The use of antibiotic-containing bead chains in the treatment of chronic bone infections

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The implantation of gentamicin polymethylmethacrylate (PMMA) chains or minichains into infected osteomyelitic cavities is a well-established local antibiotic therapy supplementary to radical debridement. The gentamicin concentrations achieved at the site of infection are far above the MICs for most common pathogens in chronic osteomyelitis. Serum and urine concentrations are low, and nephrotoxic and ototoxic side-effects of this form of gentamicin application are not to be feared. Under local antibiotic therapy with gentamicin PMMA chains, primary wound healing as in aseptic surgery can be expected. Prolonged systemic antibiotic therapy is unnecessary. In a series of 405 cases, a success rate of 90.4% was obtained.

Keywords Gentamicin PMMA chain, chronic osteomyelitis, local antibiotic therapy

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INTRODUCTION

Chronic osteomyelitis is the result of either bacterial contamination in compound fractures or of infection following operative stabilization of fractures by intramedular (IM) nailing or plating and other orthopedic operations such as alloplastic joint replacement. Chronic osteomyelitis can develop after acute hematogenous osteomyelitis, but this condition is rather rare in countries with good medical care.

The two main features of chronic osteomyelitis are a draining sinus from the focus of the purulent bone infection and sequestration of devitalized bone fragments. Chronic osteomyelitis is a surgical disease, and the primary treatment must be surgical. A sequestrum has no blood supply, and bacteria in the center of such a piece of dead bone cannot be eradicated by antibiotic therapy alone—either by systemic administration or by local application. Radical debridement with removal of all dead bone fragments and alloplastic implants is mandatory (Figure 1).

GENTAMICIN PMMA CHAINS AND MINICHAINS

The local implantation of gentamicin polymethylmethacrylate (PMMA) chains or minichains into an infected bone cavity after debridement allows local antibiotic therapy over a prolonged period of time with one single application [1–3].

The bone cement PMMA is an ideal carrier material for the protracted release of the antibiotic substance by diffusion.

Gentamicin sulfate is the antibiotic substance of choice for the admixture to PMMA because of the broad antibacterial spectrum of action, the bactericidal action, the low rate of primarily resistant pathogens, the low allergy rate, the good thermostability—which is important for the manufacture of the gentamicin PMMA beads—and the good solubility in water.

PHARMACOKINETIC STUDIES

In the in vitro studies of Wahlig et al, the release of gentamicin was investigated by elution of the beads in phosphate buffer solution. Up to 600 mg/L of gentamicin per bead was eluted on the 1st day, 120 mg/L on the 10th day, and 10 mg/L even on the 80th day (Figure 2).

In in vivo pharmacokinetic studies, only traces of gentamicin could be measured in the serum of patients a few days after implantation of the beads. Gentamicin could be measured in the urine several months after implantation, with low concentrations of under 7 mg/L. On the other hand, high concentrations of gentamicin between 50 and 80 mg/L were measurable in the wound secretion.

These concentrations after local implantation of gentamicin PMMA beads were compared with those after intramuscular injection of 80 mg of gentamicin.

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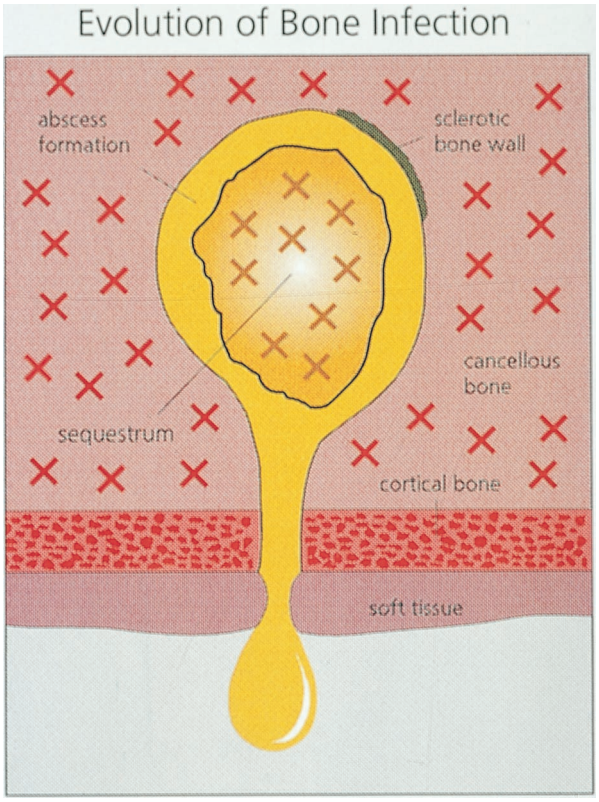

Figure 1 Sequestration of infected devital bone fragments is the main feature in chronic osteomyelitis; radical surgery with removal of such sequestrum should proceed any antibiotic treatment – whether systemically or locally applied.

