Evaluating the Safety Profile and Outcomes of Antibiotic-Loaded Synthetic Calcium Sulfate Beads: A Level 1 Trauma Center Hospital Experience

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INTRODUCTION: Postoperative infection is a significant source of morbidity and mortality throughout orthopaedics, and <br bcx0="">recent advances in prevention and treatment have led to the use of antibiotic-loaded synthetic calcium sulfate (CaS) beads for local antibiotic delivery and infection control. Offering advantages of osteoconductive properties and rapid reabsorption, CaS has been used with increasing frequency in a variety of procedures, particularly in the management of periprosthetic joint infections with bone void. Yet, to our knowledge, few studies have examined the safety and postoperative outcomes after the use of CaS beads, particularly as questions have been raised regarding the potential risks of the local introduction of nephrotoxic antibiotics including tobramycin and vancomycin, which are both used with CaS beads. Thus, this study aimed to examine the safety and postoperative outcomes after the use of CaS beads across a range of orthopaedic procedures at a single institution. This study evaluated: 1) indication for CaS bead use; 2) baseline inflammatory markers; 3) reoperation rates; and 4) pre-to-postoperative changes in trends in serum calcium levels and renal function.

METHODS: We retrospectively reviewed all orthopaedic procedures that used CaS beads (Stimulan®, Wilmington, NC) between August 21, 2015 to August 22, 2019. Patient's preoperative and postoperative diagnoses, procedures, indication for CaS use, and inflammatory markers including white blood cell count (WBC), neutrophil percentage (PMNs), erythroid sedimentation rate (ESR), and C-reactive protein (CRP) were recorded. Baseline measures of serum calcium (Ca2+), BUN, and creatinine (Cr) from preoperative labs, postoperative day 1, and at each subsequent postoperative visit were extracted. Readmission and reoperation rates for each procedure were recorded.

RESULTS: A total of 56 patients have undergone primary procedures performed by 9 surgeons. Open reduction and internal fixation (ORIF) for open fractures was the most common indication for use of CaS (n=14, 25%), followed by infected nonunions (n=12, 21%), and osteomyelitis (n=9, 16%) (Table 1). Analysis of preoperative labs revealed a mean WBC count of 9.09 x 109 /L, and 63.9% PMNs. Mean ESR and CRP at time of operation were 78.5 mm/hr and 79.5 mg/L respectively. The mean follow-up period for all patients was 224 (range, 6 to 789) days. Preoperative and peak postoperative serum Ca2+ (9.2 to 9.1 mg/dL, p=0.330) and BUN (13.6 to 13.4 mg/dL, p=0.679) values were comparable. However, peak postoperative serum creatinine (0.93 mg/dL) was significantly higher than pre-surgical peak (0.88 mg/dL), p=0.042. Of the 56 original procedures, 8 (14%) required reoperation (Table 2), with a mean time to reoperation of 2.6 months.

DISCUSSION AND CONCLUSION: The use of antibiotic-loaded synthetic CaS beads demonstrated adequate clinical outcomes in patients with or at high risk for infection and significant increases in serum creatinine, though no difference in serum Ca2+ and BUN. Given the antibiotic protocol for CaS-based bone grafts, an increase in serum creatinine could be expected and should therefore be monitored, given the renal toxicity of some of the antibiotics utilized. Despite not being statistically significant from its preoperative peak, the observed post-surgical decrease in serum calcium may be suggestive of osteogenesis and fracture healing. This study suggests antibiotic-loaded synthetic CaS beads can be used safely and efficaciously to treat in patients with or at high risk for infections.

Indication	Number of Cases
ORIF of open fracture	14
Infected nonunion	12
Osteomyelitis	9
Infection	6
Periprosthetic fracture	4
Failure/aseptic loosening	3
Periprosthetic joint infection	3
ORIF of closed fracture	3
High infection risk	2
Revision surgery	2

Case Number	Indication
1	Soft tissue abscess and infected nonunion following open intra-articular distal tibial fracture + metadiaphyseal comminution and extension; infected nonunion
2	Infection, status post right femur malunion reconstruction
3	Right foot diabetic Charcot arthropathy
4	Osteomyelitis, soft tissue abscess connecting to proximal left tibia, nonhealing proximal medial wound
5	Infected nonunion, left femoral neck and shaft
6	Right thigh infection secondary to buttocks, postoperative decubitus ulcer following right femoral cephalomedullary nailing
7	Wound dehiscence following right revision total hip arthroplasty
8	Polytrauma: A. Left acetabular posterior column ORIF + I&D, beads, VAC placement B. I&D degloving injury site, CaS beads, deep and superficial VAC

Table 2. Reoperation Details.