Use of antibiotic-loaded polymethyl methacrylate beads in the management of musculoskeletal sepsis — a retrospective study

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ABSTRACT

Purpose. To assess the use of antibiotic-loaded polymethyl methacrylate beads in the management of chronic osteomyelitis of different aetiologies: infected osteosynthesis, infected open fractures, and haematogenous osteomyelitis.

Methods. Records of 49 patients with chronic osteomyelitis who were treated at Department of Orthopaedics, Kasturba Medical College, from 1995 to 1999 were studied retrospectively. The diagnosis of chronic osteomyelitis was made on the basis of clinical and radiographic features. Of the 49 patients, 4 had haematogenous osteomyelitis, which later proved to be tuberculosis, and were thus excluded. Antibiotic-loaded acrylic beads were implanted in the remaining patients after thorough debridement. The implant was removed primarily in 16 patients with infected osteosynthesis, who then underwent decompression and sequestrectomy. All wounds were closed primarily. Peri-operative antibiotics were given for 7 days. Beads were removed at the end of 3 weeks followed by bone grafting in 26 patients. Patients were followed up for an average period of 3.7 years.

Results. The infective organisms were sensitive to gentamycin in 26 cases and resistant in 19 cases; 14 cases were sensitive to cefuroxime, 11 to cloxacillin, 8 to ampicillin, and 5 to cotrimoxazole. Seven cases were resistant to all antibiotics tested. Of the 19 patients with gentamycin-resistant infection, only one had a poor result. No adverse systemic side-effects such as ototoxicity or nephrotoxicity were seen. Infection did not recur in 39 patients, but 6 patients had low-grade persistent infection at the last follow-up visit.

Conclusion. In chronic infections, especially those following osteosynthesis, antibiotic beads are a valuable adjuvant. The most valuable advantage is that the wound can be closed primarily, thereby reducing the incidence of nosocomial infections and requirement of nursing care.

Key words: antibiotic-loaded polymethyl methacrylate beads; chronic osteomyelitis
INTRODUCTION

Optimal treatment of musculoskeletal infections often requires a combined surgical and antimicrobial approach. Osteomyelitis, however, is not consistently treated with success in this way, despite the extensive array of antibiotics currently available. Although such drugs have vastly improved the prognosis of acute osteomyelitis, they have not been successful in the management of chronic osteomyelitis or in surgical sepsis following internal fixation. The frequent recurrence of sepsis, despite intensive treatment with both surgery and prolonged parenteral administration of antimicrobial agents, may result in persistence or relapse of the infection and suggests that many fundamental questions remain unanswered. Buchholz et al.\textsuperscript{1} proposed the concept of local delivery of antibiotics as a means of preventing infection associated with replacement arthroplasty. Klemm\textsuperscript{2} later extended this concept to the treatment of chronic osteomyelitis. In this study, we assessed the efficacy and difficulties encountered during the use of antibiotic-loaded polymethyl methacrylate (PMMA) beads in different types of chronic osteomyelitis.

MATERIALS AND METHODS

We studied records of 49 patients, who had chronic osteomyelitis of various aetiologies, and were treated in our institution from July 1995 to June 1999 retrospectively. Four patients had haematogenous osteomyelitis, but the infection was later shown to be tuberculosis, and these patients were thus excluded from the study. Of the 45 patients, 37 were men and 8 were women. The median age at presentation was 34.8 years (range, 18.0–58.0 years). The diagnosis of chronic osteomyelitis was made on the basis of clinical and radiographic features of infection that were present for more than 12 weeks. Patients were divided into 3 groups according to the primary cause of infection: patients with infected osteosynthesis (Group 1), those with infection following open fractures (Group 2), and those with haematogenous osteomyelitis (Group 3). All patients had undergone at least one operation before admission, with an average of 3 operations, in an attempt to eradicate the infection before implantation of antibiotic-loaded PMMA beads.

Preoperative protocol

Samples of discharge from all sinuses and wounds were taken for culture and antibiotic sensitivity assays. Radiographic assessment was made to detect the presence of sequestra and implant loosening.

Operative procedure

Surgery was performed in 2 stages. In the first stage, the wound was explored through the pre-existing scar. If the draining sinus tract was found to be away from the previous scar, it was left alone. All osteosynthetic materials when present were removed except for those in 6 patients in whom there was no loosening of the implants and the fractures had not healed well. The implants were not removed with the hope of allowing the fracture to unite. All unhealthy granulation tissue was removed. The cavities were decompressed, curetted, and thoroughly washed out with copious quantities of normal saline.