The concentration of gentamicin in the serum was 3–5 mg/L, and that in the urine was 80–200 mg/L, whereas the concentration in the wound secretion was only 0.4 mg/L. This means that the local gentamicin concentrations after application of the gentamicin PMMA chains are far above the MICs and MBCs for most common pathogens. With low concentrations

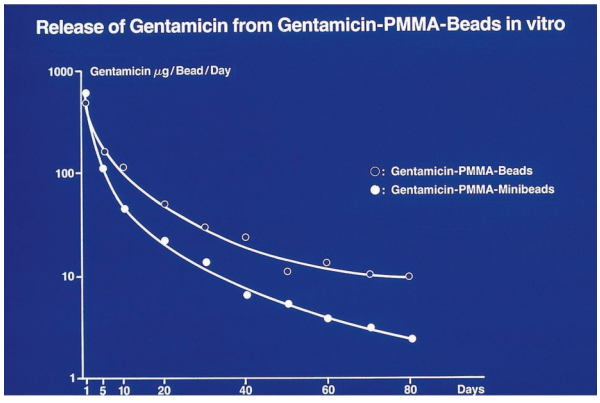

Figure 2 Release of gentamicin from gentamicin PMMA beads in vitro.

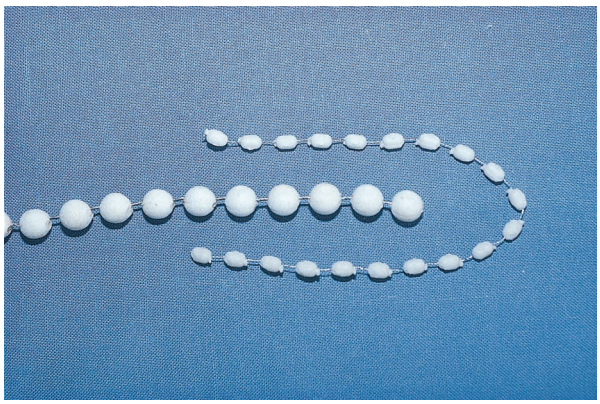

Figure 3 Gentamicin PMMA chain and minichain for local antibiotic therapy by implantation in infected bone cavities, depending on the size of the defect.

in th serum and urine, ototoxic and nephrotoxic side-effects are not to be feared [4,5].

Gentamicin PMMA chains are commercially available in two sizes under the trade name Septopal chains (Figure 3).

The standard-size chain has beads with a diameter of 7 mm. Each bead contains 7.5 mg of gentamicin sulfate, equivalent to 4.5 mg of gentamicin base, and zirconium oxide as a contrast medium to make the chain visible on X-ray.

One chain consists of 10, 30 or 60 beads threaded onto a multistrand surgical wire. The use of the smaller gentamicin PMMA minichain is indicated for implantation into small infected bone cavities, in hand surgery, in maxillofacial surgery and in pediatric surgery.

CLINICAL APPLICATION

In clinical practice, gentamicin PMMA chains can be used in three different ways [2,3]. Short, temporary application is

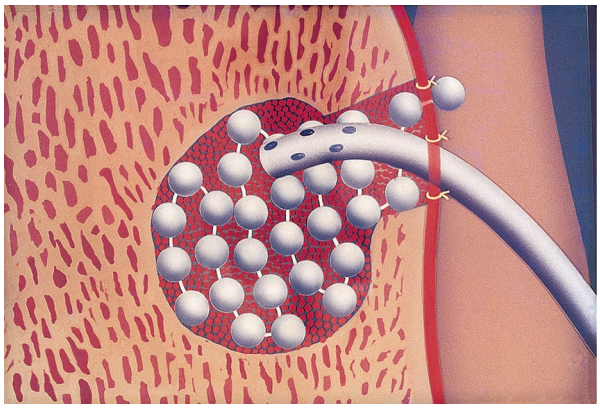

Figure 4 By implantation of a gentamicin PMMA chain into an infected bone cavity after sequestrectomy, local antibiotic therapy can be administered at local concentrations of gentamicin far above the MICs for most common pathogens in chronic osteomyelitis.

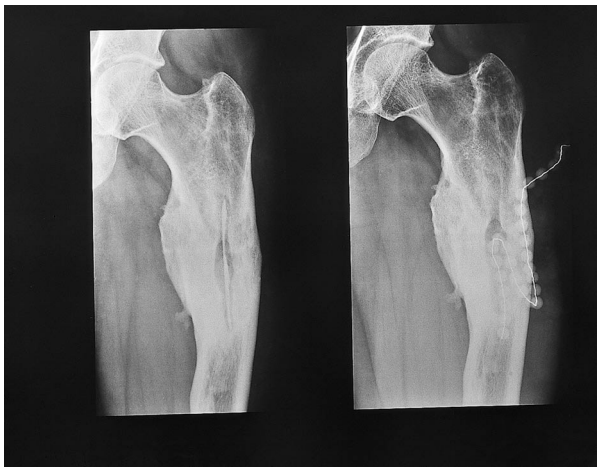

Figure 5 Sequestrating osteomyelitis after plate osteosynthesis of a fracture in the subtrochanteric region; temporary implantation of a gentamicin PMMA chain following sequestrectomy.

