Antibiotic-Loaded Hydrogel Coating for the Prevention of Local Infection after Vertebral Surgery: A Retrospective Cohort Analysis

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ABSTRACT

Objectives: To preliminarily assess the effectiveness of a highly viscous antibiotic-loaded hydrogel used as a coating for the prevention of superficial and deep Surgical Site Infections (SSIs) after laminectomy and fusion in instrumented vertebral surgery.

Methods: We performed a retrospective cohort analysis on 73 consecutive patients who underwent surgery from June 2018 to December 2019 for degenerative spinal disorders (DSD) or traumatic fractures with segmental instability. Patients received the antibiotic-loaded hydrogel over the implants perioperatively and were observed postoperatively for 12 months.

Results: Postoperative evaluations showed no adverse events in the study population. None of the patients reported significant pain or functional limitation after surgery. Post-surgically, computed tomography scans confirmed the correct positioning of instruments. At 12 months follow-up, no infection was recorded in the overall population.

Conclusion: This retrospective investigation highlights the importance of adopting measures to prevent SSIs in instrumented vertebral surgery. The intraoperative local use of an antibiotic-loaded hydrogel, complementary to systemic antibiotic therapy, appears to minimize the risk of superficial and deep infection.

INTRODUCTION

While advances in drug development and innovations in surgical technique and patient postoperative care have reduced the infection rate in patients undergoing spinal surgery, Surgical Site Infections (SSIs) and Postoperative Peri-Implant Spine Infections (PPSIs), are still significant concerns in vertebral surgery, and are associated with high morbidity and mortality.[1] Additionally, substantial increases in social costs for the healthcare provider system have been reported because SSIs in spinal surgery often require reoperations and increased hospital stay.[2]

For example, in the U.S., it was estimated that SSIs for a single patient can increase the cost of care up to four times the cost of the initial spine surgery: costs range between $15,800 and $43,900 per SSI.[3]

Moreover, a retrospective clinical investigation reported that, in a cohort of 836 consecutive patients who underwent spine surgery, the overall unexpected readmission rate was 8.4% at 30 days and 12.3% at 90 days. Patients with multiple level fusion had higher rates of readmission in comparison with single fusions and SSIs accounted for 45.6% of readmissions.[4] A retrospective study to determine the financial impact and length of stay associated with readmissions for SSI following spine surgery found that the average cost of spine SSI treatment at a single tertiary referral center was $16,242 per case.[5]

The epidemiological data reported regarding the incidence of SSIs (deep and superficial) in spine surgery are divergent. While some studies have reported a range from 2% to 13% as described by McClelland et al.,[6] other papers have given values of 1%-4%.[7] These variations as well the type and the extent of the infection depend on the indications for surgery, the anatomic site, the surgical approach, and whether it is an instrumented surgery. SSIs rates ranged from as low as 0.07% in patients undergoing anterior cervical discectomy and fusion, to 2.94% in posterior cervical surgery, 2.4% in spinal tumour, 8.8% in primary lumbar fusion, and 12.2% in revision lumbar fusion.[8-10] A systematic review reported that, among the different indications, the highest incidence of SSIs was in neuromuscular scoliosis patients (13.0%) and the lowest incidence was in idiopathic scoliosis patients (2.6%).[11] Therefore, the risk of SSIs after spine surgery increases with the complexity of the procedure and patient-related factors. Furthermore, obesity and diabetes associated with other comorbidities may further increase the risk for SSIs.[12] Some studies have shown that older age is a significant risk factor independent of comorbidities.[13] While the most common source of SSIs is the patient's endogenous skin flora, Staphylococcus aureus is the pathogen that is mainly associated with SSI in spine surgery and most patients present a significant percentage of methicillin-resistant bacteria, especially after revision surgery.[14] Gram-negative organisms are seen less frequently. Apparently, infection from gram-negative agents can be related to surgery in the lower lumbar spine and sacroiliac area.[15] Therefore, preventive strategies to reduce the rate of SSIs after spine surgery have become critically important and it is imperative that surgeons develop and implement methods to reduce the rate of SSIs and associated costs. Strategies to prevent infection in spinal surgery may include three main steps: preoperative optimization of patient-related risk factors, and intraoperative and postoperative measures to prevent peri-implant infections and subsequent superficial and deep SSIs. Nevertheless, as with other surgical implants, the pathogenesis of periprosthetic infection in instrumented surgery is quite complex. Bacteria colonize the implant in the early phase of surgery, and the characteristics of the metallic surfaces of devices for arthrodesis such as roughness, hydrophobicity, and electrostatic charge play a crucial role in bacterial adhesions. Gasik et al.[16] described how a hydrophobic surface might be a suitable substrate for bacterial colonization, while a hydrophilic surface can prevent biofilm formation. Bacteria exhibit adhesive ligands (adhesins), which present charges that interact with hydrophobic surfaces of implants leading to bacterial adhesions and proliferation with consequent formation of biofilm, an agglomerate of extracellular polymeric matrix and bacteria that adheres to an implant.[17] These pathological conditions alter the immune defences at the site of implantation and conventional systemic antibiotic therapies alone fail to eradicate bacterial growth within biofilm.[18] Biofilm protects pathogens and promotes antibiotic resistance, leading to persistent infection.

