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Accelerating lumbar fusions by combining rhBMP-2 with allograft bone: a prospective analysis of interbody fusion rates and clinical outcomes

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Abstract

BACKGROUND CONTEXT: Recombinant human bone morphogenetic protein-2 (rhBMP-2) is an osteoinductive protein approved for use in the anterior lumbar interspace. High fusion rates with rhBMP-2 have been reported with threaded interbody allograft dowels. There may be a clinical benefit for the patient by adding rhBMP-2 to the allograft.

PURPOSE: To compare the fusion rates and clinical outcomes of patients treated with allograft interbody fusions with and without the addition of rhBMP-2.

STUDY DESIGN: Prospective consecutive patient enrollment with minimum 24-month follow-up.

PATIENT SAMPLE: Seventy-five patients with lumbar interbody fusions at 1–3 spinal segments.

OUTCOMES MEASURES: Clinical: Numerical Rating Scale (NRS) and Oswestry Disability Index (ODI). Radiographic: X-ray and computed tomographic scan analysis using the Molinari-Bridwell fusion scale.

METHODS: Seventy-five patients scheduled for lumbar fusion were enrolled sequentially. Group 1: 30 patients had anterior interbody allografts alone. Group 2: 45 patients had anterior interbody allograft filled with rhBMP-2. All cases had posterior pedicle screw instrumentation. A total of 165 surgical levels (62 allograft alone/103 allograft+BMP) were included. Fusion data and clinical outcomes were collected for a minimum of 2 years after surgery.

RESULTS: Statistically higher fusion rates were observed in the patients with BMP at all time points compared with allograft alone. Group 2 (+ BMP) fusion rates were 94%, 100%, and 100% at 6, 12, and 24 months after surgery. Group 1 (-BMP) fusion rates were 66%, 84%, and 89% at the same time intervals. Clinical outcomes were significantly improved in Group 2 compared with Group 1 at 6 months. There were no revisions (0%) in the BMP group and 4 revision fusion surgeries (13%) in the allograft group. No untoward effects were attributable to the rhBMP-2.

CONCLUSIONS: Our study confirms the efficacy of an innovative lumbar fusion technique: an interbody femoral ring allograft, combined with an osteoinductive stimulant (rhBMP-2), protected by pedicle screws. This combination of a structural interbody allograft with rhBMP-2 eliminates the insult of iliac crest harvest, allows for reliable radiographic analysis, and results in successful fusion formation in 100% of the cases in this study.

Keywords: rhBMP-2; Bone morphogenetic protein; BMP; InFuse Bone Graft; Lumbar fusion; Arthrodesis; Clinical outcomes; Allograft; Low back pain

Introduction

Recombinant human bone morphogenetic protein-2, rhBMP-2, (InFuse Bone Graft; Medtronic Sofamor Danek, Memphis, TN) is an osteoinductive protein approved for use in the anterior lumbar interspace. Summary analysis of prospective studies has shown that the rhBMP-2 placed within two titanium interbody cages is superior to autograft in obtaining fusion success [1–3]. Ongoing clinical research

FDA device/drug status: approved but not for this indication (rhBMP-2).

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is encouraging, and expectations for continued success with BMP remain high [4–7].

Successful interbody fusions with rhBMP-2 have been reported with threaded, allograft bone dowels [8,9]. Allograft bone is commonly used as structural interbody graft in the lumbar spine, but fusion rates vary widely and time to incorporation is often prolonged. An advantage of using allograft is that it can be visualized on computed tomographic (CT) scans or radiographs without metal artifact. This allows for more direct and accurate fusion assessment using these readily available radiographic tests [10].

Anterior lumbar interbody fusions (ALIF) are an effective treatment option for symptomatic lumbar disc disease [2,3,11–18]. ''Stand-alone'' grafts (no pedicle screw instrumentation) have been associated with high rates of pseudarthrosis and clinical failure [13,18–20]. Even with the addition of rhBMP-2, stand-alone femoral allograft interbody constructs are not mechanically stable enough to heal reliably [21].

The emergence of rhBMP-2 as a viable alternative to traditional bone grafting is based on two important clinical challenges [7]. The first is to eliminate the need to harvest bone from the iliac crest or other sites when performing a spinal fusion. There is increased pain and morbidity in these operative procedures. The second reason is to try to eliminate or greatly reduce the number of nonunions observed in reconstructive spinal surgeries.

There are extensive data published on the results of lumbar fusions with anterior allograft stabilized with pedicle screw fixation [11,13,15,22]. Although the results of these techniques are generally good, there are still a significant number of failures. Concerning issues with allograft fusions include prolonged time to heal, incomplete graft incorporation, and mechanical failure [20,23–25].

As BMP is osteoinductive and allograft bone is osteoconductive, it is logical to combine the two in an effort to improve the reliability and rapidity of a lumbar arthrodesis. Based on the very high fusion rates noted with rhBMP-2, the authors began placing two sponges of rhBMP-2 (InFuse Bone Graft) inside the center of allograft femoral rings in a small number of ALIF cases. We observed rapid incorporation of the grafts with no untoward effects. A formal prospective analysis was therefore initiated. The purpose of this study is to determine if rhBMP-2 will safely accelerate allograft interbody fusions, as compared with allograft alone, and significantly reduce the number of pseudarthrosis.

Methods

A prospective, single-center study of patients undergoing arthrodesis at 1–3 levels of the lumbar spine was conducted with institutional review board approval from September 2002 to July 2004. Group 1 (control) consisted of 30 patients enrolled consecutively. The next 45 patients were then enrolled successively, comprising Group 2 (investigational).

Study population

Seventy-five consecutive patients with 165 fusion levels were enrolled. Group 1 had ALIF with femoral ring allograft (Precision Regeneration Technologies Inc., Alachua, FL) filled with allograft chips; Group 2 had Precision grafts filled with rhBMP-2 (InFuse). All patients had posterior pedicle screw fixation. No iliac crest was harvested and no posterior fusions were performed in either group.

Inclusion criteria

Patients were included in the study if they had painful degenerative disc disease of the lumbar spine (L3–S1), Grade I–II spondylolisthesis, or degenerative scoliosis. All patients had predominant low back pain that was refractory to nonsurgical treatment including physical therapy, spinal injections, medications, or other accepted treatments.

Exclusion criteria

Patients were excluded if they had disc disease at greater than 3 lumbar levels, high-grade spondylolisthesis, tumor, infection, or psychological contraindications.

Outcome measures

Clinical outcomes were measured by comparing preoperative and postoperative Numerical Rating Scale (NRS) (0=no pain, 10=worst pain) and Oswestry Disability Indexes (ODI) [26,27]. To assess statistical significance, a paired *t* test was used.

Radiographic outcomes were measured by X-rays and CT scans at 6, 12, and 24 months. All studies were reviewed by three independent reviewers, blinded to group status, using the Molinari-Bridwell grading to assess anterior fusion [24]. For the purpose of this analysis, Grades I–II were considered ''fused'' at the level of surgery and Grades III and IV were considered ''not fused'' (Table 1).

Surgical technique

All patients underwent anterior retroperitoneal approach to the lumbar spine. Complete discectomy and segmental distraction and end plate preparation were performed using

Table 1
Anterior fusion grades

Fusion	Description of fusion
Grade I	Fused with remodeling and trabeculae present
Grade II	Graft intact, not fully remodeled and incorporated, no lucency
Grade III	Graft intact, potential lucency present at the top or bottom graft
Grade IV	Fusion absent with collapse/resorption of graft