites, bone allografts, xenografts, and alloplasts may be used. While the supply of these products is virtually unlimited, they do not contain the viable cells that are present in autogenous grafts. To solve this problem, a novel and simple surgical technique that retains the standard of autogenous bone grafting without its inherent drawbacks and limitations has been developed.[1] This technique utilizes the patient's own iliac crest as the source for obtaining adult stem cells that can differentiate to osteogenic progeny for osteoblast formation and hematopoietic stem cells for endothelial cell formation.[2] The vital cells and growth factors are aspirated through the iliac crest with a minimally invasive needle aspirating technique. While this is technically a secondary surgical site, patient morbidity associated with the needle aspiration is minimal. The aspirate is then combined with allograft, xenograft , or alloplast graft materials that serve as a scaffold or a matrix for the grafting site. The aim of this study is to introduce and evaluate, by two clinical case reports, the technique proposed.

Unlike the procedures for harvesting autogenous bone, the aspiration of bone marrow does not require an open surgical site. This technique was developed in 2005[3] and is a relatively simple procedure with minimal morbidity or complication that can be performed in an outpatient setting. The bone marrow aspirant is combined with a matrix used to augment osseous defects. The large flat bones of the body are rich in red active marrow and are an excellent source of adult stem cells and osteoprogenitor cells. Three possible locations are available for harvesting bone marrow from an adult patient: 1) the anterior iliac crest; 2) the posterior ileum; 3) the sternum. The anterior Iliac crest is selected as the primary location due to its relative ease of access and safety.

Bone marrow aspirant is not used alone to augment bony defects. An osteoconductive scaffold is necessary to serve as a matrix and vehicle for the aspirated cells to attach and mature. The authors recommend the use of a porous, slowly resorbable, biodegradable, and biocompatible scaffold material. Beta-tricalcium phosphate β-TCP) is an excellent material of choice as it will facilitate cell ingrowth and vascularization of the graft from the surrounding tissues.[4-6] If other materials such as block allografts are used, the graft material must be stabilized at the recipient site with screws, guided bone regenerative membranes, and/or titanium mesh depending on the procedure.

Smiler and Soltan[7,8] published their clinical findings and histomorphomeric analysis for bone marrow aspiration procedures mixed with various grafts for oral bone grafting sites in 2007. After 4-7 months of heal-

ing, percentages of vital bone ranged between 31-54% depending on the healing time and type of graft used. Published histomorphometric results from studies using conventional methods of autogenous bone grafts mixed with various scaffolds typically demonstrate percentages of vital bone between 27-38%.[9-16] Comparing the percentages of vital bone from bone marrow aspirant and autogenous bone grafts, the bone marrow aspirant offers higher osteogenic induction.

MATERIALS AND METHODS

Two patients were treated with grafting procedures mixed with bone marrow aspirant. In both cases, bone marrow aspirant was obtained from the anterior iliac crest. When obtaining bone marrow aspirant, the aspiration site is identified and marked under sterile conditions. The skin at the surgical site is cleansed with iodine and anesthetized with local anesthesia through infiltration of the subcutaneous tissue. A larger needle is used to anesthetize the periosteum and probe to confirm the precise location of the bone to be aspirated. A bone marrow aspiration needle is then inserted through the cortical bone into the cancellous compartment. Penetration through the cortical bone is achieved with steady pressure, rotating the aspiration needle back and forth until a change in resistance is felt. Once the aspiration needle is in the cancellous compartment, 2 to 4cc of marrow aspirate is obtained. With higher aspiration volumes, dilution of the marrow-derived cells by peripheral (venous) blood will occur. Therefore, the needle should be redirected or a new aspiration site selected if more than 4 cc of marrow aspirate is needed.

Figure 1: Pre-surgical appearance of the severely atrophied anterior ridge from Case 1.