Rough and jagged edges of the bone were rounded off so as to prevent entanglement of the bead chain. The antibiotic bead chain was then implanted; the number of beads and the size of the chain were determined by the size of the cavity. All wounds were closed primarily. If the wound closure was found to be under tension, as in cases of tibial wound closure, release incisions were made before the closure. The limb was immobilised in plaster of Paris cast or using an external fixator.

Noncommercial fabrication of beads

In 14 cases which the commercially prepared PMMA beads (Septopal; E. Merck, Hamburg, Germany) were not available, handmade beads impregnated with cefuroxime were used.

As gentamycin in powder form was not available in India and liquid gentamycin does not mix uniformly with bone cement, cefuroxime was used in this study:

Figure 1 Prefabricated Septopal bead chain (above) a chain of handmade beads (bottom).
8 g of cefuroxime powder was mixed homogenously in a sterile bowl with 40 g of PMMA polymer. To this, 20 ml of PMMA monomer liquid was added. When the mixture became doughy and non-sticky, beads of 5- to 8-mm size were handrolled. The beads were threaded onto a steel wire and the ends were knotted (Fig. 1).

**Postoperative protocol**

Systemic antibiotics, to which organisms were sensitive, were given for 7 days. If organisms were found to be resistant to all antibiotics, broad-spectrum antibiotics were administered. Overflow drains were used without suction for the first 24 to 48 hours. Sutures were removed after 10 days. After 3 weeks, the beads were removed and bone grafting was done in 26 cases, depending on the status of the fracture and the size of the cavity (Fig. 2). In 5 cases of infected gap nonunion, ring fixators were applied and bone transport was performed.

**Follow-up**

All patients were followed up at 6-week intervals in the initial 3 months, then every 3 months for at least 2

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**Figure 2** Radiographs of a patient with fracture shaft of femur treated by locked intramedullary nail with chronic osteomyelitis: (a) chronic osteomyelitis of the femur with implant in situ, (b) after removal of the implant and gentamycin beads, (c) following the removal of the beads and bone grafting, and (d) at last follow-up, showing healed fracture with no evidence of infection.
years. The mean follow-up period was 3.7 years (range, 2.0–5.0 years). The results were graded as follows:

**Good:** No clinical features of infection with erythrocyte sedimentation rate returning to normal levels, primary healing of the wound without any recurrence of the discharging sinus, and complete healing of fracture.

**Fair:** No clinical signs of infection with erythrocyte sedimentation rate returning to normal levels, primary healing of the wound, and delayed fracture healing.

**Poor:** Recurrence of the sinus with discharge, and radiographic signs of infected nonunion.

**RESULTS**

Site of infection, duration of infection, and organism responsible for the infection are shown in Tables 1, 2, and 3, respectively. The organisms were found to be sensitive to gentamycin in 26 cases and resistant in 19 cases. They were sensitive to cefuroxime in 14 cases, cloxacillin in 11, ampicillin in 8, and cotrimoxazole in 5; in 7 cases, the organisms were resistant to all antibiotics tested. 38 wounds healed primarily, whereas 7 healed by secondary intention, of which 4 healed by epithelisation and 3 required secondary closure. At 6 weeks’ follow-up, there was recurrence of drainage in 6 cases, all of which belonged to Group 1.

### Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Site</th>
<th>Femur</th>
<th>Tibia</th>
<th>Forearm</th>
<th>Humerus</th>
<th>Spine</th>
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<tr>
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<td></td>
<td>12</td>
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<td>1</td>
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<td>2</td>
<td>4</td>
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### Table 2

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<th>Duration of infection (months)</th>
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<td>&lt;3</td>
<td>5</td>
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<tr>
<td>3–6</td>
<td>8</td>
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<tr>
<td>&gt;6</td>
<td>9</td>
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<tr>
<td>Total</td>
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### Table 3

<table>
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<th>Organism</th>
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<tr>
<td><em>Staphylococcus aureus</em></td>
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</tr>
<tr>
<td><em>Pseudomonas</em> spp</td>
<td>7</td>
</tr>
<tr>
<td><em>Klebsiella</em> spp</td>
<td>2</td>
</tr>
<tr>
<td><em>Haemolytic streptococcus</em></td>
<td>1</td>
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<tr>
<td><em>Proteus</em></td>
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<tr>
<td>Mixed infections</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>45</td>
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</table>
There was no difference in the clinical outcome between the cases treated with Septopal or those treated with handmade beads.

