Prophylactic use of antibiotic laden poly methyl methacrylate beads in the management of open fractures: a novel approach for control of orthopaedic infection

Hariprasad Seenappa, Prabhulingreddy Patil*, Harsha Madamanchi, Sakthikesavan Sivanandan

INTRODUCTION

Open fractures are often contaminated and the development of infection is a major complication. The primary cause of infection has multiple etiologies; it can arise from haematogenous, post-traumatic or post-operative colonisation.1,2 The aims of treatment are salvage of the limb, fracture healing without infection and restoration of function.3

Current management of open fractures includes wound irrigation, serial radical debridement, systemic administration of broad-spectrum antibiotics, stabilisation of the bone and, if the wound is sterile, early provision of soft-tissue cover.4,5

Control of infection in open fractures is a challenge in orthopaedic surgery. The critical factors in the treatment of any orthopaedic infection are adequate surgical

ABSTRACT

Background: Control of infection in open fractures is a challenge in orthopaedic surgery. The literature provides evidence that antibiotic-laden bead chains are a useful adjuvant with systemic antibiotics in the prevention of infection in open fractures.

Methods: Between February 2018 and January 2019, sixty four patients with open type fractures admitted in emergency room were analysed for this study. In this 64 patients, 32 in Group A received antibiotic laden PMMA (Poly methyl methacrylate) beads with standard care. Another 32 in Group B received standard care.

Results: There were 54 males and 10 females with a mean age of 41 and follow up 6 months. Among 64 patients 37 patients were stabilised with external fixators and remaining 17 patients underwent a definitive fixation either an intramedullary nailing (12 patients) or internal fixation with a plate (5 patients). 10 patients were stabilised with k wires. The infection rate in group A and B was 6.25% and 21.8% respectively which is statistically not significant (p=0.072).

Conclusions: Although the final infection control rate was comparable between the bead group (30/32, 93.75%) and the non bead group (25/32, 78.12%), few complications were noted in the bead group (9.37%, 3/32) than in the group B (15.62%, 5/32). Hence the prophylactic use of antibiotic cement beads is advantageous in preventing post traumatic orthopaedic infection, lessens hospital stay as well the financial burden to the patients.

Keywords: PMMA beads, Open fractures, Orthopaedic infection

INTRODUCTION

Open fractures are often contaminated and the development of infection is a major complication. The primary cause of infection has multiple etiologies; it can arise from haematogenous, post-traumatic or post-operative colonisation.1,2 The aims of treatment are salvage of the limb, fracture healing without infection and restoration of function.3

Current management of open fractures includes wound irrigation, serial radical debridement, systemic administration of broad-spectrum antibiotics, stabilisation of the bone and, if the wound is sterile, early provision of soft-tissue cover.4,5

Control of infection in open fractures is a challenge in orthopaedic surgery. The critical factors in the treatment of any orthopaedic infection are adequate surgical
debridement, integrity of the host immune system, and adequate antibiotic levels. The literature provides evidence that antibiotic-laden bead chains are a useful adjuvant with systemic antibiotics in the prevention of infection in open fractures. Local antibiotic therapy via antibiotics impregnated in bone cement was first used to treat infected arthroplasties.

Antibiotic loaded bone cement is popular as it is a proven way to deliver high concentrations of the drug locally, even to avascular areas that are inaccessible by systemic antibiotics. Another advantage of local antibiotic delivery is that the high concentrations of the drug achieved locally would be effective against organisms that are resistant to drug concentrations achieved by systemic antibiotics. Its use results in only low serum antibiotic concentrations and hence less toxicity than that associated with systemic administration.

Aminoglycosides can safely achieve high levels at the site of infection when implanted locally (e.g., in antibiotic impregnated polymethyl methacrylate cement).

Antibiotic-laden PMMA beads is a useful method for the local antibiotic delivery adjuvant to systemic antibiotics. Bead chains are a practical method of local antibiotic therapy when the wounds can be closed. Antibiotic release from cement is biphasic, with most occurring during the first hours to days after implantation and the remaining eluting for weeks, and sometimes years.

In this study, we intend to evaluate a novel approach of using antibiotic laden PMMA (poly methyl methacrylate) beads for prophylactic usage in the management of open fractures.

Aims of the study

- To assess the rate of surgical site infection (SSI) in the study group.
- To analyze the results of antibiotic laden PMMA (Poly methyl methacrylate) beads in the control of infection in open fractures.
- To assess the complications associated with this treatment.

