Retrospective Study of Posterior Cervical Fusions With rhBMP-2

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abstract

Posterior cervical decompression and fusion can be performed for various spinal conditions. Previous rates of pseudoarthrosis have been reported in up to 38% of patients. The use of bone morphogenic protein (BMP) has been approved for use in certain anterior lumbar interbody fusion techniques to decrease the incidence of pseudoarthrosis. Bone morphogenic protein in the anterior cervical spine carries a potential increased risk of airway complications; however, few data exist on the safety and efficacy of BMP in the posterior cervical spine. The purpose of this study was to evaluate fusion success, safety, and heterotopic bone formation using BMP in posterior cervical fusion.

Twenty-nine patients who received posterior cervical fusion with BMP were followed for a minimum of 12 months. Computed tomography scans were obtained at a minimum of 12 months postoperatively to evaluate for solid arthrodesis and the presence of heterotopic bone formation. Patients’ demographic data and adverse events were evaluated. All patients underwent posterior cervical decompression and instrumented fusion of at least 1 level between 2006 and 2008. Of 37 patients eligible for the study, 29 agreed to participate. Three (10.3%) of 29 patients developed pseudoarthrosis, as found on computed tomography scan. None of these went on to further surgery. No evidence existed of heterotopic bone formation outside of the lateral masses or bone growth over the spinal canal or neuroforamen. No adverse events were related to the use of BMP in this series of posterior cervical fusions. Bone morphogenic protein can be used safely in posterior cervical spine fusion, but additional larger studies are recommended. Even with the use of bone morphogenic protein, the possibility of pseudoarthrosis exists.
P osterior cervical decompression and instrumented fusion can be used for a variety of cervical spine disorders. It is generally considered to be a safe and effective technique, but pseudarthrosis has been reported in up to 38% of patients. Autologous iliac crest bone remains the gold standard graft substance for achieving a solid fusion, but it has associated risks and comorbidities. In a recent prospective study, Kim et al reported the incidence of donor site pain and comorbidities associated with posterior iliac crest bone graft harvest up to 1 year postoperatively. At 1 year, the mean harvest site pain score was 16.1 of 100, and 16.5% of patients had greater levels of pain from the harvest site than the primary surgical site. Additional comorbidities included numbness (29.1%), difficulty ambulating (15.1%), difficulty with recreation (12.9%), and difficulty with employment (5.2%). Other reported complications from posterior iliac crest graft harvest include fracture, vascular injuries, and unsatisfactory cosmesis.

In an attempt to reduce the comorbidities associated with autologous graft harvest, various bone graft substitutes have been developed. The most effective of these is generally believed to be recombinant human bone morphogenic protein (rhBMP). The use of rhBMP on an absorbable collagen sponge (ACS) carrier (INFUSE; Medtronic Sofamor Danek, Memphis, Tennessee) was granted premarket approval by the United States Food and Drug Administration (FDA) for use in anterior lumbar interbody fusion for the treatment of degenerative disk disease.

Despite the fact that rhBMP is only approved for use in specific anterior lumbar procedures, its use in other spinal fusion applications is increasing. Off-label use of rhBMP is reported to account for at least 85% of its overall use. Cahill et al performed a review of the use of rhBMP in spinal fusion procedures. They reported a significant increase in the overall use of rhBMP in all spinal fusions between 2002 and 2006, from 0.69% to 24.89%. Complications associated with anterior cervical fusions were significantly increased with the use of rhBMP, from 4.68% to 7.09%, with an odds ratio of 1.43. However, no statistically increased risks were associated with rhBMP use in posterior cervical fusions. Other investigators have reported similar increased complication rates with rhBMP in anterior cervical fusions, including increased hospital stay, reintubations, tracheotomies, dysphagia, dyspnea, respiratory failure, and intensive care unit admission. Because of the increased risk of complications, the FDA issued a public health notification warning of the increased potential serious risks associated with the use of rhBMP in cervical spine procedures. Despite the fact that the majority of reported complications were associated with anterior cervical disectomy and fusion, the FDA did not make a distinction between anterior vs posterior procedures in this notification.

