Combination Use of Antibiotic-Loaded Calcium Sulfate Beads in Spinal Surgery for Patients with Spondylodiscitis: A Clinical Retrospective Study

Xiaojie Tang  
Department of Orthopedics, Yantai Affiliated Hospital of Binzhou Medical University

Jianyi Li  
Department of Orthopedics, The Affiliated Hospital of Qingdao University

Chunxiao Wang  
Department of Orthopedics, Yantai Affiliated Hospital of Binzhou Medical University

Fang Liu  
Department of Orthopedics, Yantai Affiliated Hospital of Binzhou Medical University

Jianwei Guo  
Department of Orthopedics, The Affiliated Hospital of Qingdao University

Jiangwei Tan (✉ tanbyytfy@126.com)  
Department of Orthopedics, Yantai Affiliated Hospital of Binzhou Medical University

Qinyong Song  
Department of Orthopedics, Yantai Affiliated Hospital of Binzhou Medical University

Haifei Cao  
Department of Orthopedics, Yantai Affiliated Hospital of Binzhou Medical University

Yao Zhang  
Department of Orthopedics, Yantai Affiliated Hospital of Binzhou Medical University

Research Article

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Abstract

Background.

Various surgical techniques for treating spondylodiscitis have been proposed, but the optimal surgical treatment remains controversial. In this study, we propose a new procedure that is implanting antibiotic-loaded calcium sulfate (CS) beads into the disc after infection site debrided by Quadrant channel combined with percutaneous fixation through a single-stage posterior approach for the treatment of spondylodiscitis. Thus, the purpose of this study is to assess the safety and efficacy of this procedure.

Methods.

This study collected 32 patients’ clinical data of whom had spine spondylodiscitis treated in our department from July of 2015 to August of 2020. The Demographic data included age, gender, involved segment and complications were collected. The intra-operative details, results of culture, functional outcome, radiologic outcome, and length of hospital stay, laboratory examination were recorded.

Results.

The mean age of the 32 patients was 61.1 ± 9.7 years old. The mean operative time was 135.0 ± 30.6 minutes, and the mean blood loss was 243.4 ± 92.1 ml. The positive rate of culture was 72%. The mean Visual analogue scale (VAS) and Oswestry Disability Index (ODI) score significantly improved from 7.5 to 1.6 and from 65–10%. Cobb angle was significantly improved and could be maintained at final follow-up. Solid bone fusion was achieved in all patients. There were no recurrences of infection in our study.

Conclusions.

The procedure we proposed is effective in the treatment of spondylodiscitis, the infection site can be debrided and controlled exactly, and spinal stabilization can also be achieved.

Background

Spondylodiscitis is an uncommon but potentially life-threatening bacterial infection involving the intervertebral disc and adjacent vertebrae[1]. The annual incidence of spondylodiscitis ranges from 0.5 to 2.2/100,000 inhabitants in Europe[2, 3], and the infection commonly tends to affect elderly or chronically debilitated patients aged over 50 years[4]. Spondylodiscitis shows mortality rates from 2–20% and a morbidity rate of more than 7%[5]. It can be managed either by non-operative measures, including intravenous/oral antibiotics and immobilization or by surgical intervention[6]. Surgery for spondylodiscitis is indicated for instability, deformity, neurological deficits, unbearable pain, or disease
progression[7]. The surgical goal in spondylodiscitis is to debride the infection, identify and reduce the pathogens, stabilize the deformed and instable segments, and decompress the neural structures[8].

Anterior, posterior and combined approaches have been used for the treatment of spondylodiscitis[9–16]. However, the optimal surgical treatment remains controversial. The defects require reconstruction to ensure stability after radical debridement and decompression, which should be filled with graft. Antibiotic-loaded CS is widely used in osteomyelitis as a filler of bone defects, but separate reports on spondylodiscitis are few relatively[17]. The objective of this retrospective study was to verify the efficiency of antibiotic-loaded CS beads applied in a single-stage posterior approach for the treatment of spondylodiscitis.

