SPINE

Multiple-Day Drainage when Using Bone Morphogenic Protein for Long-Segment Thoracolumbar Fusions Is Associated with Low Rates of Wound Complications

Dwight Saulle[1], Kai-Ming G. Fu[2], Christopher I. Shaffrey[1], Justin S. Smith[1]

Key words
- Bone morphogenetic protein
- Complications
- Drainage
- Infection
- Seroma

Abbreviations and Acronyms
BMP: Bone morphogenic protein
FDA: U.S. Food and Drug Administration

From the [1]Department of Neurosurgery, University of Virginia, Charlottesville, Virginia; and [2]Department of Neurosurgery, Weill Cornell Medical College, New York, New York, USA

To whom correspondence should be addressed: Justin S. Smith, M.D., Ph.D. [E-mail: jss7f@virginia.edu]

Citation: World Neurosurg. (2013) 80, 1/2:204-207.
http://dx.doi.org/10.1016/j.wneu.2012.08.003

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

BACKGROUND: **Concerns over increased wound complication rates have been raised when bone morphogenic protein (BMP) is used as an adjunct for fusion in spinal surgery. This study evaluated 87 consecutive patients undergoing long-segment thoracolumbar spinal fusions with BMP to assess drain output and the rates of reoperation for infection or seroma.**

METHODS: **Inclusion criteria included patients undergoing 4 or more levels of posterior instrumented thoracolumbar fusion, use of BMP, age >18 years, and a perioperative follow-up of ≥60 days. Drain output, length of time of drainage, and need for reoperation for wound seroma or infection were reviewed.**

RESULTS: **A total of 87 patients met inclusion criteria and had a mean age of 58.5 years (SD 16, range 20 to 81). The average number of levels instrumented and arthrodesed with BMP was 9.2 (SD 3.7; range 4 to 18), and the average dose of BMP used was 31.2 mg (SD 9.6, range 12 to 48) or 2.6 large sponges. Patients required drainage for a mean of 4.9 days (SD 1.3, range 3 to 9). The average total output was 1923 mL (SD 865, range 530 to 4310 mL). The wound infection rate was 2.3% (2 cases of deep wound infection that required reoperation). There was one (1.1%) hematoma, and one (1.1%) sterile seroma, both requiring evacuation. No other wound complications were noted.**

CONCLUSIONS: **Use of BMP for long-segment posterior thoracolumbar fusions may be associated with significant drain output, requiring multiple days of drainage. However, when drained adequately, infections and seromas occur infrequently.**

INTRODUCTION

The off-label use of bone morphogenetic protein (BMP) as an adjunctive aid for posterior spinal arthrodesis has increased 4-fold in the past decade (2, 15). Accompanying this usage have been reports of associated complications, including radiculitis, ectopic bone formation, and neuroinflammation (1-3, 13, 16, 20). One area of concern has been the potential for inflammatory seromas, which has led to the U.S. Food and Drug Administration (FDA) warning about BMP use in cervical spine surgery (14, 21). However, concern over the inflammatory effects of BMP has not been limited to the cervical spine. Several studies have reported inflammatory-related wound complications associated with the use of BMP in posterior thoracolumbar fusions (9, 16). Owens et al. reported a wound complication rate of 4.9%, including infection, hematoma, or persistent drainage (16). Garrett et al. reported that 4.6% of patients treated with lumbar fusion using BMP experienced painful, sterile seromas requiring drainage either surgically or via computed tomography–guided aspiration (9).

Given the reported rates of wound complications, developing and using management techniques to minimize the potential risk when using BMP is important. One management strategy when using BMP in posterior thoracolumbar fusions is to use the lowest effective dose. This dosage remains the subject of debate in the literature (6, 7). A second strategy is the effective use of perioperative closed drainage systems. Subfacial drain placement at the time of surgery has been used to help reduce the occurrence of seromas and hematomas in lumbar spine surgery without a reported increase in infection (18). Previous studies of drainage from fusions with BMP indicate that large volumes of serous fluid can be induced (12). However, most management of drains is predicated on the time of drainage, for example, removal on the second postoperative day, rather than on the volume of drainage. The objective of this study was to assess the rates of wound complications in a series of patients undergoing BMP-augmented long-segment thoracolumbar spinal fusions with routine use of postoperative wound drainage and standardized criteria for removal of these drains based on volume of output.

