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Clinical Study

Clinical sequelae after rhBMP-2 use in a minimally invasive transforaminal lumbar interbody fusion

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Abstract

BACKGROUND CONTEXT: Recent reports of postoperative radiculitis, bone osteolysis, and symptomatic ectopic bone formation after recombinant human bone morphogenetic protein-2 (rhBMP-2) use in transforaminal lumbar interbody fusions (TLIFs) are a cause for concern.
PURPOSE: To determine the clinical and radiographic complications associated with BMP utilization in a minimally invasive transforaminal lumbar interbody fusion (MIS-TLIF) environment.
STUDY DESIGN/SETTING: Retrospective clinical case series at a single institution.
PATIENT SAMPLE: Five hundred seventy-three consecutive patients undergoing an MIS-TLIF.
OUTCOME MEASURES: Reoperation rates and total costs associated with complications of rhBMP-2 use and pseudarthrosis.
METHODS: A retrospective review of 610 consecutive patients undergoing an MIS-TLIF (2007–2010) by a single surgeon at our institution was performed (mean age 48.7 years, range 26–82 years). All patients underwent an MIS laminectomy with bilateral facetectomy, single TLIF cage, unilateral pedicle screw fixation, and 12 mg (large kit) or 4.2 mg (small kit) of rhBMP-2. The BMP-2 collagen-soaked sponge was placed anteriorly in the disc space, followed by local bone graft, and then the cage was filled only with local bone and no BMP-2. Patients were evaluated at 6 months and 1 year with computed tomography (CT) scan. Those demonstrating neuroforaminal bone growth, osteolysis/cage migration, or pseudarthrosis were reviewed, and cost data including direct cost/procedure for both index and revision surgeries were collected.
RESULTS: Of the 573 patients, 10 (1.7%) underwent 15 additional procedures based on recalcitrant radiculopathy and CT evidence of neuroforaminal bone growth, vertebral body osteolysis, and/or cage migration. Thirty-nine patients (6.8%) underwent reoperation for clinically symptomatic pseudarthrosis. Bone overgrowth was associated with nerve impingement and radiculopathy in all 10 patients (small kit, n=9; large kit, n=1). Osteolysis and cage migration occurred in 2 (20%) of these same 10 patients. Average total costs were calculated per procedure ($19,224), and the costs for reoperation equaled $14,785 per encounter for neuroforaminal bone growth and $20,267 for pseudarthrosis.
CONCLUSIONS: Symptomatic ectopic bone formation, vertebral osteolysis, and pseudarthrosis are recognized complications with the use of rhBMP-2 in MIS-TLIFs. Potential causes include improper dosage and a closed space that prevents the egress of the postoperative BMP-2 fluid collection.

FDA device/drug status: Not approved for this indication (Infuse).

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Management of these complications has a substantial cost for the patient and the surgeon and needs to be considered with the off-label use of rhBMP-2.

Keywords: rhBMP-2; Neuroforaminal; Bone growth; MIS-TLIF; Pseudarthrosis

Introduction

The clinical use of purified recombinant osteoinductive proteins to enhance spinal fusion has now entered its second decade. Recombinant human bone morphogenetic protein-2 (rhBMP-2, Infuse; Medtronic Sofamor Danek, Memphis, TN, USA) received US Food and Drug Administration (FDA) approval for the indication of anterior lumbar interbody fusion (LIF) in conjunction with a lumbar-tapered cage (Medtronic Sofamor Danek). In this application, rhBMP-2 is applied to a collagen sponge that serves as a biologic carrier [1–3]. In the anterior fusion clinical trials, no adverse events were reported, and it was noted that clinical outcomes improved in the rhBMP-2–treated group. Once approved by the FDA, the off-label use began in clinical practice in the anterior/posterior cervical and posterolateral lumbar spine in an effort to improve fusion rates. Subsequent reports have demonstrated that application of Infuse in the anterior lumbar spine is not without risk [4,5]. The recently published Yale University Open Access Data (YODA) project meta-analyses have demonstrated that the original studies (RCTs and cohort projects) investigating the complications associated with BMP-2 utilization have underreported or even missed some adverse events because of nontransparent data sharing, selective reporting, duplicate publications, and conflicts of interest [4,5]. Therefore, this article will emphasize the limitations of the published BMP-2 complication literature as reported in the YODA project meta-analyses.

Complications in the cervical spine (wound complications, dysphagia, dysphonia) have surfaced over the last several years prompting the FDA to issue a public health warning in 2008 for the off-label use of BMP-2 in this application [5]. Ectopic bone formation has been reported in both the epidural space and the insertional track when rhBMP-2 was used in posterior LIFs, but the harm data were too inadequate to achieve statistical significance in the YODA project [5–7]. Clinically significant neural compromise was noted by Chen et al. [8] in a case series of four patients after the off-label use of rhBMP-2 after minimally invasive transforaminal lumbar interbody fusions (MIS-TLIFs), but the YODA project noted that this outcome measure was poorly classified in the literature with variable reporting of neurologic events [5].

This institutional review board–approved study reviews a single surgeon/single institution experience of more than 500 patients who underwent MIS-TLIFs with rhBMP-2 over a 4-year period including clinical sequelae and direct cost per procedure for both index and revision surgeries. None of the contributing authors have conflicts of interest with Medtronic Sofamor Danek.

Materials and methods

Patient data

After institutional review board approval, a retrospective review of all consecutive patients undergoing an MIS-TLIF by a single surgeon was performed. Patients receiving rhBMP-2 along with an interbody graft were identified. Patients were evaluated based on routine CT evaluation (at 6 months) and with additional diagnostic imaging if neurologic or radiculopathic findings were present (CT myelography).

Data were collected with regard to patient age, diagnosis at index procedure, operative time, interbody graft preparation and materials, time to onset of initial symptoms, and the subsequent revision surgery (hospital direct costs and physician charges). Diagnoses for the primary procedure included recurrent herniated nucleus pulposus, spinal stenosis associated with a degenerative spondylolisthesis, and degenerative disc disease. Demographic data are presented in Tables 1 and 2. Statistical testing was performed to compare age, gender, smoking status, rhBMP-2 doses, and surgical levels between patients who underwent revisions to those who did not. p Values less than .05 were considered statistically significant.

Surgical technique

A unilateral approach was undertaken through a paramedian skin incision using the Wiltse technique under fluoroscopy. Unilateral pedicle screws were placed percutaneously over a guide wire. The laminectomy, bilateral facetectomy, and TLIF were performed through a unilateral 21-mm nonexpandable tube retractor. No posterolateral fusion was performed. Midline muscular and ligamentous structures were all preserved during the procedure. Local bone graft that had been harvested from the laminectomy and facetectomy was collected in a bone trap and mixed with either a small (4.2 mg) or a large (12 mg) kit of rhBMP-2. The large kit was routinely used for earlier cases because of its hospital formulary availability. At the time of the earlier cases in this series, there were limited data on complications related to BMP. However, once complications started to be case reported, the senior surgeon switched from using a large kit to a small kit of rhBMP-2.

Follow-up

Standard postoperative follow-up included visits at 6 weeks, 3 months, 6 months, and 1 year. Patients were evaluated with routine postoperative CT scans at 6 months