Of the 19 cases in which the organism was found to be resistant to gentamycin, only one case had a poor result. No adverse systemic side-effects such as ototoxicity or nephrotoxicity were seen. In 39 (87%) cases, the results were good (Fig. 3); in 6 (13%) cases, the results were poor.

**DISCUSSION**

Musculoskeletal sepsis is a chronic debilitating disease. In particular, osteomyelitis is more difficult to treat than other infectious disorders because the systemically administered antibiotics fail to reach the site of infection owing to relative avascularity. Infection in the bone can persist despite thorough debridement, sequestrectomy, saucerization, and long-term systemic antibiotic therapy. With the increasing popularity of internal fixation, the problem of infected osteosynthesis is increasing.

The principle of depot administration of antibiotic is based on a well-accepted fact that the drug leaches out locally over a period of time. The resulting bactericidal tissue concentration at the site of infection is therefore higher than the concentration achievable by systemic antibiotic administration.

Various materials have been tried as a carrier of local antibiotic. Of these, PMMA has the best elution characteristics. Of the antibiotics available, gentamycin is the most suitable: it is thermostable, has a broad spectrum of activity, and is bactericidal; in addition, primary resistance is uncommon.

In this study, the most common type of chronic osteomyelitis was due to infected osteosynthesis (49%), followed by open fractures (29%), and haematogenous osteomyelitis (22%). Galey and Uhthoff reported an incidence of 51%, 30%, and 19%, respectively. In addition, Hedstrom et al. found incidences of 77% postoperative infections, 17% haematogenous osteomyelitis, and 12% infections following open fractures. In contrast, Majid et al. identified haematogenous osteomyelitis (51%) as the most common aetiological factor. Furthermore, the incidence of musculoskeletal infection in our series was higher among relatively young individuals, probably because of their susceptibility to open fractures and subsequent complications.

*Staphylococcus aureus* was the most common pathogen (58%), followed by Pseudomonas species in 16% of cases, whereas mixed infections were seen in 18% (Table 3). Other authors have also reported *Staphylococcus aureus* as the most common pathogen, followed by Pseudomonas species. In 42% of cases in our series, the organisms were gentamycin resistant. Majid et al. reported that 58% of cases in their series...
were sensitive to gentamycin. Postoperative cultures were sterile in all patients in our series except in one case of failure, which was similar to the observations of Galey and Uthhoff.10 This study showed a success rate of 87%. This finding is comparable to the results reported by Galey and Uthhoff10 (67%) and Majid et al. (78%).12 Six out of 45 cases were classified as failures in our series; of these, 2 were cases of infected Kuntscher’s nails that were not removed at the time of first-stage surgery, because there was not adequate sign of union at the fracture site. Furthermore, one patient had an infected total hip arthroplasty and the remaining 3 had infected osteosynthesis with plates and screws (Table 4). In these cases, infection could be controlled only for 6 weeks, following which there was recurrence of the draining sinus. These implants were left in situ with the hope of salvaging the osteosynthesis but with little success. Even though sequestra were not visible radiologically, they were found underneath the plates after implant removal. The wound and sinus healed after implant removal, sequestrectomy, and debridement.14 Of the cases in our series were treated with handmade beads and 31 with Septopal beads. There was no difference in the outcome between these 2 groups. The handmade beads were slightly more difficult to remove because of their uneven surface and size. However, they were less expensive and offered flexibility regarding the choice of antibiotic used, which depended on the sensitivity of the organism.

Of the 19 patients with infections in which the organism was found to be gentamycin resistant, only one had poor result. This shows that the antibiotic-loaded PMMA beads are effective even in the presence of resistant organisms. This observation could be explained by the fact that when the organisms are exposed to a very high concentration of antibiotics, they are eradicated, as postulated by Salvati et al.3 Usually, antibiotic sensitivity testing is done with a 10-µg disc, whereas the antibiotic concentration achieved following the implantation of PMMA beads is more than 50 µg/ml. In addition, Mackowiak et al.13 were of the opinion that sinus tract cultures may not be representative of the actual pathogen.

**CONCLUSION**

Radical debridement is the cornerstone in the management of musculoskeletal infections. For chronic infections, especially those following osteosynthesis, the use of antibiotic beads is a valuable adjuvant. In the presence of infected implants that prevent accessibility to the underlying sequestra and infected tissues, the role of these beads becomes limited. They help to eradicate infection when implanted only after removal of dead and infected material. The most valuable advantage of this method is that the wound can be closed primarily, thereby reducing the incidence of nosocomial infections and the requirement for nursing care. The technique also reduces the need for multiple procedures for wound closure as well as the overall cost of treatment.

**REFERENCES**