ORIGINAL RESEARCH

To determine difference between radiological and functional outcome in TLIF surgery with use of BMP 2 VS without bmp 2 in adult patients

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ABSTRACT

Background: Bone morphogenetic proteins (BMP) are multi-functionalgrowth factors that belong to the transforming growth factor beta (TGF-beta) superfamily. The purpose of the study is to determine difference between radiological and functional outcome in TLIF surgery with use of BMP 2 vs without BMP 2 in adult patients.

Methods: The present study evaluated data obtained between May 2016 and July 2017 on patients in whom BMP-2 was used in conjunction with TLIF. 150 fulfilled the study criteria whose mean age was 54.6 years [range 25–65 years]). Twenty-five patients (33.8%) had previously undergone lumbar surgeries (discectomy, fusion, and decompression).

Result: Both groups had similar gender distribution and average age at surgery (48.9 ± 12.2years for the BMP group and 44.6 ± 13.7 years for the non-BMP group, $p>0.05$). As expected, the BMP group had a shorter median follow-up time of 5.05 ± 7.10 years while the non-BMP group was followed for a median of years 5.06 ± 12.6.

Conclusion: It is important that clinicians explain these findings to patients so that they can make informed choices about the type of surgery they would prefer. The use of BMP safe and effective in the context of TLIF procedures, and thoughtful discussion with patients about the pros and cons of BMP utilization during surgery is recommended

Keywords: Bone morphogenetic protein; transforaminal lumbar interbody fusion; spine surgery; BMP-2

INTRODUCTION

Bone morphogenetic proteins (BMP) are multi-functionalgrowth factors that belong to the transforming growth factor beta (TGF-beta) superfamily, they were introduced in themedical scenario to promote bone healing with the proposalof less morbidity compared to the usual methods of bone graftharvest; it is the only bone inducer with level I of clinical evidence. The Food and Drug Administration (FDA) approved itsuse in July of 2002 for anterior approaches of lumbar spinefusion procedures.

Human bone morphogenetic protein-2 (BMP-2) is widely used as an alternative to iliac crest bone graft (ICBG) to promote fusion in spinal surgery.[1]Since the U.S. Food and Drug Administration (FDA) approved rhBMP-2 for anterior lumbar interbody fusion (ALIF) surgery,[3] its use has grown rapidly, including off-label indications.[2,4]

Several recently developed BMPs have been shown to possess osteoinductive potential capable of stimulating the formation of new bone.[5] This growth factor is thought to promote increased fusion rates more reliably and faster.[6,7]

The availability of rhBMP-2 for use in clinical practice could theoretically resolve numerous problems related to spinal fusion. Although preclinical experimental results seem promising, initial clinical applications are still in the early phases of study. Several different materials and techniques have been explored in an effort to improve spinal fusion rates. Allograft bone used alone in lumbar fusion has yielded inconsistent results, with arthrodesis rates ranging from approximately 50 to 95%.[8-11]

With numerous benefits of BMP, recombinant human bone 16 morphogenetic protein-2 (rhBMP-2), a subtype of BMP, has only obtained FDA approval for use in single level anterior lumbar interbody fusions (ALIF) inside an LT-CAGE

The purpose of the study is to determine difference between radiological and functional outcome in TLIF surgery with use of BMP 2 vs without BMP 2 in adult patients.

MATERIALS AND METHODS

The present study evaluated data obtained between May 2016 and July 2017 on patients in whom BMP-2 was used in conjunction with TLIF. 150 fulfilled the study criteria whose mean age was

54.6 years [range 25–65 years]). Twenty-five patients (33.8%) had previously undergone lumbar surgeries (discectomy, fusion, and decompression). The criteria for determining to undertake an open approach or a minimally invasive approach depended on whether the patient had previously undergone lumbar surgery, the presence of bilateral disease. In determining these factors open surgery was performed in preference to the minimally invasive procedure. Depending on the surgical approach and the number of surgically treated spinal levels, patients were divided into one of two groups: Group I- TLIF surgery with use of BMP 2 and Group II - TLIF surgery without BMP 2 in adult patients.

All patients underwent extensive preoperative evaluation to isolate the cause of their pain. Indications for surgery included painful degenerative disc disease (with or without radiculopathy), spinal instability, spinal stenosis, facet joint arthropathy, or degenerative spondylolisthesis.