METHODS

The University of Virginia Department of Neurosurgery Complex Spinal Disorders Database was queried for all patients undergoing thoracic and/or lumbar fusion from January 2007 to December 2009. Further inclusion criteria included age older than 18 years, 4 or more levels arthrodesed, documented usage of BMP with dosage, wounds drained per standard protocol, and a perioperative follow-up of

a minimum of 60 days. Collagen sponges were used as the carrier for BMP, and care was taken to not place BMP sponges overlying the dura. No specific sealants or barriers were used. Fusions were performed posterolaterally (intertransverse process) in the lumbar spine and posteriorly in the thoracic spine. All levels fused were also instrumented with pedicle screw and rod constructs. The quantity of BMP from interbody fusions was included in cases in which the approach was posterior (thereby providing a direct path for BMP diffusion into the surgical bed). Interbody fusions were performed via transforaminal lumbar interbody fusion and used either allograft spacers or titanium cages, morselized autograft, and BMP. Vertebrectomies, if performed, were done via costotransversectomy and used expandable titanium cages, morselized autograft, and BMP. Additional cancellous allograft was used when the quantity of morselized autograft was insufficient. For cases in which iliac bolts were placed, a limited amount of iliac crest bone was typically harvested and also used for arthrodesis.

Database information included demographics, diagnosis, operation performed, and complications necessitating return to the operating room. Database information was supplemented with retrospectively reviewed drainage sheets to determine total drainage from indwelling drains. Standard drain protocol included the placement of a minimum of two 1/8˝inch Hemovac drains in the subfascial space and tunneled through separate incisions. Drains were monitored on a per-shift basis, with drainage recorded every 8 hours on a drainage-specific worksheet. These shift outputs were used to inform the total length of active drainage, as drains were only actively removed when 2 consecutive shifts passed with <30 mL of recorded drainage. Patients were treated with prophylactic intravenous antibiotics while drains were in place. The first-line antibiotic used was Ancef, with vancomycin used for cases in which Ancef was contraindicated. Drains were also generally kept in place until the patients had been mobilized. In patients undergoing staged procedures consisting of an initial anterior procedure followed by posterior fusion, only the drainage from the posterior stage was included in the present study. Additional data collected from review of operative notes included dosage of rh-BMP-2 used, length of surgical procedure, blood loss, and operative details.

Statistical analyses were performed using a Pearson correlation for comparisons of drain output volume, duration of drain use, and the dosage of BMP used. Approval to conduct this study was obtained through the University of Virginia Internal Review Board. The applications of BMP in the patient population described herein are off-label uses of this product.

RESULTS

A total of 87 consecutive cases meeting the inclusion criteria were identified (Table 1). The mean age of the patients was 58.5 years (SD 16.2; range 20 to 81); 62 (71.3%) of the patients were women. All patients carried a diagnosis of deformity, including 42 kyphoscoliosis (48%), 29 scoliosis (33%), 9 kyphotic deformity (10%), 5 proximal junctional kyphosis (6%), 5 spondylolisthesis (6%), and 1 patient with lumbar instability (1%). Forty-seven (54%) patients were undergoing revision surgery.

The mean number of levels treated with instrumentation and arthrodesis was 9.2 (SD 3.7; range 4 to 18), and the mean estimated blood loss was 2250 mL (SD 2137 mL). Operative length ranged from 114 minutes to 585 minutes, with a mean of 362 minutes and an SD of 97 minutes. The mean dose of BMP used was 31.2 mg (SD 9.6 mg, range 12 to 48 mg), or the equivalent of 2.6 large kits. The mean dose per level was 3.4 mg. There were 6 durotomies, with operative notes indicating watertight primary closure in each instance. There was no significant difference in total drainage in patients who incurred a durotomy compared with those who did not (1780 mL vs. 1862 mL, $P = .8$).

