

The Use of rhBMP-2 to Achieve Posterior Cervical Fusion Without Internal Fixation: Report of Three Cases in Adults

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Citation

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Abstract

The use of bone morphogenetic proteins (BMPs) to achieve bony fusion has been reported in conjunction with internal fixation in different locations of the spine. Three cases are presented in which the patients were deemed to have poor quality bone and spinal anatomical abnormalities that prevented the use of traditional fusion methods. Posterior cervical fusion using rh-BMP-2 alone after application of a halo ring and vest was used in these three patients as an alternative method of achieving fusion. To the authors' knowledge, no studies have yet described the use of rh-BMP-2 (INFUSE®) in achieving posterior cervical fusion without internal fixation.

DISCLOSURE

In the effort of full disclosure, Peter Shedden MD serves as a medical consultant for Medtronic. Dr. Shedden has not received and will not receive any compensation of any form for the publication of this work. Dr. Shedden also has no benefit of any kind that would result from this publication. The article has been written with full scientific integrity and accurate reporting of all results and discussion.

INTRODUCTION

Surgeons have been searching for decades to find bone-grafting materials that would allow them to achieve higher fusion rates and/or eliminate the need for autogenous iliac crest bone harvesting. Fusion rates are known to be impacted by several factors including but not limited to fusion method, age of patient, bone quality, history of smoking, and diabetes mellitus.^{18,20,36,38,40} Recent advances in material-based technology and molecular biotechnology have led to the development of new interbody spacers and osteoinductive agents that hold tremendous promise for the future of spine surgery.

Bone morphogenetic proteins (BMPs), discovered and named by Marshall Urist, are a component of the bone matrix and are part of a large, multigene family – the transforming growth factor beta (TGF-β) superfamily.

Numerous BMPs have been identified with upwards of 20 distinct proteins and can be divided into subgroups based on sequence similarity.^{13,14,28,48,49,50,51} BMPs

are extracellular, dimeric, low molecular weight, non-collagenous glycoproteins that are involved in regulating proliferation, apoptosis, and differentiation.^{13,21,25,26,42,44,45} They differ from other proteins (e.g., growth factors) in that they are morphogens.^{21,25,26,42,51,52}

Several but not all of the BMPs have been shown to be able to induce de novo osteogenesis acting as local mediators of osteogenesis with their affect being concentration dependent.

Preclinical studies indicate that they induce osteogenesis in a sequential manner and their mode of action includes chemotaxis of cells to the implant site, proliferation of these cells, and finally differentiation of these cells into active osteoblasts.^{14,25,26,42,51} The bone tissue that is formed is histologically normal.^{38,39}

Rh-BMP-2 (INFUSE®, Medtronic Sofamor-Danek, Memphis, TN) which has osteoinductive capacity has been demonstrated to play a critical role in development.

The safety and efficacy of rh-BMP-2 was extensively studied for decades prior to receiving FDA approval for human use.^{21,39,46,51,54} ^{23,44,45,46,52}

Several human clinical trials have reported rh-BMP-2 usage in oral maxillofacial procedures and in human orthopedic clinical trials for tibial fractures.^{3,7,8,15,17,19,22,24,47,53} Although this new technological advance has been known and applied in the lumbar spine for several years, its use in the cervical spine has been limited to the anterior approach in the few sporadic reports in the literature.^{2,4,6,6,9,10,11,12,18,20,29,34}

We report the clinical outcomes obtained in three patients who underwent posterior cervical fusion using rhBMP-2 with only external fixation. To our knowledge, the use of rhBMP-2 for posterior cervical fusion without internal fixation has not been previously reported.

CASE MATERIAL

CASE 1

A 77-year-old female presented with pain radiating to behind the left ear compatible with occipital neuralgia. She had no complaints of pain, numbness, or tingling in either the shoulder or arm, and was neurologically intact. She had no history of physical injury and the medical history included chronic lymphocytic leukemia and osteoarthritis. Cervical spine x-rays and CT imaging revealed cervical spondylitic disease and severe left C1-C2 facet arthropathy. The patient had failed all conservative options and it was recommended that the patient try a halo to see if external fixation could decrease the pain. The patient had complete resolution of pain and thus fusion was recommended as an option.

