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CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Absorbable Delivery Products for Treatment of Patients with Periprosthetic Infections: Clinical and Cost-Effectiveness

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Research Questions

1. What is the clinical effectiveness of the surgical implantation of absorbable delivery products for local antibiotic treatment of osteomyelitis in the treatment of patients with periprosthetic infections?
2. What is the cost-effectiveness of the surgical implantation of absorbable delivery products for local antibiotic treatment of osteomyelitis in the treatment of patients with periprosthetic?

Key Findings

One randomized control trial and four non-randomized studies were identified regarding absorbable delivery products for the treatment of patients with periprosthetic infections.

Methods

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, and economic studies. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2012 and March 26, 2017. Internet links were provided, where available.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Patients with periprosthetic infections
Intervention	Surgical implantation of absorbable delivery products for local antibiotic treatment (e.g., calcium sulfate beads infused with antibiotics)
Comparator	Q1-2: Antibiotic infused bone cement; No comparator
Outcomes	Q1: Clinical effectiveness for treatment of infection; harms Q2: Cost-effectiveness
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic evaluations

Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, and economic evaluations.

One randomized control trial and four non-randomized control trials were identified regarding absorbable delivery products for the treatment of patients with periprosthetic infections. No relevant health technology assessments, systematic reviews, meta-analyses, or economic evaluations were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

One randomized controlled trial (RCT)[1] and four non-randomized studies[2-5] were identified regarding absorbable delivery products for the treatment of patients with periprosthetic infections.

The identified RCT examined the use of Defensive Antibacterial Coating (DAC), a resorbable hydrogel coating for the prevention of infection during closed fracture internal osteosynthesis.[1] The group who received antibiotic-loading DAC had reduced post-surgical infection rates when compared to the control group who received no DAC; however, wound healing, clinical scores, laboratory tests, and radiographic findings were not significantly different between the two groups. No adverse events or side effects were noted with the use of the DAC.[1]

Four non-randomized studies[2-5] were identified, two of which used bio-degradable beads in infection treatment[2,4] and one of which used bio-degradable sponges.[5] Three studies[2-4] examined calcium sulphate as the bio-composite. Two of these studies solely used calcium sulphate[2,4] and the third used a calcium sulphate/hydroxyapatite mixture.[3] Two of the studies investigated the use of absorbable delivery products in revision or primary arthroplasty,[4-5] one in chronic osteomyelitis,[3] and one in vascular graft prosthetics.[2]

In vascular graft prosthetics, bio-absorbable calcium sulphate beads successfully suppressed infection, preserved the graft, and contributed to the salvaging of limbs in a cohort of six patients.[2] Bio-absorbable calcium sulphate beads used in revision arthroplasty were reported in another study; however, the results were not reported directly in the abstract text.[4] The authors recommended the measurement of serum calcium levels after the implantation of calcium sulphate beads.[4] A calcium sulphate/hydroxyapatite mixture was used in patients with chronic osteomyelitis, with infection being eradicated in 96 out of 100 patients in one procedure.[3] Adverse events were not common, with only three fractures, six wound leaks, and three unrelated deaths occurring after follow up.[3] Finally, the authors of the last study used a gentamicin loaded sponge to treat infection after hip arthroplasty, observing that 25 of 34 patients with a deep infection were treated successfully with the biodegradable sponge, with no permanent complications in any patient.[5]

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

No literature identified.

Randomized Controlled Trials

1. Malizos K, Blauth M, Danita A, Capuano N, Mezzoprete R, Logoluso N, 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 Feb 2.
PubMed: PM28155060

Non-Randomized Studies

2. Genovese EA, Avgerinos ED, Baril DT, Makaroun MS, Chaer RA. Bio-absorbable antibiotic impregnated beads for the treatment of prosthetic vascular graft infections. Vascular. 2016 Dec;24(6):590-7.
PubMed: PM26896286