Drains were removed once output had decreased to <30 mL for 2 consecutive 8-hour shifts. Based on this criterion, patients required drainage for 3 to 9 days, with a mean time of drainage of 4.9 days (SD 1.3 days). There was no significant difference in days of drainage between revisions and first-time procedures, (4.6 vs. 5.2, $P = .08$); however, there was significantly less total drainage for revisions compared with initial procedures (mean 1639 mL for revisions vs. a mean of 2068 mL for initial surgeries, $P = .01$). All patients required drainage for a minimum of 3 days (Figure 1). By day 5, 60% of the patients still required drainage, decreasing to 14% at day 7. Drain output was substantial, with a mean total output of almost 2 L (1856 mL, SD 787 mL, range 530 to 4310 mL). Drain output was the greatest on day 1 (Figure 2), with a mean output of 693 mL (SD 281 mL). Mean drainage decreased by 49% on day 2 (355 mL), but remained with a mean above 100 mL daily until day 5. Dosage of BMP correlated with the total amount of drain output ($R = 0.396$, $P = .001$) and the duration of drainage required ($R = 0.51$, $P = .001$). There was a moderate correlation between total drainage and number of levels fused ($R = 0.388$, $P = .02$, but no significant correlation between number of levels and number of days of drainage required ($R = .177$, $P = .1$). For none of the cases was there documentation to suggest premature drain failure or unintentional removal.

Wound complications requiring a return to the operating room were noted in 4 patients (4.6%). Two patients were identified with wound infections requiring debridement and reclosure. One patient's infection was diagnosed and treated on postoperative day 17, whereas the second patient's infection was identified on postoperative day 7. One patient was noted to have a painful seroma requiring incision and drainage on postoperative day 5. The 4th patient returned to the operating room on the same day of surgery for concern of a postoperative hematoma.

Table 1. Patient Demographics

Total patients	87 (25 male, 62 female)
Age (mean)	58.5 (SD 16.2, range 20–81)
Diagnosis	Kyphoscoliosis 48%
	Scoliosis 33%
	Kyphotic deformity 10%
	Proximal junctional kyphosis 6%
	Spondylolisthesis 6%
	Lumbar instability 1%
Revisions	47 (54%)
Levels fused (mean)	9.2 (SD 3.7, range 4–18)
BMP dose, mg (mean)	
Total	31.2 (SD 9.6, range 12–48)
Per level	3.4

BMP, bone morphogenic protein.

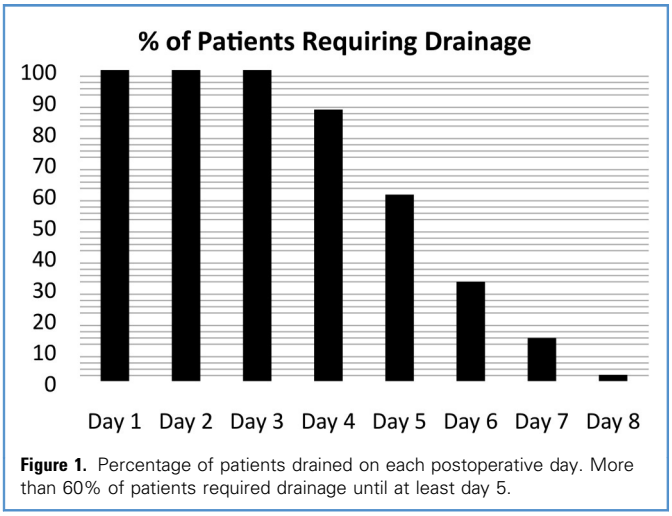

Figure 1. Percentage of patients drained on each postoperative day. More than 60% of patients required drainage until at least day 5.