SURGICAL PROCEDURE

The patient was brought to the operating room and was intubated with a cuff endotracheal tube. Initially a right hip graft was harvested from the patient for later use. Subsequently, the patient was placed prone on bolsters, in the halo, and her head was supported and placed in neutral position. At that point the occipital area was shaved, prepped, and draped in an appropriate fashion. Standard approach was performed to expose the occiput, C1, and C2 posterior elements. Intra-operative examination revealed that the C1 arch was fused to the occiput. Although several options were possible, there was concern that adequate internal fixation could not be accomplished successfully. At this point the surgery proceeded with bilateral decortication of the lamina of C1, C2, and also the base of the occiput. Two INFUSE soaked collagen sponges were wrapped around MASTERGRAFT PUTTY and the harvested autogenous bone. These sponges were placed in complete contact with the occiput, C1, and C2 on both sides. No irrigation was done at this point. Standard closure procedures were done. There were no complications during this procedure. Patient remained in halo for 3 months.

CASE 2

An 80-year-old female presented with a complaint of bilateral weakness in both arms and tingling in her hands. Weakness was grade 2/5 in her proximal arms. It was noted

that the patient had her head in a fixed-tilted position looking to the left. The patient also had deafness in the left ear along with numbness around the left ear and into the left jaw. The medical history was unremarkable except for a fall the patient had 2-years prior to presentation. She had seen multiple physicians over that time and was told there was nothing that could be done for her. After investigations, which included CT/MRI/plain films of cervical spine, she was admitted to the hospital and placed in a halo with 10 lbs of traction. The patient responded to the traction and was able to lift both arms above her head. The investigations had revealed rotation of the dens, medullo-cervical junction compression, and previous C2 fracture with displacement. Application of halo ring and vest were completed and posterior cervical fusion was recommended. Because of experience in case #1 the patient was made aware of the possible use of rh-BMP-2 and the current FDA recommendations.

SURGICAL PROCEDURE

The patient was taken to the operating room and fiberoptically intubated. All standard preventions were taken for positioning. Her occipital area and post-cervical area were shaved, prepped and draped in appropriate fashion. Standard approach allowed exposure of the occiput, C1, and C2. Very thin bone, poor bone quality, and misaligned C1 and C2 prevented the use of internal fixation of any type. The suboccipital area, the arch of C1, the lamina and the spinous process of C2 were then decorticated. Vitoss® soaked in INFUSE® was used, and was packed from the occiput down to C2 on both sides and along the lamina and spinous processes. There was no irrigation and standard closure procedures were done. There were no complications with the procedure. Patient remained in halo for 3 months.

CASE 3

A 71-year-old female patient presented to the emergency room after falling backwards on the tiled kitchen floor, she had a brief loss of consciousness, and noticed some left upper extremity weakness. She was seen in the emergency room and was diagnosed with a C2 avulsion fracture. She was discharged from the ER in a collar and was referred to our office one month later. The fracture was deemed unstable and fortunately the patient was neurologically intact. Evaluation revealed what appeared to evidence of bilateral C2 pars fracture and also a fracture extending through the body of C2. The patient was admitted to the hospital and required 10 lbs of cervical traction for

realignment. A long discussion took place with the patient's family and the patient about her various surgical options. Her bone quality was extremely poor. She had multiple medical problems including diabetes mellitus, prior history of smoking, and hypertension. With a halo ring and vest in place, a posterior approach was suggested with the goal of lateral fusion using rh-BMP-2. From our experience with case #1 and 2, the patient was made aware of rh-BMP-2 and what the FDA had approved for its usage.

SURGICAL PROCEDURE

The patient was brought to the operating room and fiberoptically intubated in standard fashion. All standard preventative measures were taken for positioning. The posterior neck was then shaved, prepped, and draped in appropriate fashion and a standard approach was done to expose the base of the occiput, and thru the C1-C3 vertebra. A generous decortication of the lamina of C1, C2, C3, and the facet joints at C2-3 followed. Options were reviewed and internal fixation was deemed unsafe and not possible. At this point, an INFUSE® soaked collagen sponge was wrapped around MASTERGRAFT® GRANULES (Medtronic Sofamor-Danek, Memphis, TN). It was placed down laterally over the facet joints extending from C1 to the C2/C3 facet joint and along the C3 lamina. There was no irrigation done. Hemostasis was controlled. Standard closure procedures were done. There were no complications during this procedure. Patient remained in halo for 3 months.