The use of preoperative antimicrobial prophylaxis is a conventional procedure to inhibit peri-implant infections, and its efficacy is related to the timing of administration.[19] Nevertheless, standard systemic antibiotic prophylaxis showed conflicting results, particularly regarding the ideal timing and the most effective preoperative skin antisepsis. Hence, the optimal duration of systemic antibiotic treatment with surgical concepts of curing wound and device-related orthopaedic infections is still unclear.[20]

Several authors have reported that standard systemic antibiotic prophylaxis associated with the local administration of antibiotic prevents SSIs and deep peri-implant infection, thus reducing the risk of associated morbidity in patients undergoing instrumented spine surgery. Intra-wound vancomycin appears to be safe and cost-effective for reducing postoperative SSIs with a low rate of morbidity.[21,22] In addition, the combination of bone graft materials loaded with vancomycin and gentamycin has been experimentally and clinically demonstrated to reduce infections in vertebral arthrodesis procedures without affecting the fusion rate.[23,24]

The use of a commercially available coating based on natural polymers such as hyaluronan (HY), DAC® (Defensive Antibacterial Coating) gel (CE0426) (Novagenit Srl, Mezzolombardo, Italy), and loaded with antibiotic may be an effective approach for reducing bacterial adhesion, and consequently the onset and persistence of periprosthetic joint infections. The gel, which is spread over the implant surface perioperatively, has been proven to be effective in primary and revision arthroplasty procedures in the hip and knee and in traumatology.[25,26]

The current retrospective case series presents a 12-month safety and preliminary efficacy follow-up in a cohort of 73 consecutive patients who were treated with antibiotic-loaded DAC® gel, which was used as a physical coating over implants to prevent bacterial adhesion and infection in the early operative phase in instrumented vertebral surgery.

MATERIALS AND METHODS

Study Population and Data Collection

This retrospective data collection was conducted in a single center and was

approved by the hospital institutional review board (IRB). All medical records of patients were retrospectively reviewed and data were processed anonymously so as not to permit the identification, even indirectly, of the subjects. A signed informed consent was obtained from each patient.

Between June 2018 and December 2019, clinical data on 73 consecutive patients who underwent primary or revised instrumented lumbar vertebral fusion for degenerative spinal disorder with segmental instability and who received additional antibiotic-loaded hydrogel coating treatment were collected. Next, electronic and paper medical records of all patients were reviewed to identify the presence of comorbidity, operation time, average length of hospital stay, need for additional antibiotic therapy, adverse events/complications and infection onset.

All patients arrived at the emergency room showing neurogenic claudication claiming severe pain in the buttock and/or leg that did not respond to pharmacologic therapies. Patients were scheduled for diagnostic investigation and hospital admission.

The most frequent diagnosis was lumbar or lumbosacral segmental instability defined by stenosis of the vertebral canal, and degenerative spondylolisthesis. Clinical and neurologic examinations and imaging studies, including X-ray and magnetic resonance imaging (MRI), confirmed the levels responsible for the symptoms. Therefore, patients were scheduled to have surgery.

Surgery

The same surgeon performed all of the operations using standard surgical procedures. According to the standard antibiotic prophylaxis, intravenous antibiotics were administered 30-60 min before the skin incisions, with redosing after 4 hours during longer surgeries.

Systemic antibiotics were administered preoperatively, including gentamycin 1.5 mg/kg (n = 2), vancomycin 15 mg/kg (n = 50), cefazolin 25mg/kg (n = 9), and cefazolin/vancomycin 25mg/kg-1.5mg/kg (n = 12).