DISCUSSION

Concerns regarding complications associated with the usage of BMP in spine surgery have increased as its off-label usage has become more prevalent (3). Previous reports have demonstrated that BMP can cause a significant serous inflammatory response. This was a factor leading to the recommendation against using BMP in anterior cervical spine surgery. Several studies have also reported a problematic inflammatory response with the use of BMP when used in posterolateral thoracic and lumbar fusions, with rates approaching 5% (see **Table 1**). Garrett et al. (9) specifically looked at seroma formation in the off-label use of BMP in posterolateral lumbar fusions. They reported that 6 patients required reoperation for exploration of sterile seromas. These seromas occurred in patients treated with varying doses of BMP, suggesting that the inflammatory response was not dose related. Whether or not these patients were drained was not reported. In the study by Mok et al. (12), designed to evaluate the extravasation of BMP, the investigators reported large amounts of drainage in 9 patients. Over 2 days, the drainage ranged from 345 mL to 1840 mL, with a mean drainage of 1224 mL. The investigators did not maintain drains in place to evaluate long-term serous output. Given the potential for morbidity from the significant amount of serous inflammatory fluid production that can occur with the use of BMP in thoracic and lumbar spinal arthrodesis, longer perioperative drainage would be an intuitive method of minimizing this complication.

Our method of managing patients treated with BMP includes drainage until the amount collected decreases to under 30 mL for 2 consecutive 8-hour shifts. In the patients included in this study, this equated to a minimum of 3 days of drainage and was as long as 9 days. A majority of patients had drainage at least until postoperative day 5. Large amounts of drainage were noted, with the mean approaching 2 L. The largest amounts of drainage were present on day 1 and likely reflect some continuing blood loss. However, drainage in large quantities persisted in patients through day 5, suggesting a serous inflammatory response. This is consistent with the findings by Smucker et al., in which anterior cervical discectomy and fusion augmented with BMP had postoperative swelling complications present an average of 4.2 days after surgery (21). In the present series, not draining after day 2 would have resulted in a mean of 563 mL of fluid potentially remaining to form a seroma.

The large number of levels fused in this study (average 9.2) could lead to the assumption that the large quantities of drainage were simply attributable to the magnitude of procedures and the extent of tissue dissection. However, this is refuted by the poor correlation of numbers of levels fused with the number of days of drainage required, while concurrently there is a significant correlation between the dose of BMP and total drainage ($R = 0.396$, $P = .001$). Additionally, the extended duration of drainage would support an active inflammatory process continuing to produce fluid, as opposed to drainage being caused primarily by surgical tissue disruption.

Even with long perioperative drainage, 1 patient required evacuation of a seroma. It should be noted that 1 patient was treated on the same day as the initial operation for evacuation of an epidural hematoma. In this patient, long-term drainage ensued after the reclosure without further event. The rate of seroma formation was less than the rates previously reported in the thoracic and lumbar spine for studies in which patients did not receive wound drains, but similar to rates found in studies in which subfacial drains were used (2, 6, 9, 10, 12, 16). The number of spinal levels fused was substantially fewer in these studies (1 to 4 levels) compared with the present study (mean of 9.2 levels). The study by Garrett et al. reported an incidence of 4.6% for sterile seromas requiring reoperation in 6 patients who had an average BMP dose of 8.4 mg and an average of 3.5 levels fused (9). Glassman et al. reported sterile hematoma/seroma requiring drainage at a rate of 0.96% in a series of 1037 patients, with an average of 1.8 levels fused and with 6.8 mg BMP per level (11). The present series had an average of 3.4 mg of BMP used per level and 9.2 levels

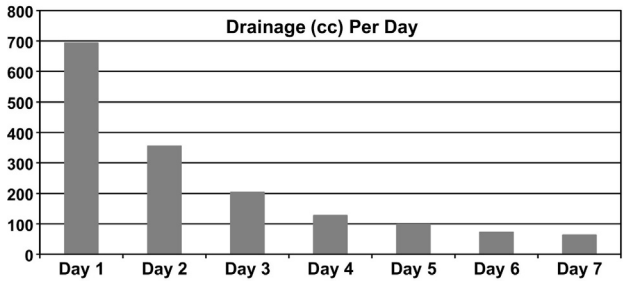

Figure 2. Mean amount of drainage per day. Persistent drainage of 100 mL per day was present until day 5.

fused. These are substantially larger fusions and quantities of BMP, yet seroma formation rates were lower than those reported in studies not using drains or equivalent in studies using them.