DISCUSSION

The three cases presented have shown the effective use of rhBMP-2 in achieving posterior cervical spinal fusion in patients that could not undergo traditional fusion procedures due to poor bone quality and poor cervical anatomy. All three of the patients obtained excellent fusion results, although all had to be treated with a halo ring and vest for 3 months post-surgery. The patient in case 1 had resolution of her pain after fusion. The patient in case 2 obtained increased stability from the fusion and normal neurological function was restored. The patient in case 3 obtained increased stability from the fusion and had minimal complaints of muscular pain. All three patients used a different carrier and bulking agent; however, the specific carrier seems to be independent of successful fusion. Successful fusion seems to be dependent solely on the use of INFUSE® as the source for rh-BMP-2. Figures 1-3 show the x-rays of the posterior fusion achieved in each of the cases. No patient suffered any complication from the surgery, or

from the use of rhBMP-2.

Figure 1

Figure 1: Flexion (left) and extension (right) x-rays of case #3 are shown. Arrows indicate fusion between occiput, axis (C1), and atlas (C2).

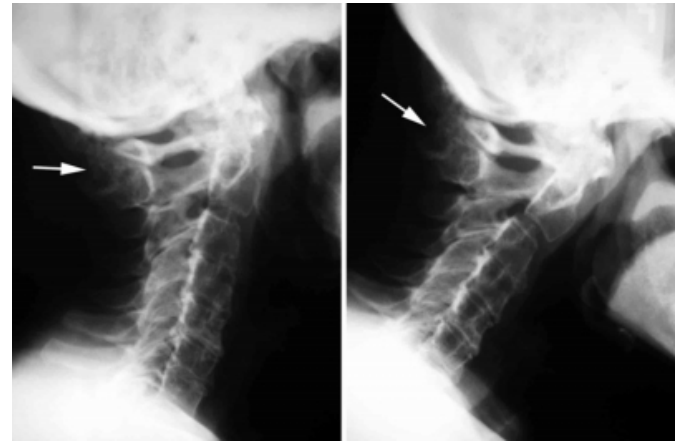


Figure 2

Figure 2: Flexion (left) and extension (right) x-rays of case #2 are shown. Arrows indicate fusion between occiput, axis (C1), and atlas (C2).

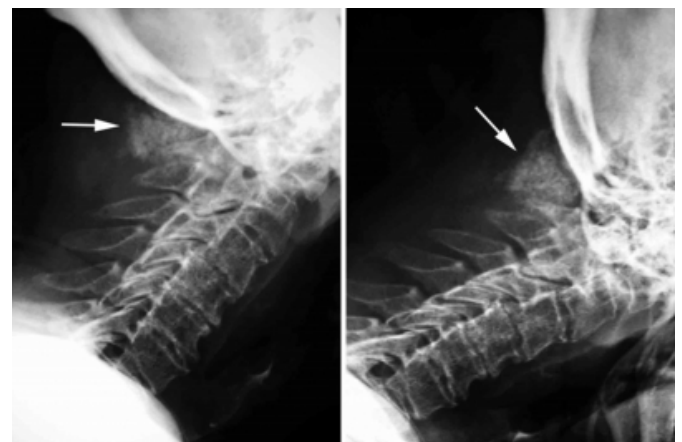


Figure 3

Figure 3: Flexion (left), normal (center), and extension (right) x-rays of Case #1 are shown. Arrows indicate fusion between occiput and axis (C1).



A few studies have indicated adverse responses to the use of rhBMP-2 in anterior cervical fusion such as swelling, increased difficulty in swallowing and breathing.^{37,40,41} These adverse effects appear to be associated with higher doses of rhBMP-2 and seem to be minimized through proper planning and usage.⁴⁰ Although these studies have noted risk of adverse effects with the use of BMPs, these three cases support the possibility for the safe and effective use of rhBMP-2 in achieving posterior cervical fusion in patients with external fixation. To the author's knowledge, this provides the first report of rh-BMP-2, independent of carrier and bulking agent, used to achieve posterior cervical fusion without use of traditional internal fixation techniques.

CONCLUSIONS

Although the use of rhBMP-2 in achieving spinal fusion has been well described, limited literature exists on its use in the cervical region. The limited literature that does exist only describes the use of BMPs in achieving anterior cervical fusion. To the author's knowledge no literature has described the use of rhBMP-2 to achieve posterior cervical fusion. These three cases show the use of rhBMP-2 with external fixation to achieve posterior cervical spinal fusion in patients with poor bone quality and poor cervical anatomy where internal fixation was deemed unsafe.

CORRESPONDENCE TO

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