Surgical access was achieved through a posterior midline approach with the patient in a prone position. In addition to the posterolateral lumbar arthrodesis, laminectomies, foraminotomies, and/or discectomies were performed at the treated segment or at an adjacent segment when needed.

The entrance point of a pedicle screw was identified by using anatomic landmarks. Wound irrigation was completed before instrumentation procedures and rods with pedicle screw systems were coated with the antibiotic-loaded gel (DAC® gel). The gel was prepared by hydrating DAC® powder with a 5% aqueous solution of gentamycin (Fig. 1). The antibiotic-loaded gel was uniformly spread to cover all implant surfaces, including rods and screws (Fig. 2), and the procedure was then completed via pre-drilled transpedicular canals. An average volume of 10 mL of antibiotic-loaded DAC® gel was applied.

Wound closure was performed layer by layer.

Clinical evaluations

All the intraoperative and postoperative complications associated with surgery and adverse events associated with the use of DAC® gel were reported and followed-up. Clinical outcome was evaluated based on postoperative infection onset. Medical and surgical complications were recorded using information from the retrospective chart review and infections were classified as superficial (above lumbosacral fascia) or deep (below lumbosacral fascia), and as early onset (within 2 weeks postoperatively) or late onset. A deep SSI was defined as an infection involving the deep soft-tissue muscle and fascia, which was in contrast to a superficial SSI involving only infected skin and subcutaneous tissue. All patients were followed-up at 3, 6 and 12 months and fusion was assessed using static and dynamic plain X-rays at the last follow-up.

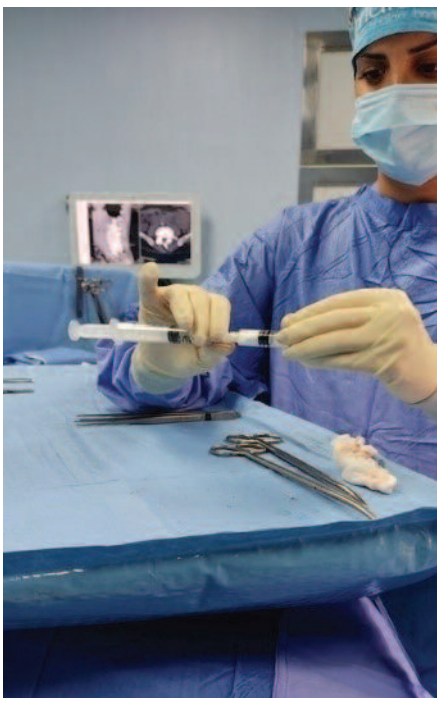

Figure 1. DAC® powder hydrated with a 5% aqueous solution of gentamycin.

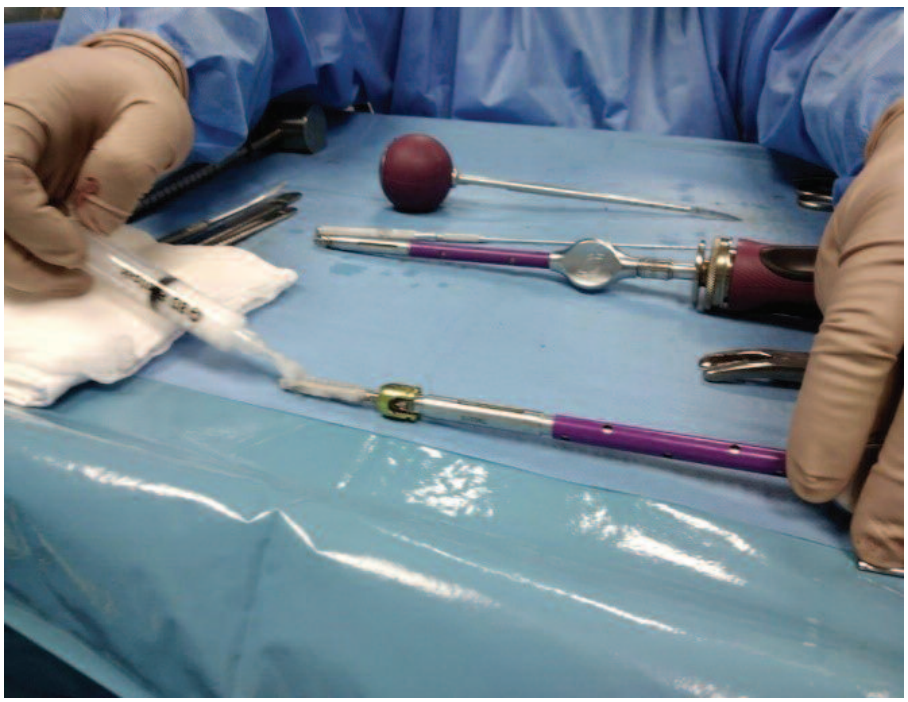

Figure 2. Screws being coated with antibiotic-loaded DAC® gel.

