The Effect of Recombinant Human Bone Morphogenetic Protein-2 in Single-Level Posterior Lumbar Interbody Arthrodesis


The authors reported a single-center, single-surgeon, prospective, randomized, controlled trial undertaken to assess the clinical and imaging findings of the use of recombinant human bone morphogenetic protein-2 (rhBMP-2) vs autologous bone in patients treated with an instrumented single-level posterior lumbar interbody arthrodesis with polyetheretherketone cages.

Forty patients were randomized into either treatment with 8 mg of rhBMP-2 (study group; n = 20) or treatment with 2.5 mL of autologous bone harvested unilaterally from the iliac wing (control group; n = 20).

Inclusion criteria included lytic and degenerative spondylolisthesis, disk degeneration that was not responsive to nonoperative treatment modalities for at least 6 months, disk herniation in patients with severe disk degeneration and persisting sciatica despite epidural steroid injections, and single-level disk abnormality.

Exclusion criteria included a history of spinal surgery other than diskectomy; chronic use of corticosteroids or nonsteroidal anti-inflammatory drugs; skeletally immature patients or patients older than 70 years; history of osteoporosis, systemic disease, or a malignant lesion; disk abnormality at adjacent levels; and patients undergoing multilevel surgery.

A posterior lumbar interbody arthrodesis with posterior pedicle screw fixation was performed. Pedicle screws were placed under fluoroscopic guidance, followed by a complete laminectomy and discectomy. The vertebral body endplates were prepared by curetting until point bleeding was seen. A titanium segmental instrumentation rod system (Colorado 2; Medtronic Sofamor Danek, Memphis, Tennessee) was used for posterior instrumentation, and 2 polyetheretherketone cages (Telamon; Medtronic Sofamor Danek) were used for interbody arthrodesis. The bone morphogenetic protein used was rhBMP-2 on an absorbable collagen sponge (InductOs; Wyeth Europa, Taplow, United Kingdom).

Clinical results were measured using the Oswestry Disability Index, the Short Form 36, and the visual analog scale for pain preoperatively and at 3, 6, 12, and 24 months postoperatively. Imaging results were measured using anterior, lateral, and flexion-extension radiographs of the lumbar preoperatively and at 3, 6, and 12 months postoperatively, and computed tomography scans with coronal and sagittal reconstructions at 3, 6, and 12 months postoperatively. Using the computed tomography scans, the status of the interbody fusion was quantified using the bridging trabecular bone scale.

Baseline demographic data showed no significant difference between groups, except for body mass index, which was higher in the study group ($P = .032$). The operative procedure took significantly longer ($P = .010$) and blood loss was significantly higher ($P = .008$) in the control group.

No significant differences existed in the clinical results between the groups at each postoperative visit. At 3 months, endplate resorption was noted around the cages in all patients in the study group. Bridging trabecular bone scale scores and bone density measures were significantly lower in the study group. Osteolysis and ectopic bone formation occurred in 7 of 19 patients in the study group and did not occur in the control group.
Review
Norman B. Chutkan, MD
Georgia Health Sciences University

In this well-designed and well-executed prospective, randomized, controlled trial, Michielsen et al evaluated the effect of recombinant human bone morphogenetic protein-2 (rhBMP-2) in a single-level posterior arthrodesis of the lumbar spine. Since its approval for use in the spine by the Food and Drug Administration in 2002, rhBMP-2 has seen an explosion of use in this country, with most of it occurring off-label. The dramatic increase in so-called minimally invasive approaches was due in no small part to the use of rhBMP-2. The idea that implanting a sponge of rhBMP-2 could overcome limited access to the surgical site was attractive to surgeons. Recombinant human bone morphogenetic protein-2 was heralded as the future of fusion surgery that would render autologous bone grafting obsolete.

As is often the case with new technology, the promise of what would be has proven to be somewhat less than reality. Concerns about potential side effects have increased with widespread use, and some surgeons have begun to question whether the clinical results are as good as those advertised. The significant financial relationship between many of the early proponents of rhBMP-2 and the manufacturer has also been a source of concern, raising the possibility of bias and underreporting of adverse events. Two independent reviews sponsored by the Yale University Open Data Access project concluded that rhBMP-2 has little or no clinical benefit over bone graft.\textsuperscript{1,2} Significant limitations were found with both of these reviews that are beyond the scope of this commentary, and certainly evidence exists in the literature about the benefit of rhBMP-2 in complex, multilevel spinal reconstructions.

Into this somewhat charged and controversial arena, we can now add this well-done study. Although both the rhBMP-2 and control groups achieved a high level of clinical and radiographic success, no significant difference was found between the 2 groups. Endplate resorption, osteolysis, and ectopic bone formation were frequently seen in the rhBMP-2 group, but this did not seem to effect the clinical outcome. Successful fusion was achieved in all patients in both groups. These data suggest that rhBMP-2 has little or no advantage over conventional bone grafting techniques in posterior lumbar interbody fusions. As for the ideal indications for rhBMP-2, the jury is still out.

REFERENCES


doi: 10.3928/01477447-20130821-08

At 1 year postoperatively, computed tomography scans showed osseous healing in all patients.

Clinical results between the groups at 24 months postoperatively were not significant with regard to improvement in visual analog scale scores ($P=.987$), Oswestry Disability Index scores ($P=.577$), and both the Short Form 36 physical ($P=.536$) and mental ($P=.278$) component summary scores between the groups.

Imaging results revealed that bone density measures were significantly different between the groups at 3, 6, and 12 months postoperatively ($P=.002$, .024, and .014, respectively). A significant difference was also found between the groups with regard to interbody healing on the bridging trabecular bone scale at 3, 6, and 12 months postoperatively ($P=.021$, .004, and .014, respectively). Fusion on the computed tomography scan (a bridging trabecular bone scale score of 3, 4, or 5) was ultimately achieved in all patients.

No clinical difference was found when rhBMP-2 was used in posterior lumbar interbody arthrodesis compared with autologous bone. On computed tomography scans, fusion was equally achieved when rhBMP-2 was used; however, trabecular bone formation occurred at a slower rate and interbody bone density was lower within the first postoperative year after surgery when rhBMP-2 was used.