Anterior Cervical Discectomy and Fusion: Comparison of Fusion, Dysphagia, and Complication Rates Between Recombinant Human Bone Morphogenetic Protein-2 and Beta-Tricalcium Phosphate

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■ INTRODUCTION: **Anterior cervical discectomy and fusion (ACDF) is one of the most common spinal procedures performed. A direct comparison of the fusion and complication rates between recombinant human bone morphogenetic protein-2 (rhBMP2) and beta-tricalcium phosphate (bTCP) has not been reported.**

■ METHODS: **A retrospective study of 191 consecutive patients who underwent ACDF with polyetheretherketone plastic fusion spacers during a 2-year period with either rhBMP2 (n = 84, 46%) or bTCP (n = 107, 56%) was performed. Patients underwent 1- (35%), 2- (41%), 3- (20%), and 4- (4%) level operations. The primary outcome measure was mature arthrodesis, with secondary measures including clinical outcomes and complication occurrence. Fusion was graded on plain lateral radiographs, with median length of follow-up of 12 months.**

■ RESULTS: **Rates of cervical fusion were significantly greater for patients treated with rhBMP2 than bTCP at both 6 months (70% vs. 26%, P = 0.000) and 12 months (99% vs. 85%, P = 0.000). Postoperative dysphagia was reported in 35 patients (18%), with no difference in dysphagia incidence between rhBMP2 and bTCP (20% vs. 17%, P = 0.5); however, dysphagia was more severe in the rhBMP2 group, with greater rates of readmission and steroid use (both P < 0.05). A multivariable sensitivity analyses to control for patient characteristics and number of spinal fusion levels showed no differences in dysphagia rate between rhBMP2 and bTCP.**

■ CONCLUSIONS: **In our cohort, the rate of mature arthrodesis after ACDF was greater with rhBMP2 compared with bTCP with no increased incidence of postoperative dysphagia; however, dysphagia severity was greater in the rhBMP2 cohort.**

INTRODUCTION

Anterior cervical discectomy and fusion (ACDF) remains one of the most common and successful spinal procedures; however, the durability of this operation is predicated on achieving solid arthrodesis. Before the introduction of stored allograft (both structural and morcelized) and various osteoinductive or osteoconductive compounds, a separate incision was required to obtain autograft from a remote site (e.g., anterior iliac crest), which causes additional morbidity, increased operative time, and, in some cases, chronic pain. Both the osteoinductive recombinant human bone morphogenetic protein 2 (rhBMP2) and the osteoconductive beta-tricalcium phosphate (bTCP) have been used in ACDF to facilitate fusion.

Off-label use of osteoinductive rhBMP2 for ACDF remains controversial. Studies report fusion rates nearing 100% with rhBMP2[1-3] with excellent neurologic outcomes[4]; however, several prospective and retrospective studies reveal a greater incidence of clinically significant postoperative complications associated with the use of rhBMP2 in anterior cervical fusion operations.[2,3,5-9] Large doses of rhBMP2 in many of the early

Key words
- Anterior cervical fusion
- Bone morphogenetic protein

Abbreviations and Acronyms
ACDF: Anterior cervical discectomy and fusion
bTCP: Beta-tricalcium phosphate
CI: Confidence interval
ICU: Intensive care unit
IQR: Interquartile range
LOS: Length of stay
PEEK: Polyetheretherketone
rhBMP2: recombinant human bone morphogenetic protein 2
RR: Rate ratio

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published reports in ACDF were thought to be responsible for the reported complication rates.[1,4,7,10] Also, the lack of containment of the rhBMP2 within the disc space or spacer or graft is felt to be a factor in the development of complications such as swelling or dysphagia.

The first controlled trial of bTCP use in the cervical spine demonstrated solid fusion in all patients by 6 months with or without anterior plating.[11] Compared with hydroxyapatite, bTCP was shown to produce superior fusion rates at 6 and 12 months without any complications attributable to the compound.[12]

Postoperative dysphagia is a common and potentially morbid complication associated with ACDF.[13-17] Dysphagia in these patients is a multifactorial complication, which can result from preoperative patient factors, postoperative soft-tissue swelling, altered pharyngeal and esophageal motility and sensation, as well as changes in cervical alignment. The incidence of postoperative dysphagia after ACDF reported in the literature varies widely, between 1% and 80%.[18-22] Although a number of patient and surgical factors have been studied as risk factors for postoperative dysphagia, their definitive significance has not been demonstrated reliably.[19-28]