RESULTS

Patient characteristics

The patients' demographic characteristics are summarized in Table I. The average patient age at the time of surgery was 61.6 years (range 33-82 years, SD = 10.6) and the study cohort included 36 women and 37 men. Sixteen of the 73 patients (21.9%) had no comorbidity, 25 (34.2%) had one comorbidity, 19 (26%) had 2 comorbidities, and 13 (17.8%) had 3 or more comorbidities. Among these, the most frequent comorbidities and risk factors were hypertension (n=43; 58.9%), diabetes (15; 20.5%), heart disease (10; 13.7%), smoking (9; 12.3%), thyroid disease (7; 9.6%), and vasculopathy (7; 9.6%). Diagnoses were stenosis (61; 83.6%), spondylolisthesis (4; 5.5%), instability (3; 4.1%) and other (5; 6.8%), respectively.

Overall, 116 levels were treated; 38 (52.0%) patients were treated for 1 level, 28 (38.4%) for 2 levels, 6 (8.2%) for 3 levels and 1 (1.3%) for 4 levels respectively. The most fused level was L4-L5 (n=56 levels; 48.3%), followed by L3-L4 (39 levels; 33.6%) and L5-S1 (13 levels; 11.2%), and L2-3 (8 levels; 6.9%). Primary surgery was performed in 52 patients (71.2%) and 21 patients (28.8%) underwent revision surgery. The mean operation time was 3.5 hours (range 1.12-6.50 hours, SD = 1.2).

Table I
Demographic characteristics of the patients

No. of Patients	73
Age (years)	61.6 (SD = 10.6)
Female	36 (49.3%)
Male	37 (50.7%)
Comorbidities	
0	16 (21.9%)
1	25 (34.2%)
2	19 (26%)
3 or more	13 (17.8%)
Most frequent comorbidities (% of population)	
Hypertension	43 (58.9%)
Diabetes	15 (20.5%)
Heart disease	10 (13.7%)
Smoking	9 (12.3%)
Thyroid disease	7 (9.6%)
Vasculopathy	7 (9.6%)
Diagnoses	n. (%) of patients
Stenosis	61(83.6%)
Spondylolisthesis	4 (5.5%)
Instability	3 (4.1%)
Other	5 (6.8%)
Fusion levels	
1	38 (52.1%)
2	28 (38.4%)
3	6 (8.2%)
4	1 (1.3%)
Levels	
L4-L5	56 (48.3%)
L3-L4	39 (33.6%)
L5-S1	13 (11.2%)
L2-L3	8 (6.9%)
Primary surgery	52 (74.4%)
Revision of previous surgery	21 (25.6%)
Operation Time	3.3 (SD = 1.2)

Early peri- and post-operative complications

The postoperative evaluations showed no adverse events in the early postoperative period. None of the patients reported significant pain or functional limitation after discharge. Post-surgically, computed tomography scans confirmed the correct positioning of instruments. The mean post-surgery hospital stay was 7.7 days (SD = 3.6) and 33 of the 73 patients (45.2%) received antibiotic treatment postoperatively. The average duration of therapy was 3.4 days (SD = 3.0) and the antibiotics administered were vancomycin in 23 patients (69.7%), ciprofloxacin in 3 (9.1%), cefazolin in 3 (9.1%), amoxicillin in 2 (6.1%), gentamicin in 1 (3.0%) and levofloxacin in 1 (3.0%).

Problems with wound closure were observed in 2 patients, but no infections were observed, as confirmed by bacterial swab; among these, one patient with comorbid rheumatoid arthritis was re-treated for wound cutaneous and subcutaneous closure 4 days after surgery and a prolonged hospital stay was required (20 days).

Infection onset

None of the patients in the cohort developed an early infection 2 weeks after surgery or at 3, 6 or 12 months follow-up. At 12 months follow-up, radiographic examination showed that fusion was achieved in all of the patients.