CASE REPORTS

Case 1:

A 33 year old healthy male patient presented with a severely atrophic maxillary anterior ridge spanning from right lateral incisor to left central incisor (figure 1). Patient history revealed that he had gone through two prior unsuccessful bone grafting surgeries. The first failed surgery utilized particulate allograft with a non-resorbable membrane while the second failed surgery utilized autogenous bone blocks harvested from patient's symphysis. As a consequence of the multiple surgeries, the patient developed dense scar tissue at the surgical site. Despite previous unsuccessful attempts, the patient still desired a fixed prosthesis to replace his missing anterior teeth. After obtaining an informed consent from the patient, the bone marrow aspiration technique was performed for the patient. The patient was locally anesthetized and an alveolar crestal incision was made in the

Figure 2: Initial entry of ridge defect from Case 1.

Figure 3: Tomography showing block allograft fixated with bone screw.

Figure 4: Re-entry of Case 1 graft site after 6 months of healing.

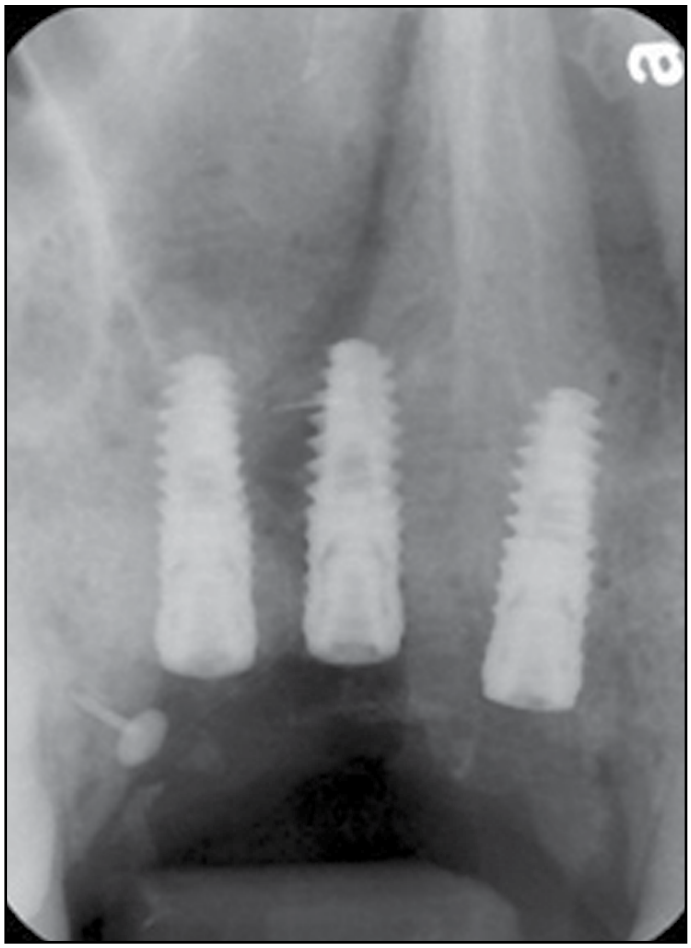

Figure 5: Immediate post-surgical radiograph of 3 implant fixtures delivered in Case 1.

edentulous ridge with adjacent vertical releasing incisions (figure 2). A wide base full thickness mucoperiosteal flap was raised to ensure adequate blood flow to the flap and the periosteum. The recipient site was then prepared by decorticating the labial bone using a small round #6 carbide bur with copious irrigation. Two block allografts were contoured to fit within the prepared recipient sites at the lateral and central incisor regions. When contouring the block allografts, care was taken to avoid remov-

Figure 6: Pre-surgical panoramic radiograph from Case 2.

Figure 7: Obtaining marrow aspirate from anterior iliac crest.

Figure 8: Marrow aspirate/alloplast mixture is injected into prepared maxillary sinuses.

ing the cancellous component. Preparation in this manner enables the bone marrow aspirate to fully saturate the cancellous compartment of the block graft. Four millilitres of hepranized bone marrow aspirate was obtained from the patient's anterior iliac crest and impregnated into the bone blocks. The two blocks were then stabilized with bone screws (figure 3). Excess graft was grounded with a bone mill, mixed with the bone marrow aspirate, and mortised around and over the fixated bone blocks. A periosteal releasing incision was used with the mucoperiosteal flap to allow for primary closure.