**Materials And Methods**

A retrospective review of patients who underwent surgical treatment for lumbar/thoracic spondylodiscitis at our department. The 32 consecutive patients were identified from July of 2015 to August of 2020 and their data were retrospectively investigated. All the patients were treated with the proposed procedure. Patients with neurological deficits, instability, progressive pain, or progression on MRI/CT despite conservative treatment underwent surgical treatment. Demographic data, including age, gender, involved segment, clinical outcomes and complications were recorded (Table 1). The intra-operative details, results of culture, functional outcome, radiologic outcome, blood loss, ASIA classification and length of hospital stay were recorded (Table 2). The Cobb angle, VAS, ODI at the time of initial diagnosis, the 7 post-operative day, and the last follow-up were compared (Table 3). Radiological investigations such as X-rays and computed tomography (CT) were done to document endplate erosion, cavitation, reduction in disc space, and instability, and magnetic resonance imaging (MRI) was serially done for evaluation of response to treatment pre-op and post-op routinely (Fig. 1). Clinical evaluation was performed using the ASIA classification, ODI and VAS. The functional outcome of the study was measured by the modified criteria of Kirkaldy-Willis. All the patients were treated by empirical antibiotic therapy or antibiotics according to the results of microbial culture and sensitivity when available. Patients were treated with intravenous broad spectrum antibiotics for 6–8 weeks followed by oral antibiotics for a total period of 3 months. The antibiotic therapy was withdrawn based on clinical improvements and the infection related laboratory test results, such as the average levels of CRP and ESR.
Table 1
Clinical data of patients.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>18</td>
</tr>
<tr>
<td>Male</td>
<td>14</td>
</tr>
<tr>
<td>Age, average, y</td>
<td>61.1 ± 9.7</td>
</tr>
<tr>
<td>Affected levels</td>
<td></td>
</tr>
<tr>
<td>Thoracic</td>
<td>8</td>
</tr>
<tr>
<td>Thoracolumbar</td>
<td>4</td>
</tr>
<tr>
<td>Lumbar/lumbosacral</td>
<td>20</td>
</tr>
<tr>
<td>Concurrent disease</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>11</td>
</tr>
<tr>
<td>Rheumatism</td>
<td>1</td>
</tr>
<tr>
<td>Nephritis</td>
<td>1</td>
</tr>
<tr>
<td>ASIA classification (pre-op)</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>3</td>
</tr>
<tr>
<td>D</td>
<td>16</td>
</tr>
<tr>
<td>E</td>
<td>13</td>
</tr>
</tbody>
</table>

Operative Procedure

After general anesthesia, patients were carefully placed in a prone position, and the surgery was performed through a posterior approach. The anteroposterior (AP) view was then used to identify the affected segment and the location of pedicle with C-arm fluoroscopy. A 1–2 cm incision is proposed and marked just lateral to the lateral border of the pedicle. The entry point is usually selected to be at or just lateral to the lateral border of the pedicle in the AP view. Instrumentation with percutaneous pedicle screw placement into the infected vertebra and the adjacent vertebra above and below the infected segment was performed on the mild side. Pedicle screw was inserted 1 level above and 1 level below the most destroyed vertebra on the opposite side. A median longitudinal incision around 3 cm in length was made 2 cm beside the midline on the affected side. The skin, subcutaneous tissue, and lumbar fascia were cut in turn, and then the paravertebral muscles were separated out by a Quadrant instrument to establish the channel on the infected segment. The lateral edge of the upper lamina and superior articular process
were exposed. Forceps was used to remove part of the lateral edge of the upper lamina and superior articular process on the affected side of the lesion segment in a transformational approach (Fig. 2). After exposure, drained all pus debrided granulomatous tissue and/or necrotic material. Radical debridement was performed by using a rongeur and curette until sclerosing bone was completely removed and healthy, bleeding margins were obtained. The kit containing 5ml calcium sulfate powder (STIMULAN, Biocomposites Ltd, England) was mixed with 0.5 g of vancomycin hydrochloride powder plus the 2.5-3 ml sterile water, all the components were mixed for 30 s to form a paste, which was pressed into 4.8-mm-diameter hemispherical cavities in a flexible mold. The beads were left undisturbed for 20 min to set. When set, the beads were removed by flexing the mold and implanted into the debrided site to reconstruct the anterior column and control the infection. Finally, posterior instrumentation was finished and the debrided material was sent for histopathologic examination as well as antibiotic sensitivity testing.