DISCUSSION

Infection remains a leading cause of failure of spinal surgery, with associated severe morbidities and socio-economic issues. Current therapeutic procedures to prevent post-operative peri-implant infections in instrumented vertebral surgery follow a multidisciplinary approach based on preoperative assessment, optimization of patient-related risk-factors and patient selection considering age, gender, nutritional status, comorbidities and the risks related with the surgical technique. Smoking cessation, glucose control, skin asepsis, and bacterial decontamination can all mitigate infection onset and prevent disastrous outcomes.

While preoperative antibiotic prophylaxis appear to be the gold standard procedure, the use of i.v. antibiotics in the surgical setting may be limited by issues such as hematoma, soft tissue impairment around the anatomical site and other comorbidities, and therefore may limit the availability of the drug at the required concentrations at the operative site.[27]

Recent studies have shown that intraoperative local prophylactic use of intrawound vancomycin in posterior instrumented spine surgery significantly decreases the incidence of wound infections without adverse effects and reduce revision surgery with a noteworthy cost savings.[28,29] Nevertheless, some authors recommend care in the use of intrawound vancomycin due to the lack of well-designed prospective studies that evaluate the efficacy of this antibiotic and outline appropriate systems to capture drug-related complications.[30] The local delivery of antibiotic through a biocompatible carrier has also been shown to be a smart approach to decrease the risk of SSIs in spine surgery. Yang et al. proved that the use of $CaSO_4$ in the form of absorbable beads as a carrier system was effective for the local delivery of vancomycin and gentamycin in a transforaminal lumbar interbody fusion (TLIF) procedure for lumbar pyogenic spondylodiscitis. The procedure was safe and there was no impairment of vertebral fusion.[31]

Among various strategies aimed at the inhibition of implant-related infection, antibacterial coatings based on HY and its derivatives appear to be an attractive and effective option to prevent bacterial colonization over an implant surface. Because a hydrophobic surface might be a suitable substrate for bacterial colonization, while a hydrophilic surface might prevent such colonization, experimental studies have shown the an HY coating can change the hydrophobicity of an implant surface to a hydrophilic surface, thereby significantly reducing bacterial attachment and biofilm formation.[32] In addition, some authors have described that biopolymers, such as HY, can provide an antagonistic effect against the hyaluronidase expressed by many pathogens to penetrate the healthy connective tissues of the host.[16]

DAC® hydrogel is a highly viscous, biocompatible, HY-poly-D-L-lactic acid derivative solution that was designed to act as a physical absorbable barrier when spread over an implant surface. The solution is very sticky and stable, and protects metallic implants from bacterial adhesions in the early phase of surgery. *In vitro* studies have proven that it has a barrier effect that reduces bacterial adhesion and biofilm formation.[33] Furthermore, DAC® hydrogel has synergistic activity in combination with antibiotics and antibiofilm substances, and simultaneously provides a barrier effect and a local delivery of antibacterial agents.[34] Antibiotic-loaded DAC® gel was shown to be effective for reducing peri-implant infection in an *in vivo* rabbit model by delivering locally high concentrations of gentamycin or vancomycin and being absorbed within a few days without systemic antibiotic prophylaxis agents. Moreover, bone integration with the implant was not impaired.[35]

Successive randomised controlled trials have confirmed the experimental findings, and have proven a significant reduction in the incidence of periprosthetic joint infection in primary and revision arthroplasty procedures, in the hip and knee, after coating of implant surfaces.[25] Furthermore, the same positive trend was confirmed in two clinical studies in either trauma surgery using osteosynthesis devices or in a large and complex bone reconstruction trial using joint mega-prosthesis.[26,36] Lastly, a recently published cost-benefit study demonstrated how the clinical use of antibiotic-loaded DAC® gel may limit the costs associated with periprosthetic infection and related septic revision procedures.[37]

The present retrospective investigation exhibited for the first time that an antibiotic-loaded hydrogel, DAC® gel, acting as antibacterial barrier and delivering a locally high concentration of gentamycin, may reduce the incidences of SSIs and deep infection in instrumented vertebral surgery, which confirms previous clinical outcomes in arthroplasty and traumatology. This could be a noteworthy advantage if we consider the incidence of post-operative peri-implant infections in instrumented vertebral surgery. A series of literature articles related to thoracic-lumbar stabilization reported that infection was present in 2.0 to 13.0% of cases (Table II), and the infection rate appeared to be higher in patients undergoing posterior spinal instrumented surgery for traumatic injuries.[38] No perioperative or postoperative device-related adverse events were recorded, thus confirming the safety and tolerability of antibiotic-loaded DAC® gel.