Clinical findings were consistent with mechanical back pain with or without radiculopathy, which limited the patient's ability to function. Clinically relevant levels were determined based on their history, physical examinationstatus, and diagnostic studies. Although infrequently performed, provocative discography was used to identify a specific intervertebral disc space as a source of pain. A diagnosis of degenerative disc disease was considered if one or more of the following imaging findings were present: decreased disc height and hydration, osteophyte formation, ligamentous thickening, Modic changes, disc herniation, instability, or facet joint degeneration. Lumbar instability was demonstrated on functional flexion–extension radiographs and the diagnosis was established when dynamic anteroposterior translation was greater than or equal to 3 mm and/or angulation was greater than or equal to 10°. All patients underwent conservative therapy for a minimum of 6 months before the surgery unless their symptoms were progressive or existed in conjunction with radiographically documented gross spinal instability.

OUTCOME MEASURES

Plain radiography was conducted to evaluate fusion status and possible ectopic bone formation at 3, 6, 12, and 24 months and thin-cut 1-mm CT scanning was performed at 12 and 24 months. Complications related to the surgical procedure, additional surgical interventions, and allergic reactions were documented. Fusion was defined as an evidence of trabecular bone bridging documented on CT scans; furthermore, it was defined on plain radiographs as less than a 5° difference in angular motion between flexion and extension and the absence of radiolucency lines greater than 2 mm in thicknesscovering more than 50% of the superior or inferior surface of the grafts.[12,13]

SURGICAL TECHNIQUE

After pedicle screw placement, an inferior facetectomy is performed with osteotomes through the ipsilateral pars. The interspinsous ligament between the operative levels is resected and a laminar spreader is utilized to help distract the disc space in preparation of the discectomy. Secondary distraction is utilized with ipsilateral pedicle screw distractors. A high-speed burr or osteotome is utilized to resect the superior facet to be flush with the distal pedicle, which exposed the transforaminal corridor. Once the bone is removed, the ligamentumflavum on the ipsilateral side is resected with kerrisons exposing the thecal sac and traversing nerve root, if a contralateral decompression is necessary based on preoperative symptoms. All bone around the caudal pedicle is resected with kerrisons so that clear visualization of the neural structures is achieved. The disc space is identified and bipolar cautery is used to coagulate epidural veins. A right-angled neural protector is used to retract the thecal sac medially as well as protect the exiting nerve root. A discectomy is then performed with disc space shavers, currettes and rasps. Trials are utilized to ensure that an appropriate height and width cage is used, with the goal of placing the widest TLIF cage that can be utilized to maximize surface contact area. The TLIF cage is filled with BMP-2 on absorbable collagen sponge wrapped around Mastergraft Matrix. The dose of BMP-2 varied during the study time frame, with gradual reduction of the anterior BMP-2 dose from 12mg to 4mg towards the end of the study time frame. Local autograft was used tosupplement the BMP in the BMP group, and local autograft and iliac cress autograft were used ifthe non-BMP group. The TLIF cage 1 was placed anterior in the disc space and the disc space was backfilled with autograft in both groups.

STATISTICAL ANALYSIS

The results are reported as means 6 SDs and percentages when applicable. Statistical significance was set at a probability value of 0.05. The Student t-test was performed for independent continuous quantitative variables. The chi-square or the Fisher exact test was used to analyze categorical values. Analysis of variance was conducted to assess Patient Satisfaction with Results data.

RESULTS

Table 1: Summary of demographic data stratified by procedure

Category	BMP (n=75)	NON-BMP (n=75)	t (p)
Age at surgery	48.9±12.2	44.6 ± 13.7	-1.80 (0.053)
Follow up time	5.05 ± 7.10	5.06 ± 12.6	3.04 (<0.003)
Sex			
Male	45	35	
Female	30	40	
TLIF-related complications	7	4	0.018 (0.894)
Diabetes	8	5	6.635 (0.01)

Baseline characteristics between the two cohorts were statistically similar (Table 1). Both groups had similar gender distribution and average age at surgery (48.9 ± 12.2years for the BMP group and 44.6 ± 13.7years for the non-BMP group, p>0.05). As expected, the BMP group had a shorter median follow-up time of 5.05 ± 7.10 years while the non-BMP group was followed for a median ofyears 5.06 ± 12.6.

Table 2: Frequency of Anterior Lenke Grades

Lenke Grade	BMP levels fused = 75	Non-BMP levels fused = 75	X2 (p)
A	35	40	3.16 (0.35)
B	30	25	
C	5	6	
D	5	4	

Table 3: Frequency of Posterior Lenke Grades

Lenke Grade	BMP levels fused = 75	Non-BMP levels fused = 75	X2 (p)
A	30	35	10.25 (<0.02)
B	30	20	
C	10	10	
D	5	10	

There is no statistically significant difference in the distribution of anterior Lenke grades between groups 3.16, p=0.35). However, the distribution of posterior grades was statistically significant with the BMP group having a more favorable distribution with fewer grades C or D than the non-BMP group 10.25, p<0.02).