Statistical analysis

All patients with complete initial data were considered for inclusion in the retrospective analysis. All values are expressed as mean ± SD. Repeated measurement data of continuous numerical variables were analyzed by repeated measurement ANOVA, comparisons between the two groups were analyzed using the student’s paired t test. All statistical evaluations were performed with SPSS 22.0 (IBM, Armonk, New York). P < 0.001 was considered statistically significant.

Results

The demographic details and patients’ characteristics are presented in Table 1. Thirty-two consecutive patients who underwent this surgery for spondylodiscitis had been identified from 2015 to 2020 and their data were retrospectively investigated. The mean duration of follow-up was 25.16 ± 8.1 months (range 12 to 36 months). The surgical incisions were healed without chronic infection, fistula formation and recurrence. All patients had significant improvement in constitutional symptoms and back pain after surgery. Early ambulation was permitted the next day after the surgery in all patients. No perioperative complications related to instrumentation or decompression were reported.

The mean patient age was 61.1 ± 9.7 years (range 43–82), with 56 % of the cases being female. The intra-operative amount of blood loss was 243.4 ± 92.1 ml (range 120 to 520 ml) and the duration of surgery was 135.0 ± 30.6 min (around 100 to 240 mins). The majority of the cases involved the lumbar region (62.5%), of which 25% involving the thoracic spine and 12.5% at the thoracolumbar segment. The cultures of 32 cases were taken, 14 cases (44%) were Staphylococcus aureus, 5 cases (16%) were Escherichia coli, 3 cases (9%) were Mycobacterium tuberculosis, 1 case (3%) was Propionibacterium acnes, and 9 cases (28%) were culture negative.

The average Cobb angle was significantly improved at 19.8 ± 5.1° post-op and had resolved to 19.2 ± 4.9° at final follow-up. This result had statistically significant differences compared with the pre-op Cobb angle (P < 0.001), and there was significant difference between the post-op angle and the final follow-up.
VAS and ODI values of the seven-day post-op and the last follow-up were significantly lower compared with pre-op (P < 0.001), and significant differences were found between the post-op and last follow-up. ESR and CRP returned to normal levels in all patients in 3 months after surgery. The average hospital stay was 52.3 ± 10.0 days. The average fusion time was 4.6 ± 1.1 months (range 3–6 months), judging by plain radiograph and/or CT scan. On last follow-up, neurological recovery was observed in 20 patients with previous neurological deficit; specifically, of which 16 cases with grade D deficits, 1 case with grade C recovered to grade E and 2 cases with grade C improved to grade D. According to the Kirkaldy-Willis functional criteria, 14 patients were finally evaluated as “excellent”, 17 patients were “good” and one patient was “fair”.

Table 2
Summary of treatment outcomes, mean ± SD

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operation time, min</td>
<td>135.0 ± 30.6</td>
</tr>
<tr>
<td>Blood loss, mL</td>
<td>243.4 ± 92.1</td>
</tr>
<tr>
<td>Hospitalization, d</td>
<td>52.3 ± 10.0</td>
</tr>
<tr>
<td>Duration of follow-up, m</td>
<td>25.1 ± 8.1</td>
</tr>
<tr>
<td>ASIA classification (post-op)</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>0</td>
</tr>
<tr>
<td>D</td>
<td>3</td>
</tr>
<tr>
<td>E</td>
<td>29</td>
</tr>
</tbody>
</table>