This study has several limitations. First, it is a retrospective review of cases at a single medical center, and prospective randomized clinical trials will be needed to confirm the results. Nevertheless, the aim of this study was to report our preliminary experience following the

Table II
Infection (expressed as %) reported in the literature after instrumented vertebral surgery

Author	Sample Size (Patients)	Infection (%)	Follow-up months
Abdul-Jabbar A et al.[15]	7,529	3.2	12
Adogwa O et al.[39]	1,200	2.8	3
Hey HWD et al.[40]	272	4.7	12
Emohare O et al.[29]	207	3.4	24
Godil SS et al.[41]	54	13.0	24
Haimoto S et al.[21]	268	5.6	6
Janssen DMC et al.[42]	898	6.9	18
Lopez WY et al.[43]	3,231	2.0	24
Martin JR et al.[44]	174	6.9	1
O'Neill KR et al.[38]	56	13.0	6
Pereira PL et al.[45]	521	4.9	1
Pereira BJ et al.[46]	164	7.3	1
Rao SB et al.[47]	1,587	3.6	1
Rosenthal NA et al.[2]	13,212	3.4	6
Schairer WW et al.[4]	836	5.6	3
Strom RG et al.[48]	97	11.0	12
Sweet FA et al.[49]	821	2.6	30

efficacy previously validated in arthroplasty and traumatology, and we demonstrated that this approach is even feasible to prevent SSI in instrumented vertebral surgery without impairment of fusion.

CONCLUSION

The use of DAC® gel with the local delivery of antibiotic for the prevention of peri-implant infection in instrumented vertebral surgery is promising and might mitigate uncommon but severe complications that can cause prolonged hospitalization, additional systemic antibiotic therapy and risk of revision surgery with impairment of quality of life for the patients and cost concerns for the national health system. STI

AUTHORS' DISCLOSURES

The authors declare that there are no conflicts of interest related to this study.

