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Nerve injury and recovery after lateral lumbar interbody fusion with and without bone morphogenetic protein-2 augmentation: a cohort-controlled study

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Abstract

BACKGROUND CONTEXT: Despite common use of intraoperative electrophysiologic neuromonitoring, injuries to the lumbar plexus during lateral lumbar interbody fusion (LLIF) have been reported. Emerging data suggest that recombinant human bone morphogenetic protein-2 (rhBMP-2) use during an anterior or transforaminal lumbar interbody fusion may be associated with an increased risk of neurological deficit. Clinical data on the sequelae of rhBMP-2 implantation in close proximity to the lumbosacral plexus during LLIF remains to be understood.

PURPOSE: The purpose of this study was to compare the incidence of neurologic deficits and pain in patients undergoing LLIF with and without rhBMP-2.

STUDY DESIGN/SETTING: Retrospective outcome analysis in controlled cohorts undergoing the lateral exposure technique for LLIF with and without rhBMP-2.

METHODS: The electronic medical records of patients undergoing LLIF with and without supplemental posterior fusion for degenerative spinal conditions were retrospectively reviewed over a 6-year period. Patients with previous lumbar spine surgery or follow-up of less than 6 months were excluded. Patients were divided into 2 groups, Group 1 (rhBMP-2 use; n=72) and Group 2 (autograft/allograft use; n=72), and were matched according to the age at the time of surgery, gender, weight, body mass index, side of approach, total number of treated spinal segments, use of supplemental posterior fusion, and length of follow-up.

RESULTS: Immediately after surgery, a sensory deficit was recorded in 33 patients in Group 1 and 35 patients in Group 2 (odds ratio [OR] 0.895; 90% confidence interval [CI] 0.516–1.550; p=.739). At last follow-up, a persistent sensory deficit was identified in 29 patients whose LLIF procedure

FDA device/drug status: Approved: Interbody Fusion Cage: XLIF (Nuvasive, Inc., San Diego, CA, USA); Interbody Fusion Cage: COUGAR (Depuy Spine Inc., Raynham, MA, USA). Not Approved: Bone Morphogenetic Protein-2: INFUSE Bone Graft (Medtronic, Inc., Memphis, TN, USA).

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The disclosure key can be found on the Table of Contents and at www.TheSpineJournalOnline.com.

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was supplemented by rhBMP-2 and 20 patients in whom autograft/allograft was used (OR 1.754; 90% CI 0.976–3.151; p=.115). A motor deficit was recorded in 37 patients immediately after the rhBMP-2 procedure and 28 patients treated with autograft/allograft (OR 1.661; 90% CI 0.953–2.895; p=.133). A persistent motor deficit was recorded in 35 and 17 patients in Groups 1 and 2, respectively, at last follow-up (OR 3.060; 90% CI 1.681–5.571; p=.002). During the first postoperative examination, 37 patients in Group 1 and 25 patients in Group 2 complained of anterior thigh or groin pain (OR 1.987; 90% CI 1.133–3.488; p=.045). At last follow-up, there was a significantly higher number of patients in Group 1 who complained of persistent anterior thigh or groin pain than Group 2 (8 vs. 0 patients) (OR 16.470; 90% CI 1.477–183.700; p=.006).

CONCLUSIONS: Our results provide evidence of an increased rate of postoperative neurologic deficit and anterior thigh/groin pain after LLIF using rhBMP-2, when compared with matched controls without rhBMP-2 exposure. This study suggests a potential direct deleterious effect of rhBMP-2 on the lumbosacral plexus.

Keywords: Nerve injury; LLIF; XLIF; rhBMP-2; Thigh pain; Transforming growth factor-β

Introduction

Lateral lumbar interbody fusion (LLIF) may be complicated by injury to the lumbosacral plexus. Although several intraoperative electrophysiologic neuromonitoring systems are commercially available to prevent iatrogenic nerve injury, nerve injuries during the lateral retroperitoneal transpsoas approach to the spine have been reported with an incidence of 0.7% to 23% [1–6]. Lumbosacral plexus injury is usually the result of nerve root traction or compression during the lateral transpsoas approach [1,3]. Dissection under direct visualization of the psoas with identification and protection of the lumbosacral plexus is recommended. Operative time and inclusion of the L4–L5 level have been identified as independent risk factors for iatrogenic nerve injury during LLIF [6,7]. However, motor and/or sensory nerve deficits and postoperative pain still occur when levels other than L4–L5 are treated even by the most experienced spine surgeons.

Currently, recombinant human bone morphogenetic protein-2 (rhBMP-2) is approved by the US Food and Drug Administration (FDA) for anterior lumbar interbody fusion (ALIF) and long-bone fracture repair [8]. Postoperative complications in spine surgery associated with the off-label use of rhBMP-2 include heterotopic bone formation, vertebral body osteolysis in the lumbar and thoracic spine, soft tissue swelling in the cervical spine, and radiculitis [9–14]. Retrograde ejaculation has also been reported in the original FDA trial on rhBMP-2 use in ALIF and confirmed by more recent studies [15,16].

Through BMP receptors, which are present in both the central and peripheral nervous system, BMPs act as instructive signals for neuronal lineage commitment and promote neuronal differentiation [17]. Evidence suggests that BMPs may be involved in neuronal regeneration and axonal growth through an injury-induced signaling regulation with BMP pathway activation being predominantly permissive in the peripheral nervous system and inhibitory in the central nervous system [18–21]. In a dog model of lumbar spine laminectomy defect, Meyer et al. [22] reported the safety of rhBMP-2. However, more recent studies suggest that rhBMP-2 may impede neurologic recovery in patients with an open dural spinal cord injury [23].

Prior reports suggest that rhBMP-2 following ALIF or transforaminal lumbar interbody fusion (TLIF) procedures is associated with an increased risk of direct neurological deficit. Data on the clinical sequelae of rhBMP-2 implantation during LLIF remains to be reported. We hypothesized that in a matched cohort of patients, those undergoing LLIF with rhBMP-2 had a higher incidence of postoperative neurological deficits and pain.

Methods

Study population

After obtaining institutional review board approval, the electronic medical records of patients who underwent LLIF with or without supplemental posterior spinal fusion between March 2006 and April 2012 were retrospectively reviewed. Inclusion criteria were as follows: (1) patients who underwent LLIF with the supplementary use of rhBMP-2, cancellous allograft, or iliac crest bone autograft for stimulation of bone growth; (2) patients who underwent fusion for degenerative spinal conditions; and (3) follow-up of more than 6 months. Patients with prior thoracolumbar spine surgery were excluded.

All patients underwent a minimally invasive lateral retroperitoneal transpsoas approach and lumbar interbody fusion at one or more levels using either the extreme lateral interbody fusion system (XLIF-Nuvasive, Inc., San Diego, CA, USA) or the COUGAR system (COUGAR-Depuy Spine, Inc., Raynham, MA, USA). Intraoperative electromyography and active-run electromyography were used in every patient. Our standard rhBMP-2 dosing protocol was to load each LLIF cage with 4.2 mg (concentration: 1.5 mg/mL) of the adjunct (INFUSE Bone Graft; Medtronic, Inc., Memphis, TN, USA), administered via a sterile absorbable collagen sponge, which was soaked for at least 15 minutes before application according to the