Bone grafts and bone morphogenetic proteins in spine fusion

Munish C. Gupta* and Sukanta Maitra
Department of Orthopaedics, Davis Medical Center, University of California, Suite 3800, 4860 Y Street, Sacramento, CA 95817, USA; *Author for correspondence (e-mail: munish.gupta@ucdmc.ucdavis.edu; phone: 916-734-2988; fax: 916-734-7904)

Received 10 August 2002; accepted in revised form 17 February 2003

Key words: BMPs, Bone grafts, GDF-5, Hydroxyapatite, Spine fusion, Tricalcium phosphate

Abstract

Spinal fusions are being performed for various pathologies of the spine. Stabilizing vertebral segments by eliminating motion across those segments becomes critical in dealing with pathologies of the spine that lead to instability. The use of autograft has been the gold standard for spine fusion. However, due to complications such as donor site morbidity, increased operating time, and limited supply, the use of allograft as a graft extender has become an acceptable practice especially in fusions spanning multiple segments. The discovery and isolation of novel proteins (i.e., bone morphogenetic proteins, BMPs), which initiate the molecular cascade of bone formation, have experimentally been shown in numerous animal studies to be as effective as autografts. Although the use of BMPs has exciting applications in spine surgery, long-term clinical studies must be evaluated for its efficacy in various applications in humans. The use of biomimetic materials such as hydroxyapatite (HA), or tricalcium phosphate (TCP) has also been examined in several animal models as bone graft substitutes or carriers. Although these materials have shown some promise in specific site applications, more work remains in elucidating an efficacious combination of these materials and BMPs that can be as effective as autografts. This review will present the status of bone grafts, bone morphogenetic proteins, gene therapy, and work that has been done to facilitate spinal fusion and simultaneously eliminate the need for bone graft.


Introduction

More spinal fusions are done today than ever before by orthopedic and neurologic surgeons. The procedure is used to stabilize the spinal segments that are affected by a myriad of pathologies such as infection, trauma, tumors, and spinal deformities caused by idiopathic, neuropathic, or myopathic diseases. Degenerative conditions of the spine often result in neural compression requiring decompression, which may require a concomitant spinal fusion. Some spinal fusions are performed for painful degenerative conditions where the discs and facet joints are considered to be the cause of pain. Recently, the thought of fusion or immobilization of the spine to relieve pain has been changed to preserving motion by total disc replacement. The total disc replacement is similar to total joint arthroplasty in the knees and hips where fusion used to be the treatment of choice at one time but is done now in only limited circumstances. Whether total disc replacement will replace fusion in spine surgery for at least some degenerative conditions remains to be seen. Spinal fusion still continues to be a procedure of choice for many conditions of the spine. Therefore, any advance that can facilitate, simplify, and eliminate the negative aspects of fusion
such as autograft bone harvest or pseudoarthrosis will be advantageous. A radiograph of a patient with severe degenerative scoliosis requiring a large multi-level fusion is depicted in Figure 1. Such a patient has to have instrumentation to correct the spinal deformity and then fusion with an autograft that has to be augmented due to the large surface area to be fused. Patients such as these are challenging because they are usually elderly, with some degree of osteoporosis besides other health problems. This patient in particular had rheumatoid arthritis for which she was on prednisone for over twenty years and methotrexate. To fuse the spine of such a patient reliably, one can use instrumentation, which corrects the spine and holds it steady until the fusion takes place. Harvesting of both iliac crests for an autograft is still not sufficient. Therefore, one can augment the autologous bone with allograft bone; demineralized bone (DBM); ceramics e.g., tricalcium phosphate (TCP); or hydroxyapatite (HA). In this review the present status of bone grafts, bone morphogenetic proteins, gene therapy, and work that has been done to facilitate spinal fusion and simultaneously eliminate the need for any kind of bone graft will be presented.

**Biology of spine fusion**

Spinal fusion is performed by decortication of the bony elements to expose marrow elements that provide the necessary cells and factors needed for a successful fusion. After the decortication, a bone graft is laid to bridge the required area of the fusion. Eventually, the bone graft goes through remodeling and results in a solid bone with a cortical rim and marrow elements within. Clinically, fusion is seen on radiographs with bridging trabeculae between the transverse processes or interbody space confirming a successful fusion.

The difficulty in achieving a fusion depends on