USE OF HIGH CONCENTRATE DEMINERALIZED BONE MATRIX IN ANKLE AND HINDFOOT ORTHOPEDIC PROCEDURES

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INTRODUCTION

One of the most common complications of ankle and hindfoot orthopedic procedures remains delayed or nonunion. For example, the nonunion rate of ankle fusions is approximately 10-12%. To maximize the likelihood of obtaining an adequate union, the appropriate environment at the site must be created. On the gross level, this includes well-vascularized surfaces, adequate bone apposition, and the appropriate fixation.

On the micomolecular level there are three essential elements necessary for bone regeneration. They are bone morphogenic proteins (BMPs), osteogenic precursor cells, and a structural matrix. BMPs provide the signal (osteoinduction), which leads to the differentiation of mesenchymal cells into osteoblasts (osteogenesis), which in turn lay down new bone with the give lattice network (osteoconduction).[1-4]

Autografts such as iliac bone crest have long been the standard utilized for bone grafting. It provides all three of the necessary components of bone healing: osteoinduction, osteogenesis, and osteoconduction. However, there are several drawbacks associated with using this type of graft. They include morbidity at the harvest site, limited quantity available for harvest, variable bone quantity, increased operating room time, and the inherent technical difficulties associated with the harvesting procedure itself.[5-7] Alternatives to iliac bone crest include freeze-dried cadaveric bone and other synthetics which exhibit only osteoconductive properties.[8]

DBM is an alternative grafting substitute which has been introduced. It is a form of allograft derived from human cortical bone. All minerals are removed leaving the proteinaceous BMPs which are necessary for osteoinduction.[9,10] Many of the products can be used to form a composite graft by adding cancellous bone chips, bone marrow aspirate, or synthetics to gain the remaining two elements necessary for bone healing: osteogenesis and osteoconduction.

Thordarson et al[11] demonstrated that the application of DBM in ankle/hindfoot fusion procedures did not produce a statistically significant decrease in rate of nonunions. However, the DBM used in this study was Orthoblast which contains only 36% DBM with cancellous bone chips. The remaining 64% of the product is an inert carrier molecule.[12] For our study we used DBM100 in 20 procedures and Connexus in 4 procedures.

The purpose of this study was to assess the union rate in hindfoot and ankle orthopedic procedures when utilizing a high concentration DBM.

METHODS

Between October 2003 and August 2004 we performed 24 ankle and hindfoot orthopedic procedures on 16 patients. In all cases high concentrate DBM was utilized. An external fixation device was then applied to all patients to stabilize the bones. If the gap between the fragments was felt to be too large for effective consolidation, bone chips were incorporated into the graft to provide adequate scaffolding for bone ingrowth. If the patient was medically compromised in ways which impede bone healing a composite graft was produced. The composite graft included DBM, cancellous bone chips, and bone marrow aspirate (BMA) from the calcaneus. BMA was added due to the intrinsic bone-forming potential present within its osteogenic cells. Therefore, the composite graft

Figure 2A. AP radiograph of patient with severe osteoarthritis of ankle and subtalar joint with lateral displacement of the talus inside the ankle mortise. Patient has history of ankle fracture and dropfoot secondary to poliomyelitis.

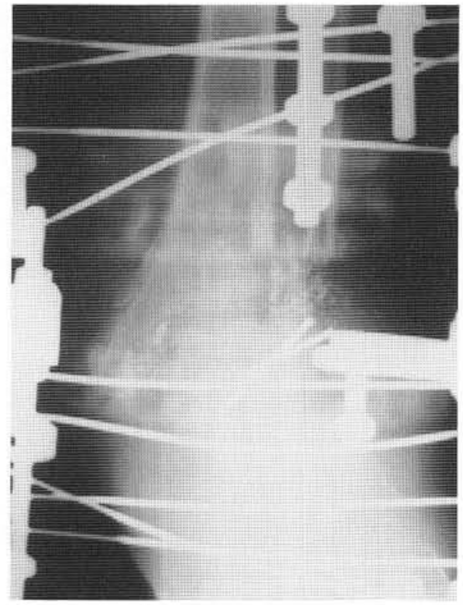

Figure 2B. AP radiograph of ankle joint at the time of removal of external fixation device. Here at 8 weeks a line of radiolucency seen at the ankle joint demonstrates nonunion. Nonunion was confirmed with motion at the joint under fluoroscopy intraoperatively. A composite graft had been incorporated into the fusion sites consisting of DBM100.

removed and under fluoroscopy the patient was found to have a nonunion of the ankle joint. The fusion was immediately revised using a retrograde intramedullary nail (Figure 2).