One concern regarding longer perioperative drainage is the potential for increased infection (4, 17). However, this concern is controversial, with different studies showing conflicting results (19). At our institution (and in patients included in the current study), we use prophylactic intravenous antibiotics, administered before incision and continued until after the final drain is removed, in an effort to minimize the chance of infection developing both during surgery and via percutaneous dissemination through drain tracts. In the present study, there were 2 wound infections requiring operative treatment for a rate of 2.3%. This rate is comparable to or lower than rates previously reported in the literature (2, 5, 8-11, 16), despite the previously reported rates being based on substantially shorter fusion constructs. Patients in this study had low seroma and low infection rates, suggesting the efficacy and safety of longer perioperative drainage when using BMP as an adjunct to fusion.

There are limitations to this study. First, fusion patients treated without BMP were not available for a comparison of the amount of drainage or length of drainage required. Therefore, we cannot comment on how much drainage is directly related to BMP usage. Second, this study focused on perioperative wound complications, and other early or delayed complications were not assessed. Finally, it could be postulated that patients discharged on the day of final drain removal may have simply been kept as inpatients while waiting for drainage to decrease. However, documenting in the medical record that a patient was kept in house for no reason other than continued drainage is not generally done. The added cost of prolonged hospitalization could be an argument against the use of BMP. However, once BMP is used, the cost of any potential prolonged hospitalization may be offset by the savings achieved by decreased surgeries for seroma evacuation and further offset by the reduction of revision procedures for pseudarthrosis. Future studies may be performed to fully evaluate this issue.

CONCLUSIONS

The use of BMP for spinal fusion is associated with significant serous fluid production. Drainage of this fluid with subfacial drains can be done safely with acceptable rates of infection and reoperation, thereby reducing the morbidity from seroma formation.

REFERENCES

1. Benglis D, Wang M, Levi A: A comprehensive review of the safety profile of bone morphogenetic protein in spine surgery. Neurosurgery 62 (Suppl 2):ONS423-431; discussion ONS431, 2008.

2. Cahill K, Chi J, Day A, Claus E: Prevalence, complications, and hospital charges associated with use of bone-morphogenetic proteins in spinal fusion procedures. JAMA 302:58-66, 2009.

3. Carragee E, Hurwitz E, Weiner B: A critical review of recombinant human bone morphogenetic protein-2 trials in spinal surgery: emerging safety concerns and lessons learned. Spine J 11:471-491, 2011.

4. Cobb J: Why use drains? J Bone Joint Surg Br 72: 993-995, 1990.

5. Coe J, Smith J, Berven S, Arlet V, Donaldson W, Hanson D, Mudiyam R, Perra J, Owen J, Marks M, Shaffrey C: Complications of spinal fusion for scheuermann kyphosis: a report of the scoliosis research society morbidity and mortality committee. Spine (Phila Pa 1976) 35:99-103, 2010.

6. Dawson E, Bae H, Burkus J, Stambough J, Glassman S: Recombinant human bone morphogenetic protein-2 on an absorbable collagen sponge with an osteoconductive bulking agent in posterolateral arthrodesis with instrumentation: A prospective randomized trial. J Bone Joint Surg Am 91:1604-1613, 2009.

7. Deutsch H: High-dose bone morphogenetic protein-induced ectopic abdomen bone growth. Spine J 10:e1-4, 2010.

8. Fu K, Polly D Jr, Perra J, Sansur C, Berven S, Broadstone P, Choma T, Goytan M, Noordeen H, Knapp D Jr, Hart R, Zeller R, Donaldson W 3rd, Boachie-Adjei O, Shaffrey C: Morbidity and mortality in the surgical treatment of 10,329 adults with degenerative lumbar stenosis. J Neurosurg Spine 12:443-446, 2010.

