IN VITRO RELEASE OF ANTIBIOTICS FROM PMMA BEADS AND ARTICULATING HIP SPACERS

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Introduction

Deep infection after total hip arthroplasty (THA) is currently seen in approximately 1-2% of all cases. Treatment of an infected THA can be a major challenge. Although some centers have excellent results with one-stage procedures, the two-stage procedure still appears to be most effective for the control of infection and therefore remains the gold standard for treatment.

The traditional use of antibiotic-loaded polymethylmethacrylate (PMMA) beads works well to cure infection, but the second stage is often complicated because of peri-articular soft-tissue contractures, disuse osteopenia and poor interim functionality. Multiple in vivo studies have shown the benefits of articulating cement spacers regarding these complications and show similar results regarding the infection-free rates. In almost all of these studies, PMMA with a high concentration of hand-mixed antibiotics was used. However, in clinical practice many surgeons use commercially available, pre-mixed antibiotic bone cements for the preparation of a spacer, which have a much lower antibiotic content. As antibiotic release is a surface diffusion phenomenon and therefore release from a spacer with a relative low surface area as compared to beads will be lower, this may result in subtherapeutic antibiotic concentrations. Until now, no data have been published to answer this question for spacers made of pre-mixed cements.

In this study we determined the in vitro antibiotic release pattern of articulating hip spacers, made of 2 types of pre-mixed antibiotic bone cement in comparison to a clinically representative amount of preformed antibiotic PMMA beads.

Materials and Methods

We compared 3 groups of antibiotic carriers (Figure 1). Each group had a sample size of n=3. Group 1 consisted of hip spacers made of Refobacin-Palacos®-R bone cement, containing 0.5g of gentamycin per 40 g PMMA (Biomet Orthopaedics, Kerzer, Switzerland). Group 2 consisted of hip spacers made of Antibiotic-Simplex-P® bone cement, containing 1g of tobramycin per 40g PMMA (Howmedica Int. Limerick, Ireland). Group 3 consisted of 2x60 Septopal® beads, containing in total 0.54 g gentamycin (Biomet Merck, Darmstadt, Germany). Except for Septopal® beads in the USA and Europe.

Preparation of the spacers/beads

Palacos®-R and Simplex-P™ bone cement are provided in a sterile pack, containing 40 g of dry PMMA and 20 ml of liquid monomer. Both cements were mixed according to the manufacturer’s guidelines, using either the Optivac (Palacos) or ACM (Simplex) mixing and delivery system. To slightly increase porosity we did not use a vacuum. After mixing, the cement was injected in a silicone hip spacer mold. The spacer mold used, was a collarless hi-metric style stem with an endo-style head (Biomet Orthopedics, Inc., Warsaw, IN, USA) Stem size: 9mmx125mm, Head size: 51mm Ø. Mold content is +/- 150 ml. The Septopal® beads were preformed and consisted of chains of 60 beads. Each bead has a diameter of 7mm and contains 4.5mg gentamycin.

Release testing

Spacers and beads were placed in 1500ml beakers, containing 1000 ml phosphate buffered saline (PBS, pH 7.4), at 37°C. An aliquot of PBS was collected on 16 time points, with a gradually expanding interval during a period of 6 weeks (day 1-7, 9, 11, 13, 16, 19, 23, 28, 35 and 42) and stored at -20°C until further analysis. Antibiotic concentrations were determined using fluorescent polarizing immunoassay (AxSym, Abbott).

Results

All 3 groups showed a burst release during the first day, which rapidly decreased during the next few days (Figure 2). For both the Palacos and Simplex spacers there was hardly any additional release after the first week, whereas for the Septopal beads, the antibiotic concentration in the buffered saline persistedly increased for at least two weeks. Additionally the beads had an average release of 2.4±0.6 mg/g/day during week 3 to 6. The cumulative release after 6 weeks was 7.5±2.3 mg for Palacos, 23.8±0.2 mg for Simplex and 188.3±9.3 mg for Septopal. This represented 2.14%, 0.93% and 34.87% respectively of the total amount of antibiotics present. At all time points the release from the Septopal beads was significantly higher compared to both other groups (p<0.0001). The difference between Palacos and Simplex was not significant.

Discussion

The Septopal beads showed to have an antibiotic release, which was much higher and persisted for a longer period of time as compared to articulating hip spacers made of Refobacin-Palacos-R or Antibiotic Simplex-P bone cement. Both spacers had a comparable release, even though the Palacos spacers contained only half the amount of antibiotics. The use of Septopal beads has been proven effective in both experimental and clinical research; even though we do not exactly know how high the antibiotic concentration should be and for what period of time.

The idea of the spacer is, that it should stay in place for at least 6 weeks. Masri et al. previously showed, that by using high dose antibiotic bone cement adequate antibiotic concentrations could be maintained for such a period of time. In our study however, the release of the spacers lasted for only 1 week. Although this may be sufficient in some cases, and it should be realized that the use of a spacer in infected hip revision has other surgical and clinical advantages, it also creates the risk of having a foreign body in situ, which prolongs the infection instead of curing it. We therefore conclude, that although an in vitro experiment is only a simplification of the in vivo situation, where factors as stability and filling dead space also have an influence on curing the infection, one should be cautious toward using standard, premixed antibiotic bone cement for spacers in the treatment of an infected prosthesis.

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References


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