METHODS

Between February 2018 and January 2019, sixty four patients with open long bone fractures were identified after their admission to the emergency department. It was an open label, parallel group, observational, randomised control trial. Informed consent was obtained for all patients and consent to publish was obtained for the patients whose information appears in this publication. The study was authorized by the Institutional Ethics Committee of to Sri Devaraj Urs Medical College, Kolar, Karnataka, India and was performed in accordance with the ethical standards of the 2013 Declaration of Helsinki.

A proforma was formulated for patient data, with variables analyzed subsequently. This proforma was completed after the signing of the consent terms by the patient or patient attender or legal guardian, maintaining assurance in its methodology of the right to confidentiality and to the freedom of non-inclusion in the study at the beginning as well as at any time.

Patients from the department of orthopaedics meeting the inclusion criteria and who are willing to participate as per our treatment protocol were recruited after obtaining informed written consent. The inclusion criteria were all the patients of either gender and skeletally mature with a diagnosis of open fracture of long bones with Gustilo Anderson classification type I, II, IIIA, IIIB. The exclusion criteria was patients with chronic orthopaedic infections, patients with blood diseases, metabolic diseases, immunodeficiency, hepatitis B and hepatitis C, HIV positive, patients not willing to give consent and patients with known allergies to the antibiotics. Four patients were excluded from the study: all the four patients met inclusion criteria but three lost to follow up and another patient lost due to mortality.

Sixty four patients with open long bone fractures were analysed for this study between February 2018 and January 2019. Among 64 patients 32 in Group A received antibiotic laden PMMA beads along with standard care. Another 32 in Group B received standard care (systemic antibiotic therapy, wound debridement, skeletal stabilization) as we realized the potential advantages of preventing the post-operative infection in open long bone fractures. The culture and sensitivity of the wounds was sent as a routine according to the protocol and the participants were explained about the various advantages and disadvantages of the treatment modalities (standard care i.e. systemic antibiotic therapy, wound debridement, skeletal stabilization and antibiotic laden PMMA beads with standard care) for open fracture management.

The antibiotic laden PMMA beads were prepared by the surgical team member by mixing 40 grams of PMMA powder with 2 grams of vancomycin powder under room temperature mixed with the monomer solution in sterile conditions until it attains a doughy state, then small beads are prepared over a stainless steel wire of diameter 16G. The ends of the wire are bent to form a loop to avoid the complication of lost bead while removal and to facilitate easy removal. An important topic in the use of antibiotic-loaded spacers is the impregnation of the bone cement itself with antibiotics. Not every antibiotic qualifies equally for incorporation into bone cement: desirable characteristics include: its availability in powder form, wide antibacterial spectrum, bactericidal at low concentrations, elution from PMMA in high concentrations for prolonged periods, thermal stability, low or no risk of allergy or delayed hypersensitivity, low influence on the mechanical properties of the cement and low serum protein binding.
Aminoglycosides and glycopeptides are known to be the two groups of antibiotics that fulfill most of these criteria. The combination of these antibiotics has the advantage of a wide antimicrobial spectrum with good elution kinetics. Vancomycin is good for treating orthopaedic-related infections since Staphylococci are the most common bacteria causing such infections, and vancomycin possesses an excellent efficacy against these strains, especially resistant strains.11

Randomization plan

Subjects with open fractures were evaluated. After fulfillment of inclusion and exclusion criteria the subjects were randomized into two groups, Group A and Group B.

The treatment of open long bone fractures often requires adequate debridement and proper wound care to prevent wound infection. The various modalities of containing the infection include systemic antibiotics, thorough wound debridement, soft tissue coverage and skeletal immobilization. Treatment of post-traumatic osteomyelitis requires adequate management of dead space created by debridement. There are a number of options for the reconstruction of bone defects, including antibiotic impregnated cement beads, which have been used in the treatment of chronic osteomyelitis for more than 20 years. Their use is well established: bone defects created by debridement are filled with temporary PMMA antibiotic-impregnated beads. Encouraging results have been demonstrated with the use of antibiotic-impregnated beads in the treatment of chronic osteomyelitis.12-16

Statistical analysis

The data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square was the test of significance. Continuous data was represented as mean and standard deviation. Independent t test was the test of significance to identify the mean difference between two groups. P value <0.05 was considered as statistically significant.

RESULTS

There were 54 males and 10 females with a mean age of 41 (range 20–71) and follow-up of 6 months (range 6–36 weeks). 14 patients were having diabetes mellitus and hypertension, 8 patients were suffering from chronic obstructive pulmonary disease and 3 patients had ischemic heart disease. Microbiological analysis revealed infection in 7 patients of group B, the organisms isolated were Staph aureus and Pseudomonas in 2 patients, E. coli, Klebsiella and MRSA in 1 patient each. 2 patients of group A had the following organisms isolated, 1 E. coli and Klebsiella respectively. The infection rate in group A was 6.25% and in group B was 21.8% which is statistically not significant (p=0.072).