Although the patients involved in the additional 23 procedures had comorbidities which included smoking, diabetes, obesity, and osteoporosis which are commonly recognized to significantly reduce bone healing, they went on to full union.

DISCUSSION

Often in ankle and hindfoot orthopedic procedures many of the necessary factors of bone healing may not be adequate (bone apposition, vascularization, BMPs, stem cells, etc.). This makes it much more difficult for timely, effective healing to occur. Under these circumstances, delayed or nonunion is likely. Other factors that might lead to delayed or nonunion include smoking, patient non-compliance, obesity, and technical errors during the procedure.

When grafting material is needed, autograft has historically been used. However, alternatives have been devised due to the inherent technical difficulties, variable quality, and morbidities associated with the harvesting process.[5-7] These include allograft and synthetic materials such as calcium phosphate pellets. Unfortunately, these materials possess only osteoconductive properties.[13,14]

Demineralized bone matrix is a new approach to bone grafting. DBM is prepared from human

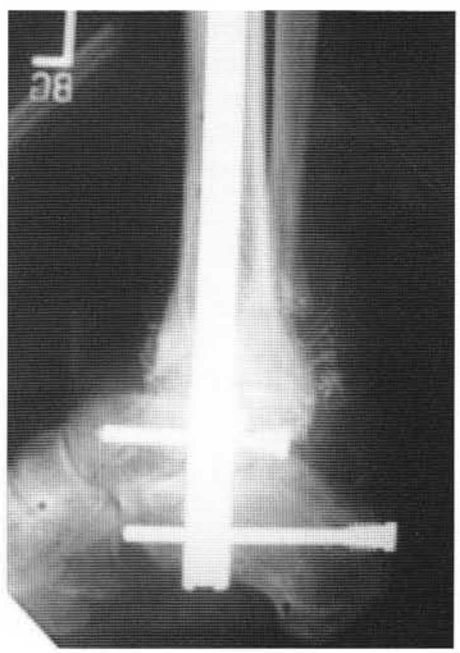

Figure 2C. Patient was immediately revised with a retrograde intramedullary nail. Radiographic fusion seen here at 13 weeks.

cortical bone. All of the minerals within the bone are removed leaving only the BMPs. These BMPs contain osteoinductive properties which cause mesenchymal cells to differentiate into osteoblasts.[9,10,15-19]

There are several different DBM products currently on the market. First generation DBMs contained a much smaller concentration of actual DBM than the newer second generation products. A significant portion of the material was an inactive carrier molecule. Second generation DBM products contain up to 100% DBM. The result is an increased concentration of BMPs at the fusion site leading to an increased osteoinductive capacity. This concept is known as proportional osteoinduction. In essence, as the signal increases (BMPs) the amount of bone deposition increases proportionately.[20,21]

A possibility for the increased success of our union rates was the initial introduction of an external fixation device as opposed to internal fixation. External fixation allows for micromovement at the site. This process stimulates bone healing allowing for significant reductions in consolidation time.[22-24] However, in earlier cases in which we implemented external fixation without incorporating DBM we did not detect a noteworthy decrease in nonunion rates compared to internal fixation.

Obtaining favorable unions in complex ankle and hindfoot orthopedic procedures remains a challenge. Bone healing is a comprehensive subject matter. We have demonstrated that the use of high concentrate DBM in conjunction with additional modalitities may help to facilitate superior results compared with traditional methods. However, we feel that additional studies on a larger patient population with a more intense statistical analysis may be warranted to further substantiate our findings.

In conclusion, we evaluated the efficacy of two different high concentrate DBM products to facilitate ossification of ankle and hindfoot orthopedic procedures. The patient population studied was diverse with various comorbidities which impede bone healing. We found a significantly lower percentage of nonunions than would generally be expected in this complex population.