Limited information exists regarding the safety and efficacy of using rhBMP in posterior cervical spine fusions. Crawford et al performed a retrospective review of 77 patients undergoing posterior cervical fusion and compared the use of rhBMP vs iliac crest graft. They reported a greater incidence of wound complications requiring treatment in those receiving rhBMP (14.6%) compared with those receiving an iliac crest graft (2.5%), although this was not statistically significant ($P=0.113$).

The purpose of this study was to evaluate the safety and efficacy of using rhBMP in posterior cervical decompression and fusion in terms of radiographic evidence of fusion and risk of heterotopic bone formation and other postoperative complications.

Materials and Methods
All patients undergoing posterior cervical decompression and fusion by 3 fellowship-trained spine surgeons (S.D.H.) between 2006 and 2008 were considered for this study. Inclusion criteria included posterior decompression and fusion of at least 1 level, postoperative follow-up for a minimum of 12 months, use of rhBMP on an ACS, and patient willingness to undergo computed tomography (CT) scan postoperatively to assess for fusion. Exclusion criteria included use of a bone growth stimulator, mental incompetence, incarceration, pregnancy, history of cancer, current infection, or prolonged use of steroids. Thirty-seven patients qualified for the study based on the inclusion and exclusion criteria, and 29 of these agreed to participate. Eight of the 37 eligible patients chose not to participate in the study. A total of 69 operative levels existed. The study was approved by the Western Institutional Review Board prior to patient enrollment.

The surgery consisted of placing instrumentation in the operative level (lateral mass screws from C3-C6 with pedicle screws at C2 and C7) and a posterior decompression in which a trough was created in the lamina bilaterally with a high-speed burr. A Kerrison rongeur was used to free the underlying ligamentum flavum, and the lamina was removed. The Kerrison rongeur was then used to perform foraminotomies bilaterally. Following posterior cervical decompression, the remaining bony surfaces and facet joints of the levels to be fused were decorticated with a high-speed burr. The BMP was injected on the ACS, wrapped around the morselized local autograft or allograft bone, and packed along the posterolateral gutters bilaterally. None of the patients used a cervical collar postoperatively.

Patients’ demographic data, including age, sex, body mass index, use of tobacco, presence of diabetes mellitus, operative levels, previous cervical spine surgery, preoperative diagnosis, and medical history, were reviewed to search for any potential variables affecting the results. Statistical significance was set at $P<0.05$.

Determination of solid arthrodesis was made by a postoperative CT scan evaluat-
ing for evidence of solid trabecular bone across all operative levels with no signs of lucency between levels. All images were evaluated by a single neuroradiologist. The presence of fusion was determined for each operative level. If any operative level showed signs of pseudoarthrosis, the patient was considered to have a pseudoarthrosis. Data were calculated for the patients as a whole, as well as for each operative level. Computed tomography scans were also evaluated for signs of heterotopic ossification, with emphasis on bone growth in the spinal canal or neural foramen. Patients were monitored for signs of postoperative wound infection, seroma, dehiscence, or the presence of radiculitis.

RESULTS

Demographic data of the study population are summarized in the Table. All patients received rhBMP combined with either allograft, local autograft, or hydroxyapatite:tricalcium phosphate ceramic matrix at each operative level. The dose of rhBMP varied among patients and was left to surgeon discretion, but the mean dose used was 1.4 cc (2.1 mg)/level. All operative levels were stabilized with instrumentation, including lateral mass screw fixation in the subaxial cervical spine and pedicle screw fixation at C2 and C7.

Computed tomography scans with sagittal and coronal reconstructions were obtained at a minimum of 12 months. Three (10.3%) of 29 patients and 4 (5.8%) operative levels had CT evidence of pseudoarthrosis. None of these patients required additional surgery. No evidence of any heterotopic bone formation existed in the spinal canal, neural foramen, or other locations for any patient.