After 6 months, a second surgery was performed to remove the fixation screws and place three implants 3.4 x 10mm in size (figures 4, 5). Five additional months after implant placement, all implants had osseointergrated successfully and a 3 unit anterior bridge was delivered.

Case 2:

A 59 year old woman presented with a completely endentulous maxillary arch and expressed the desire to have a complete fixed prosthesis to replace her existing denture. Panoramic radiographic evaluation revealed bilateral pneumatization of the maxillary sinuses with minimal residual bone height (figure 6). Evaluation of anterior maxilla revealed adequate bone height and width for implant placement. The patient's history revealed a compromised medical condition of osteoporosis and the patient had been on oral bisphosphonate therapy for the past year and a half. After consultation with her attending physician and obtaining clearance,

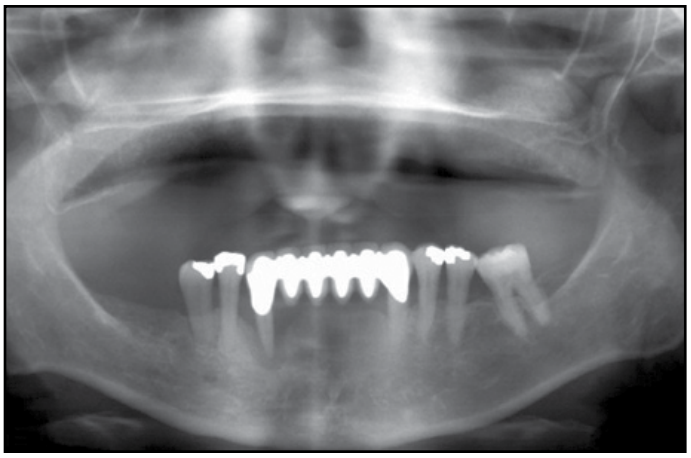

Figure 9: 4 month post-surgical panoramic radiograph

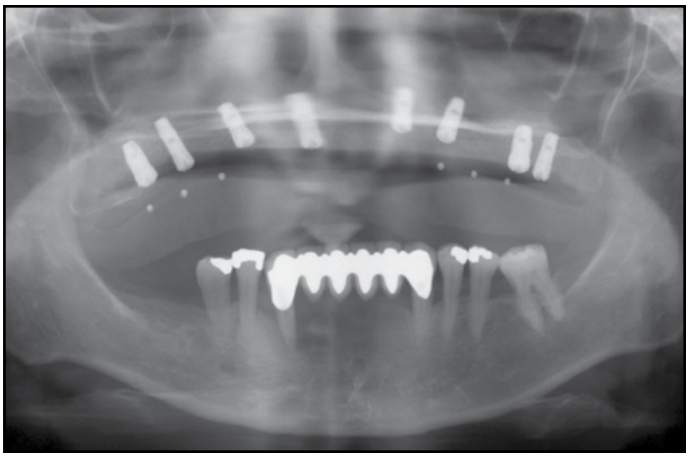

Figure 10: Panoramic radiograph following dental implant delivery.

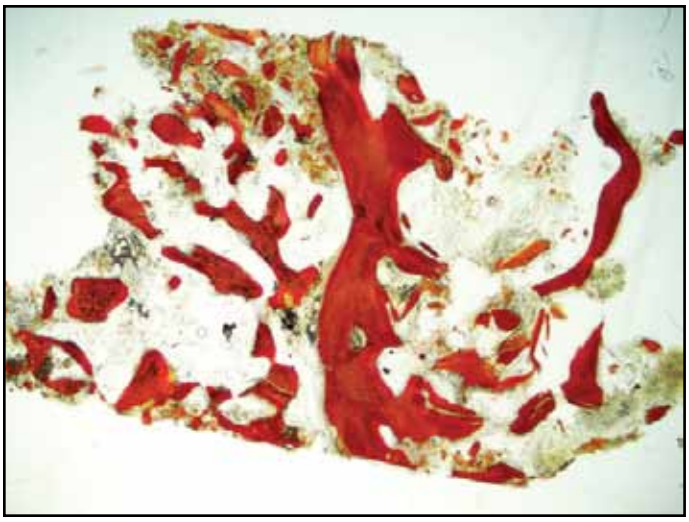

Figure 11: Histologic core sample from Case 2 demonstrating the trabecular pattern of newly formed bone. Vital bone is stained in red.