3. McNally MA, Ferguson JY, Lau AC, Diefenbeck M, Scarborough M, Ramsden AJ, et al. Single-stage treatment of chronic osteomyelitis with a new absorbable, gentamicin-loaded, calcium sulphate/hydroxyapatite biocomposite: a prospective series of 100 cases. Bone Joint J. 2016 Sep;98-B(9):1289-96.
PubMed: PM27587534

4. Kallala R, Haddad FS. Hypercalcaemia following the use of antibiotic-eluting absorbable calcium sulphate beads in revision arthroplasty for infection. Bone Joint J. 2015 Sep;97-B(9):1237-41.
PubMed: PM26330591

5. Kuiper JW, Brohet RM, Wassink S, van den Bekerom MP, Nolte PA, Vergroesen DA. Implantation of resorbable gentamicin sponges in addition to irrigation and debridement in 34 patients with infection complicating total hip arthroplasty. Hip Int. 2013 Mar;23(2):173-80.
PubMed: PM23397196

Economic Evaluations

No literature identified.

Appendix — Further Information

Systematic Reviews – Animal Models

6. Inzana JA, Schwarz EM, Kates SL, Awad HA. Biomaterials approaches to treating implant-associated osteomyelitis. Biomaterials [Internet]. 2016 Mar [cited 2017 Apr 6];81:58-71. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4745119 PubMed: PM26724454

Non-Randomized Studies

Alternate Populations

7. Morley R, Lopez F, Webb F. Calcium sulphate as a drug delivery system in a deep diabetic foot infection. Foot (Edinb). 2016 Jun;27:36-40. PubMed: PM26338082

8. White TL, Culliford AT, Zomaya M, Freed G, Demas CP. Use of Antibiotic-Impregnated Absorbable Beads and Tissue Coverage of Complex Wounds. Am Surg. 2016 Nov 1;82(11):1068-72. PubMed: PM28206933

9. Humm G, Noor S, Bridgeman P, David M, Bose D. Adjuvant treatment of chronic osteomyelitis of the tibia following exogenous trauma using OSTEOSET(®)-T: a review of 21 patients in a regional trauma centre. Strategies Trauma Limb Reconstr [Internet]. 2014 Nov [cited 2017 Apr 6];9(3):157-61. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4278971 PubMed: PM25540119

Review Articles

10. Galarraga-Vinueza ME, Mesquita-Guimaraes J, Magini RS, Souza JC, Fredel MC, Boccaccini AR. Anti-biofilm properties of bioactive glasses embedding organic active compounds. J Biomed Mater Res A. 2017 Feb;105(2):672-9. PubMed: PM27750384

11. Cook GE, Markel DC, Ren W, Webb LX, McKee MD, Schemitsch EH. Infection in Orthopaedics. J Orthop Trauma. 2015 Dec;29 Suppl 12:S19-S23. PubMed: PM26584261

12. Howlin RP, Brayford MJ, Webb JS, Cooper JJ, Aiken SS, Stoodley P. Antibiotic-loaded synthetic calcium sulfate beads for prevention of bacterial colonization and biofilm formation in periprosthetic infections. Antimicrob Agents Chemother [Internet]. 2015 Jan [cited 2017 Apr 6];59(1):111-20. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4291338 PubMed: PM25313221

13. Lyndon JA, Boyd BJ, Birbilis N. Metallic implant drug/device combinations for controlled drug release in orthopaedic applications. J Control Release. 2014 Apr 10;179:63-75. PubMed: PM24512924

14. Knaepler H. Local application of gentamicin-containing collagen implant in the prophylaxis and treatment of surgical site infection in orthopaedic surgery. Int J Surg. 2012;10 Suppl 1:S15-S20.
PubMed: PM22659311

Additional References

15. Antibiotic-impregnated calcium sulfate beads for controlling infection in orthopedic surgery [Internet]. Plymouth Meeting (PA): ECRI Institute; 2012 [cited 2017 Apr 6]. Available from: www.ecri.org. Subscription required.

16. Stimulan Rapid Cure (Biocomposites Ltd.) resorbable, biocompatible bone graft material [Internet]. Plymouth Meeting (PA): ECRI Institute; 2013 [cited 2017 Apr 6]. Available from: www.ecri.org. Subscription required.