In considering the use of osteoinductive and conductive adjuncts, one must assess not only the efficacy and speed of arthrodesis but also the cost as well as any effects on the complication rate. Autograft, the gold standard and less-expensive bone graft option, often is associated with significant donor site morbidity.[29,30] Although rhBMP2 reliably promotes interbody arthrodesis for ACDF, the high per-case cost and reports of increased rates of dysphagia and ectopic bone production have limited its widespread use.[31-33]

In contrast, bTCP has been shown to be associated with less-robust fusion rates (between 46% and 97%), with greater rates of pseudoarthrosis with an increasing number of levels despite similar high associated costs.[11,12,34] In this investigation, we sought to compare fusion rates, incidence, and severity of postoperative complications between consecutive patients who underwent ACDF operations that used rhBMP2 or bTCP during a 2-year period in a high-volume academic spine surgery center.

MATERIALS AND METHODS

Patient Population

A retrospective chart review was performed to identify all ACDF procedures performed by 2 Department of Neurosurgery faculty members at Emory University–affiliated hospitals during a 2-year period from April 2011 to April 2013 (N = 206). All patients in whom allograft or polyetheretherketone (PEEK) cages with rhBMP2 or bTCP bone graft substitute were implanted were included (N = 191). Patients in whom autograft or allograft were used exclusively were excluded (n = 15). Pre- and postoperative clinical and radiographic records of all cases were reviewed. The choice of bone graft supplement, either rhBMP2 or bTCP, was made through a collaborative decision by the surgeon and patient based on patient-specific clinical and surgical characteristics, e.g., single versus multilevel procedures. bTCP was mixed with local, morselized autologous local bone graft and blood aspirate in all cases.

The most common indications for surgery were any or a combination of the following: cervical myelopathy, radiculopathy, spondylosis, and anatomic instability. Risk factors for failure of cervical fusion pseudoarthrosis, including diabetes mellitus, current or previous tobacco use, obesity, end-stage renal disease, and immunosuppression also were collected. Previous cervical fusion (n = 16, 8.4%) also was considered to be a risk factor for pseudoarthrosis and surgical complications. Pre- and postoperative notes were reviewed to characterize and document the persistence or resolution of neurologic deficits after surgery. Obesity was defined by Centers for Disease Control and Prevention guidelines as a body mass index greater than 30. A Smith-Robinson anteromedial approach was used in all cases; all bone graft supplements were secured fully inside the PEEK cage or allograft and were combined with autologous bone marrow aspirate and morcelized osteophyte fragments when bTCP was used. An anterior cervical plate was applied in all cases. Dosing of rhBMP2 and bTCP were approximately 0.5 mg and 1.2 mL per cervical level, respectively.

Fusion

Fusion was assessed by evaluating for evidence of motion across the cervical segment or within the construct and lucency between the graft and adjacent vertebral body endplates with the use of plain radiographs, flexion-extension lateral radiographs, or computed tomography studies at clinic follow-up. Fusion was defined as a binary outcome, with complete fusion versus incomplete fusion at both 6- and 12-month endpoints. As such, partial or incomplete fusion was not counted in statistical analysis. Pseudoarthrosis was defined as failure of fusion at postoperative clinical follow-up beyond 6 months.

Dysphagia Calculations

Episodes of postoperative dysphagia were identified from documentation in the electronic medical record. A liberal definition of dysphagia included all patient-reported, subjective reports that were documented as well as objective clinical measures. Clinically significant dysphagia was defined and stratified as mild, moderate, or severe.[3] Mild dysphagia was defined as dysphagia that prolonged postoperative hospitalization length of stay (LOS) by 48 hours or more. Moderate dysphagia was defined as dysphagia that prolonged postoperative hospitalization by 72 hours or more and required a speech therapy evaluation or modification of diet. Severe dysphagia was defined as inability to sustain adequate oral nutrition requiring supplemental nutrition by a nasal feeding tube or gastrostomy tube. Administration of intravenous and oral postoperative steroids also was collected. For patients with postoperative dysphagia, the Nurick Myelopathy Score and Ranawat Classification of Neurologic Deficit were calculated for time of last follow-up.[35,36]

Statistical Analysis

Statistical analyses were conducted with SPSS v22 (IBM Corp., Armonk, New York, USA). Descriptive statistics were calculated for all variables of interest and include means and standard deviations or medians and interquartile ranges (IQRs) for continuous variables or counts and percentages, as appropriate. Multivariable logistic regression was conducted to assess the association of