REFERENCES

1. Helm GA, Dayoub H, Jane Jr. Gene-based therapies for the induction of spinal fusion. *Neurosurg Focus* 2001;10:1-5.
2. Kalfas IH. Principles of bone healing. *Neurosurg Focus* 2001;10:1-4.
3. Pilitsis JG, Lucas DR, Rengachary SR. Bone healing and spinal fusion. *Neurosurg Focus* 2002;13:6.
4. Urist MR. Formation by autoinduction. Science 1965;150:893-9.
5. Kurz LT, Garfin SR, Booth RE. Harvesting autogenous iliac bone grafts: a review of complications and techniques. *Spine* 1989;14:1324-31.
6. Fennyhough JC, Schimandle JJ, Weigel MC, Edwards CC, Levine AM. Chronic donor site pain complicating bone graft harvesting from the posterior iliac crest for spinal fusion. *Spine* 1992;17:1474-80.
7. Kurz LT, Garfin SR, Booth RE. Harvesting autogenous iliac bone grafts: a review of complications and techniques. *Spine* 1989;14:1324-31.
8. Sammarco VJ, Chang L. Modern issues in bone graft substitutes and advances in bone tissue technology. *Foot Ankle Clin* 2002;7:19-41.
9. Shigeyama Y, D'Errico JA, Stone R, Sommerman MJ. Commercially prepared allograft material has biological activity in vitro. *J Periodontal* 1995;66:478-87.
10. Reddi AH. Initiation of fracture repair by bone morphogenetic proteins. *Clin Orthop* 1998;355S:S66-72.
11. Thordarson DB, Kuehn S. Use of demineralized bone matrix in ankle/hindfoot fusion. *Foot Ankle Int* 2003;24:557-60.
12. Data on file. *IsoTis OrthoBiologics*. www.isotis.com.
13. Betz RR. Limitations of autograft and allografts: new synthetic solutions. *Orthopedics* 2002;25:561-70.
14. Gazdag AR, Lane JM, Glaser D, et al. Alternatives to autogenous bone graft: efficacy and indications. *J Am Acad Orthop Surg* 1995;3:1-8.
15. Einhorn TA, Lane JM, Burstein AH, Kopman CR, Vigorita VJ. The healing of segmental bone defects induced by demineralized bone matrix. *J Bone Joint Surg Am* 1984;66:274-9.
16. Feighan JE, Davy D, Prewett AB, Stevenson S. Induction of bone by a demineralized bone matrix gel: a study in a rat femoral defect model. *J Orthop Res* 1995;13:881-91.
17. Martin GJ, Boden SD, Titus L, Scarborough NL. New formulations of demineralized bone matrix as a more effective graft alternative in experimental posterolateral lumbar spine arthrodesis. *Spine* 1999;24:637-45.
18. Michelson JD, Curl LA. Use of demineralized bone matrix in hindfoot arthrodesis. *Clin Orthop* 1996;325:203-08.
19. Geesink GT, Hoefnagels NHM, Bulstra SK. Osteogenic activity of OP-1 bone morphogenetic protein (BMP-7) in human fibular defect. *J Bone Joint Surg Br* 1999;81):710-8.
20. Han B, Tang B, Nimni ME. Quantitative and sensitive in vitro assay for osteoinductive activity of demineralized bone matrix. *J Ortho Res* 2003;648:654.
21. Atti E, Abjornson C, Diegmann M, et al. High resolution X-ray computed tomography as a technique to study osteoinductivity of demineralized bone matrix. Proceedings of the NASS 18th Annual Meeting. *Spine J* 2003;3:120S.
22. Kenwright J, Richardson JB, Cunningham JL, et al. Axial movement and tibial fractures, a controlled radomised trial of treatment. *J Bone Joint Surg Br* 1991;73:654-9.
23. Wallace WA, Howard PW. A decade of tibial fractures at Nottingham and Derby. *Int J Orthop Trauma Suppl* 1993;3:61-3.
24. Foxworthy M, Pringle RM. Dynamization timing and its effect on bone healing when using the Orthofix Dynamic Axial Fixator. *Injury* 1995;26:117-9.