REFERENCES

1. Anderson PA, Savage JW, Vaccaro AR, et al. Prevention of surgical site infection in spine surgery. Neurosurgery 2017;80(3 suppl):S114-S123.
2. Rosenthal NA, Heinrich KH, Chung J, Yu H. Cost and hospital resource utilization of Staphylococcus aureus infection post elective posterior instrumented spinal fusion surgeries in U.S. hospitals: a retrospective cohort study. Spine (Phila Pa 1976) 2019;44:637-46.
3. McGirt M, Parker SL, Lerner J, Engelhart L, Knight T, Wang MJ. Comparative analysis of perioperative surgical site infection after minimally invasive versus open posterior/transforaminal lumbar interbody fusion: analysis of hospital billing and discharge data from 5170 patients. J Neurosurg Spine 2011;14:771-8.
4. Schairer WW, Carrer A, Deviren D, et al. Hospital readmission after spine fusion for adult spinal deformity. Spine (Phila Pa 1976) 2013;38:1681-9.
5. Blumberg TJ, Woelber E, Bellabarba C, Bransford R, Spina N. Predictors of increased cost and length of stay in the treatment of postoperative spine surgical site infection. Spine J 2018;18:300-6.
6. McClelland S, Takemoto RC, Lonner BS, et al. Analysis of postoperative thoracolumbar spine infections in a prospective randomized controlled trial using the Centers for Disease Control surgical site infection criteria. Int J Spine Surg 2016;10:14.
7. Nota SP, Braun Y, Ring D, Schwab JH. Incidence of surgical site infection after spine surgery: what is the impact of the definition of infection? Clin Orthop Relat Res 2015;473:1612-9.
8. Ghobrial GM, Harrop JS, Sasso RC, et al. Anterior cervical infection: presentation and incidence of an uncommon postoperative complication. Global Spine J 2017;7(1 suppl):12S-16S.
9. Karhade AV, Vasudeva VS, Dasenbrock HH, et al. Thirty-day readmission and reoperation after surgery for spinal tumors: a national surgical quality improvement program analysis. Neurosurg Focus 2016;41:E5.
10. Sebastian A, Huddleston P, Kakar S, Habermann E, Wagie A, Nassr A. Risk factors for surgical site infection after posterior cervical spine surgery: an analysis of 5441 patients from the ACS NSQIP 2005-2012. Spine J 2016;16:504-9.
11. Zhou J, Wang R, Huo X, Xiong W, Kang L, Xue Y. Incidence of Surgical Site Infection After Spine Surgery: A systematic review and meta-analysis. Spine (Phila Pa 1976) 2020;45:208-16.
12. Meng F, Cao J, Meng X. Risk factors for surgical site infections following spinal surgery, J Clin Neurosci 2015;22:1862-6.
13. Chaichana KL, Bydon M, Santiago-Dieppa DR, et al. Risk of infection following posterior instrumented lumbar fusion for degenerative spine disease in 817 consecutive cases. J Neurosurg Spine 2014;20:45-52.
14. Yin D, Liu B, Chang Y, Gu H, Zheng X. Management of late-onset deep surgical site infection after instrumented spinal surgery. BMC Surg 2018;18:121.
15. Abdul-Jabbar A, Berven SH, Hu SS, et al. Surgical site infections in spine surgery: identification of microbiologic and surgical characteristics in 239 cases. Spine (Phila Pa 1976) 2013;38:1425-31.
16. Gasik M, Van Mellaert L, Pierron D, et al. Reduction of biofilm infection risks and promotion of osteointegration for optimized surfaces of titanium implants. Adv Healthc Mater 2012;1:117-27.
17. Zimmerli W, Sendi P. Orthopaedic biofilm infections. APMIS 125 (2017) 353-64.
18. Arciola CR, Campoccia D, Montanaro L. Implant infections: adhesion, biofilm formation and immune evasion. Nat Rev Microbiol 2018;16:397-409.
19. Watters WC, Baisden J, Bono CM, et al. North American Spine Society Antibiotic prophylaxis in spine surgery: an evidence-based clinical guideline for the use of prophylactic antibiotics in spine surgery. Spine J 2009;9:142-6.
20. Mujagic E, Zwimpfer T, Marti WR, et al. Evaluating the optimal timing of surgical antimicrobial prophylaxis: study protocol for a randomized controlled trial. Trials 2014;15:188.
21. Haimoto S, Schär RT, Nishimura Y, Hara M, Wakabayashi T, Ginsberg HJ. Reduction in surgical site infection with suprafascial intrawound application of vancomycin powder in instrumented posterior spinal fusion: a retrospective case-control study. J Neurosurg Spine 2018;29:193-8.
22. Bakhsheshian J, Dahdaleh NS, Lam SK, Savage JW, Smith ZA. The use of vancomycin powder in modern spine surgery: systematic review and meta-analysis of the clinical evidence, World Neurosurg 2015;83:816-23.
23. Shiels SM, Raut VP, Patterson PB, Barnes BR, Wenke JC. Antibiotic-loaded bone graft for reduction of surgical site infection in spinal fusion. Spine J 2017;17:1917-25.
24. Borkhuu BB, Borowski A, Shah SA, Littleton AG, Dabney KW, Miller F. Antibiotic-loaded allograft decreases the rate of acute deep wound infection after spinal fusion in cerebral palsy. Spine (Phila Pa 1976) 2008;33:2300-4.
25. Romanò CL, Malizos K, Capuano N, et al. Does an antibiotic-loaded hydrogel coating reduce early post-surgical infection after joint arthroplasty? J Bone Jt Infect 2016;1:34-41.