RADIOGRAPHIC OUTCOMES

Radiography demonstrated successful fusion in all patients by 10 months. The mean time to fusion was 4.1 months (range 2–10 months) (Fig. 1). Solid fusion at the surgically treated level(s) at 12 and 24 months was confirmed on thin-cut CT scans. No ectopic bone formation was identified.

DISCUSSION

The use of rhBMP-2 in spine surgery has increased substantially since the FDA approved its use in single-level ALIFs. In comparison to iliac crest bone graft, rhBMP-2 has proven to be equal to or better than ICBG in posterior spinal fusions, with the potential to reduce donor site pain and morbidity.13-15 While there are many benefits to its use, rhBMP-2 has its own set of complications such as radiculitis, ectopic bone formation, andosteolysis, all related to BMP inflammatory mechanism.

The purpose of the study is to determine difference between radiological and functional outcome in TLIF surgery with use of BMP 2 vs without BMP 2 in adult patients.

In the aforementioned PLIF and BMP-2 studies,[13,16,17]cylindrical threaded cages were used as the carrier, and the authors reported posterior ectopic bone formation, perhaps related to surgical technique or the rhBMP-2 carrier itself. Poynton and Lane33 reviewed the available literature for safety issues including bone overgrowth and uncontrolled bone formation, interaction with exposed dura mater, and osteoclastic activation. They concluded that bone overgrowth might have been related to incorrect placementinadequate retention by some carriers, excessively bleeding bone surfaces, and inadvertent exposure of the adjacent levels. The TLIF approach differs from that of PLF (in theory) by requiring a more lateral-to-medial trajectory, thus necessitating less retraction of the exiting (superior) nerve root and thecal sac. This slight change in trajectory could potentially eliminate the ectopic bone formation that

has been reported in the anterior epidural space posterior to the fixation devices. Moreover, we placed the BMP-2 and locally harvested autograft anteriorly in the disc space and then inserted one or two structural allografts posteriorly. Although we found no evidenceof ectopic bone formation in the anterior epidural space posterior to the structural allografts, one allograft migrated posteriorly into the epidural space and caused postoperative nerve root impingement and radiculopathy, thus requiring surgical intervention and removal of the graft. Baskin, et al.,[18] reported the results of a pilot study in which they evaluated the safety and efficacy of rhBMP-2–soaked collagen carrier placed inside an allograft ring in patients undergoing anterior cervical fusion.

Minimally invasive TLIF can in theory involve only minimal iatrogenic tissue injuries and still accomplish the traditional goals of surgery. The radiographically documented efficacy of BMP-2–induced fusion was not dependent on whether open or minimally invasive surgery was used or the number of treated spinal levels.

Previous studies have examined the efficacy of rhBMP-2 use in TLIF procedures. Singh et al.[19] reported a pseudarthrosis rate of 39 out of 573 patients, or 6.8%. Patients underwent MIS- TLIF with BMP with two anterior doses of rhBMP-2: 4.2 mg (small kit) and 12 mg (large kit).Crandall et al., on the other hand, reported a lower pseudarthrosis rate of 8 out of 872 discs, or 0.92%.

The spinal fusion is a tool for the treatment of degenerative,traumatic, neoplastic and infectious conditions of the spine,it can be achieved with interbody fusion, posterior or posterolateral fusion and circumferencial fusion. The most usedexamples of BMP's are recombinant human BMP-2 (rhBMP-2is approved for anterior lumbar interbody fusions – ALIF) andrecombinant human BMP-7 (rhBMP-7 has received a human-itarian device exemption for revision posterolateral lumbarfusion operation).

CONCLUSION

The use of BMPs is effective but depending of the location of usage (cer-vical spine, lumbar spine or sacrum) and the medical status ofthe patient (presence of comorbidities, tobacco usage) its moreprobable to exhibit complications, such as neuroforaminalbone growth, osteolysis, pseudarthrosis, seroma, hematoma. The use of BMP-2 in spinal fusion surgery increases the likelihood of successful fusion at up to 24 months, but this does not seem to translate into a clinically significant reduction in pain.It is important that clinicians explain these findings to patients so that they can make informed choices about the type of surgery they would prefer. The use of BMP safe and effective in the context of TLIF procedures, and thoughtful discussion with patients about the pros and cons of BMP utilization during surgery is recommended.

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