Table 3
Laboratory findings and VAS/ODI/Cobb angle x ± s

<table>
<thead>
<tr>
<th>ESR (mm/h)</th>
<th>CRP (mg/L)</th>
<th>VAS</th>
<th>ODI</th>
<th>Cobb angle(*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-op</td>
<td>82.37 ± 27.11</td>
<td>78.19 ± 27.48</td>
<td>7.50 ± 1.16</td>
<td>65.41 ± 13.46</td>
</tr>
<tr>
<td>Post-op</td>
<td>53.88 ± 19.89</td>
<td>44.22 ± 17.19</td>
<td>4.44 ± 1.48</td>
<td>27.59 ± 9.64</td>
</tr>
<tr>
<td>FFU</td>
<td>19.06 ± 8.21</td>
<td>8.12 ± 5.12</td>
<td>1.66 ± 0.65</td>
<td>10.03 ± 5.08</td>
</tr>
<tr>
<td>F</td>
<td>131.427</td>
<td>122.721</td>
<td>225.452</td>
<td>351.766</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Pre-op pre-operative, Post-op post-operative, FFU final follow-up
Discussion

Spondylodiscitis is a most common spinal infection, which affects the vertebral bodies, intervertebral disk, paraspinal tissues, and also the posterior bony elements occasionally[18]. Traditionally, conservative treatment including immobilization and systemic administration of antibiotics is the first choice for pyogenic spondylitis[19, 20]. Surgical treatment is indicated in patients with progressive biomechanical pain, refractoriness to antibiotic therapy, epidural abscesses, neurological impairment or segmental instability[21]. Surgical intervention is recommended as it could relieve pain, maintain vertebral column balance, improve neurologic function, and bring higher quality life[22].

Debridement and reconstruction are two main principles of the surgical treatment of pyogenic spondylitis[23, 24]. The anterior approach provides direct visualization for radical debridement and decompression without affecting the posterior elements, which is the best way to control the infection and promote definitive healing, and it also can warrant adequate and strong reconstruction with modern instrumentation tools[10–12]. However, anterior surgery alone does not adequately correct kyphosis and could not bear physiological loads, the recurrence of kyphosis following it are difficult to treat[9, 25]. In order to overcome these limitations, some authors advocated posterior spinal stabilization and fusion. Posterior approach could give better kyphotic deformity correction and vertebral stabilization, less complications and less surgical invasiveness[16]. Meanwhile, the infected intervertebral discs, vertebral endplates, and vertebral body tissues could be adequately debrided through a posterior-only approach to assure the excellence of the radiographic and clinical results[13, 15]. But a considerable portion of authors believed that the posterior-only approach has the drawbacks of insufficient removal of infected tissue compared with the anterior approach[26]. Thus a combination of anterior debridement with posterior fixation is widely used for the treatment of lumbar pyogenic spondylodiscitis[14, 27–29]. Nevertheless, the combined approach increases the risk of morbidity associated with the prolonged duration of operation, anesthesia times, the additional blood loss and operative trauma[28].

Antibiotic-loaded cement (AIBC) is widely used to treat or prevent infections in total hip and knee arthroplasty because it can lead to a locally high antibiotic concentration[30]. Nonetheless, burst release of antibiotics and microbial colonization of the non-degradable cement has led to advanced investigation for more antibiotic delivery[31]. Calcium sulphate has a long history as antibiotic carrier material, which is a resorbable osteo-conductive scaffolds without requiring to be removed after implantation[32]. It also can be mixed with heat-sensitive antibiotics because there is very little temperature rise on curing[17, 33]. The mechanical strength of CS is comparable to cancellous bone, and is hydrolyzed slowly in bone, lasting for about 6–12 weeks[34]. The antibiotic-loaded beads demonstrated high bioactivity in preventing and eliminating the residual bacteria, with long periods of sustained efficacy[37]. It’s a good solution for the shortcoming of insufficient removal of infected tissue in the posterior procedure. The cement beads could be absorbed completely in about 8–12 weeks after surgery, and new bone gradually formed while antibiotics released to control the infection. The imaging examination showed the infected site healing well with no recurrence during the follow-up in our series. Percutaneous pedicle screw instrumentation was used to avoid unnecessary muscle dissection and tissue disruption, decrease blood
loss and complications, provide immediate stability[35]. Meanwhile, pedicle screws were inserted into the infected and adjacent vertebra to avoid decreasing mechanical stability by longer fixation levels[36].