26. Malizos K, Blauth M, Danita A, et al. Fast-resorbable antibiotic-loaded hydrogel coating to reduce post-surgical infection after internal osteosynthesis: a multicenter randomized controlled trial. J Orthop Traumatol 2017;18:159-69.
27. Naresh-Babu J, Arun-Kumar V. Do prophylactic antibiotics reach the operative site adequately? A quantitative analysis of serum and wound concentrations of systemic and local prophylactic antibiotics in spine surgery. Spine (Phila Pa 1976) 2020;45:196-E202.
28. Chiang HY, Herwaldt LA, Blevins AE, Cho E, Schweizer ML. Effectiveness of local vancomycin powder to decrease surgical site infections: a meta-analysis. Spine J 2014;14:397-407.
29. Emohare O, Ledonio CG, Hill BW, Davis RA, Polly DW, Kang MM. Cost savings analysis of intrawound vancomycin powder in posterior spinal surgery. Spine J 2014;14:2710-2715.
30. Ghobrial GM, Cadotte DW, Williams K, Fehlings MG, Harrop SH. Complications from the use of intrawound vancomycin in lumbar spinal surgery: a systematic review. Neurosurg Focus 2015;39:E11.
31. Yang K, Zhang S, Liu H, Wu W. Transforaminal lumbar interbody fusion with antibiotics delivered by CaSO4 drug carrier system for pyogenic spondylodiscitis World Neurosurg 2019;132:e447-e454.
32. Harris L, Richards RG. Staphylococci and implant surfaces: a review. Injury 2006;37:S3-S14.
33. Romanò CL, De Vecchi E, Bortolin M, Morelli I, Drago L. Hyaluronic acid and its composites as a local antimicrobial/antiadhesive barrier. J Bone Jt Infect 2017;2:63-72.
34. Drago L, Boot W, Dimas K, et al. Does implant coating with antibacterial-loaded hydrogel reduce bacterial colonization and biofilm formation in vitro? Clin Orthop Relat Res 2014;472:3311-23.
35. Giavaresi G, Meani E, Sartori M, et al. Efficacy of antibacterial-loaded coating in an in vivo model of acutely highly contaminated implant. Int Orthop 2013;38:1505-12.
36. Zoccali C, Scoccianti G, Biagini R, Daolio PA, Giardina FL, Campanacci DA. Antibacterial hydrogel coating in joint mega-prosthesis: results of a comparative series. Eur J Orthop Surg Traumatol 2021;doi:10.1007/s00590-021-02884-7. Online ahead of print.
37. Trentinaglia MT, Van Der Straeten C, Morelli I, Logoluso N, Drago L, Romanò CL. Economic evaluation of antibacterial coatings on healthcare costs in first year following total joint arthroplasty. J Arthroplasty 2018;33:1656-62.
38. O'Neill KR, Smith JG, Abtahi AM, et al. Reduced surgical site infections in patients undergoing posterior spinal stabilization of traumatic injuries using vancomycin powder. Spine J 2011;11:641-6.
39. Adogwa O, Elsamadicy AA, Sergesketter A, et al. Prophylactic use of intraoperative vancomycin powder and postoperative infection: an analysis of microbiological patterns in 1200 consecutive surgical cases. J Neurosurg Spine 2017;27:328-34.
40. Hey HWD, Thiam DW, Koh ZSD, et al. Is intraoperative local vancomycin powder the answer to surgical site infections in spine surgery? Spine (Phila Pa 1976) 2017;42:267-74.
41. Godil SS, Parker SL, O'Neill KR, Devin CL, McGirt MJ. Comparative effectiveness and cost-benefit analysis of local application of vancomycin powder in posterior spinal fusion for spine trauma: clinical article. J Neurosurg Spine 2013;19:331-5.
42. Janssen DMC, Kramer M, Geurts J, Rhijn LV, Walenkamp GH, Willems PC. A retrospective analysis of deep surgical site infection treatment after instrumented spinal fusion with the use of supplementary local antibiotic carriers. J Bone Jt Infect 2018;3:94-103.
43. Lopez WY, Rider SM, Nwosu K, et al. The impact of vancomycin and cefazolin as standard preoperative antibiotic prophylaxis on surgical site infections following instrumented spinal fusion. Spine (Phila Pa 1976) 2019;44:E366-E371.
44. Martin JR, Adogwa O, Brown CR, Kuchibhatla M, Bagley CA, et al. Experience with intrawound vancomycin powder for posterior cervical fusion surgery. J Neurosurg Spine 2015;22:26-33.
45. López Pereira P, Díaz-Agero Pérez C, López Fresneña N, et al. Epidemiology of surgical site infection in a neurosurgery department. Br J Neurosurg 2017;31:10-5.
46. Pereira BJ, de Holanda CV, Ribeiro CA, et al. Spinal surgery for degenerative lumbar spine disease: predictors of outcome. Clin Neurol Neurosurg. 2016; 140:1-5.
47. Rao SB, Vasquez G, Harrop J, et al. Risk factors for surgical site infections following spinal fusion procedures: a case-control study. Clin Infect Dis 2011; 53:686-92.
48. Strom RG, Pacione D, Kalhorn SP, Frempong-Boadu AK. Lumbar laminectomy and fusion with routine local application of vancomycin powder: decreased infection rate in instrumented and non-instrumented cases. Clin Neurol Neurosurg 2013;115: 1766-9.
49. Sweet FA, Roh M, Sliva C. Intrawound application of vancomycin for prophylaxis in instrumented thoracolumbar fusions: efficacy, drug levels, and patient outcomes. Spine (Phila Pa 1976) 2011;36:2084-8.