![Figure 1 (A-C): Radiographs showing antibiotic coated cement beads in various open fractures along with different external fixators and internal fixator.](image)

Among 64 patients 37 patients were stabilised with external fixators and remaining 17 patients underwent a primary definitive fixation either an intramedullary nailing (12 patients) or internal fixation with a plate (5 patients). 10 patients were stabilised with k wires. 19 patients underwent secondary procedures with reconstructive soft tissue coverage done by the plastic surgery team. There were 8 free vasularised flaps, 6 rotational flaps and remaining 5 split skin grafting.

Out of 64 patients 8 patients had complications which included ankle stiffness (4 patients), knee stiffness(2 patients), posterior interosseous nerve palsy and foot drop( 1 patient). 29 patients in group A had primary wound healing and remaining 3 patients had secondary wound healing. In group B 15 patients had primary wound healing and 17 patients had secondary wound healing.
The complications in group A were ankle stiffness in 2 patients and another patient had foot drop. In group B the ankle stiffness was found in 2 patients, knee stiffness in 2 patients and posterior interosseous nerve palsy in 1 patient. The complications have no correlation, specific to the treatment modalities.

DISCUSSION

With the use of antibiotic-impregnated beads, infection control rates in the literature range from 78% to 100% in the treatment of chronic osteomyelitis with or without systemic antibiotics.12-16 Calhou et al evaluated the effectiveness of gentamicin in PMMA beads in the treatment of osteomyelitis and found that 89.3% (25/28) of patients’ infections were successfully treated with gentamicin beads.13 In a retrospective study, Patzakis et al found no recurrence of infection in 100% (12/12) of patients treated with gentamicin antibiotic-impregnated beads.14 Walenkamp et al reported on a series of 100 patients who underwent surgery using gentamicin PMMA beads with a follow-up period of 5 years.15 They found that the infection control rate was 78% after a single treatment period, while it was 92% after two or three treatment periods.

In the present study, the infection control rate was 93.75% (30/32) in the bead group, which was similar to outcomes reported in the literature. It should be mentioned that although the final infection control rate was comparable between the bead group (30/32, 93.75%) and the non-bead group (25/32, 78.12%), few complications were noted in the bead group (9.37%, 3/32) than in the group B (15.62%, 5/32); these may not have been due to the internal fixations being used as definitive fixation, but could be due to external fixation and prolonged immobilisation in both groups leading to ankle and knee stiffness. The other complications like posterior interosseous nerve and common nerve palsy was related to primary trauma.