Antibiotics targeted toward the causative pathogen appears to be the most important factor to determine the success rate of treatment. Identifying the causative pathogens is one of the key factors to achieve cure in our studies. Positive culture was obtained in 23 patients (72%) while Staphylococcus aureus is the most frequent pathogen (73%) in our studies. Systemic antibiotic treatment duration ranged from 6 weeks to 12 weeks, which was consistent with the previous literature description[22]. Appropriate antibiotic therapy based on the causative pathogen is crucial and can lead to good clinical results. After sending blood culture and disc space aspiration, all patients immediately started empirical intravenous antimicrobial therapy. Then, an appropriate antibiotic was administrated according to the results of microbial culture and sensitivity[37].

Our data showed the pain was significantly relieved and the ODI index was significantly increased after surgery, all patients could return to normal life. The patients' ESR and CRP levels decreased significantly 7 days after surgery and returned to normal in a mean of 4 weeks after surgery, indicated that inflammation indexes were well controlled. The CS antibiotic bone granules were absorbed in 2 to 3 months gradually, and the bony fusion was observed in all patients in a mean of 4.1 months after surgery. The Cobb Angle was significantly improved at 7 days post-op and last follow-up, and there was significant difference between the post-op angle and the final follow-up, which meant the Cobb Angle was maintained at the final follow-up with no kyphotic deformity aggravated compared with the post-op. All the 20 patients with preoperative dysfunction recovered to different degrees after operation, and the excellent and good rate reached to 94.4%.

However, this study also has limitations. The current study is a small-scale retrospective data analysis in a single institution, and there is no matching control group. We need a prospective controlled study and a large number of patients to identify the effectiveness of this technique in the future.

**Conclusion**

Based on the investigation of our studies, it suggests that this procedure may be a safe and effective operative procedure for spondylodiscitis. Most patients improved significantly not only their general conditions but also neurological status after this posterior surgery without any serious complications in our study. Early diagnosis and an optimal approach can reduce the morbidity of the patients and the incidence of complications.

**Abbreviations**

CS: calcium sulfate; CT: computed tomography; MRI: magnetic resonance imaging; VAS: visual analogue scale; ODI: Oswestry Disability Index; Pre-op: pre-operative; Post-op: post-operative; FFU: final follow-up;
Declarations

Acknowledgements

Not Applicable.

Authors’ contributions

JW G, HF C, Y Z and QY S performed the data analysis. XJ T and JY L wrote the manuscript. CX W and FL contributed to the manuscript revise. XJ T, JY L and CX W contributed to literature search and data extraction. JW T conceived and designed the study. All authors have read and approved the final version of the manuscript.

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Availability of data and materials

The data used and analyzed during the current study are available in anonymized form the corresponding author on reasonable request.

Ethics approval and consent to participate

This article is designed and submitted acting on guideline of the Institutional Review Board of Yantai Affiliated Hospital of Binzhou Medical University. Written informed consent was obtained from all patients. No children (under 16 years old) were included in this study.

Consent for publication

Not Applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

1 Department of Orthopedics, Yantai Affiliated Hospital of Binzhou Medical University, 717 Jinbu Street, Muping District, Yantai 264000, Shandong Province, People's Republic of China.

2 Department of Orthopedics, The Affiliated Hospital of Qingdao University, 16 Jiangsu Road, Qingdao 266003, Shandong Province, People's Republic of China.
References


Figures
Figure 1

Preoperative sagittal CT and MRI a, b, c showing spondylodiscitis involving L2/3 segment. Post-operative AP radiograph and CT d, e, f at 4 days after surgery showing interbody space filled with calcium sulfate beads. Postoperative sagittal CT and MRI g, h at 3 months follow-up showing beads has been absorbed and infection has been controlled.
Figure 2

Illustration of transforaminal approach for spondylodiscitis though posterior approach only. The range of excision including part of the lateral edge of the upper lamina and superior articular process without disturbance of the spinal canal and the posterior elements.