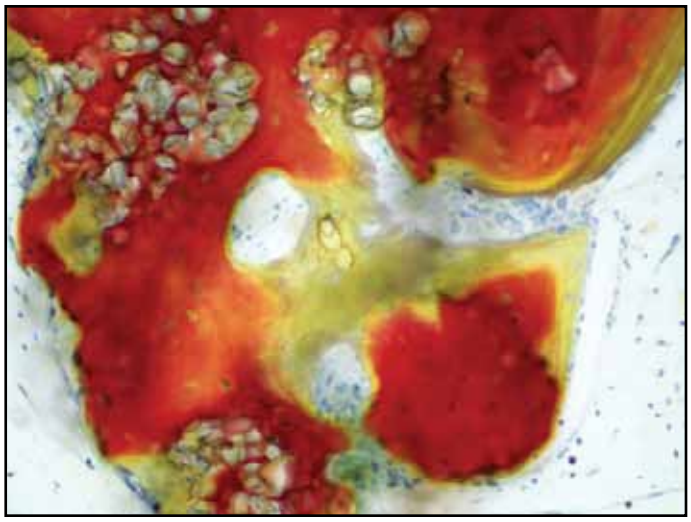

Figure 12: High power histomorphometric image showing new bone formation (stained red), osteoid (stained brown), osteoblasts (stained blue), and residual β-TCP particles

the bisphosphonate therapy was terminated two months prior to seeking implant therapy.

To facilitate implant delivery, bilateral maxillary sinus lifts with bone marrow aspirate were performed. A #6 round carbide bur and a piezoelectric surgical unit were used for the osteotomy of the sinus window. Using a specially designed sinus lifting elevator, the sinus membrane was carefully lifted without any perforations. Four millilitres of bone marrow aspirate was obtained from patient's anterior iliac crest in the manner previously described (figure 7) and mixed with 10cc of pure phase β-TCP particulate of 500-1000μm in size. The

mixture was syringed into the prepared sinus cavities (figure 8); care was taken not to over compact the graft material to ensure space for angiogenesis and cellular apposition. The lateral windows were covered with resorbable membranes and the flaps were primarily closed.

Approximately five months later, a total of eight implants were delivered (figures 9,10). During implant placement, a 3mm diameter trephine core sample was taken from the left molar region. Histomorphometric analysis (figures 11, 12) of the bone core showed 36% new bone with 91% vitality. The remainder of the core included 9% residual graft and 55% interstitial material. Five months after implant delivery, the implants were restored with a fixed appliance.

DISCUSSION

Muschler et al[17] determined that in a healthy adult, 2cc of marrow aspirate provides an average of 36 million marrow nucleated cells, of which 360 stem cells would be available for bone regeneration. An average ratio of 1 stem cell per 100,000 marrow cells is found in healthy individuals, with the highest majority of the marrow cells belonging to the various hematopoietic lineages. In vitro studies have shown that a mean of 2,400 alkaline phosphate positive colony forming units for osteoblasts can be plated from 2cc of marrow. This number diminishes with age and in the presence of systemic disease.

The histologic analysis of the trephine core from Case 2 (36% new bone) compares favorably to previous research of bone marrow aspirates and autogenous bone grafts. The two cases described in this report were successfully treated with dental implants in spite of previous failed attempts at bone augmentation. The combination of bone allografts, alloplasts, and adult stem cells aspirated from bone marrow of the anterior iliac crest eliminated the need for harvest of secondary autogenous bone.

CONCLUSION

The efficacy of the bone marrow aspirating procedure to reconstitute defective sites in the oral region is evident clinically and through histomorphometric analysis of bone core samples. Aspiration of bone marrow cells from the iliac crest in conjunction with a non-viable matrix is an effective procedure and results in less patient morbidity than grafting with conventional autogenous bone harvesting techniques. The promising results of this case report and other studies evaluating bone marrow aspirate for treatment of dental defects may warrant additional studies and clinical trials. ●

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Disclosure:
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