

G52: Is there a role for the use of resorbable agents that can deliver antibiotics locally for prevention of infection in patients undergoing major orthopaedic surgery?

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Response/Recommendation:

Yes. There appears to be a role for the use of resorbable agents for delivery of local antimicrobials. Although a whole host of resorbable agents exist, the most studied are calcium sulfate and hydrogel agents.

Level of Evidence: Limited

Delegate Vote:

Rationale:

A total of nine studies were identified (1–9), including three randomized controlled trials (RCTs) (3,8,9), one case control study (1), three retrospective cohort studies (4,6,7), and two case series (2,5). Eight of nine studies (88.9%) included patients undergoing primary or aseptic revision arthroplasty (including megaprotheses for oncologic reconstruction) (1,3–9), while one study included spine surgery patients (2). A total of 1205 patients were included (57.9% female).

Five studies evaluated the use of calcium sulfate beads (Stimulan®), with or without vancomycin added (2,4,5,7,8). Two studies evaluated an antibiotic loaded hydrogel coating (DAC®) (1,3). One study evaluated a hydroxyapatite-collagen scaffold loaded with vancomycin (Pro Osteon®) (9). Finally, one study evaluated calcium carbonate beads loaded with gentamicin (HERAFILL®).

Of the five studies evaluating the use of calcium sulfate beads, the four comparative studies were pooled for analysis (Figure 1). All studies enrolled patients with some type of risk factor for infection – such as non-modifiable patient risk factors, high risk surgery (e.g. revision or spine surgery), or previous infection in the same joint. The comparative groups were either no calcium sulfate beads, or one study which used calcium sulfate beads without antibiotics. All studies added vancomycin to the sulfate beads, while two studies also added tobramycin, and one study added tobramycin and cefazolin. Three of the four studies found significantly reduced infection rates with the use of calcium sulfate beads, while the non-comparative study found a 0% infection rate with the use of calcium sulfate beads.

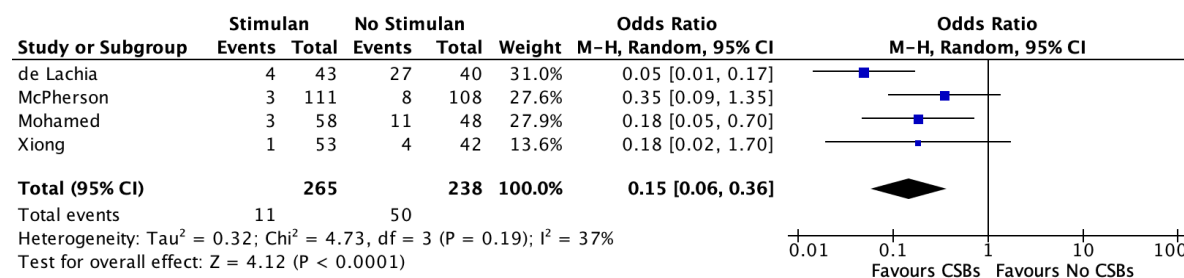


Figure 1 – pooled data for calcium sulfate beads

Based on the pooled data from four studies (N=50, Figure 1), there was a significantly reduced rate of infection with the use of antibiotic-loaded calcium sulfate beads (Odds Ratio [OR]: 0.15, 95% Confidence Interval [CI]: 0.06 to 0.36, $p < 0.0001$, $Z = 4.12$) with moderate heterogeneity ($I^2 = 37\%$). Only one study had an industry-related conflict of interest directly related to the calcium sulfate bead product.

Data were pooled for two studies comparing antibiotic-loaded hydrogel coating to standard of care (N = 459) (1,3). There was a significant reduction in infection rates (OR: 0.08, 95%CI: 0.01-0.41, $p = 0.003$, $Z = 2.99$), with no heterogeneity ($I^2 = 0\%$). One study had an industry-related conflict of interest (**Figure 2**) (3).

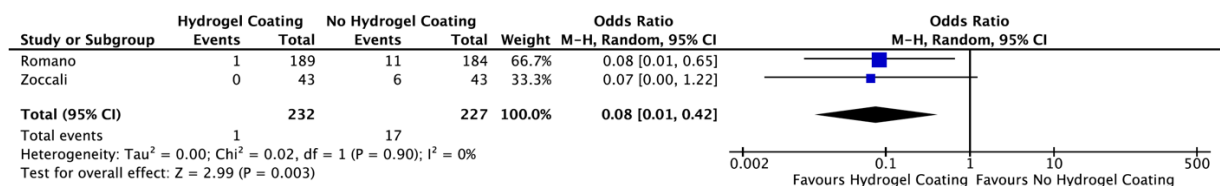


Figure 2– pooled data for antibiotic-loaded hydrogel coating

One RCT evaluating a vancomycin loaded hydroxyapatite-collagen scaffold in total knee arthroplasty patients found a significant reduction in rates of prosthetic joint infection (0% vs. 4.1%, $p = 0.014$) (9). Finally, one study evaluating calcium carbonate beads loaded with gentamicin found a significant reduction in re-infection rate in second-stage total knee arthroplasty for previous prosthetic joint infection (0% vs. 17.9%, $p = 0.025$) (6).

One study reported an adverse event potentially related to the resorbable agent – Lum et al., in their non-comparative study, reported 1 case of prolonged serous drainage (1.9%) which required irrigation, debridement, and liner exchange, however was negative for infection workup (5). A previous systematic review has also raised concerns about possible hypercalcemia with the use of calcium sulfate beads, with a rate of 4.2%, and a rate of 0.28% of patients requiring active management of the hypercalcemia (10).

Overall, nearly all studies evaluating resorbable antibiotic delivery agents have found low or reduced infection rates compared to standard of care, including in one study, compared to non-antibiotic loaded calcium sulfate beads plus antibiotic powder. Thus, there is likely a role for these agents in high-risk patients. However, the effect sizes in the pooled data should be interpreted with caution given the overall small number of relatively low-quality studies available. As well, it is unclear whether the resorbable delivery agent itself matters, however the slow elution and resorption over time does seem to be important given that one study using plain beads plus antibiotic powder in the control group still found a significant effect favouring antibiotic loaded beads.

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