Few studies have specifically focused on antibiotic impregnated spacers (Masquelet technique) in the treatment of osteomyelitis defects.17,18 Recently, Masquelet reviewed twelve patients with segmental bone defects resulting from infected non-unions of the tibia treated with the induced membrane technique and showed no cases of recurrent infection.18 In the present study, the induced membrane technique was not only used for the treatment of segmental bone defects but also for the treatment of partial segmental bone defects. The overall infection control rate for the spacer group was 90.9% (20/22), and it was 89.5% (17/19) for partial segmental bone defects, which was comparable to the bead group (88.9%). It is interesting that the release of antibiotics from bone cement was influenced by the size of bone cement; more antibiotics were released in the bead group than in the spacer group.19 However, it seems that a greater release of antibiotics did improve the infection control rate in the bead group.
There may be two reasons for this phenomenon. First, surgical debridement is critical to the success of treatment in post-traumatic open fractures. Mader et al noted that treatment failures occur if surgical debridement was inadequate, independent of the type of antibiotic used or duration of the treatment. Second, although more antibiotics were released in the bead group, the local antibiotic concentration was also greater than the minimum inhibitory concentration in the systemic antibiotic group. Therefore, our study indicates that prophylactic usage of antibiotic impregnated beads are also an effective method for the treatment of open fractures in terms of infection control. However, the sample size was small; a larger sample size is needed for definitive conclusions about infection control rates. Removing PMMA antibiotic beads is simpler technique and less time consuming. One patient with PMMA antibiotic beads had failure of removal in the present study. This outcome may have been due to deeply seated beads within the muscular plane. Compared with spacers, beads leave an irregular membrane that is less than ideal for the containment of cancellous bone grafts. Therefore, vascularized bone grafts, such as vascularized fibula flaps, are needed for the reconstruction of large/segmental bone defects when cement beads are used.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Lazzarini L, Mader JT, Calhoun HJ. Osteomyelitis in long bones. J Bone Joint Surg Am. 2004;86:2305–18.
2. Lew DP, Waldvogel FA. Osteomyelitis. Lancet (London, England). 2004;364:369–79.
3. Ostermann PAW, Seligson D, Henry SL. Local antibiotic therapy for severe open fractures a review of 1085 conclusive cases J Bone Joint Surg [Br]. 1995;77:93–7.
4. Felson DT, Zhang Y, Anthony JM, Naimark A, Anderson JJ. Weight loss reduces the risk for symptomatic knee osteoarthritis in woman. The Framingham study. Ann Intern Med. 1992;116(7):535-9.
5. Bellamy N, Campbell J, Robinson V, Gee T, Bourne R, Wells G. Intraarticular corticosteroid for treatment of osteoarthritis of the knee. Cochrane Database Sys Rev 2006;19:CD005328.
6. Brien WW, Salvati EA, Klein R, Brause B, Stern S. Antibiotic impregnated bone cement in total hip arthroplasty. An in vivo comparison of the elution properties of tobramycin and vancomycin. Clin Orthop Relat Res. 1993;(296):242-8.
7. Buchholz HW, Engelbrecht H. Depot effects of various antibiotics mixed with Palacos resins. Chirurg. 1970;41:511–5.
8. Munukka E, Lepparanta O, Korkeamaki M, Vaahitio M, Peltola T, Zhang D et al. Bactericidal effects of bioactive glasses on clinically important aerobic bacteria. J Mater Sci Mater Med. 2008;19:27–32.
9. Seligson D, Berling S. Antibiotic-laden PMMA bead chains for the prevention of infection in compound fractures: current state of the art. Eur J Orthop Surg Traumatol. 2015;25(6):969-74.
10. Wininger DA, Fass RJ. Antibiotic-impregnated cement and beads for orthopaedic infections. Antimicrob Agents Chemother. 1996;40:2675–9.
11. Anagnostakos K, Kelm J. Enhancement of antibiotic elution from acrylic bone cement. J Biomed Mater Res B Appl Biomater. 2009;90:467–75.
12. Blaha JD, Calhoun JH, Nelson CL, Henry SL, Seligson D, Estehri JL Jr, et al. Comparison of the clinical efficacy and tolerance of gentamicin PMMA beads on surgical wire versus combined and systemic therapy for osteomyelitis. Clin Orthop Relat Res. 1993;295:8–12.
13. Calhoun JH, Henry SL, Anger DM, Cobos JA, Mader JT. The treatment of infected nonunions with gentamicin-polyethylenehexacrylate antibiotic beads. Clin Orthop Relat Res. 1993;295:23–7.
14. Pat zakis MJ, Mazur K, Wilkins J, Sherman R, Hol tom P. Septopal beads and autogenous bone grafting for bone defects in patients with chronic osteomyelitis. Clin Orthop Relat Res. 1993;295:112–8.
15. Walenkamp GH, Kleijn LL, de Leeuw M. Osteomyelitis treated with gentamicin- PMMA beads: 100 patients followed for 1-12 years. Acta Orthop Scand. 1998;69(5):518–22.
16. Mohanty SP, Kumar MN, Murthy NS. Use of antibiotic-loaded polymethyl methacrylate beads in the management of musculoskeletal sepsis—a retrospective study. J Orthop Surg (Hong Kong). 2003;11(1):73–9.
17. Chadayammuri V, Hake M, Mauffrey C. Innovative strategies for the management of long bone infection: a review of the Masquelet technique. Patient Saf Surg. 2015;9:32.
18. Mauffrey C, Hake ME, Chadayammuri V, Masquelet AC. Reconstruction of Long Bone Infections Using the Induced Membrane Technique: Tips and Tricks. J Orthop Trauma. 2015;30(6):e188–93.
19. Shin sako K, Okui Y, Matsuda Y, Kunimasa J, Otsuka M. Effects of bead size and polymerization in PMMA bone cement on vancomycin release. Biomed Mater Eng. 2008;18(6):377–85.
20. Mader JT, Cripps MW, Calhoun HJ. Adult posttraumatic osteomyelitis of the tibia. Clin Orthop Relat Res. 1999;360:14–21.
21. Tu YK, Yen CY. Role of vascularized bone grafts in lower extremity osteomyelitis. Orthop Clin North Am. 2007;38(1):37–49.

Cite this article as: Seenappa H, Patil P, Madamanchi H, Sivanandan S. Prophylactic use of antibiotic laden poly methyl methacrylate beads in the management of open fractures: a novel approach for control of orthopaedic infection. Int J Res Orthop 2019;5:624-8.