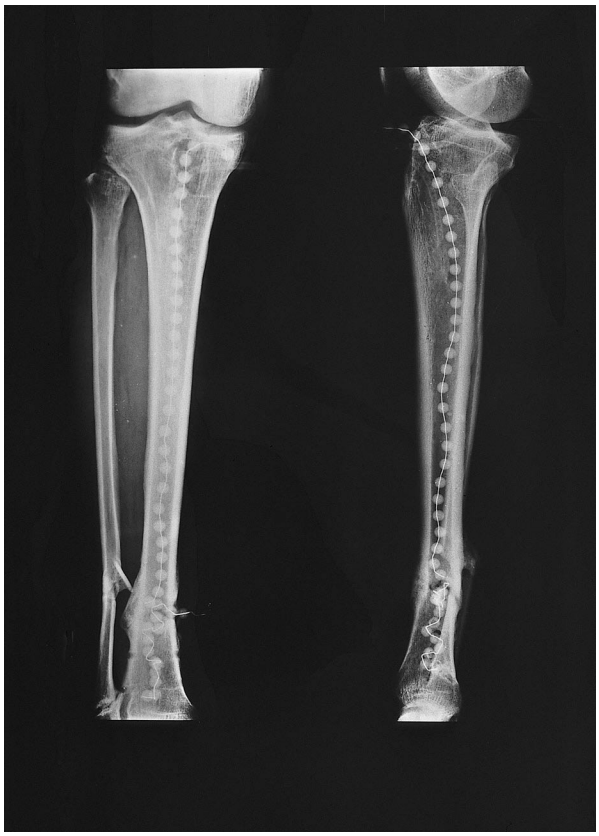

Figure 6 Temporary implantation of a gentamicin PMMA chain in the medullary canal of the tibia after removal of an infected interlocking nail.

indicated for antibiotic therapy in high concentrations in connection with the operative revision of an osteomyelitic process when no secondary operation is planned or needed. Following sequestrectomy the gentamicin PMMA chain is implanted into the infected bone cavity in such a way that the last bead of the chain is protruding above the surface of the skin. This makes it possible to extract the chain later without further operation by pulling on the free end of the chain (Figures 5 and 6).

It is very important that the wound is closed as in an aseptic operation to achieve high local concentrations of the antibiotic, which is leached out by the postoperative hematoma from the beads by diffusion.

The chain should be extracted within 7–10 days. If the chain is left for a longer period of time, granulation tissue will form around the beads and hold them in place; difficulties may then arise when one tries to extract the chain.

In such cases of localized osteomyelitis, additional parenteral antibiotic therapy is limited to the perioperative phase of 1–2 days. Prolonged systemic antibiotic therapy is not necessary.

In longer-term temporary application, the gentamicin PMMA chain is buried completely in the infected cavity following debridement to ensure antibiotic activity of longer duration and because of the necessity of a second operation such as bone grafting some weeks later. In the intervening time period, the chain serves as a space holder for the cancellous bone chips to be implanted. In these cases, the chain is removed operatively at the second operation.

In cases of longstanding chronic osteomyelitis with a bone cavity which cannot be filled with vital tissue like bone chips or pedicled muscle graft, permanent filling of such a bone defect with gentamicin PMMA chains may be indicated. In one case, the permanent filling was performed 15 years ago and no reinfection occurred. But if infection recurs, it is always worth trying it again, if the bacteriology reveals continuing good sensitivity to gentamicin.

RESULTS

At the Department of Posttraumatic Osteomyelitis of the B.G. Trauma Clinic in Frankfurt/Main, Germany, the treatment of chronic osteomyelitis with local antibiotic therapy with gentamicin PMMA chains was introduced in 1976. In spite of the intensive use of gentamicin PMMA chains over 7 years from 1977 to 1983, intraoperative wound smears did not reveal increased gentamicin resistance over 4 mg/L.

At the 13th International Congress of Chemotherapy 1983 in Vienna, the results of 405 cases of chronic sequestrating osteomyelitis with temporary implantation of gentamicin PMMA chains following radical debridement were demonstrated.

The postoperative observation period was between 6 and 78 months. Cure of the infection could be obtained in 90.4% of the cases; the infection persisted in 9.6% [6].

CONCLUSION

In conclusion, it can be stated that radical debridement should proceed any antibiotic treatment systemically or locally applied.

The implantation of gentamicin PMMA chains allows local antibiotic therapy in high concentrations with minimal inhibitory concentrations far above the MBCs of the relevant pathogens as an adjuvant therapy to good surgery.

Nephrotoxic or ototoxic side-effects are not to be feared.

Primary wound healing as in aseptic operations can be expected.

It is a very comfortable treatment for the patient, because prolonged bedrest and prolonged hospitalization can be avoided.

The cost of treatment of chronic osteomyelitis can be considerably reduced.

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