9. Garrett M, Karkarla U, Porter R, Sonntag V: Formation of painful seroma and edema after the use of recombinant human bone morphogenetic protein-2 in posterolateral lumbar spine fusions. Neurosurgery 66:1044-1049; discussion 1049, 2010.

10. Glassman S, Gum J, Crawford C 3rd, Shields C, Carreon L: Complications with recombinant human bone morphogenetic protein-2 in posterolateral spine fusion associated with a dural tear. Spine J 11:522-526, 2011.

11. Glassman S, Howard J, Dimar J, Sweet A, Wilson G, Carreon L: Complications with rhBMP-2 in posterolateral spine fusion: a consecutive series of one thousand thirty-seven cases. Spine (Phila Pa 1976) 36:1849-1854, 2011.

12. Mok J, Durrani S, Piper S, Hu S, Deviren V, Berven S, Burch S: Extravasation of rhBMP-2 with use of postoperative drains after posterolateral spinal fusion. Spine (Phila Pa 1976) 33:1668-1674, 2008.

13. Mroz T, Wang J, Hashimoto R, Norvell D: Complications related to osteobiologics use in spine surgery: a systematic review. Spine (Phila Pa 1976) 35 (Suppl):S86-104, 2010.

14. Notification, FDA Public Health: Life-threatening complications associated with recombinant human bone morphogenetic protein in cervical spine fusion. Available at: www.fda.gov/medicaldevices/safety/alertsandnotices/publichealthnotifications/ucm062000.htm. Updated July 1, 2008. Accessed January 2012.

15. Ong K, Villarraga M, Lau E, Carreon L, Kurtz S, Glassman S: Off-label use of bone morphogenetic proteins in the United States using administrative data. Spine (Phila Pa 1976) 35:1794-1800, 2010.

16. Owens K, Glassman S, Howard J, Djurasovic M, Witten J, Carreon LY: Perioperative complications with rhBMP-2 in transforaminal lumbar interbody fusion. Eur Spine J 20:612-617, 2011.

17. Parker M, Roberts C: Closed suction surgical wound drainage after orthopaedic surgery. Cochrane Database Syst Rev 4; CD001825, 2001.

18. Payne D, Fischgrund J, Kerkowitz H, Barry R, Kurz L, Montgomery D: Efficacy of closed wound suction drainage after single-level lumbar laminectomy. J Spinal Disord 9:401-403, 1996.

19. Scuderi G, Brusovanik G, Fitzhenry L, Vaccaro A: Is wound drainage necessary after lumbar spinal fusion surgery? Med Sci Monit 11:CR64-CR66, 2005.

20. Shahlaie K, Kim K: Occipitocervical fusion using recombinant human bone morphogenetic protein-2: adverse effects due to tissue swelling and seroma. Spine (Phila Pa 1976) 33:2361-2366, 2008.

21. Smucker J, Rhee J, Singh K, Yoon S, Heller J: Increased swelling complications associated with off-label usage of rhBMP-2 in the anterior cervical spine. Spine (Phila Pa 1976) 31:2813-2819, 2006.

Conflict of interest statement: Justin S. Smith is a consultant for Medtronic, Depuy, and Biomet; receives honoraria for teaching from Medtronic, Depuy, Biomet, and Globus; and receives research study group support from Depuy. Christopher Shaffrey is a consultant for and holds a patent with Biomet, receives royalties from and holds a patent with Medtronic, is a consultant for Depuy, and has received grant funding from the National Institutes of Health and the Department of Defense.

Received 14 January 2012; accepted 13 August 2012; published online 25 August 2012

Citation: World Neurosurg. (2013) 80, 1/2:204-207. http://dx.doi.org/10.1016/j.wneu.2012.08.003

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

1878-8750/$ - see front matter