All 3 patients who developed a pseudoarthrosis had a previous anterior cervical spine operation, whereas 7 (24.1%) patients had no prior cervical spine surgery, and each of these went on to solid fusion ($P = .30$). Eight (27.6%) patients had a previous anterior pseudoarthrosis, and 1 (12.5%) developed pseudoarthrosis. Ten (34.5%) patients had a previous anterior fusion at an adjacent level, and 2 (20%) of these went on to a pseudoarthrosis. One of the 3 patients with a pseudoarthrosis was a smoker, and none had diabetes mellitus. Mean body mass index of those with a solid fusion was 29.3 vs 27.4 for those with a pseudoarthrosis. None of the demographic variables reached statistical significance.

No complications were directly related to the use of rhBMP, including no wound problems or infections, no airway complications, no radiculitis, and no excessive hematoma or seroma formation that required a return to the operating room.

DISCUSSION

In an attempt to reduce the risk of pseudoarthrosis in spinal fusion, the use of rhBMP is becoming more frequent in spinal fusion surgery. Rates of pseudoarthrosis in posterior cervical fusion have been reported to range from 0% to 38%. However, a wide variety of surgical indications, number of levels fused, patient comorbidities, and surgical techniques are used in these studies. As a result, it is difficult to provide an accurate rate of pseudoarthrosis following posterior cervical fusion. Another limitation in accurately defining the rate of pseudoarthrosis in posterior cervical fusion is the difficulty in determining whether a solid fusion exists using plain radiographs. A CT scan provides the best evidence for solid fusion, but this study is not routinely ordered postoperatively. In the current study, a pseudoarthrosis rate of 10.3% was achieved with the use of posterior instrumentation and rhBMP.

Although numerous adverse events have been related to the use of rhBMP in the anterior cervical spine, few data exist for its use in posterior cervical applications. Cahill et al performed a retrospective review of 328,468 patients who underwent spinal fusion between 2002 and 2006 and reported a significant increase in the use of rhBMP during this time frame, from 0.69% to 24.89% of all spinal fusions. The immediate postoperative complications were compared as a function of rhBMP use, and no differences were found for lumbar, thoracic, or posterior cervical fusion cases. Similar findings were reported by Williams et al in a retrospective review of 55,862 spinal fusion cases from the Scoliosis Research Society. No significant differences were found in overall complications, wound infections, or epidural hematomas based on the use of rhBMP for thoracic, lumbar, and posterior cervical fusions. Significantly greater complications were observed with anterior cervical fusions overall and with wound complications specifically. Despite this, the FDA warning against the use of rhBMP in the cervical spine does not make a distinction between anterior vs posterior applications.

Previous studies have shown a small, but not statistically significant, increase in wound-related problems with the use of rhBMP in the posterior cervical spine. In the current study, no patient developed any wound-related complications when rhBMP was used in the posterior cervical spine. It is possible that some of the
adverse events related to rhBMP use in the anterior cervical spine could be dose-related. The current study used a mean of 1.4 cc (2.1 mg)/level. The authors did not attempt to identify an optimal dose to maximize arthrodesis while minimizing adverse events. The dose of rhBMP used in the current study was left to the surgeons’ discretion.

In addition to the potential risks associated with the use of rhBMP, another common criticism is the cost. A direct cost-benefit analysis was beyond the scope of the current study. Previous studies have documented the increased cost associated with rhBMP in spinal fusion that can lead to increases between 11% and 41% of total hospital costs.3

A potential limitation of the current study is the lack of clinical outcomes data. The goal was to evaluate the safety and efficacy of rhBMP in achieving arthrodesis radiographically in the posterior cervical spine. Although no patient with pseudoarthrosis required additional surgical treatment, a direct clinical comparison of the 2 groups is not available. Another limitation is the lack of a control group of patients with posterior cervical instrumented fusion without the use of rhBMP. When compared with historical control data, the results of the current study are favorable. Finally, this study group was heterogeneous in terms of indications, levels fused, and use of other bone graft materials.

**Conclusion**

Based on the results of this study, rhBMP can be safely and effectively used in instrumented fusions of the posterior cervical spine with no increased risks. Despite the use of rhBMP and its associated increased cost, a pseudarthrosis rate of 10.3% occurred. Surgeons must decide on an individual case basis if the use of rhBMP is justified for this off-label application.

**References**


